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CASE REPORTS

Original Article

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Morphometry of the Central Sulcus in the Brain of Uttar Pradesh Region

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Abstract

Background: Central sulcus is an important structural landmark of the cerebral hemisphere as it is located between the primary motor and the primary somatic sensory cortex. Variations in the morphology of the central sulcus are seen with respect to the length and depth of the central sulcus. This study was done to establish a normal standard in length and depth of central sulcus in the population of Uttar Pradesh region.

Materials and Methods: An analytical cross-sectional study was conducted in 34 brains taken from the anatomy department of Rohilkhand Medical College, Bareilly, Uttar Pradesh. Morphology of the central sulcus was studied with regards to its dimension and contour.

Result: The mean length and depth of the central sulcus was found and compared with other similar studies on a different population.

Conclusion: Knowledge of morphometry of central sulcus is not only important during neurosurgery of brain but also holds tremendous significance in diagnosis and management of diseases of the cerebral cortex.

Key words: Central sulcus, Cerebral hemisphere, Motor cortex, Somatic sensory cortex

INTRODUCTION

The highest level of nervous function resides in the cerebral cortex. It contains the primary sensory and motor areas, as well as multiple association areas. Cerebral cortex which is the primary storehouse for memory also controls the function of lower brain centers. Each area of the cerebral cortex receives specific inputs, which helps in evoking response in a specific part of the body. The surfaces of the cerebral hemisphere are molded into a number of gyri separated by sulci. These sulci and gyri provide a natural topographic partition in the cerebral cortex, which lie on the outer surface of the cerebral hemispheres. The study of the shape, size, and configuration of the sulci has been a subject of interest as many functional zones runs along the bed of the major or minor sulci. The central sulcus is one of the most important structural landmarks of the cerebral hemisphere as it separates the primary motor from the primary somatic sensory cortex. The study of the central sulcus using post-mortem samples was undertaken in the past by many workers including Broca,[1] Campbell,[2] Cunningham,[3] and White. *et al*.,[4]. The central sulcus or the fissure of Rolando extends across the lateral convex surface of the cerebral hemisphere interrupting the general longitudinal course of the gyri and sulci. The central sulcus begins at the superomedial border near the vertex or the highest point of the hemisphere, somewhat behind the midpoint of the longitudinal fissure. It passes outward, downward, and forward to end near the middle of the fissure of sylvius, the posterior limb of which it sometimes joins. Like most other sulci and gyri, the central sulcus also shows marked variation in size, shape, and configuration.[5] Typically a central sulcus is divided into three parts by two bends, the upper third facing downward and backward, middle third downward and forward and the lower third vertically downward.[3] Depth of the central sulcus is approximately two cm except near its two extremities where it becomes shallower. The depth

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however may vary with age, manual skill and handedness. The right-handed person has a slightly deeper central sulcus in the left cerebral hemisphere as compared to the right hemisphere.[5] During neurosurgical resection it's important to plan out the neurosurgical approach. This needs a sound knowledge of the location, configuration, and morphometry of the central sulci to avoid any damage to the primary motor cortex which forms its anterior wall. Some degenerative diseases may also affect the cerebral cortex, e.g., Alzheimer's disease which is the commonest cause of dementia in elderly.[6] The aim of the study was to put more light to the morphometry of the central sulcus, with respect to the length and the depth, in the brain of Uttar Pradesh region.

MATERIALS AND METHODS

The current study was done on post-mortem cerebral hemispheres obtained from the Museum of the anatomy department, from Rohilkhand Medical College, Bareilly. Total of 18 brains were obtained. The morphometric measurement was done on both the cerebral hemispheres. As two of the cerebral hemispheres were damaged, a total of 34 specimens were studied. The meninges were carefully stripped of from the superolateral surface avoiding tearing of the cerebral cortex by the larger blood vessels lying at the bottom of the sulcus. The length of the sulci was measured in millimetres by following the curves of the sulci by a thin wire shown in Figure 1. The depth of the sulci was measured by placing vertically a calibrated scale in the sulci at different locations shown in Figure 2.

RESULTS

Our study which was done on the central sulcus in the brain of samples obtained from Uttar Pradesh region measured the length and depth of the central sulcus. Table 1 and Graph 1 show the length of the central sulcus found in the right hemisphere and left hemisphere. Table 2 compared the mean length of the central sulcus in the right hemisphere which was found to be 94.75 mm with that in the left hemisphere where it measured 96.06 mm (N = 17, standard deviation [SD] = 7.73). The conclusion derived was that the length in the left hemisphere was more than that in the right hemisphere. The P value was however found to be insignificant at 0.6242. Table 3 shows the depth of the central sulcus in both the hemisphere. The average maximum depth on the right side was found to be 18.06 mm and on the left side 18.41 mm. The average minimum depth found was 4.88 mm on the right side and 5.47 mm on the left side. The average depth thus measured on the right side was 11.52 mm (N = 17, SD = 1.64) and on the left side 12.05 mm (N = 17, SD = 1.62). Table 4

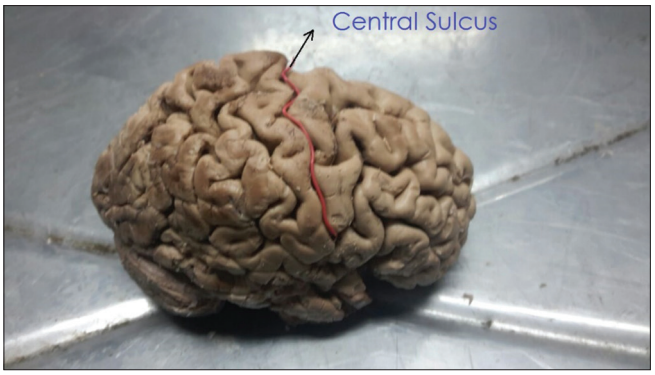


Figure 1: Central sulcus

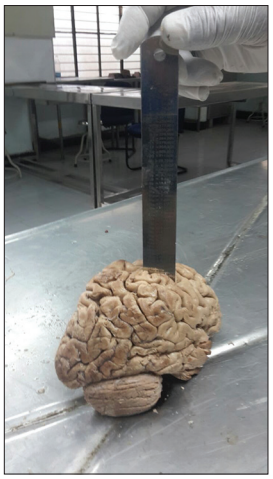
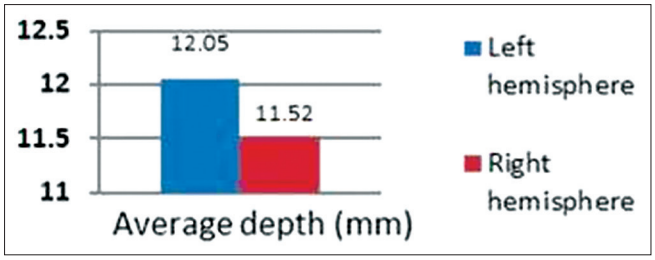
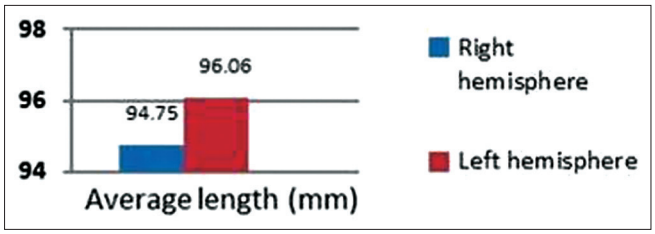


Figure 2: Central sulcus depth being measured



Graph 1: Average depth



Graph 2: Average length

and Graph 2 compared the depth of the central sulcus in both the hemispheres. The depth was found to be more in the left hemisphere compared to the right hemisphere. The P value of the depth was insignificant at 0.3526. Table 5 shows a comparative analysis of both the length and depth

of the central sulcus. In our study on the brains of Uttar Pradesh region, both the length and the breadth of the central sulcus were found to be more in the left hemisphere.

DISCUSSION

Human central sulcus divides the frontal and parietal lobe. Its anterior wall is formed by primary motor cortex (Brodmann's area 4) and posterior wall by major portion of primary somatic sensory cortex (Brodmann's area 3). The study of the central sulcus using post-mortem samples have been a subject of interest for many workers in the past. Of all the sulci present in the cerebral hemisphere the central sulcus is the most suited for the study of morphometry as it develops as early as the 20th week of fetal life,[7] has a more or less constant macroscopic features and very predictably divides two very significant Brodmann's area.[4,5] This has led to a detailed analysis of the various aspects of central sulcus by many researchers. Blanton *et al*.,[8] worked on the normal and abnormal sulcal development while Lohmann *et al*.[9] worked on genetic control over the sulcal shape. Amunts *et al*.[10] demonstrated the structure function relationship in the primary sensorimotor cortex. He also worked on the effect of handedness on central sulcus morphology. Boling *et al*.[11] worked on the potential of using sulcal feature for somatotopic localization. The drawback of some of these studies were that since a lot was based on observer's judgment the ability of investigators to provide quantitative markers to recognize landmarks in the central sulcus was limited. One well-known landmark "pli di passage frontoparietal moyen" was however provided by Broca. This appeared as an elevation in the floor of the mid part of the central sulcus. Later studies by White *et al*.,[4] showed that it corresponded to the somatotopic hand area.

Crossman[12] postulated that the central sulcus ran downward and forward for 8-10 cm before ending a little above the posterior rami of the lateral sulcus. According to Brown and Bottjer[13] length of central sulcus was >80 mm while Sun *et al*.,[14] estimated it to be 93.28 mm on the left side and

Table 1: Length of the central sulcus

Sample no	Right cerebral hemisphere (mm)	Left cerebral hemisphere (mm)
1	99	96
2	80	91
3	100	107
4	96	95
5	95	97
6	108	113
7	102	92
8	84	82
9	89	102
10	92	94
11	85	86
12	105	104
13	91	95
14	95	90
15	92	90
16	99	98
17	99	101

Table 2: Statistical analysis of length of the central sulcus

Side of cerebral hemisphere	*N*	Mean	SD	*P* value
Right hemisphere	17	94.75	7.53	0.6242
Left hemisphere	17	96.06	7.73	

SD: Standard deviation

Table 3: Depth of the central sulcus

	Right hemisphere			Left hemisphere		
Sample no.	Maximum depth (mm)	Minimum depth (mm)	Average depth (mm)	Maximum depth (mm)	Minimum depth (mm)	Average depth (mm)
1	15	6	10.5	17	7	12
2	22	4	13	21	6	13.5
3	14	5	9.5	15	4	9.5
4	18	4	11	21	6	13.5
5	17	3	10	17	4	10.5
6	21	8	14.5	21	9	15
7	16	4	10	19	5	12
8	18	5	11.5	18	13	11.5
9	19	3	11	20	5	12.5
10	18	5	11.5	17	4	10.5
11	17	3	10	18	5	11.5
12	17	5	11	18	6	13
13	18	4	12	18	5	11.5
14	18	3	10.5	15	5	10
15	17	6	11.5	17	4	10.5
16	21	5	13	23	7	15
17	21	10	15.5	18	8	13

Table 4: Statistical analysis of depth of the central sulcus

Side of cerebral hemisphere	*N*	Mean	SD	*P* value
Right hemisphere	17	11.52	1.64	0.3526
Left hemisphere	17	12.05	1.62	

SD: Standard deviation

Table 5: Comparison of the length and depth of the central sulcus in both the cerebral hemisphere

Side of cerebral hemisphere	Average length of central sulcus	Depth of central sulcus		
		Maximum	Minimum	Average
Right hemisphere	94.75	18.06	4.88	11.5
Left hemisphere	96.06	18.41	5.47	12.05

84.59 mm on the right side. Kline *et al*.,[15] stated it to be 70-125 mm in autopsied body, average being 94 mm. In our study, which was done on the central sulcus in the brain of samples obtained from Uttar Pradesh region, the average length of the central sulcus found in the right hemisphere was 94.7 mm and on the left hemisphere 96.06 mm. This was in accordance to the findings of studies done on length of central sulcus by Crossman[12] and Brown and Bottjer,[13] Sun *et al*.[14] and Kline *et al*.[15] Cykowski *et al*.[16] stated that the average maximum depth of the central sulcus on the left side was 16.6 cm while on right side was 16.4 mm. In our study, the average maximum depth was slightly higher being 18.06 mm on the right side and 18.41 cm on a left side.

CONCLUSION

As sulci and gyri are the natural routes to deep brain structure a knowledge of morphometry of the sulci was essential for the surgical planning. It also holds great significance in diagnosis and management of diseases of the cerebral cortex, e.g., in Alzheimer's disease there is a marked decrease in sulcal depth. Sulcal morphometric features can also be used for somatotopic localization.

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Original Article

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Impact of Medical Education Technology Workshops in a Rural Medical College of Bihar: A Questionnaire Study

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Abstract

Background: An evaluation study on the impact of medical teacher's training workshop on concept and comprehension of the trained medical teachers was designed at Mata Gujri Medical College, Kishanganj, Bihar. The study comprised of different components of medical teachers training (namely: Group dynamics, principles of adult learning *viz*., andragogy, teaching learning process, large group and small group teaching, and integrated teaching). The study was carried out with the aim to find out the effectiveness of workshop in changing knowledge and attitude toward medical teaching.

Materials and Methods: Pre-designed and pre-tested semi-structured questionnaire was distributed to all of the participant medical teachers of MGM Medical College before the start of the workshop. Instruction was provided during 3 days workshop with 12 h interactive sessions. The Same questionnaire was again applied on the completion of the workshop to all medical teachers. The questionnaire also included the participant medical teachers' opinion about the details of the program and its impact upon them.

Results: Using standardized questionnaires, the participants rated the quality of the workshop highly. Using comparative studies with pre- and post-workshop questionnaire the knowledge of the participants regarding medical education technology comprehension and skills was also found to have significantly improved, as analysis by paired Student's *t*-test showed significant statistical difference.

Conclusion: This workshop showed that the medical teachers' training had a positive impact on their teaching skill and attitude, and it was also highly appreciated by them. This workshop showed that there was a significant change in knowledge and attitude of trained teachers towards different aspects of medical students teaching - learning process. The results show that it is a suitable and effective educational intervention and need to be applied to all the medical teachers in all medical colleges in phased manner by organizing regular and frequent workshops in future.

Key words: Medical education, Technology, Workshop

INTRODUCTION

In recent years, the number of students in medical colleges have grossly increased and *vis a vis* number of medical colleges also. This is due to the fact that the doctor patient ratio in our country is much below the desired level which needs to be improved as advocated by WHO and other authorities. However, only the number of doctors does not suffice but the quality of the doctors should also be at par or above the desired level. For this we should induct most sophisticated and well- researched modern scientific methods in our medical education and to our medical teachers. As in other branches of knowledge there are ear-marked degrees and diplomas related to education which are essential before entering the teaching profession, no such thing exists in medical schools. Hence, the teachers a though vastly learned are not acquainted with the science of medical education and

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teaching methods. Therefore is the need of continuing medical education in the form of medical education technology (MET) workshop.

A major part in teaching medical subjects to students is hour long lecture which is convenient way to transmit large amounts of information to large numbers of students, although not necessarily an effective one.[1] The importance of taking notes during lecture has also been of a considerable significance. King (1992) noted that when this is being done the students tended to engage more actively with their notes rather than concentrating on the subject and trying to comprehend, as recorded by Burns and Sinfield.[2] There are different modules in a lecture. The teacher may have spent hours carefully planning how the lecture content will gradually develop allowing a sophisticated picture to unfurl about the subject. However, many students fail to make the connection between lectures in the module, even fewer across the modules.[3] Again, 50-60 min is a long time for an audience to sit and listen to one person talk. A number of studies suggest that the maximum and optimum attention span for a student might be as little as 10 min and as much as 20 min.[4] While with practice this can also be improved, but very few people are at their best for the full lecture. In most textbooks on communication and presentation techniques, there is reference to research that states, "93% of communication is non-verbal." While this is a glorious oversimplification of research by Mehrabian (1972), the fact remains that good non-verbal communication is so much more than the words presented.[5] The outlook of the teachers toward the student is also important just as the students' attitude towards the teacher, lecture and the process of learning. Students generally view the lecture positively.[6] They tend to like the fact that they get the lecturer's expertise mainlined directly into them. This does not necessarily mean that students do very much well with lecture notes, rather often take the quite naïve view that simply attending the lecture is going to be enough for learning. The same workers also have the view that students were less positive about working with others because they were afraid of diluting the quality of information gained during the lecture or that less - able students would hang on to their learning and in return give nothing back.[6] Some other workers found that students enjoy the opportunity to reflect, consolidate knowledge, or work on a problem with others.[7,8]

In medical education, one agenda often pushed is the need for a greater degree of interaction within lectures. Fundamentally, when well-integrated into the lecture, such activities give students the opportunity to consolidate their knowledge and the chance to give them a break from note taking for a few minutes. Huxham found that students viewed these opportunities for interaction positively and were able to recall much more from the topic they have learnt.[9] Furthermore, there may be direct evidence that some not so common activities may lead to better academic performance. Alimer *et al.* found that students who regularly completed "1 min papers" at the end of the class showed an average increase of 10% in their grades when compared to those who did not.[10]

All these above discussion show that there are large varieties of facets in medical education which need to be learnt separately and formally. Simply self-generated ideas and personal experience are not enough to make a good teacher even if he/she is a vastly learned person in his/her subject. Therefore, there is definitely a need for medical education workshops in medical colleges. However, there is also a need to know how far the existing workshops are useful and acceptable and hence our venture in this study to do the job.

MATERIALS AND METHODS

Two sets of pre-designed and pre-tested semi-structured questionnaires were prepared. One set is testing the knowledge of the participant teachers regarding the topics taught during the medical education workshop. The second set comprised of questions in Likert scale regarding how the workshop changed the attitude and activities of the teacher during actual application in the further teaching process. These questionnaires were distributed to all of the participant medical teachers of MGM Medical College, Kishanganj before the start of the workshop. During the 3 days of the workshop, lectures were given with audio-visual aids covering the various aspects of MET. The lectures were interspersed with various activities such as microteaching by the participants, role-playing skits, group activities and 12 h of exhaustive interpersonal, intragroup and intergroup interactions and discussions. Three months after this workshop the same questionnaires were again applied to all participant medical teachers. The data were analyzed not only on the effect of the workshop on the participant teachers, but each and every question given was also analyzed regarding its difficulty index and overall acceptability. The data were put on excel sheet, and the results were analyzed applying paired two-tailed Student's *t*-test using IBM SPSS 20.

RESULTS

The results obtained are depicted in the form of tables and graphs which are self-explanatory.

The impact of workshop on teacher's knowledge of teaching methods according to their designations like Assistant Professor, Associate Professor and Professor (Figure 1). The means, the standard deviations have been also calculated which can be seen in Table 1.

The impact of workshop on teacher's knowledge of teaching methods question-wise (20 questions) has been depicted in Figure 2. The means, the standard deviations hves been also calculated which can be seen in Table 2.

DISCUSSION

The results show that the 3-day teaching method workshop did have some effects on teachers' knowledge and attitude of teaching methods. The average marks for an Assistant Professor before the course was 45, that of an Associate professor was 46 and in case of a Professor it was 50. After the completion of the course the test, marks became 50, 51 and 60 for Assistant Professor, Associate Professor, and Professor respectively. The *P* value of paired differences in a two-tailed Student's *t*-test was 0.0001 in all three cases with designations of Assistant Professor (degree of freedom that is, df = 10), Associate Professor (df = 8) and Professor (df = 4). Therefore the differences between pre- and post-course test scores are highly statistically significant. Again when question-wise data were analyzed the results showed a rise in marks for most of the questions and for all the teachers during post-test scoring compared to the pre-test scoring. The results were not statistically significant in the case of question numbers 9, 12, 15, 16 and 20. For all other questions, the paired differences were statistically significant. This raises the fact that not all questions are properly chosen in all cases of question setting and ambiguity in the questions might lead to confusion.

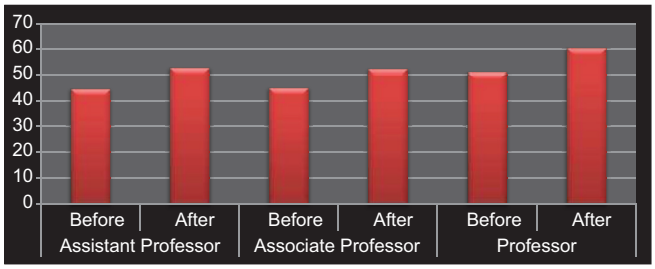

Figure 1: Impact of workshop on teacher's knowledge of teaching methods designation-wise

The primary aim of all MET workshops is to train medical teachers so as to bring about a change in the medical education system for betterment of teaching - learning mainly at the undergraduate level. The basic emphasis is that teaching should be interactive, and the teachers should become a facilitator to develop active learning by students.[11] Several medical schools in India have accepted a certificate course as a criterion for academic promotions.[12] The process of faculty development deals with the sensitization and training of teachers in carrying out their professional tasks, which lead to improvement in the quality of teaching.[13] The workshops are usually planned to present new methods and information to encourage in the teacher-participants more favorable attitude towards medical education.[14]

However, the true effectivity of the MET workshops should be evidence-based. Some workers have reported that short-term educational workshops are effective methods for influencing medical teachers.[15] The impact of the training on actual teaching is not always quantitatively assessed.[16] Nagdeo and Chari made a quantitative assessment and found just as our studies have revealed that the MET program workshops do enhance the efficiency and teaching the knowledge of the medical teachers.

CONCLUSION

In our short study in a limited setup, it has been found that the 3 days basic MET workshop increases the teachers' knowledge regarding medical education. After the course, the teachers are sensitized to new teaching methods and undertake these methods in implementing

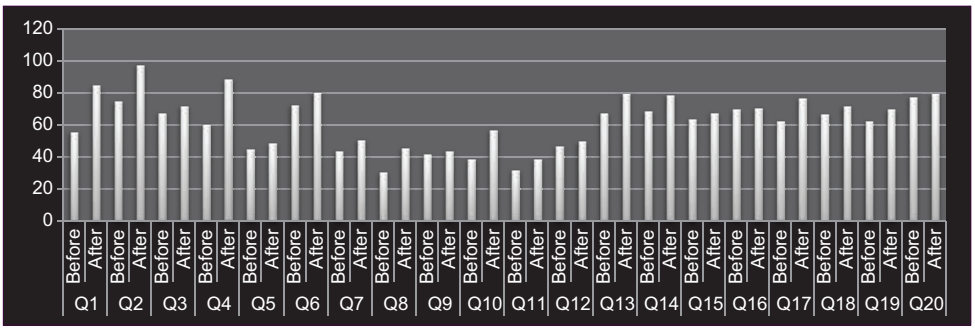

Figure 2: Impact of workshop on teacher's knowledge of teaching methods question-wise

Table 1: Mean, SD, SEM, 95% CI and level of significance regarding impact of workshop on teacher's knowledge of teaching methods designation-wise

Designation	Paired differences					*t* value	Degree of freedom	*P* value (two-tailed)
	Mean	SD	SEM	95% CI of the difference				
				Lower	Upper			
Assistant Professor	−8.18182	1.94001	0.58493	−9.48513	−6.87850	−13.988	10	0.0001
Associate Professor	−7.33333	1.80278	0.60093	−8.71907	−5.94760	−12.203	8	0.0001
Professor	−9.40000	1.51658	0.67823	−11.28308	−7.51692	−13.860	4	0.0001

SD: Standard deviation, SEM: Standard error of mean, CI: Confidence interval

Table 2: Mean, SD, SEM, 95% CI and level of significance regarding impact of workshop on teacher's knowledge of teaching methods question-wise

Questions	Paired differences					*t* value	Degree of freedom	*P* value (two-tailed)
	Mean	SD	SEM	95% CI of the difference				
				Lower	Upper			
Q.1	−1.16	0.62	0.13	−1.42	−0.90	−9.29	24	0.0001
Q.2	−0.92	0.49	0.10	−1.12	−0.72	−9.33	24	0.0001
Q.3	−0.16	0.37	0.07	−0.31	−0.01	−2.14	24	0.043
Q.4	−1.12	0.67	0.13	−1.39	−0.85	−8.41	24	0.000
Q.5	−0.16	0.37	0.07	−0.31	−0.01	−2.14	24	0.043
Q.6	−0.32	0.48	0.09	−0.52	−0.12	−3.36	24	0.003
Q.7	−0.28	0.62	0.12	−0.53	−0.03	−2.28	24	0.032
Q.8	−0.60	0.96	0.19	−0.10	−0.20	−3.13	24	0.005
Q.9	−0.08	0.28	0.06	−0.19	0.03	−1.44	24	0.161
Q.10	−0.72	0.84	0.16	−1.07	−0.37	−4.27	24	0.000
Q.11	−0.28	0.54	0.11	−0.50	−0.06	−2.59	24	0.016
Q.12	0.01	0.82	0.16	−0.33	0.34	0.01	24	1.000
Q.13	−0.48	0.59	0.12	−0.72	−0.24	−4.10	24	0.000
Q.14	−0.40	0.50	0.10	−0.61	−0.20	−4.00	24	0.001
Q.15	−0.17	0.56	0.12	−0.41	0.07	−1.45	23	0.162
Q.16	−0.04	0.54	0.11	−0.26	0.18	−0.37	24	0.714
Q.17	−0.56	0.58	0.12	−0.80	−0.32	−4.80	24	0.000
Q.18	−0.20	0.41	0.08	−0.37	−0.03	−2.45	24	0.022
Q.19	−0.28	0.54	0.11	−0.50	−0.06	−2.59	24	0.016
Q.20	−0.08	0.28	0.06	−0.019	0.03	−1.445	24	0.161

SD: Standard deviation, SEM: Standard error of mean, CI: Confidence interval

newer teaching - learning and assessment method to students. This is a pilot study and needs further studies on a larger infrastructure and resources, preferably multicentric to come to more conclusive evidence regarding the effectivity of these workshops. This also does by no way means that the present frameworks of MET workshops are full and final, as they also need to be periodically reassessed as new researches and findings crop up.

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Original Article

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Evaluation of Placental Weight Ratio in Preterm Births and Small for Gestation Age Babies in Preeclampsia in Sikkimese Population

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Abstract

Background: Studies have established placental weight ratio (PWR) as a relevant marker of fetal uteroplacental function which reflects whether the fetal and placental growth is proportionate. It decreases across gestation as the placental growth slows and fetal growth accelerates. Preeclampsia and preterm birth are both risk factors of small for gestational age (SGA) off springs with the smaller placenta. The PWR is elevated in both these conditions which share a common pathophysiology.

Aim: The study aims to determine if PWR is a reliable indicator of placental function and fetal growth and to evaluate the PWR by gestational age in preterm births in preeclampsia in Sikkimese population.

Methods: A total of 150 placentae were analyzed, out of which 100 were from normotensive mothers and 50 from pre-eclamptic mothers. Data analysis was done using Statistical Package of Social Sciences 17. Student's *t*-test and Fisher's Chi-square test. $P < 0.05$ was considered to be statistically significant.

Results: Significantly, higher PWR was observed in pre-eclamptic pregnancies (0.001) and in both preterm (0.009) and term (0.048) births. The elevated ratio was observed only in SGA off springs (0.037) of pre-eclamptic mothers and not in normotensive mothers. Decreasing PWR across gestation was documented only in pre-eclamptic patients. The mean birth weight (0.004) and placental weight (0.0001) were significantly reduced in pre-eclamptic pregnancies while the PWR was elevated. The peak placental growth was delayed by several weeks in preeclampsia. No significant difference between preterm and term off springs of cohorts or controls was observed.

Conclusion: Preeclampsia is a confounding variable in SGA leading to raised PWR and is a reliable indicator of pregnancy complications. The influence of gestational age on this ratio and uteroplacental function could not be established. The PWR is not a relevant marker of fetal growth as it is not raised in all SGA off springs.

Key words: Gestation, Preeclampsia, Weight

INTRODUCTION

Placental weight ratio (PWR) is regarded by many as an appropriate marker of uteroplacental function and reflects the balance between fetal and placental growth.[1-4] It is predictive of maternal diseases, obstetric outcomes, perinatal mortality, morbidity, childhood development, and fetal origin of adult onset diseases.[5-9] It is postulated to decrease across gestation as the placental growth slows and fetal growth accelerates.[3,10-12] Although, the placental and birth weights are lower in small for gestational age (SGA) neonates. and preeclampsia the PWR is said to be elevated in them.[4,5,13-16] Insufficient implantation and impaired placental development in preeclampsia cause low placental weight and subsequently intrauterine growth restriction (IUGR).[17] The placenta compensates to minimize fetal growth restriction with lower weight and higher PWR to increase transfer of substrates.[2,10] Elevated PWR indicates an inefficient placenta unable to meet fetal growth requirement while lower ratio indicates increased placental efficiency.[18-20] Neonates with elevated PWR had increased incidence of meconium-stained liquor, low 1 min Apgar

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scores, neonatal jaundice, and respiratory complications.[21] Preeclampsia often necessitates iatrogenic preterm delivery to curtail the placental and fetal adversities.[22] SGA is used as an indicator of fetal growth restriction and defined as birth weight <10th percentile for age and sex. Placental weight has been found to differ between SGA and average-for-gestational age (AGA) infants and in preeclampsia.[2,18,23] PWR could be a crucial indicator of pregnancy complications. The findings would be crucial in understanding the risks of mortality in preterm SGA offspring in preeclampsia and in specifically targeting the disorder for appropriate interventions.

METHODS

A prospective study of cohort design carried out in the Department of Obstetrics and Gynecology at Central Referral Hospital and the department of Anatomy at Sikkim Manipal Institute of Medical Sciences, Gangtok Sikkim from May 2008 to April 2009. A total of 150 placentae were analyzed out of which 100 were from normotensive mothers and 50 from pre-eclamptic mothers. Age matching was done to identify each cohort with two corresponding controls. The study of the gross morphology of placenta was conducted in the Department of Anatomy. After delivery, the placenta were collected from the labor room and operation theatre, examined, washed, dried, and fixed in 10% formalin. The placental weight, volume size, calcification, infarction, and PWR were observed in preterm and term births in preeclampsia and normotensive mothers. The collected data were tabulated and analyzed using the Statistical Package of Social Sciences, version 20.0 for windows. Findings were expressed in terms of proportion and depicted in the form of tables. Student's *t*-test and Fisher's Chi-square test were applied for univariate analysis to study the effect of each variable over the outcome. $P < 0.05$ was considered to be statistically significant all these 150 participants had singleton pregnancies, and their outcome was live births.

RESULTS

The PWR was significantly higher ($P = 0.001$) in pre-eclamptic pregnancies compared to normotensive controls. Decreasing PWR with increasing gestational age was observed only in pre-eclamptic mothers with the maximum at 31 (0.2) weeks and minimum (0.16) at 38 weeks demonstrating that the placental growth peak was delayed in pre-eclamptic mothers. It decreased up to the 34th week after which it was stable at 0.18 up to the 38th week nevertheless in normotensive pregnancies the PWR was constant (0.17) throughout suggesting that placental growth achieved its peak growth much earlier (34 weeks). The PWR in the term (0.048), as well as preterm births (0.009) of pre-eclamptic mothers was significantly higher. No significant difference in PWR was observed between preterm and term births in pre-eclamptic or normotensive mothers. Also, no difference between the PWR of SGA and AGA offsprings in normotensive pregnancies was observed. The mean birth weight (0.004) and placental weight (0.0001) were significantly reduced in pre-eclamptic pregnancies while the PWR was elevated (Tables 1-4).

DISCUSSION

In this retrospective study of the PWR, we observed that though the placental and birth weights were closely correlated and lower in preeclampsia and SGA offsprings the PWR was raised. The impaired endothelial invasion of cytotrophoblasts leads to reduced capillary size of terminal villi and reduced no of arteries in tertiary term villi and reduced perfusion which reduces the efficiency of the placenta as reflected by a raised PWR.[18,24-27] The increased PWR in SGA and preeclampsia as suggested by many authors appears to be an adaptive mechanism to tide over the unfavorable environment.[2,19,28] In the present study elevated PWR in SGA was observed only in preeclampsia suggesting that predetermining risk factors causing reduced placental perfusion must coexist with IUGR to exert their effect on uteroplacental function.[1] However, no significant difference in PWR was observed between SGA and AGA offsprings in normotensive pregnancies contrary to study of Macdonald *et al.* who documented elevated PWR in SGA offsprings, nonetheless he studied the PWR of SGA births in uncomplicated pregnancies.[2] We observed a PWR of 0.21 in premature deliveries of pre-eclamptic mothers and 0.16 in normotensives. Raghunathan *et al.* observed a PWR of 0.22 in premature deliveries which was similar.[4] Our PWR distribution differs from that observed by Macdonald *et al.* who observed that majority of the placental growth occurs before 33 weeks of gestation whereas in our study placenta reached its peak growth at 37-38 weeks in preeclampsia when the PWR was the least which indicates that placental efficiency was delayed in both cases.[2,23] Our observation of the highest PWR (0.2) at 31 weeks in pre-eclamptic mothers indicates that placental efficiency was the least in earlier weeks while in the normotensive mothers the PWR was lower and constant throughout gestation suggesting that placenta achieved its peak growth much earlier in normotensive pregnancies. Our study does not support the hypothesis that the placenta and fetus follow a different growth pattern with the placenta reaching its peak growth between 28 and 30 weeks while the fetus reaches its peak growth at term.[23] The mean birth and placental weight increased from SGA to large for gestational age offsprings yet the PWR significantly decreases in AGA.[2,29] Similarly,

Table 1: Comparison of placental morphometry between preeclamptic and normotensive pregnancies

Morphology of placenta	Mean (SD)		*P*-value from *t*-test
	Preeclampsia	Normotensive	
Placental weight (g)	415.44 (91.6)	484.69 (66.3)	0.0001
Placental volume (cc)	430.0 (81.3)	491.6 (65.3)	0.0001
Placental thickness	2.6 (0.33)	2.7 (0.33)	0.10
Placental diameter	19.9 (1.6)	20.3 (1.92)	0.20
Foetoplacental weight ratio	5.5 (0.40)	5.8 (0.33)	0.001
Placental coefficient/ PWR	0.18 (0.03)	0.17 (0.010)	0.001
Birth weight	2.2 (0.47)	2.8 (0.43)	0.004

P<0.05 was statistically significant, SD: Standard deviation, PWR: Placental weight ratio

Table 2: Comparison of morphometry of the placenta and birth weight between pre-term and term small for gestation age babies in preeclampsia

Placenta	Mean (SD)		*P* value from *t*-test
	Preterm SGA	Term SGA	
Birth weight	1.7 (0.34)	2.2 (0.15)	0.0006
Placental weight (g)	333 (50.4)	433.7 (27.6)	0.0002
Placental volume (cc)	330.5 (46.8)	455.7 (50.6)	0.0001
Foetoplacental weight ratio	5.3 (0.3)	5.0 (0.38)	0.34
PWR/placental coefficient	0.2 (0.03)	0.18 (0.01)	0.41

P<0.05 was considered to be statistically significant, SD: Standard deviation, SGA: Small for gestational age, PWR: Placental weight ratio

lower weighing placentas in preeclampsia have been reported by several authors.[4,5,30,31] Gestational age greatly influences placental growth with a significantly higher prevalence of smaller placenta in preterm preeclampsia compared to term preeclampsia.[32] Several studies have documented an increasing PWR with advancing gestational age.[3,10-12] Disparate to observations of most of these authors the influence of gestational age on the PWR could not be well established in our study as a decreasing PWR with increasing gestational age was again observed only in pre-eclamptic pregnancies.[1-3] This hypothesis is further strengthened by the fact that though lower weighing placenta were observed in preterm offsprings in both cohorts and controls no significant difference in the PWR was observed between preterm and term births. The slightly lower PWR across gestation observed in uncomplicated pregnancies in our study contrasts with those of other authors however our result is similar to Williams *et al.*[1-4] The mean PWR (0.16) in normotensives as well as pre-eclamptic mothers in our study at 40 weeks was lower (0.17) than that of Raghunathan *et al.*[4] and Macdonald *et al.*[2] (0.19). Lower mean PWR across all groups in our study could be attributed to pre-placental hypoxia and lower birth weight at higher altitudes as observed by various studies. Though, similar reduced placental weights and smaller placentae were revealed in

Table 3: Comparison of morphometry of the placenta and birth weight of preterm and term small for gestation age babies in normotensive pregnancies

Placenta	Mean (SD)		*P* value from *t*-test
	Preterm SGA	Term SGA	
Birth weight	2.0 (0.54)	2.4 (0.26)	0.02
Placental weight (g)	390.8 (76.9)	448.0 (40.3)	0.03
Placental volume (cc)	406.6 (55.7)	457.0 (48.5)	0.02
Foetoplacental weight ratio	5.6 (0.34)	5.4 (0.44)	0.27
PWR/placental coefficient	0.17 (0.008)	0.17 (0.001)	0.05

P<0.05 was considered statistically significant, SGA: Small for gestational age, SD: Standard deviation, PWR: Placental weight ratio

Table 4: Comparison of PWR of different studies in uncomplicated pregnancies

Authors	Year of publication	PWR
Williams *et al.*[3]	1997	0.17 (0.27)
Raghunathan *et al.*[3]	2011	0.19
Almog *et al.*[6]	2011	0.19
Macdonald *et al.*[5]	2014	0.17 (0.044)
Present study	2015	0.17 (0.011)

PWR: Placental weight ratio

our study no significant difference in PWR was elicited between term and preterm births in pre-eclamptic as well as in normotensive mothers.[32] As reported by several authors the placental weight to birth weight were highly correlated and an increased placental to birth weight ratio could be predicted by the birth weight and vice versa.[1,5,32] Considering that the PWR were observed after delivery in our sample similar ultrasound based investigations of placental morphology and PWR in the antenatal period would give more appropriate results. Also, the small size of the sample could be a drawback and studies of larger population based cross-sectional studies need to be undertaken in the near future. The findings would be crucial in understanding the risks of mortality in preterm SGA offspring in preeclampsia and in specifically targeting the disorder for appropriate interventions.

CONCLUSION

The PWR is not correlated with fetal growth as no significant difference between SGA and AGA offsprings was recognized. The PWR is not a relevant marker of fetal growth as it is not raised in all SGA off springs. Nevertheless in complications like preeclampsia, the uteroplacental function is greatly compromised resulting in elevated PWR. Preeclampsia is a confounding variable in SGA leading to raised PWR and is a reliable indicator of pregnancy complications. The influence of gestational age on the PWR and uteroplacental function in any of the groups could not be established.

The mean placental weight and birth weight were lower in preterm pre-eclamptic pregnancies while the PWR is higher with no significant difference between preterm and term births. In normotensive pregnancies, no difference across gestational age in SGA and AGA (appropriate for gestational age off-springs) was observed. The findings would be crucial in understanding the risks of mortality in preterm SGA offspring in preeclampsia and in specifically targeting the disorder for appropriate interventions.

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Original Article

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Effect of Developmental Milestones on Patterns of Teeth Eruption

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Abstract

Introduction: Developmental milestones are a set of functional skills or age-specific tasks that most children can do at a certain age range. The milestones help to check how a child is developing. Keeping in mind the importance of the developmental milestones and the teeth eruption patterns in a child's life, a study was designed.

Materials and Methods: The study was cross-sectional in nature and conducted among four to thirty 6 months old children selected from the government and private hospitals of Bhopal city, Madhya Pradesh, India. This study comprises a total of 1601 subjects from both sexes. The cases were taken from the outpatient departments of government and private hospitals in Bhopal city. The questionnaire collected information on demographic details and milestones of children were examined as per the American Academy of Pediatric Dentistry development chart of milestones. Statistical analysis was done using Statistical Package for Social Science.

Result: It was observed that teeth eruption was delayed in children irrespective of the milestones whether it was delayed or normal.

Conclusion: No significant correlation was observed between developmental milestones and tooth eruption.

Key words: Delayed eruption, Growth, Milestones, Teeth eruption

INTRODUCTION

Evolution of the human race has seen many changes in the living habits, food habits, and oral hygiene habits over a span of thousands of years which may have influenced the eruption of teeth as well. Tooth eruption is recognized as an aspect of human growth, and development could possibly be influenced by number of factors which can be both physiological and pathological like growth, caries, malnutrition, genetics, etc.[1]

"Oral health is integral to general health and should not be interpreted as separate entities. Oral diseases are progressive and cumulative and become more complex over time. They can affect our ability to perform our day to day activities. These diseases can also affect economic productivity." A healthy oral cavity is important in a growing child, as it helps to develop good speech, healthy eating habits, and good social skills.[2]

Developmental milestones are some specific skills or age-specific tasks that most children can do at a certain age range. The stages help to check how a child is developing.[3]

According to Bailey, the parents should watch for the early childhood milestones, along with the more obvious "firsts" such as walking and talking. They should compare the child with peers or older siblings. Each child is an individual. Children can achieve a particular milestone during a wide range of time. For example, children may walk as early as 9 months or as late as 14 months.[3]

Most babies have their first tooth at around 6 months. But, the baby may have his first tooth, anytime between 3 months and his first birthday, although it can come as

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late as 14 months.[4] The last teeth, which are the second molars are usually in place by the 2nd year of life. So, by the child's third birthday, he/she should have a full set of 20 primary teeth.[4]

Today, children are maturing earlier than they did at the beginning of this century and moreover, they are growing faster than their grandparents and great grandparents. Various studies have shown that an analogous correlation between skeletal and dental maturity, as is found in the relationships among growth, skeletal, sexual, and somatic maturation, does not exist.[5]

Correlation studies using dental emergence or dental formation criteria promote the concept of dental age estimation as a maturity indicator, especially with regard to chronological age. In one of the study on the inter-relationship of somatic growth variables and chronological, dental and skeletal ages concluded that there is a high correlation between dental and chronological age.[6]

Relationship between the eruption of deciduous teeth and child's development has been widely studied. However, the process being greatly influenced by genetic, ethnic, racial factors, and geographical location; growth data, derived from studies on a group of people of different genetic pools and living under different environmental conditions are inappropriate for evaluating developmental level of children residing in other geographical locations.[1]

Keeping in mind the importance of the developmental milestones and the teeth eruption patterns in a child's life, a study was designed to evaluate and compare the homogeneity in the patterns of developmental milestones and dental eruption.

MATERIALS AND METHODS

The study was cross-sectional in nature and conducted among four-thirty 6 months old children selected from the government and private hospitals of Bhopal city, Madhya Pradesh, India. Prior to the survey, permission to conduct the research and ethical clearance was obtained. This study comprises a total of 1601 subjects from both sexes. Selected cases were from outpatient departments of government and private hospitals in Bhopal city. The data collection was done by a single trained and calibrated investigator to avoid inters-examiner variability. A survey proforma and questionnaire with closed-ended questions were designed to collect reliable well-defined information from parents. Milestones of children were examined as per the American Academy of Pediatric Dentistry development chart of milestones (Table 1). Information regarding the demographic details of the child was noted. Using Statistical Package for Social Science (SPSS Version 20; Chicago Inc., USA), data comparison was done by applying specific statistical tests. Significance level was fixed at $P < 0.05$.

RESULTS

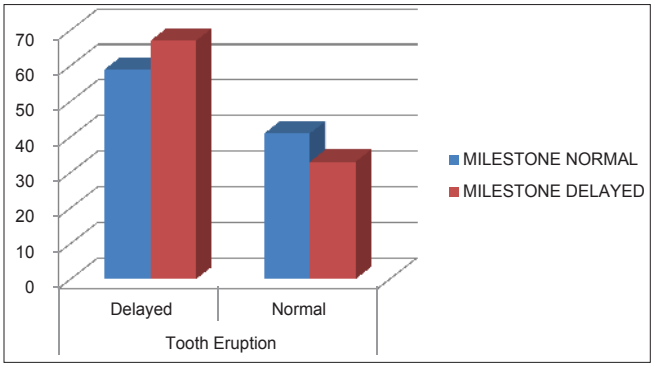
Table 2 and Graph 1 shows the comparison of the developmental milestones with the age appropriate teeth erupted in the child.

On statistical analysis, it was found that there was predominant delayed eruption in both the groups', i.e., children with normal as well as with delayed milestones. It was noticed that among normal milestones group, 40.7% children had age appropriate teeth present, whereas in delayed milestones group, 32.8% children had teeth present according to their age. i.e. if milestones were delayed age appropriate teeth were also delayed in children though the result was not statistically significant ($P = 0.03$).

It was observed that teeth eruption was delayed in children irrespective of the milestones whether it was delayed or normal.

DISCUSSION

Children grow at an amazingly fast rate during their 1st year of life. Other than the physical growth in height and weight, the major achievement stages that the children undergo during their life are referred to as the developmental milestones. These include simple skills such as rolling over, sitting up, and walking. These stages can be categorized as motor development, language development, and social/emotional development.[8]



Graph 1: The relationship of present teeth status in relationship to the developmental milestones

Table 1: Developmental milestones according to AAPD7

Hearing and understanding	Talking
Birth-3 months • Startles to loud sounds • Quiets or smiles when spoken to • Seems to recognize your voice and quiets if crying • Increases or decreases sucking behavior in response to sound	Birth-3 months • Makes pleasure sounds (cooing, gooing) • Cries differently for different needs • Smiles when sees you
4-6 months • Moves eyes in direction of sounds • Responds to changes in tone of your voice • Notices toys that make sounds • Pays attention to music	4-6 months • Babbling sounds more speech-like with many different sounds, including *p*, *b*, and *m* • Chuckles and giggles • Vocalizes excitement and displeasure • Makes gurgling sounds when left alone and when playing with you
7 months-1 year • Enjoys games like peek-o-boo and pat-a-cake • Turns and looks in direction of sounds • Listens when spoken to • Recognizes words for common items like "cup", "shoe", "book", or "juice" • Begins to respond to requests (e.g. "come here" or "want more?")	7 Months-1 year • Babbling has both long and short groups of sounds such as "tata upup bibibibi" • Uses speech or non-crying sounds to get and keep attention • Uses gestures to communication (waving, holding arms to be picked up) • Imitates different speech sounds • Has one or two words (hi, dog, dada, mama) around first birthday, although sounds may not be clear
One to two years • Points to a few body parts when asked • Follows simple commands and understands simple questions ("Roll the ball", "kiss the baby", "where's your shoe?") • Listens to simple stories, songs, and rhymes • Points to pictures in a book when named	One to two years • Says more words every month • Uses some one- or two- word questions ("where kitty?", "Go bye-bye?", "What's that?") • Puts two words together ("more cookie", "no juice", "mommy book") • Uses many different consonant sounds of the beginning of words
Two to three years • Understands differences in meaning ("go-stop", "in-on", "big-little", "up-down") • Follows two requests ("Get the book and put it on the table") • Listens to and enjoys hearing stories for longer periods of time	Two to three years • Has a word for almost everything • Uses two- or three- words to talk about and ask for things • Uses *k*, *g*, *f*, *t*, *d*, and *n* sounds • Speech is understood by familiar listeners most of the time • Often asks for or directs attention to objects by naming them
Three to four years • Hears you when call from another room • Hears television or radio at the same loudness level as other family members • Answers simple, "who?", "what?", "where?", and "why?" questions	Three to four years • Talks about activities at school or at friends' homes • People outside family usually understand child's speech • Uses a lot of sentences that have 4 or more words • Usually talks easily without repeating syllables or words
Four to five years • Pays attention to a short story and answers simple questions about them • Hears and understands most of what is said at home and in school	Four to five years • Uses sentences that give lots of details ("The biggest peach is mine") • Tells stories that stick to topic • Communicates easily with other children and adults • Says most sounds correctly except a few like *l*, *s*, *r*, *v*, *z*, *ch*, *sh*, *th* • Says rhyming words • Names some letters and numbers • Uses the same grammar as the rest of the family

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Table 2: Relationship between milestones and teeth status

Variable	Types	Teeth status (%)		*P* value
		Absent	Present	
Milestone	Normal	59.2	40.7	0.035
	Delayed	67.1	32.8	

Children tend to follow the same progression through these milestones; however, no two babies go through these milestones at exactly the same time. They also spend different amounts of time at each stage before moving on to the next.[8]

There is a wide variation in the normal age range of developmental milestones which can be because of a variation in factors such as genetic, cognitive, physical, family, cultural, nutritional, educational, and environmental factors. Many children reach some or most of these milestones at different times from the norm.[9]

Just as the milestones mark the various stages of a child's physical and emotional development, the eruption

pattern marks the oral and dental development of a child with age.

We do not usually think of a newborn as having teeth. However, at birth the crowns of the 20 "baby" or primary teeth are almost formed, and are enclosed within the jawbones. The primary teeth gradually erupt through the gums during the first 2.5 years of life.[10]

This study, hence, aimed to evaluate if the developmental milestones and dental eruption patterns are interdependent.

From the results, we can conclude that children having appropriate timings of various developmental milestones had normal dental eruption patterns. However, even in case of delayed developmental milestones, the dental eruption pattern was not necessarily found to be delayed in all cases but was normal in some.

According to our knowledge, there is no previous literature showing comparison between the milestones and the eruption pattern of teeth.

As per the literature dental eruption and skeletal growth are strongly associated with each other.[11] Eruption of teeth is found to be positively related to somatic growth. The reason may be the breastfeeding as it has an important influence on thrust and growth of mandible.[12]

Although, a study was done by Folayan *et al*.[13] in which he compared teeth eruption with feeding habits but failed to establish any link between eruption timing and duration of breastfeeding.

Though breastfeeding and teeth eruption were compared, and it may be related to somatic growth or developmental stages, we cannot say that tooth eruption is directly dependent upon developmental milestones.

CONCLUSION

We would like to conclude that no significant correlation exists between developmental milestones and tooth eruption. It is not necessary if a child has delayed milestones his teeth eruption will also be delayed. A person cannot decide the timing of tooth eruption on the basis of the developmental milestone of a child.

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Original Article

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Ectopic Pregnancy - A Rising Trend

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Abstract

Introduction: Ectopic pregnancy remains the leading cause of maternal death in early pregnancy. This retrospective analysis was done to determine the incidence, clinical features, risk factors, treatment, and morbidity and mortality associated with ectopic pregnancy in a tertiary care center.

Objective: To know the age group, parity, risk factors, clinical presentation, intervention required, and outcome of the ectopic pregnancy.

Materials and Methods: This retrospective study was conducted over a period of 1-year from January 1 to December 31, 2014 in Department of Obstetrics and Gynecology at Indira Gandhi Government Medical College, Nagpur, Maharashtra. A total of 52 cases reported during this frame with ectopic pregnancy and were admitted at our hospital through emergency or outpatient department. Data were collected in a preconceived format. Data were collected, tabulated and analyzed.

Results: Total numbers of vaginal deliveries were 2601 during the study period. Of which 52 (1.99%) were diagnosed as ectopic pregnancy. The mean age for this study was 29.1 ± 5.42. Previous abdominal/pelvic surgery/lower segment Cesarean section (32.69%), previous abortion/medical termination of pregnancy (32.69%), pelvic inflammatory disease (25%) and ovulation induction (23.07%) were major contributing factors responsible for incidence of ectopic pregnancy. The pain was a most consistent symptom in 86.53% women. A classical triad of ectopic pregnancy (pain, amenorrhea and bleeding per vaginum) seen in 53.84% women. The incidence of tubal ectopic was maximum, i.e., 50 (96.20%) cases out of 52 cases. Among tubal ectopic pregnancy the most common site was ampulla (53.84%). 44 (86.61%) cases were of ruptured ectopic pregnancies. Partial salpingectomy (65.38%) done in maximum women. No mortality and acute renal failure were found in our study among 52 patients.

Conclusion: Proper evaluation of pregnancy with associated risk factors and early diagnosis will help preserving tube and in turn her fertility and thus help in decreasing morbidity and mortality.

Key words: Ectopic pregnancy, Partial salpingectomy, Ultrasonography, Urine pregnancy test

INTRODUCTION

An ectopic pregnancy is a challenge for the obstetrician and gynecologist due to its bizarre clinical presentation. The diagnosis of ectopic pregnancy is complicated by wide spectrum of clinical presentations, from asymptomatic cases to acute abdomen, and hemodynamic shock.[1]

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An ectopic pregnancy is assuming greater importance because of its increasing incidence and its impact on women's fertility.[2,3] Ectopic pregnancy remains the leading cause of maternal death in early pregnancy.[4] With respect to management of ectopic pregnancy, there has been a tremendous technical advance. The early diagnosis and treatment of this condition over the past two decades have allowed a definitive medical management of unruptured ectopic pregnancy even before there were clinical symptoms in these high risk women.[5,6]

Ectopic pregnancy is one of the commonest causes of first trimester maternal death in developed countries and only follows induced abortion in sub-Saharan Africa.[7] There is considerable regional variation in its incidence

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and globally it has been on the rise over the past decades. Worldwide, ectopic pregnancy complicates 0.25-2.0% of all pregnancies.[7] In Europe and North America, the incidence is estimated at 2% of live births. In the developing world, however, data are few and often out of date. Nonetheless, ectopic pregnancy accounted for 0.5-2.3% of all live births in Africa from the 1960s to the mid-1980s.[8]

An ectopic pregnancy is the cause of pregnancy-related deaths. Its incidence is increasing and has been risen from 4.9/1000 pregnancies in 1970 to 9.6/1000 pregnancies in 1992.[9] The reason for this increase has not been fully elucidated, but the possible contribution of pelvic inflammatory disease (PID), ovulation inducing drugs, previous abdominal-pelvic surgeries and intra-uterine contraceptive device use has been cited as contributing factors.[10] The diagnosis of ectopic pregnancy has become more frequent during the last decades, but the incidence of ectopic pregnancy rupture has declined. This declined is due to quantitative human chorionic gonadotropin measurements, minimally invasive surgeries, and transvaginal ultrasonography (USG).[11] Early diagnosis reduces the risk of tubal rupture and allows more conservative medical treatments to be employed.[12]

This retrospective analysis was done to determine the incidence, clinical features, risk factors, treatment, and morbidity and mortality associated with ectopic pregnancy in a tertiary care center.

Aims and Objectives

1. To know the age group, parity, and risk factors with respect to the ectopic pregnancy
2. To know the clinical presentation and intervention required in ectopic pregnancy
3. To know the outcome of the ectopic pregnancy.

MATERIALS AND METHODS

This retrospective study was conducted over a period of 1-year from January 1 to December 31, 2014 in Department of Obstetrics and Gynecology at Indira Gandhi Government Medical College Nagpur, Maharashtra. It is a tertiary care center getting referrals from nearby cities and other hospitals. A total of 52 cases reported during this frame with ectopic pregnancy and were admitted at our hospital through emergency or outpatient department. Data were collected in a preconceived format. The case sheets of patients with ectopic pregnancy were traced through labor ward registers and operation theatre registers. Information regarding total number of deliveries during study period, details of demographic characteristics, presenting clinical symptoms and signs, parity, use of contraception, diagnostic tool used, detail obstetric history, risk factors for ectopic pregnancy, site of ectopic pregnancy, genital infections, line of management as well as morbidity and morbidity were obtained. Relevant investigations included complete blood picture, blood group, urine pregnancy test (UPT), and ultrasound. Based on thorough evaluation, type of management was decided. Data were collected, analyzed and tabulated.

Inclusion criteria's: All women with confirmed ectopic pregnancies.

Exclusion criteria: None.

RESULTS

Total numbers of vaginal deliveries were 2601 during the study period. Of which 52 (1.99%) were diagnosed as ectopic pregnancy. In all cases, urine pregnancy was done for provisional diagnosis. USG helped in 44 cases in diagnosing ectopic pregnancy. Gestational age ranges between 4 and 14 weeks, and the most frequent gestational age was around 6-8 weeks. Right sided ectopic (29 patients) were more common than the left side.

Table 1 depicts that maximum number of cases were above the age of 25, which is around 69.22%. This shows the maximum incidence of ectopic pregnancy in higher age group. The mean age for this study was 29.1 ± 5.42. The maximum incidence of ectopic pregnancy in the higher age group and with nulliparous.

Table 2 shows that previous abdominal/pelvic surgery/lower segment Cesarean section, previous abortion/medical termination of pregnancy (MTP), PID, ovulation induction, and use of intrauterine device were major contributing factors responsible for incidence of ectopic pregnancy.

Table 3 shows pain was most consistent symptom in 86.53% women. A classical triad of ectopic pregnancy (pain, amenorrhea and bleeding per vaginum) seen in 53.84% women.

Table 4 depicts that incidence of tubal ectopic was maximum which was 50 (96.20%) cases out of 52 cases of ectopic pregnancy. Among tubal ectopic pregnancy the most common site was ampulla (53.84%) followed by fimbrial (17.30%), isthmus (11.53%), cornual/interstitial (7.6%) and tubal abortion (5.7%). Two cases were at the extra tubal site, i.e., one was ovarian ectopic, and other was in the rudimentary horn of the bicornuate uterus.

Table 5 shows that 44 (86.61%) cases were of ruptured ectopic pregnancies, out of which amount of

Table 1: Demographic parameters

Age group (years)	Number of cases (%)	Gravida	Number of cases (%)	Parity	Number of cases (%)
<20	01 (1.9)	1	12 (23.07)	0	22 (42.30)
20-25	15 (28.84)	2	13 (25)	1	10 (19.23)
26-30	15 (28.84)	3	12 (23.07)	2	11 (21.15)
31-35	13 (25)	4	12 (23.07)	3	09 (17.30)
>35	08 (15.38)	>4	03 (5.7)	>3	00 (00)

Table 2: Distribution of cases according to risk factors associated with ectopic pregnancy

Risk factor	Number of cases	Percentage
Age>35 years	08	15.38
Tubal surgery/tubal ligation	05	9.6
Previous abortion/MTP	17	32.69
Previous ectopic pregnancy	03	5.7
PID	13	25
H/O tuberculosis	02	3.8
Oral contraceptive pill use	04	7.6
Intrauterine device	10	19.23
Ovulation induction	12	23.07
Previous abdo-pelvic surgery/LSCS	17	32.69

LSCS: Lower segment Cesarean section, MTP: Medical termination of pregnancy, PID: Pelvic inflammatory disease

Table 3: Distribution of cases according to presenting signs and symptoms

Sign/symptoms	Number of cases	Percentage
Pain	45	86.53
Bleeding per vaginum	34	65.38
H/O amenorrhea	42	80.76
Classic triad	28	53.84
Shock	27	51.92
Abdominal tenderness	37	71.15
Abdominal distension	27	51.92
Abdominal mass	10	19.23
Cervical tenderness	43	82.69
Mass felt through fornices	35	67.30

hemoperitoneum <500 ml found in 11 (21.15%) cases and ≥500 ml of hemoperitoneum in 33 (63.46%) cases.

Table 6 depicts that partial salpingectomy (65.38%) done in maximum women.

Table 7 gives an idea about the morbidity associated with ectopic pregnancy. Blood transfusion (≥2 pints) needed in 30 (57.69%) cases. 11 out of 52 patients required more than 10 days post-operative hospital stay. Among 5 patients with wound complication, 2 cases had burst abdomen, and 3 had wound gape. 7 patients needed immediate intensive care unit admission in the post-operative period. Out of 52 cases 27 (51.92%) cases required general anesthesia, 24 (46.15%) cases required spinal anesthesia and one required no anesthesia which was managed by a medical line of treatment. No mortality and acute renal failure were found

Table 4: Distribution of cases according to site of ectopic pregnancy

Site of ectopic pregnancy	Number of cases	Percentage
Ampulla	28	53.84
Isthmus	06	11.53
Fimbrial	09	17.30
Cornual/interstitial	04	7.6
Ovarian	01	1.9
Rudimentary horn	01	1.9
Tubal abortion	03	5.7
Heterotrophic/abdominal	00	00

Table 5: Distribution according to condition of tube and amount of hemoperitoneum

Condition of ectopic pregnancy	Number of cases	Percentage
Ruptured	41	86.61
Un-ruptured	08	15.38
Tubal abortion	03	5.7
Hem peritoneum <500 ml	11	21.15
Hem peritoneum ≥500 ml	33	63.46
No hem peritoneum	08	15.38

Table 6: Distribution according to line of management

Line of management	Number of cases	Percentage
Linear salpingectomy	01	1.9
Partial salpingectomy	34	65.38
Complete salpingectomy	10	19.23
Salphingo-oophorectomy	02	3.8
Milking	03	5.7
Uterine/corneal/horn reconstruction	02	3.8
Medical line of treatment	01	1.9

Table 7: Morbidity and mortality associated with ectopic pregnancy

Indicators	Number of cases	Percentage
Blood transfusion (≥1 pints)	30	84.61
Post-operative hospital stay (>10 days)	11	21.15
Post-operative wound complications	05	9.61
Require ICU admission	07	13.46
Require general anesthesia	27	51.92
Acute renal failure/UTI	00	00
Mortality	00	00

UTI: Urinary tract infection, ICU: Intensive care unit

in our study among 52 patients which gives information that early diagnosis and treatment can prevent severe morbidity and mortality in ruptured ectopic pregnancy.

DISCUSSION

The incidence of ectopic pregnancy was 1.99% of vaginal deliveries which is comparable to a similar study carried

by Khaleeque et al.[13] (1.3%). UPT and USG were done in 44 (84.61%) for confirmation which is comparable to study carried by Shetty and Shetty[14] (UPT - 87.1%, USG - 77%). Most frequent gestational age was around 6-8 weeks which is comparable to study carried by Khaleeque et al.[13] Right sided ectopic (55.76%) was more common then left in present study which is comparable to studies by Khaleeque et al.[13] (60%). Most common age group in this study was 20-30 years (57.68%) which is comparable to study by Khaleeque et al.[13] (57.68%). In present study, average age of patients was 29.1 ± 5.42. 12 (23.07%) patients were primigravida and rest 40 (76.93%) were multigravida in present study with similar results in study carried out by Khan et al.[15] (primi - 24.70% and multi - 75.30%). The incidence of nulliparous (42.30%) cases found higher compared to other studies such as in Gaddagi and Chandrashekhar[16] (27%) and Singh et al.[17] (20%). The reason for the disparity in results was increasing the incidence of infertility and abortion. Previous ectopic pregnancy and tubal surgery are strongest risk factors associated with the occurrence of ectopic pregnancy.[18] In present study, previous ectopic pregnancy found in 5.7% with comparable results in study carried by Yakasai et al.[19] (4.95%) which is consistent with the hypothesis that women with previous ectopic pregnancy has greater proclivity toward a subsequent ectopic pregnancy.[20] Tubal surgeries were carried out in 9.6% in present study which shows disparity among studies carried by Singh et al.[17] (40%) and Shetty and Shetty[14] (3.2%) due to variation in sample size. In present study, H/O previous abortion/MTP found in 32.69% cases with similar to study by Singh et al.[17] (32%). PID was found in 25% cases suggesting strong evidence that PID is responsible for the ectopic pregnancy. Similar results are seen by Yakasai et al.[19] (31.68%). History of tuberculosis found in 3.8% cases. In present study, 19.23% cases were using an intrauterine device (IUD) as a method of contraception. Combining oral contraceptive pills and IUD, 26.83% cases had ectopic pregnancy which is comparable with Khan et al.[15] (21.17%). Ovulation induction resulted in an incidence of ectopic pregnancy around 23.07% cases comparable to Gaddagi and Chandrashekhar[16] (16.21%). Previous abdominopelvic surgeries including caesarean sections were responsible for 32.69% of ectopic pregnancy similar to result by Khan et al.[15] (27.05%). Most common presenting symptom was pain in abdomen which was seen in 86.53% cases followed by history of amenorrhea (80.76%) were similar with Shetty and Shetty[14] (pain = 80.6%, amenorrhea = 77.4%). Bleeding per vaginum found in 65.38% cases which is comparable with a study by Yakasai et al.[19] (64.36%). Classical triad found in 53.84% cases which is comparable to Singh et al.[17] (60%). In present study, 27 (51.92%) cases presented to the hospital in shock. On clinical examination, it is found that abdominal tenderness present in 71.15% cases which is consistent with a study carried out by Gaddagi and Chandrashekhar[16] (70.3%). Abdominal distension found in 51.92% of patients. On abdominal palpation, abdominal mass was felt in 19.23% cases which is also seen in study carried out by Gaddagi and Chandrashekhar[16] (16.2%). Cervical motion tenderness noticed in 82.69% cases which is comparable with Gaddagi and Chandrashekhar[16] (75.7%). Adnexal mass felt in 67.30% cases which is comparable with Gaddagi and Chandrashekhar[16] (70.3%). In the present study, tubal pregnancy found in 90.27% cases which is comparable to studies carried out by Yakasai et al.[19] (89.11%). Most of the patients had ampullary ectopic (53.84%) pregnancy which is consistent with studies from Khaleeque et al.[13] (58.9%). The incidence of isthmic pregnancy was similar to study carried out by Khaleeque et al.[13] (7.7%). Fimbria (17.30%) found the second most common site of tubal pregnancy with a similar result of Khaleeque et al.[13] (15.4%). One case (1.9%) was with ovarian ectopic pregnancy similar to the single case found in study carried out by Singh et al.[17] (4%). Incidence of corneal/interstitial pregnancy was comparable to Khaleeque et al.[13] (10.3%). In the present study 5.7% cases had tubal abortion and one case was of ruptured horn pregnancy. Eight cases (15.38%) cases were of unruptured ectopic pregnancy. In the present study, salpingectomy required in 84.61% cases which is similar to that found in a study carried out by Yakasai et al.[19] (89.10%). Linear salpingectomy is done in 1.9% cases similar to study by Yakasai et al.[19] (1.9%). Salphingo-oophorectomy required in 3.8% cases which is comparable to the result of a study by Khaleeque et al.[13] (2.8%). The result of milking of the tube (5.7%) is similar to Gaddagi and Chandrashekhar[16] (5.4%). Medical line of the treatment with injection methotrexate was given in 1 (1.9%) patient similar to study by Khan et al.[15] (1.9%). One patient required horn excision and one patient of corneal pregnancy needed uterus reconstruction. 84.61% patients required intra or post-operative period which is comparable to study carried by Udigwe et al.[21] (94.4%). Post-operative wound infection found in 9.61% cases which is less compared to study by Khaleeque et al.[13] (25%). Out of 52 cases 27 (51.92%) cases required general anesthesia, 24 (46.15%) cases required spinal anesthesia. 21.15% patients were discharged after a ≥10 days stay. Fortunately, no mortality was reported in our study and study carried out by Shetty and Shetty[14] and Udigwe et al.[21]

CONCLUSION

In developing countries, a majority of hospital-based studies have reported ectopic pregnancy case fatality rate of around 1-3%, 10 times higher than those reported in developed countries. There is a rising trend in ectopic pregnancy due to early diagnosis by the availability of more sensitive methods such as hormonal test, transvaginal

sonography and laparoscopy. It is the most important cause of maternal mortality and morbidity in the first trimester. Proper evaluation of pregnancy with associated risk factors and early diagnosis will help preserving tube and in turn her fertility and thus help in decreasing morbidity and mortality.

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Original Article

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Device Closure of Atrial Septal Defect in Patients of Age More than 40 Years: Immediate and Intermediate Out Come

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Abstract

Background: Transcatheter closure of atrial septal defect (ASD) is an established procedure in children and young adults, but the benefit of this procedure in older patients is still controversial. This study was performed to evaluate the immediate and intermediate outcome of transcatheter closure of ASD in patients over 40 years of age.

Materials and Methods: Between January 2009 and March 2013, 23 consecutive patients aged more than 40 years treated with percutaneous closure of ASD were evaluated. Statistical analysis was performed using Statistical Package for the Social Sciences version 16 to detect significance by applying paired *t*-test.

Results: Mean age at procedure was 46.56 ± 6.66 years (range: 40-58 years). Majority of them were having New York Heart Association (NYHA) functional Class II symptoms (2 in NYHA III) before the closure of ASD, and mean ASD diameter was 21.6 ± 4.26 mm (range 14-30 mm). ASD closure was successfully performed in all 23 patients without any major complications. During the follow-up period of 16.19 ± 5.69 months (3-23 months), there was an improvement in NYHA functional class in all patients. Right ventricular end-diastolic dimension (RVEDD) decreased from 25.52 ± 4.56 mm to 15.14 ± 5.1 mm, left ventricular end diastolic dimension (LVEDD) increased from 38.52 ± 5.96 mm to 42.6 ± 4.04 mm, RVEDD/LVEDD from 0.68 ± 0.17 to 0.36±0.10. There was a fall in systolic pulmonary artery systolic pressure from 48 ± 14.79 mmHg to 31.13 ± 12.73 mmHg ($P < 0.05$). There was a decrease in tricuspid regurgitation in 19 of 21 patients and improvement in mitral regurgitation in 2 patients.

Conclusion: Transcatheter closure of ASD in patients aged more than 40 years is safe and causes significant improvement of NYHA functional class and positive cardiac remodeling. An long-term follow-up is necessary for the detection of the occurrence of arrhythmia and RV dysfunction.

Key words: Atrial septal defect, Congenital heart defects, Patients

INTRODUCTION

Atrial septal defects (ASD) account for 25-30% of newly diagnosed congenital heart defects in adults.[1] The left-to-right shunt through an ASD results in chronic volume overload of the right heart and, if untreated, may lead to atrial arrhythmias, right heart failure, pulmonary hypertension (HTN) (PH) and/or systemic embolism,[2] atrioventricular (AV) valve regurgitation.[3] Increased arterial stiffness,[4] may cause acute congestive heart failure after ASD closure.[5] Although some patients are asymptomatic or mildly symptomatic, they may have significant reduction in cardiopulmonary function during formal exercise testing.[6-8] Left ventricular (LV) diastolic dysfunction, which is also seen as part of normal aging and frequently occurs in

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elderly individuals with HTN will further increase the atrial shunt. Hence, ASD closure has become an established therapy, being performed increasingly in adult patients. There are conflicting reports, however, that ASD closure alone is sometimes insufficient for the improvement of symptoms and heart failure in older individuals. Available literature of outcome on ASD device closure in adults is from the Western population, with no reported studies with respect to the immediate, intermediate and long-term outcome from the Indian population, to the best of our knowledge. Hence, this study was undertaken to know the immediate and short-term outcome of transcatheter closure of ASD in terms of improvement in New York Heart Association (NYHA) functional class and echocardiographic parameters.

MATERIALS AND METHODS

We studied 23 consecutive patients aged more than 40 years who underwent device closure of ostium secundum ASD at Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bangalore, between January 2009 and April 2013. The study was approved by the institutional ethics committee, and patients were followed up personally for the status of clinical symptoms. Serial echocardiographic reports were retrieved from the institutional database.

Inclusion Criteria

1. Symptoms of dyspnoea, fatigability, palpitations or giddiness
2. Right ventricular (RV) enlargement on echocardiogram as defined by RV end diastolic dimension (RVEDD) >2.1 cm on M-mode measurement in parasternal long axis view
3. Significant left-to-right shunt with Qp: Qs >1.5.

Patients with defect size >38 mm on transesophageal echocardiography (TEE), other concomitant congenital heart disease, and PH with pulmonary vascular resistance (PVR) >8 wood units were excluded.[3]

The transthoracic echocardiographic evaluation was performed before ASD closure, 1 day and 6-12 months after the procedure, and annually thereafter. Both RVEDD and LV end diastolic dimension (LVEDD) were measured from using M-mode in parasternal long-axis views. Pulmonary artery systolic pressure (PASP) was estimated by tricuspid regurgitation (TR) velocity and dimensions of the inferior vena cava.[9] The degree of TR and mitral regurgitation (MR) were quantified by color Doppler imaging as per the recommendations in the guidelines laid down by the American Society of Echocardiography.[10]

Catheter Intervention

All procedures were carried out under local anesthesia and guided by fluoroscopy and TEE. Aspirin therapy (150 mg/day) was initiated at least 2 days prior to and maintained for at least 6 months after the intervention. Intravenous heparin was administered at the start of the procedure at a dose of 5000 U and additional doses as required to maintain an activated clotting time of 200-300 s during the procedure. The invasive evaluation was performed prior to intervention when patients presented with a non-invasively estimated PASP of >50% of systemic pressure or an absolute PASP of >60 mmHg. In these patients, PVR was carefully assessed. Only patients with PVR ≤5 wood units either at baseline or after vasoreactivity testing with 100% oxygen for 10 min were considered for ASD closure.

Device Closure

Transcatheter ASD closure was performed through right femoral vein approach as described.[11] The ASD was crossed using a multi-purpose catheter over a terumo wire, and the left upper or lower pulmonary vein was engaged. The terumo wire was then exchanged for a 0.035" exchange length wire. The multipurpose catheter was then exchanged for a delivery sheath after ensuring that there was no air within the delivery sheath. Devices were chosen to exceed the measured defect size by 3-4 mm.[12,13] Lifetech ASD devices (Lifetech Scientific Inc., Schenzen, China) were used in 21 cases, Amplatzer septal occlude (AGA Medical, Plymouth, Minnesota) in one case and Cocoon device (Vascular innovations Co. Ltd., Thailand) in one patient.

Follow-up

The patients underwent serial follow-up examinations at 1 day, 3-6 months, 12 months, and then yearly after the procedure. ECG and echocardiograms were obtained during follow-up and patients were asked questions regarding their functional class.

Statistical Analysis

Statistical analysis was done using SPSS version 16. Continuous variables were expressed as mean ± standard deviation, or median with range, as appropriate. Pre device closure and post device closure parameters were compared using paired *t*-test in Statistical Package for the Social Sciences (SPSS) Version 16.0 by IBM Corporation, USA. A $P < 0.05$ was considered statistically significant.

RESULTS

Patient's baseline characteristics have been summarized in Table 1. A total of 23 patients (17 women and six men) with a mean age of 46 years (range: 40-58 years) underwent ASD

closure. Mean weight was 58.47 ± 1.39 kg, and height was 159 ± 7 cm (range: 149-170 cm). 4 (17.4%) patients were diabetic, and four patients were hypertensive. Dyslipidemia was present in 6 (26.7%) patients. Hypothyroidism and a history of recurrent respiratory tract infections in early childhood were present in one each. The mean ASD size was 18 mm (range 14-30 mm) and device sizes ranged from 20 to 36 mm. Median Qp/Qs ratio was 2.6 (1.5-3.5). Duration of follow-up was 16.19 ± 5.69 months (3-23 months).

Patient's symptoms before and after ASD device closure were analyzed and are summarized in Table 2 and Graph 1. Fatigability was the most common symptom in 14 of 23 patients followed by dyspnoea (13 of 23 patients), palpitations (8 of 23 patients), and atypical chest pain (4 of 23 patients). Exertional chest pain was present in one patient which disappeared after device closure. The giddiness was present in two cases before closure, and this disappeared following the procedure.

All patients were in sinus rhythm with right axis deviation in two patients and left axis deviation in one case. The mean PR interval was 0.20 s (0.16-0.22 s) and mean QRS duration was 0.10 s (0.08-0.12 s). The incomplete right bundle branch block (rsR') pattern was present in 19 patients and RS pattern was observed in two cases. Device delivery and implantation were successful without procedure-related complications in all patients.

One patient aged 50 years who underwent closure using a 30 mm Lifetech Device developed 2:1 AV block, 12 months after the procedure and underwent permanent pacemaker implantation. A 48-year-old lady developed leg pain after the procedure which subsided over the next 6 months. This might have been due to injury to the branches of femoral nerve at the time of obtaining transvenous access. None had hematoma at the puncture site. No patient died during the follow-up period.

Assessment of size of ASD and rims adequacy was done by using TEE in 13 out of 23 patients in whom transthoracic echocardiography was not able to delineate the rims adequately. TEE findings have been summarized in Table 3 and Graph 2. The aortic rim was deficient (<5 mm) in four patients and absent in four patients.

Various transthoracic echocardiographic parameters assessed before and after device closure have been summarized in Table 4 and Graph 3. LV internal dimensions end diastole (LVIDD), LV dimensions end systole, left atrial (LA) size and LV ejection fraction

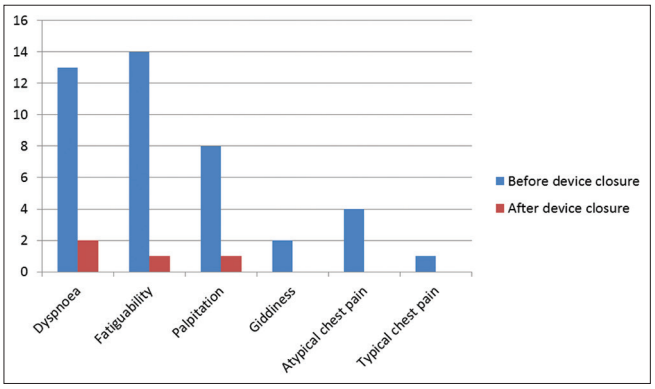
Table 1: Baseline characteristics of study population

Parameter	(Mean±SD)/frequency
Age	46.5652±6.66
Females	17 (74%)
DM	4 (17.4%)
HTN	4 (17.4%)
Dyslipidemia	6 (26.1%)
Hypothyroidism	1 (4.3%)
RRTI	1 (4.3%)
Weight (kg)	58.4783±1.39280 E1
Height	159±7 cm (max-170 cm, min-149 cm)
Hemoglobin	13.26±1.15 g/dL (range; 10.7-15 g/dL)
ASD defect	21.6±4.26 mm (max-30 mm, min-14 mm)
ASD device size	28.52±4.69 mm (max-36 mm, min-20 mm)
Follow-up	16.19±5.69 (3-23 mo)

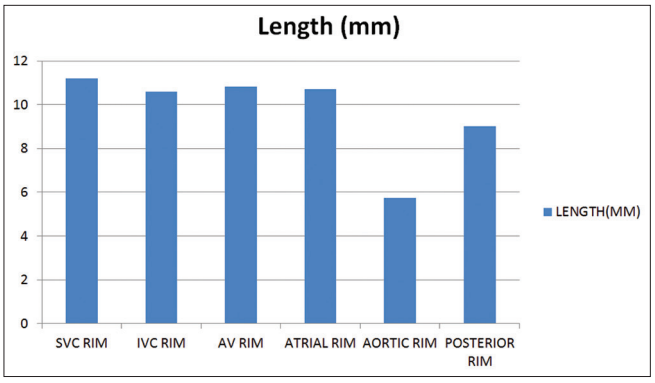
SD: Standard deviation, DM: Diabetes mellitus, HTN: Hypertension, RRTI: Recurrent respiratory tract infection, ASD: Atrial septal defect

Table 2: Symptoms before and after device closure of ASD

Symptoms	Before device closure (%)	6-12 months after closure (%)
Dyspnoea	13 (55.5)	2 (8.6)
Fatigability	14 (61)	1 (4.3)
Palpitation	8 (35)	1 (4.3)
Giddiness	2 (8.6)	0 (0)
Atypical chest pain	4 (17.2)	0 (0)
Typical chest pain	1 (4.3)	0 (0)



Graph 1: Symptoms before and after device closure



Graph 2: Lengths of various rims as assessed by transesophageal echocardiography

Table 3: TEE findings of before ASD closure

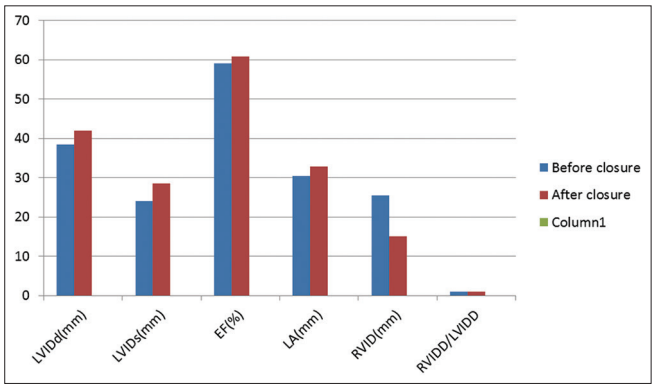
ASD rims adequacy in those who underwent device closure done (13 of 23 patients)	
SVC rim	11.2±3.12 mm (max-16 mm, min-5 mm)
IVC rim	10.58±3.40 mm (max-16 mm, min-6 mm)
AV rim	10.83±3.74 mm (max-18 mm, min-6 mm)
Atrial rim	10.7±3.24 mm (max-16 mm, min-6 mm)
Aortic rim	5.75±10.03 (max-35 mm, min-0)
Posterior rim (5 of 23 patients)	9±0.58 mm (max-10 mm, min 9 mm)
Sufficient rim	All SVC rims, IVC rims, AV rims, atrial rim, posterior rims
Aortic rim deficient	Deficient in 4 of 13 patients, absent in 4 of 13 patients

ASD: Atrial septal defect, SVC: Superior vena cava, IVC: Inferior vena cava, AV: Atrioventricular, TEE: Transesophageal echocardiography

Table 4: Transthoracic echocardiography parameters of study population before and after device closure

Parameter	Before closure	6-12 months after closure
LVIDD (mm)	38.52±5.96 mm	42.60±4.04 mm
LVIDS (mm)	24.10±4.13 mm	28.5±3.05 mm
EF (%)	59±2.45	60.83±1.23
LA (mm)	30.5±4.8 mm	32.79±3.9 mm
RV dimension (mm)	25.52±4.56 mm	15.14±51 mm^3
RVIDd/LVIDd	0.68±0.17	0.36±0.10
TR	21 (91.4%)	2 (8.6%)
TR jet	31.90±19.42 mmHg	24.25±6.3 mmHg
PASP	48±14.79 mmHg	31.13±12.73 mmHg
MVP	5	3
MR	1	0

LVIDd: Left ventricular internal dimensions end diastole, LVIDs: Left ventricular internal dimensions end systole, EF: Ejection fraction, LA: Left atrial, RVIDd: Right ventricular internal dimensions end diastole, TR: Tricuspid regurgitation, PASP: Pulmonary artery systolic pressure, MVP: Mitral valve prolapse, MR: Mitral regurgitation



Graph 3: Depicting echocardiographic parameters before and after device closure

(LVEF) improved after device closure whereas RV size, TR, TR jet, PASP, and MR decreased. TR was present in 21 of 23 patients before the procedure and in only 2 of 23 patients 6-12 months following device closure. PASP was 48 ± 14.79 mmHg. PH was present in 20 patients, with a maximum of 97 mmHg in a 40-year-old female whose ASD defect size was 24 mm. Four of the patients continued to have PASP more than 36 mmHg, 6-12 months post procedure as measured on transthoracic echocardiogram. Ventricular size regression: There was a significant decrease in RV dimensions 6-12 months post procedure (25.52 ± 4.56-15.14±3.51 mm) and also a significant decrease in LV dimensions (LVIDD) 6-12 months post procedure (38.52 ± 5.96-42.60 ± 4.04 mm).

Statistical Analysis

Paired *t*-test analysis done to analyze variables before and after device closure, which have been summarized in Table 5, showed statistically significant differences with regards to symptoms of dyspnoea, palpitation, fatigability, and echocardiographic parameters such as TR, tricuspid jet velocity, PASP, RV dimension, LVEDD, LA dimension, ejection fraction. There was no statistical reduction in giddiness following device closure, and this could be explained by the small number of patients who had it.

DISCUSSION

Treatment of ostium secundum ASD after 40 years of age has evolved over time from medical treatment to surgical treatment to transcatheter treatment. Earlier studies showed the adjusted 10-year survival rate of surgically treated patients was 95%, as compared with 84% for the medically treated patients, although arrhythmia were the problem in both group in patients aged 40 years or more when they were followed up.[14] During the follow-up for 1-17 years (mean 6.9 years), of 88 largely symptomatic sinus venosus and ostium secundum defect patients aged 40-62 years who underwent surgical correction, improvement in NYHA present in functional Class III and IV in 62% of patients pre-operatively to 82% NYHA Class I and II post-operatively was observed.[15] This is again reflective that closure of ASD irrespective age results in symptomatic improvement. In comparison between surgery and device closure. The success rate was 95.7-100% for the device group and 100% for the surgical group.[16,17] Mean age was 38 and 40 years for surgical and catheter closure respectively.[16] No statistically significant difference in the early, primary and secondary efficacy rates between the transcatheter group and surgical group ($P > 0.05$) has been reported.[17] Despite claim of 0% mortality in both transcatheter closure and surgical closure,[16,17] complication rate report has been 7.2-13% for device group and 24-28% for surgical group, values are highly significant statistical terms ($P < 0.001$).[16,17] Atrial flutter and fibrillation continued to be troublesome after surgical correction of defects after 40 years even when symptoms decrease with correction.[15] This problem of arrhythmias caused by scarring could be overcome transcatheter closure of defects as evidenced

Table 5: Paired *t*-test values of different parameters before and after device closure

Parameter	*P* value	Significance
Fatigability before closure and 6-12 months after closure	0.000	S
Palpitation before closure and 6-12 months after closure	0.005	S
Giddiness before closure and 6-12 months after closure	0.171	Ns
TR before closure and 6-12 months after closure	0.000	S
RVD before closure and 6-12 months after closure	0.000	S
Dyspnoea before closure and 6-12 months after closure	0.000	S
TR jet before closure and 6-12 months after closure	0.016	S
PASP before closure and 6-12 months after closure	0.002	S
LVID before closure and 6-12 months after closure	0.002	S
LA before closure and 6-12 months after closure	0.012	S
EF before closure and 6-12 months after closure	0.001	S

TR: Tricuspid regurgitation, RVD: Right ventricle diameter, PASP: Pulmonary artery systolic pressure, LVID: Left ventricular internal dimensions, LA: Left atrial, EF: Ejection fraction

our observation and other studies. Reported duration of hospital stay was longer by almost 2.4-4 days in surgical group difference is statistically significant ($P < 0.001$).[16,17]

Our study demonstrates that ASD closure is technically feasible with 100% success rate with least complications, when they are appropriately selected and can be performed at low risk in the older population. We observed significant improvement in symptoms and functional ability with favorable cardiac remodeling in an older population after transcatheter ASD closure. The most clinically relevant finding of our study was NYHA functional class. Little data exists with respect to intermediate and long-term outcome, particularly in Indian patients, after device closure of ASD in older patients.[3] Our study provides further evidence that transcatheter device closure of ASD in adults over the age of 40 years is not only safe and effective but also improves symptoms and NYHA functional class. Our finding is consistent with improvement in NYHA class as reported.[18]

NYHA functional class is also a predictor of survival in heart failure patients in these patients.[19] In one study, Functional status, the presence of arrhythmias, RV remodeling, and PAP were studied in 236 consecutive patients undergoing transcatheter ASD closure. 78 younger than 40 years (Group I), 84 between 40 and 60 years (Group II) and 74 older than 60 years (Group III) with similar defect and device characteristics. Although older age group had advanced clinical symptoms, post-interventionally. Symptoms were present in 13, 49, and 83% of the patients before and in 3, 11, and 34% after intervention in Groups I, II, and III. Functional status was related to pulmonary artery pressure(PAP).[20] Khan *et al.* reported that significant improvement in functional class and echocardiographic parameters as early as 6 weeks post device closure.[2] There was correlation of functional class and 6-min walk test.[2]

We observed that despite longstanding RV dilation from volume overloading, there is still potential for improvement in RV size and possible improvement in function even in those over 40 years. Closure of ASD resulted in cardiac remodeling with a significant reversal of the right to left volumetric imbalance. There was a significant decrease in RV dimensions 6-12 months post procedure (25.52 ± 4.56-15.14 ± 3.51 mm). These findings are consistent with studies by earlier authors.[2,18,20] Post-interventionally, RV size has been shown to decrease from 41 ± 7, 43 ± 7, and 45 ± 6 mm to 32 ± 5, 34 ± 5, and 37 ± 5 mm for aged <40 years, between 40 and 60 years and above 60 years, respectively ($P = 0.0001$).[20] Altinag *et al.* reported 58% patients with severe RV dilatation prior to intervention had no or mild dilatation at last follow-up. Reduction of RV dilatation was not related to age.[18]

An similar reduction in RV dimension in patients aged 40 years or more as assessed by echocardiography has been documented by echocardiography, although it was studied in in post-surgical closures patients.[15] There was a significant decrease in LV dimensions 6-12 months post procedure (38.52 ± 5.96-42.60 ± 4.04 mm). Significant improvement in RV myocardial performance iondex (MPI) and LV MPI, in one study involving 25 patients with average age of 45.5 ± 16.3 years underwent transcatheter closure.[21]

Our results are consistent with findings reported.[3] Similarly, LV end-systolic dimensions increased following device closure (24.10 ± 4.13-28.5 ± 3.05 mm), and these are consistent with findings reported by other authors.[2] These changes were evident following closure and continued to alter favorably until 6-12 months after the procedure. LV systolic function also improved soon after closing the ASD. In patients with an ASD, shunting of blood into the right heart invariably affects LV filling, akin to a "steal phenomenon." Our results support the phenomenon of ventricular interdependence, associated with RV volume overload and the "reverse Bernheim's effect" in which the septum bulges into the LV cavity leading to impaired LV filling.[22] ASD closure reduces the external work and total mechanical energy of the RV without influencing contractility. Reduced RV myocardial oxygen consumption preserves RV function.[23] Decreased in RA area is inversely proportional to age at the time of ASD closure.[24] Following device closure, left to right shunt is abolished angle filling

is improved resulting in an increase in LV dimensions and ejection fraction. A similar trend was founding a published studies.[2,25] Improvements in LV function are likely to be a major determinant of the early improvement in NYHA functional class. Schubert *et al.* have shown that ASD closure in some elderly patients may be associated with a transient increase in LA pressure and subsequent pulmonary edema due to an underlying "stiff" LV.[26] It is of interest that the improvement in LV size and function appears to occur earlier than in the RV. This may suggest that LV remodeling independent of RV remodeling.[27,28]

Device closure of ASDs leads to improvement of both RV and LV function, as well as, a reduction in LA volume. These hemodynamic improvements provide insights into the symptomatic benefits gained in the closure of ASDs using the transcatheter approach.[21] LA volume index (25.7-21.8 ml/m^2 ($P < 0.001$) after closure of ASD.[21] Our study showed some increase in LA dimension as measured in M mode on parasternal long axis. This observation is in contrast to what has been observed. In our retrospective study, only M mode dimension of LA in parasternal long axis has been taken, which does not represent the true LA volume. This could also be due to small changes in LA dimension due to inter observation variation. Moreover, Khan *et al.* reported non-significant change in the LA volume after device closure.[2]

PH was present in a significant number of patients, and mean PASP was significantly higher (48 ± 14.79 mmHg and 24.25 ± 6.3 mmHg before device closure and 6-12 months post device closure, respectively. There was statistically highly significant reduction in PASP from 48 ± 14.79 mmHg to 31.13 ± 12.13 mmHg (Table 4) in our study population. Infact, the decline was higher in contrast to other studies. Khan *et al.* reported median pulmonary artery pressure was 23 mmHg (range 12-27 mm Hg). Mean PAP >25 mm Hg was in three patients, and this was not seen at 1-year follow-up.[2] PASP decreased from 31 ± 7, 37 ± 10, and 53 ± 17 mmHg to 26 ± 5, 30 ± 6, and 43 ± 14 mmHg (P, 0.0001), respectively in 40 years, 40-60 years, >60 years after interventions in another study.[20] PH was reported to present in 63% before the procedure and was reduced to 38% at follow-up.[18] In our study, 20 of 23 patients had PH before device closure and 4 of 23 patients continued to have PH at 6-12 months follow-up. Paired *t*-test showed a statistically significant decrease in pulmonary pressure. Even those with continued PH are on follow-up and symptomatically much better.

Atrial arrhythmias are well-known in ASDs. Fortunately, all our patients had sinus rhythm in all before device closure and immediately after device closure in contrast to 21% patients with atrial fibrillation reported in one study.[2]

Complications

Despite the claim of 0% mortality in both transcatheter closure and surgical closure,[16,17] complication rate report has been 7.2-13% for the device group.[16,17] In another study, report of 8.6% early complications with transcatheter closure of ostium secundum ASD in which 2.3-2.4% needed surgical intervention either for device malposition or device embolization.[18,29] 6% were minor complications: Unsatisfactory device position or embolization, pericardial effusion, LA disc thrombus formation, right iliac vein dissection, groin hematoma, hemorrhage in the retro pharynx, and sizing balloon rupture. 0.4% late deaths due to peripheral embolization of device.[18,29]

In our study group, there was no immediate and late complications related procedure or device. One patient developed 2:1 AV block 12 months post procedure and permanent pacemaker implantation were done. However, the arrhythmia was not a feature in any of the patients at the time of device closure. 2:1 AV block in this patient is not related to device closure as it was remote occurrence, and echocardiography revealed no abnormality with device position. No patient developed signs of diastolic dysfunction or MR following ASD closure. On the contrary, there was the disappearance of MR following device closure. This shows that catheter intervention of ASD is becoming one the safest procedures with time. It has been shown that cardiac remodeling starts very shortly after transcatheter ASD closure in relatively young populations (mean age 22 ± 18 years) and that most of the cardiac remodeling appeared within a few weeks of closure. Conversely, in our study population with a mean age of 46 years), we observed that most of the improvement in RV size was very much evident in all cases at 6-12 months post device closure.

Study Limitations

Our study was a retrospective observational study with no patient aged more than 70 years. The sample size is not very large and was done in a single institute. LA dimension was assessed in a parasternal long axis which may not reflect true LA volume. This makes it essential for the data to be further confirmed in larger multicenter studies.

Longer term follow-up might have helped to assess the effect of closure on the incidence of arrhythmia and right ventricle dysfunction which are usually delayed complications of ASD.

CONCLUSIONS

Our study demonstrated that transcatheter ASD closure is technically feasible and very safe procedure when

patients with good atrial rims are chosen. Favorable cardiac remodeling in subjects aged more than 40 years as evidenced by changes in echocardiographic parameters and significant improvement in functional class on short as well intermediate-term follow-up. All ASDs should be closed irrespective of age, preferably through catheter intervention.

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Original Article

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Oral Hygiene Needs of Special Children and the Effects of Supervised Tooth Brushing

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Abstract

Introduction: Individuals with disabilities comprises 10% of the total population in developed countries and 12% in developing countries. Providing both primary and comprehensive preventive and therapeutic oral health care to individuals with special health care needs is an integral part of pediatric dentistry specialty. The aim of this study was to assess the oral hygiene status before and after supervised tooth brushing education among institutionalized differently abled children between the age of 6 and 18 years.

Materials and Methods: The oral health status was assessed for 60 children with physical and mental disabilities from a special need school in India. The Fone's/circular scrub method of tooth brushing was taught. Oral hygiene was assessed before tooth brushing education and again after 15 days expecting a distinct and significant improvement in the oral hygiene post health education. Caries index, plaque accumulation, and gingival health were assessed using decayed, missing and filled teeth index, plaque index, and gingival index, respectively.

Results: The effect of supervised tooth brushing and changes in the plaque and gingival index in mentally challenged children were statistically insignificant. The effect of supervised tooth brushing and changes in the plaque and gingival index in children with cerebral palsy were also insignificant. The group with orthopedic disability and hearing impairment showed vast improvements in their gingival and plaque index readings and significance improvement was also observed in the group with autistic children.

Conclusion: The disabled groups showed poor oral hygiene even after the education which may be attributed to the lack of coordination, understanding, physical disability or muscular limitations. More attention needs to be given to the long-term dental needs of these special children through accurate disease detection, diagnosis, prevention through habit forming and relevant treatment interventions.

Key words: Disabled children, Oral hygiene, Special needs children, Tooth brushing

INTRODUCTION

According to World Health Organization, individuals with disabilities comprises 10% of the total population in developed countries and 12% in developing countries.[1-3] According to the United Nations, 80% of all individuals with a disability live in developing countries.[4,5] The American Health Association defines a child with disability as a child, who, for various reasons, cannot fully make use of all his or her physical, mental, and social abilities[6-8] – in other words, a child who cannot play, learn, or do things that other children can of similar age. Children with disabilities have been shown to have poorer oral health than their non-disabled counterparts.[4,9,10] Variable access to dental care, inadequate oral hygiene, and disability-related factors could be the few main reasons for this observation.[11,12] The type of dental care received is determined more by the disability than the oral condition, which compounds the chronicity of dental disease.[10,13] Multiple factors including disability type and institutionalization can contribute to the observed oral health status.[14,15]

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The American Academy of Pediatric Dentistry (AAPD) recognizes that providing both primary and comprehensive preventive and therapeutic oral health care to young individuals with special health care needs (SHCN) also referred to as "The Special Child" is an integral part of the specialty of pediatric dentistry.[16] The AAPD defines SHCN as "any physical, developmental, mental, sensory, behavioral, cognitive, or emotional impairment or limiting condition that requires medical management, health care intervention, and/or use of specialized services or programs."[17] The condition may be congenital, developmental, or acquired through disease, trauma or environmental cause and may impose limitations in performing daily self-maintenance activities or substantial limitations in major life activity.[18] Health care for individuals with special needs requires specialized knowledge acquired by additional training, as well as increases awareness and attention, adaptation, and accommodative measures beyond what are considered as routine.[19]

Oral health is an integral part of overall well-being.[20] Individuals with SHCN are at an increased risk of developing oral diseases throughout their lifetime.[20-22] These individuals are also at a risk of developing systemic complication arising from oral diseases such as compromised immunity, endocarditis, etc.[23] The patients with mental, physical, or developmental disabilities who do not have the ability to understand, assume responsibility for, or cooperate with preventive oral health practices are susceptible as well.[24] The aims and objectives of this study were to assess the oral hygiene status before and after supervised tooth brushing education among institutionalized children with special needs of 6-18 years of age.

MATERIALS AND METHODS

The study was conducted under the aegis of ITS Dental College, Muradnagar, India. A total of 60 subjects between the ages of 6 and 18 years were selected for the study attending "Bhagirath Special School for Differently Abled Children," Ghaziabad, India (Figure 1). The participants were divided into five groups depending upon their disability, as follows: (1) Mentally challenged (n = 29); (2) cerebral palsy (n = 2); (3) orthopedic disabled (n = 9); (4) hearing impaired (n = 17); (5) autistic (n = 3), where "n" is equal to the number of participants. Approval from Ethical Committees and informed consent was taken from the chief inspector of the school along with the principal of our institution for conducting the study. The aim and procedure of the study were explained thoroughly to the concerned authorities. Dental examinations were done by a single examiner in school where the subject was seated on a simple chair under natural light as the illumination source. The participants did not have their teeth brushed or professionally cleaned before the examination. Dental examinations were done using a mouth mirror and probe in accordance with the World Health Organization criteria and methods.[25] The total number of decayed, missing and filled primary, and permanent teeth (decayed, missing, and filled teeth (dmft), DMFT - 1997) were recorded for each subject.[26] No radiographic examination was undertaken. The Silness and Löe index (1964) was evaluated visually by assessing the buccal and lingual surfaces of the teeth.[27] Gingival index (1963) was also taken and recorded for each subject.[28] Following these indices, an oral hygiene importance and instructional talk along with teaching the subjects the Fone's/Circular scrub method[29] of tooth brushing on a study models was performed (Figure 2). The supervising staff was also given oral health instructions and asked to ensure the practice of the taught technique amongst the children. Free samples of oral hygiene aids in the form of tooth brushes and fluoridated toothpastes were distributed (Figure 3). A subsequent visit was

Figure 1: Front of the school

Figure 2: Education about tooth brushing method

Figure 3: Free toothpaste sample distribution

made after 3 months, and all the above said procedures (examinations and oral hygiene instructions) were repeated. Statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS), Version 19.0. Armonk, NY: IBM Corp. Student's paired *t*-test was used to determine significant differences in data with the *P*-value set at 0.05.

RESULTS

The effect of supervised tooth brushing and changes in the plaque and gingival index in mentally challenged children were statistically insignificant ($P = 0.058$ and 0.187, respectively) (Table 1). The effect of supervised tooth brushing and changes in the plaque and gingival index in children with cerebral palsy were also insignificant ($P = 0.205$ and 0.090, respectively) (Table 2). The group with an orthopedic disability (Table 3) and hearing impairment (Table 4) showed vast improvements in their gingival and plaque index readings ($P < 0.001$). Significance improvement was observed in the group with autistic children after oral hygiene instructions and the improved tooth brushing technique being employed ($P = 0.034$ and 0.026) (Table 5).

DISCUSSION

Oral disease represents a major health problem among individual with disabilities.[20-22] The prevalence and severity of these diseases are much higher as compared to general population.[3,20] Poor oral hygiene was observed in the special children that were part of this study. This observation may be attributed to the reduced physical and mental abilities of these individuals and consequent difficulties in tooth brushing. Proper behavioral and habitual management are required in dealing with such cases. Oral health status and maintenance may be affected detrimentally by poor communication skills,[30] diminished motor skills,[31] the impact of anticonvulsant medications on gum health,[32] self-mutilating behaviors (excessive tooth grinding/bruxism), cariogenic effect of medicines with high sugar content, and parents having difficulty in carrying out regular oral hygiene measures.[33]

The oral hygiene condition noted during an initial examination in our study for subjects was very poor. Upon supervised brushing and providing oral hygiene instructions to the patients and their care providers, significant improvement was noticed in children with orthopedic disabilities and hearing impairments. Improvements were also observed in autistic children (although the sample size for autistic subjects was extremely low, and future studies with an increased cohort would be required to show definitive results). Children suffering from mental challenges and cerebral palsy did not show any significant improvement in oral hygiene status. This gives a clear indication that just providing instructions is not sufficient enough to improve their oral hygiene.

There is a need for the development of more clear and the efficient methods for improving oral health in such individuals to achieve a more sustainable and long-term effect. The results from our study indicate that children with special needs that were orthopedic limitations and difficulties showed an improvement after oral hygiene instructions were provided and tutorials on improved brushing techniques conducted. Conversely, children with reduced mental and/or motor skills did not show any considerable improvements in oral hygiene. It seems that learning difficulties and the inability to properly control the tooth brush to provide adequate cleaning of teeth is to be blamed. These children require not only supervised brushing and oral hygiene care, but also regular dental visits and help with tooth brushing using electronic brushes.

Our study shows that children who were more dependent on care providers for oral hygiene maintenance activities to have poorer oral health status. It has also been previously shown that children requiring tooth brushing assistance have poorer oral hygiene and more periodontal disease than those able to brush their teeth, reflecting the inadequacy or discrepancy in the efficiency with which oral care may be provided by care providers.[34-36] In assessing the oral health status of those with disabilities, it seems that the functional ability may be more important than the medical diagnosis.[31,37-39] The severity of the disability and its effect on the child's ability to accept dental treatment or the use of preventive measures can also influence disease more than the disability.[7,40-43]

Table 1: Relationship between effects of supervised tooth brushing and changes in the plaque and gingival index in mentally challenged children

Index	Paired differences					*t*	Significance (two-tailed)
	Mean	Standard deviation	Standard error	95% confidence interval of the difference			
				Lower	Upper		
PI_2-PI_1	0.00929	0.02478	0.00468	−0.00032	0.01890	1.982	0.058
GI_2-GI_1	0.00500	0.01953	0.00369	−0.00257	0.01257	1.355	0.187

PI_1: Plaque index recorded before tooth brushing education, PI_2: Plaque index recorded after tooth brushing education, GI_1: Gingival index recorded before tooth brushing education, GI_2: Gingival index recorded after tooth brushing education

Table 2: Relationship between the effects of supervised tooth brushing and changes in the plaque and gingival index in children with cerebral palsy

Index	Paired differences					*t*	Significance (two-tailed)
	Mean	Standard deviation	Standard error	95% confidence interval of the difference			
				Lower	Upper		
PI_2-PI_1	0.6000	0.2828	0.2000	−1.9412	3.1412	3.000	0.205
GI_2-GI_1	0.17500	0.03536	0.0250	−0.14266	0.4926	7.000	0.090

PI_1: Plaque index recorded before tooth brushing education, PI_2: Plaque index recorded after tooth brushing education, GI_1: Gingival index recorded before tooth brushing education, GI_2: Gingival index recorded after tooth brushing education

Table 3: Relationship between effects of supervised tooth brushing and changes in the plaque and gingival index in children with orthopedic disability

Index	Paired differences					*t*	Significance (two-tailed)
	Mean	Standard deviation	Standard error	95% confidence interval of the difference			
				Lower	Upper		
PI_2-PI_1	0.71556	0.31093	0.10364	0.47655	0.95456	6.904	0.000
GI_2-GI_1	0.40667	0.11325	0.03775	0.31962	0.49372	10.773	0.000

PI_1: Plaque index recorded before tooth brushing education, PI_2: Plaque index recorded after tooth brushing education, GI_1: Gingival index recorded before tooth brushing education, GI_2: Gingival index recorded after tooth brushing education

Table 4: Relationship between effects of supervised tooth brushing and changes in the plaque gingival index in children with hearing impairment

Index	Paired differences					*t*	Significance (two-tailed)
	Mean	Standard deviation	Standard error	95% confidence interval of the difference			
				Lower	Upper		
PI_2-PI_1	0.75294	0.30118	0.07305	0.59809	0.90779	10.308	0.000
GI_2-GI_1	0.46588	0.13440	0.03260	0.39678	0.53498	14.292	0.000

PI_1: Plaque index recorded before tooth brushing education, PI_2: Plaque index recorded after tooth brushing education, GI_1: Gingival index recorded before tooth brushing education, GI_2: Gingival index recorded after tooth brushing education

Table 5: Relationship between effects of supervised tooth brushing and changes in the plaque and gingival index in autistic children

Index	Paired differences					*t*	Significance (two-tailed)
	Mean	Standard deviation	Standard error	95% confidence interval of the difference			
				Lower	Upper		
PI_2-PI_1	1.53000	0.50090	0.28919	0.28570	2.77430	5.291	0.034
GI_2-GI_1	0.74667	0.21079	0.12170	0.22303	1.27030	6.135	0.026

PI_1: Plaque index recorded before tooth brushing education, PI_2: Plaque index recorded after tooth brushing education, GI_1: Gingival index recorded before tooth brushing education, GI_2: Gingival index recorded after tooth brushing education

Future Directions

Oral health awareness programs should be aimed specifically toward the improvement of oral hygiene in children with special needs. Personnel working at special needs schools and parents of disabled children need to be educated and made aware to the long-term importance of maintaining good oral hygiene in these children. The dental team should plan on providing comprehensive school-based initiatives and workshops, including oral health education to help children develop skills, provide fluoride supplements and sealants, offer dietary and nutrition counseling to promote oral health. Primary health care providers may influence access to dental care by assessment of oral health assessment dental referral. An epidemiological survey followed by the implementation and evaluation of a long-range public dental healthcare plan for children with disabilities and special needs is urgently required.

CONCLUSION

The subjects studied in the disabled groups showed poor oral hygiene even after the education which may be attributed to the lack of coordination, understanding, physical disability, or muscular limitations. Although improvements were observed in some of the groups, the results still highlight the urgent need for further work in this field. More attention is required directed toward the fulfillment of long-term dental needs of these special children through accurate disease detection, diagnosis, prevention through habit forming and relevant treatment interventions.

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Original Article

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Severe Acute Maternal Morbidity in a Tertiary Care Centre with Basic Intermediate Respiratory Care Units Setup

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Abstract

Introduction: Severe acute maternal morbidity (SAMM) emerges as a new quality indicator of obstetrical care. The investigation of severe maternal morbidity (SAMM) and associated risk factors is important for the global reduction of maternal mortality.

Aims and Objectives: To study the incidence, demographic factors associated with SAMM, different clinical insults responsible for SAMM, mortality to morbidity ratio, and fetomaternal outcomes in SAMM cases.

Materials and Methods: 416 SAMM cases studied in this prospective observational, analytical cross-sectional study. Data was collected by pre-defined case report format which included maternal age, socio-economic factors, obstetric history, clinical insult responsible for SAMM, complications that prompted intensive care unit admission and required intervention, length of hospital stay, and feto-maternal outcome.

Results: In our study, eclampsia leads to the cause of SAMM followed by obstetric hemorrhage and sepsis. The etiological factor for near miss event is shifting from hemorrhage to hypertensive disorders in pregnancy. In our study, maternal mortality to morbidity ratio was 1:4.95. Mortality to morbidity ratio in these categories was 1:4.6 for eclampsia with organ dysfunction, 1:6.61 for obstetric hemorrhage and 1:2.66 for sepsis respectively. 84.4% cases required blood and blood component therapy while 50% were managed in intermediate respiratory care units. Surgical intervention was required in 23.52% cases. Mortality index of our institution was 16.8% which depends on the factors such as prior health of the mother, the severity of the clinical insult, access to skilled help, and availability of medical care.

Conclusion: Severe obstetric morbidity and its relation to mortality may be more sensitive measures of pregnancy outcome than mortality alone. The lead cause of SAMM in our study is eclampsia, therefore the future demands more research into prediction, prevention, and management of hypertensive disorders in pregnancy.

Key words: Hemorrhage, Maternal mortality, and Pregnancy

INTRODUCTION

Each year nearly 289,000 women die globally due to pregnancy related causes.[1] For each maternal death, nearly 118 women suffer from life threatening event of "severe acute maternal morbidity (SAMM)".[2] In recent World Health Organization systems review of the maternal morbidity and mortality, transfer to an intensive care unit (ICU) was taken as an indicator for assessing the prevalence of SAMM worldwide.[3]

During an international seminar held in Morocco, a SAMM was defined as "any pregnant or recently delivered or aborted woman whose immediate survival is threatened and who survives by chance or because of the hospital care received."[4]

In 2013, maternal mortality in developed country was 16 per one lakh live births and that of developing country was 230 per one lakh live births.[1] Maternal mortality in India

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was178 per one lakh live births in 2011-2012.[5] Maternal mortality was used internationally as a measure of quality of obstetric care. Now, the focus is shifted from mortality to morbidity. There are very few case series on SAMM. Keeping this in mind, we are analyzing a series of SAMM cases in order to study the clinical insult responsible for SAMM and mortality to morbidity ratio. This type of study was designed for the first time in our institution and considered as a pilot study, representing this region of Marathwada.

Aim

To know the various causes of SAMM and its prevention.

Objectives

1. To study the demographic factors associated with SAMM cases
2. To study the different clinical insults responsible for SAMM
3. To find out mortality to morbidity ratio
4. To find out feto-maternal outcomes in SAMM cases.

MATERIALS AND METHODS

Study Design

This was prospective observational study carried out in the Department of Obstetrics and Gynaecology, Government Medical College, Aurangabad between the period of September 2011-January 2014. A total of 416 cases was studied. Approval of Ethical Institutional Review Board was taken.

Inclusion Criteria

1. Eclampsia with organ dysfunction
2. Severe obstetric hemorrhage
3. Severe sepsis.

Exclusion Criteria

1. Obstetric cases delivering uneventfully without any morbidity
2. Indirect causes of maternal mortality such as associated medical disorders, road accidents, and burn.

Methodology

The study population was selected from women admitted as an emergency for delivery. After applying inclusion and exclusion criteria, 416 SAMM cases were recruited for the study. A prospective study was performed including those SAMM cases which included:

Eclampsia with organ dysfunction

Eclampsia was defined as convulsions during pregnancy of >28 weeks of gestational age or in the first 10 days postpartum together with the following features within 24 h after convulsion; hypertension ≥170/110 mm of Hg and proteinuria +1, or more on random dip stick method or 0.3 g in 24 h urine analysis.

Eclampsia along with the organ dysfunction such as;

1. Hemolysis elevated liver enzymes low platelet count (HELP) syndrome (abnormal peripheral smear, lactate dehydrogenase >600, gamma glutaryltransferase >70I U/L, aspartate aminotransferase >70 IU/L, platelet count <1 lakh/L requiring platelet transfusion)
2. Pulmonary dysfunction (O_2 saturation <90%, PaO_2/FiO_2 ≤3)
3. Renal failure (oliguria ≤400 ml/24 h that does not respond to fluid infusion or blood urea >15 nmol/L, serumcreatinine >400 mmol/L)
4. Cerebrovascular accident (coma lasting for >12 h, or intracranial hemorrhage)
5. Disseminated intravascular coagulation (DIC) (acute thrombocytopenia, platelet <50,000/L requiring platelet transfusion with bleeding from multiple sites).

Severe obstetric hemorrhage

All cases of obstetric hemorrhage including antepartum and postpartum hemorrhage requiring massive transfusion of four, or more units of blood, or requiring surgical interventions in the form of obstetric hysterectomy, internal iliac artery ligation, and B-lynch brace sutures.

Severe sepsis

It includes the cases of puerperal sepsis, and postabortion sepsis presented with septicemic features. Signs and symptoms of sepsis are;

1. Fever (two or more temperature readings of >38°C)
2. Tachycardia (heart rate >100 beats/min)
3. Hypotension (blood pressure <100/60 mm of Hg)
4. Respiratory rate >20/min
5. White blood cell >17 × 10/L or <4 × 10
6. Bacteremia (positive blood culture or positive swab).

Data were collected which included the maternal age, socio-economic factors, obstetric history, clinical insult responsible for SAMM, and complications that prompted ICU admission and required intervention, length of hospital stay, and feto-maternal outcome. Women having more than one clinical insult were included in the group of primary etiology. e.g., eclampsia with abruption/DIC/hemorrhage was included in eclampsia. Data was collected by pre-defined case report format and results were expressed as numbers, or percentages.

RESULTS

During the study period, there were 35, 564 live births and we recruited 416 SAMM cases. Total number of maternal

deaths was 84, and hence, maternal mortality ratio (MMR) was 236 per lakh births. The incidence of SAMM was 11.69 per 1000 live births. Mortality:morbidity ratio was 1:4.95, this reflects for every maternal death there are 4.95 cases of SAMM. Mortality index was 16.8%.

Table 1 outlines the baseline characteristics of the patients. Mean age at which SAMM cases presented to our institute was 25.5 years. 47.11% of SAMM cases were multipara followed by primipara 41.34%. 76.92% of SAMM cases belonged to rural area, 82.21% cases were unbooked, and 48.07% cases belonged to Class IV of Kuppuswami's classification. 43.26% of SAMM cases were found in gestational age of 28-36 weeks while postpartum group includes 10.57% cases.

Table 2 shows distribution of mortality:morbidity ratio according to the individual cause responsible for SAMM. Mortality:morbidity ratio was least in obstetric hemorrhage group (1:6.61) that of eclampsia with the organ dysfunction was 1:4.6, and sepsis was 1:2.66. The lead cause of SAMM in our study was eclampsia with organ dysfunction (47.11%) followed by obstetric hemorrhage (41.34%) and sepsis (11.53%).

Table 3 shows the various interventions required and organ dysfunction associated with the SAMM cases. 69.53% of SAMM cases delivered vaginally followed by cesarean section (30.46%). About 83% cases required blood and blood component therapy while 50% cases managed in intermediate respiratory care units. Surgical intervention in the form of stepwise devascularization, B-lynch suture, and obstetric hysterectomy required in 23.07% cases. 62.5% of SAMM cases had hospital stay of 7-14 days. 27.88% cases belonged to HELLP syndrome followed by renal dysfunction (17.30%) and central nervous system dysfunction (14.42%).

48.30% babies were with the mother. 38.50% of neonates required neonatal ICU admission while 13.70% were still born (Table 4).

Table 1: Distribution of SAMM according to baseline characteristics

Baseline characteristic	Number of patients	Percentage
Age (years) (*n*=416)		
Mean age: 25.5 years		
Range: 18-38 years		
≤19	22	5.28
20-29	202	48.5
≥30	192	46.1
Parity (*n*=416)		
Nullipara (P0)	22	5
Primipara (P1)	172	41.34
Multipara (P2-P4)	196	47.11
Grandmultipara (≥P5)	26	6.25
Resident (*n*=416)		
Rural	320	76.92
Urban	96	23.07
Resistration status (*n*=416)		
Booked	74	17.70
Unbooked	342	82.21
Socioeconomic status (*n*=416)		
Class I	0	0
Class II	10	2.4
Class III	78	18.75
Class IV	200	48.07
Class V	128	30.76
State of pregnancy (*n*=416)		
<20 week	24	5.76
21-28 weeks	96	23.07
29-36 weeks	180	43.26
>36 weeks	72	17.30
Postpartum	44	10.57

SAMM: Severe acute maternal morbidity

Table 2: Distribution of mortality: Morbidity ratio according to individual clinical insults in SAMM

Cause of SAMM	Number of SAMM cases (*n*=416)	Percentage	Number of deaths	Mortality: Morbidity ratio
Eclampsia with organ dysfunction	196	47.11	40	1:4.6
Obstetric haemorrhage	172	41.34	26	1:6.61
Sepsis	48	11.53	18	1:2.66

SAMM: Severe acute maternal morbidity

DISCUSSION

In any setting, women who develops severe acute complication during pregnancy share many pathological and circumstantial factors. While some of these women die, a proportion of them narrowly escape death. By evaluating, these SAMM cases much can be learnt about the processes in place (or lack of them) for the care of pregnant women. Our current results represented a hospital based investigation of SAMM. In our study, eclampsia (47.11%) leads the causes of SAMM followed by obstetric hemorrhage (41.34%) and sepsis (11.53%). Upadhyaya and Chaudhary, Moraes *et al.* and Huseyin *et al.* also reported the hypertensive disorders in pregnancy as leading cause of maternal illness.[6-8]

While Taly *et al.*, Rööst *et al.* and Manandhar *et al.* reported hemorrhage 60%, 48% and 41.66% as most common cause of SAMM respectively.[9-11] In our study, the lead cause for SAMM was eclampsia over hemorrhage, probably due to better care at community level in the form of better antenatal care, increased number of institutional delivery along with the availability of drug like misoprostol. Though there is rampant use of drugs like magnesium sulphate to control eclamptic fit at PHC and RH level, we still need to work on prediction and prevention of hypertensive disorders in pregnancy.

Table 3: Distribution of SAMM according to maternal outcome

Parameters	Number of cases	Percentage
Mode of delivery (*n*=348)*		
Vaginal	182	52.29
Instrumental (forceps/vaccum)	60	17.24
Caesarean section	106	30.46
Intervention required (*n***)		
Intensive monitoring	204	50
Mechanical ventilation	172	41.34
Vasoactive agents	52	12.5
Blood and blood component therapy	344	82.69
Surgical intervention	96	23.07
Hospital stay (*n*=416)		
<7 days	84	20.19
7-14 days	260	62.5
>14 days	72	17.30
Organ dysfunction (*n***)		
HELLP syndrome	116	27.88
Renal dysfunction	72	17.30
CNS dysfunction	60	14.42
Pulmonary dysfunction	14	3.36
DIC	24	5.76

*Mode of delivery was applicable to gestational age >20 weeks and those delivered in our institute, **As single patient had more than one complication and required more than one intervention, so total number is more than actual number of cases, HELLP: Hemolysis elevated liver enzymes low platelet count, CNS: Central nervous system, DIC: Disseminated intravascular coagulation, SAMM: Severe acute maternal morbidity

Table 4: Distribution of SAMM according to neonatal outcome

Neonatal outcome	Number of cases (*n*=348)	Percentage
Shifted with mother	168	48.30
NICU admission	133	38.50
Still birth	47	13.70

SAMM: Severe acute maternal morbidity, NICU: Neonatal intensive care unit

The incidence of SAMM in our study was 11.69 per 1000 live births. Moraes *et al.*, Ps *et al.* and Wianwiset *et al.* reported the incidence of SAMM 15, 17.8 and 57.7 per 1000 live births respectively.[7,12,13] In our study, maternal mortality to morbidity ratio was 1:4.95. This means for every maternal death, there were 4.95 cases of SAMM.

Siddiqui *et al.*,[14] Galvão *et al.*[15] and Ps *et al.*[12] reported the maternal mortality to near miss ratio 1:5.8, 1:4.5, and 1:5.6 respectively which is consistent with our study. In the present study, the disease profile for SAMM differed from that of maternal mortality as evident by though the overall incidence of SAMM was high in eclampsia with organ dysfunction however maternal deaths were common in sepsis. Most SAMM occurred within the diagnostic categories of eclampsia with organ dysfunction, obstetric hemorrhage and sepsis. Mortality to morbidity ratio in these categories was 1:4.6 for eclampsia with organ dysfunction, 1:6.61 for obstetric hemorrhage and 1:2.66 for sepsis respectively. This observation is consistent with Rööst *et al.*[10] Fatima aparecida Lotufo *et al.* reported MMR for institution 51.6/100,000 live births, maternal near miss ratio was 4.4/1000 live births and mortality to morbidity ratio was 8.6.[16] This difference in mortality to morbidity ratio may be due to the difference in inclusion criterias and sociodemographic characteristics. Rööst *et al.* showed MMR of 187/100,000 live births and relatively low mortality index of 3.6%.[10] The mortality index gives a measure of how good the health service was with regard to managing a specific disease process. The lower the mortality index, the better the care. Mortality index of our institution was 16.8%. Galvão *et al.* and Ali *et al.* reported mortality index 18% and 19.5% respectively.[15,17] This high mortality index in our study was due to different factors such as prior health status of the mother, the severity of the clinical insult, access to skilled help, and availability of medical care.

In our study, maternal outcome was studied with respect to mode of delivery, hospital stay, intervention required along with organ dysfunction. The most common intervention was blood and blood component therapy (84.4%) followed by intensive monitoring (50%) and mechanical ventilation (37.25%). Surgical intervention was required in 23.52% cases. Siddiqui *et al.* the mean duration of hospital stay 6.17±0.58 days, and maximum stay up to 50 days.[14] Sepsis (33.33%) is the main reason for secondary morbidities and prolonging the hospital stay. Hemorrhage was the leading cause for the operative intervention. Fatima aparecida Lotufo *et al.* also reported prolonged hospital stay, high incidence blood transfusion and operative intervention in near miss event.[16] Huseyin *et al.* reported transfusion of blood products in 40% and artificial ventilation in 19.5% cases.

In our study, about half of the neonate suffered from mortality and morbidity, with take-home baby rate around 48.27%. Fatima aparecida Lotufo *et al.* also reported similar observation.[16] High perinatal morbidity and mortality were attributed to unbooked cases, preterm birth, and hypoxic insult due to eclampsia, and sepsis.

CONCLUSION

Severe obstetric morbidity and its relation to mortality may be more sensitive measures of pregnancy outcome than mortality alone. Including SAMM in maternal death audit will increase the rapidity with which the health system problem can be identified.

For meaningful comparisons to be made, standardized, simplified definitions need to be designed and agreed on as the benchmark for future research. So there is a clear need to set uniform criterias to classify SAMM. The lead cause of SAMM in our study is eclampsia, which demands more research into prediction, prevention, and management of hypertensive disorders in pregnancy.

To conclude, any pregnant woman can develop life threatening complication with little or no advance warning. All women need to access the quality maternal health services that can diagnose and manage life threatening complications. In developing countries, woman's lower socioeconomic status, poor obstetric services, and lack of emergency transfer contributes significantly to morbidity and mortality. Obstetric ICU setup with team approach consisting of treatment by obstetricians, intensive care specialists, and anesthesiologists are essential to save a maternal life. Our study recommends introduction of SAMM audit in parallel to maternal mortality audit as the causes of maternal death can be very different from the causes of SAMM. This understanding between morbidity and mortality will help in reducing substandard care and the global burden of death and long-term morbidity.

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Original Article

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Role of Ultrasound as a Diagnostic Tool in Superficial Facial Space Infections

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Abstract

Background: The purpose of this study is to show the role of ultrasound as a diagnostic tool for superficial facial space infections. Plain radiographs, computed tomography (CT), magnetic resonance imaging (MRI) are valuable diagnostic aids. However, the CT scan and MRI are both expensive. Also, the CT scans expose the patient to relatively large doses of radiation and MRI is time - consuming and not suitable for every patient.

Materials and Methods: The study consists of 10 patients. Aspiration of pus was positive in 8 patients. In these cases, pus evacuation was the prime consideration. Incision and drainage has been planned under local anesthesia and other two patients were given appropriate antibiotic and anti-inflammatory drugs.

Results: In all the cases, the spread of infection was odontogenic in nature. Ultrasound was accurate in assuming the exact location, an extent of spread, presence of pus collection, and the ultrasound imaging were concordant with the other radiological investigations.

Conclusion: Ultrasonography is a safe investigatory and an inexpensive method in diagnosing superficial facial space infections.

Key words: Computed tomography, Magnetic resonance imaging, Ultrasonography

INTRODUCTION

Dental disease is the underlying cause of most of inflammatory swellings which occurs either in or around the jaws. Inflammation may commence at either the root apices or gingival margins of erupted teeth, or in the soft tissues which surround and overlie the crown of an unerupted or partially erupted tooth.[1-3] Inflammation around the apices of tooth root may result in the formation of pus. The pus tracks along the line of least resistance and perforates the bone at the site where it is thinnest and weakest and involves the surrounding soft tissues. Once the infection enters the tissues it may resolve, become localized or spread. These infections may range from superficial to deep neck infections. The infections generally spread by following the path of least resistance through connective tissues and along facial planes. The infections spread to a site, distant to its origin, causing considerable morbidity and occasionally death.[4,5]

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Certain microorganisms produce spreading factors and spreading infections whilst others produce localizing factors and localizing infection.[6] Thus, some Streptococci produce hyaluronidase, an enzyme which dissolves the intercellular cement substance and fibrinolysin which breaks down fibrin.[7,8] The presence of these substances in the tissues will facilitate the spread of inflammatory process, some Staphylococci produce a substance called coagulase, which produces fibrin from plasma, which tends to localize the inflammatory lesion.[1] In cases of acute odontogenic infection, the oral and maxillofacial surgeon needs to know whether the inflammatory process is in a stage of abscess formation, requiring primary evacuation of pus and administration of antibiotics or a cellulitis that can generally be treated with antibiotics alone. It is often difficult to diagnose the stage of infection and to define its exact anatomic location. Plain

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radiographs, computed tomography (CT), magnetic resonance imaging (MRI) are valuable diagnostic aids. However, the CT scan and MRI are both expensive.[9-12] Also, the CT scans expose the patient to relatively large doses of radiation and MRI is time-consuming and not suitable for every patient.

An alternative diagnostic tool that is widely available, relatively inexpensive and non-invasive is ultrasonography (USG). High-resolution USG has recently been shown to be an effective tool to confirm pre-operatively any fluid collection or abscess in superficial facial spaces.[13-18]

In diagnostic ultrasound, highfrequency sound waves are transmitted into the body by a transducer and echoes from tissue interface are detected and displayed on a screen.[5] The transducers are designed to produce longitudinal waves, hence, only those waves can pass through tissues get reflected, audio frequency of a sound wave is 20 KHz. Anything below this is called infrasonic and above this is ultrasound. Medical ultrasound uses the frequency of 1-15 MHz. The transducer has a special property called piezoelectric effect; they can convert sound waves into electrical waves and vice versa.

All body tissues except bone behave like liquids and, therefore, they all transmit sound at about some velocity, a velocity of 1540 m/sec is used as an average for body tissues. No echoes are returned by fluids and thus USG is very sensitive in detecting tissue fluid collection. Unlike radiography and MRI, adverse effects of USG are not yet been reported.[19-23]

Aims

The aim of this study is to introduce inexpensive, non-invasive, non-radiation investigations in the diagnosis of superficial facial space infection.

Objectives

- To introduce a safe investigation method in diagnosing superficial facial space infections
- To find out an inexpensive method of investigation in superficial facial space infections
- To find out an alternative modality in the investigation to reduce the radiation exposure as in the case of radiographs, CT, and MRI
- To find out the difference between abscess and cellulitis
- To evaluate the extension of the swelling by using USG
- To subject the inflammatory swellings of the maxillofacial region with USG examination before a medical or surgical intervention
- To evaluate the usefulness of USG findings in the management of superficial facial space infections.

MATERIALS AND METHODS

The study was done in division of oral and maxillofacial surgery, Rajah Muthiah Dental College and Hospital, Annamalai University, Tamil Nadu, India. The study consists of 10 patients suffering from acute odontogenic infections of superficial facial spaces.

Inclusion Criteria

- Patients were of all age groups
- Patients are of both sexes
- Patients who were suffering from unilateral inflammatory swelling in the maxillofacial region of odontogenic origin.

Exclusion Criteria

- Patients with non-inflammatory swellings like soft tissue and bony cyst, tumors, and developmental anomalies
- The contralateral side of the patient with pathologies and variations most likely to show USG changes were excluded from the study
- Patients with parotid swellings were excluded from the study.

Patient Assessment

A proforma with a detailed history comprising of patient's demographic data, medical history was taken. A thorough clinical and radiological examination to locate the focus of infections should be done for all the patients, and then they were subjected to USG examination. Those agreeing to take part in the study will be asked to sign an informed consent form.

Ultrasound Examination

An ultrasound examination will be performed using a diagnostic ultrasound machine.[9] The ultrasound probes will be covered with a disposable film for control of infection and then covered with a layer of ultrasound gel.[11] The probe will be positioned outside the mouth on the skin overlying the swelling. The position of the probe will be changed several times to obtain an adequate number of transverse scans (axial plane) and longitudinal scans (sagittal plane) to define the extent of the lesion. All the lesions will be measured in 3 planes; anteroposterior, superoinferior and mesiodistal and dimensions will be recorded. Color Doppler will be applied to the images to visualize the arteries and veins.[13] No echoes are returned by fluids and thus USG is very sensitive in detecting fluid collection.

A tentative differential diagnosis will be based on the following principles:

1. Cellulitis: A poorly defined hypoechoic area, showing the scanty collection of fluids

2. Abscess: A hypoechoic area was showing diffuse margins filled with fluid and with no evidence of internal vascularization on color Doppler examination.

Procedure for USG Examination done in our Hospital

Position of patient

All examinations should be performed with the patient in the supine position.

Transducer used

A 10 MHz linear array probe and ultrasound transmission gel was used as a coupling agent. The transducer was directly applied over the skin, covering the suspected area in transverse and axial sections to determine the presence or absence of the fluid collection; if dimensions of the abscess cavity were present, depth from the skin surface up to the center of cavity and amount of collection were recorded.[21]

If ultrasound images showed no collection and only thickness of subcutaneous tissue and muscle involved were increased, then the diagnosis was made as cellulitis. In such cases, conservative management was of prime consideration. Any foci of infection if present were removed and patients were kept on supportive care to help their own body defenses in combating the infection.

When a collection was identified, diagnosis was made as an abscess. Dimensions of abscess cavity, amount of pus collected and depth of the center of abscess cavity from the skin surface were recorded.[23] Pus evacuation was then the prime consideration either by needle aspiration or by incision and drainage.

Methods

The study was successfully done in 10 patients. Aspiration of pus was positive in 8 patients. In these cases, pus evacuation was the prime consideration. Incision and drainage was done under left ventricular in these patients and other two patients were given appropriate antibiotic and anti-inflammatory drugs.

The ultrasound machine used in this study is Siemens and frequency was 10 MHZ (Table 1).

Case 1

USG findings: A well-defined hypoechoic foci of size 37 mm × 8 mm × 5 mm was seen below the body of the mandible in the superficial plane.

USG diagnosis: Abscess
Aspiration: Positive
Diagnosis: Right sub-mandibular space infection

Treatment done: Incision and drainage followed by extraction of the affected tooth (Figure 1 and 2).

Case 2

USG findings: A poorly defined hypoechoic foci with thickening of subcutaneous tissue was seen in the right buccal space region.

USG diagnosis: Cellulitis
Aspiration: Negative
Diagnosis: Cellulitis

Treatment done: Extraction of the affected teeth followed by medical management by antibiotic therapy (Figure 3 and 4).

RESULTS

In all the cases, the spread of infection was odontogenic in nature. Ultrasound was accurate in assuming the exact location of the infection, extent of spread, presence of pus collection,[21] and the ultrasound imaging were concordant with the other radiological investigations. The usual ultrasound scan examination took <10 min, and none of the patients found the procedure painful or uncomfortable. We can conclude that USG is an inexpensive and non-invasive diagnostic technique that should be used to supplement clinical examination in patients with superficial facial space infection.

USG is valuable in diagnostic as well as therapeutic help in the management of superficial facial space infections.[28] Sometimes clinical diagnosis alone is difficult to differentiate between cellulitis and abscess; in such cases USG provides accurate imaging of the superficial structures of head and neck region, delimited medially by a bony skeleton. Compared to clinical examination, ultrasound is much superior in defining the exact location of abscess because of its real-time processing. Out of 10 cases, 8 cases were diagnosed ultrasonographically as abscess and 2 cases were diagnosed as cellulitis.

Graph 1 depicts the number of patients and it suggests male patients are more prone for infections rather than females.

Graph 2 depicts the USG findings; it was easier in differentiating between abscess and cellulitis.

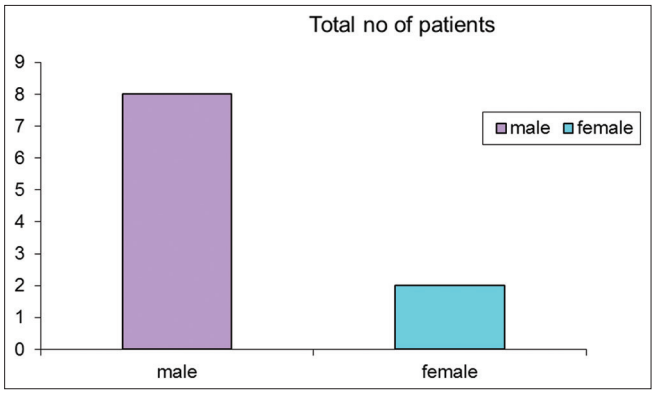
DISCUSSION

Odontogenic infections are one of the major sources of facial space infections in the head and neck region. The examination of inflammatory facial swellings is

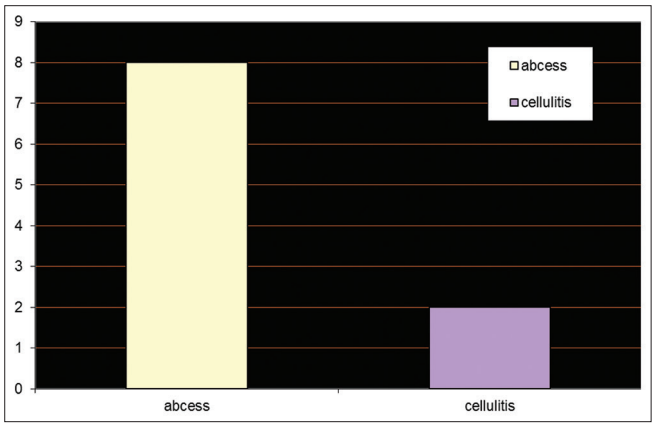
Table 1: Total number of patients - 10

Name	Age/sex	Investigations	Diagnosis	Treatment done	GA/LA
Ananth	22/M	USG	Abscess	Incision and drainage	LA
Vairam	45/F	USG	Abscess	Incision and drainage	LA
Sachin	14/M	USG	Abscess	Incision and drainage	LA
Govindarajan	60/M	USG	Cellulitis	Conservative management by antibiotics	
Paneerselvam	30/M	USG	Abscess	Incision and drainage	LA
Prabakaran	43/M	USG	Abscess	Incision and drainage	LA
Rani	45/F	USG	Abscess	Incision and drainage	LA
Thirumurugan	14/M	USG	Abscess	Incision and drainage	LA
Arumugam	26/M	USG	Abscess	Incision and drainage	LA
Velmurugan	50/M	USG	Cellulitis	Conservative management by antibiotics	

USG: Ultrasonography, LA: Left ventricular



Graph 1: Total no of patients



Graph 2: Ultrasonographic findings

largely restricted to clinical techniques of evaluation, such as inspection and palpation. However, because of the complicated anatomic structure of the head and neck, facial space infections are often difficult to be determined by clinical examinations alone. Techniques such as USG, CT, and MRI have revolutionized the field of diagnostic radiology.[24-29] These powerful diagnostic tools have minimized the therapeutic dilemma for Dental surgeons. CT scanning and MR1 are effective in diagnosing inflammatory conditions. The choice between these two techniques usually depends on the anatomic area involved. However, both techniques are expensive and radio-invasive procedure. USG has several advantages over other modalities as it is harmless, uses no ionizing radiation, is widely available, easy-to-use, non-radio-invasive, inexpensive and unaffected by metal artifacts such as dental restorations.[29-32] It can be performed without heavy sedation.[23] Ultrasound causes no health problems.

Sonography was introduced in the medical field in the early 1950's. The steady development and upgrading of the ultrasound equipment has helped the medical field and now in oral and maxillofacial surgery as well.[33] In diagnostic ultrasound, highfrequency sound waves are transmitted into the body by a transducer and echoes from tissue interface are detected and displayed on a screen. The transducers are designed to produce longitudinal waves, hence only those waves can pass through tissues and get reflected. Audio frequency of a sound wave is 20 KHz. Anything below this is called infrasonic and above this is ultrasound. Medical ultrasound uses the frequency of 1-15 MHz (2.5, 3.5, 7.5 and 10 MHz). The transducer has a special property called piezoelectric effect, i.e., they can convert sound waves into electrical waves and *vice versa*. USG examination of the inflammatory swelling was performed in cases of facial space infections. If ultrasound images showed no collection and only thickness of subcutaneous tissue and muscle involved were increased, then the diagnosis was made as cellulitis. When collection was identified, diagnosis was made as abscess. Dimensions of abscess cavity, amount of pus collected, and depth of the center of the abscess cavity from the skin surface were recorded. Pus evacuation was then the prime consideration either by needle aspiration or by incision and drainage.

Rega *et al.*,[1] conducted a study on microbiology and antibiotic sensitivities of head and Neck space infections of odontogenic origin and concluded that the bacteria were found to be 63.5% Gram-positive. Gram-positive cocci were isolated in 57.7% of specimens and Gram-negative rods were isolated in 33.0%. The most common bacteria isolated were Viridians streptococci, Staphylococci, and Peptostreptococcus.

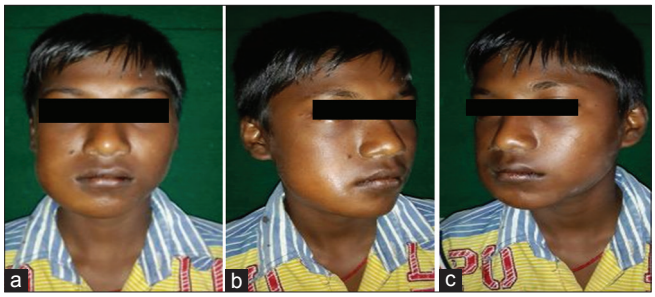


Figure 1: Ultrasonography

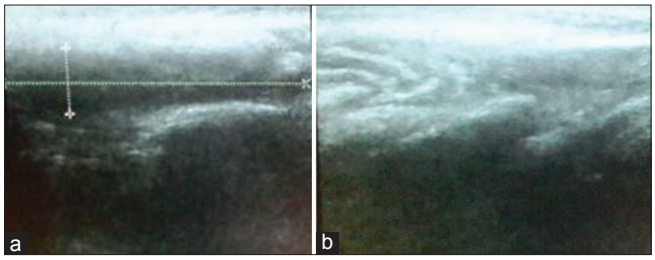


Figure 2: (a) Affected side, (b) Contralateral side

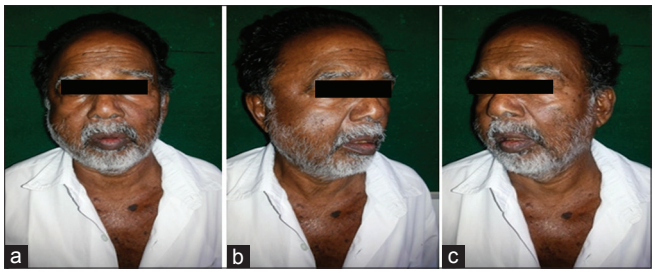


Figure 3: Ultrasonography (b) Contralateral side

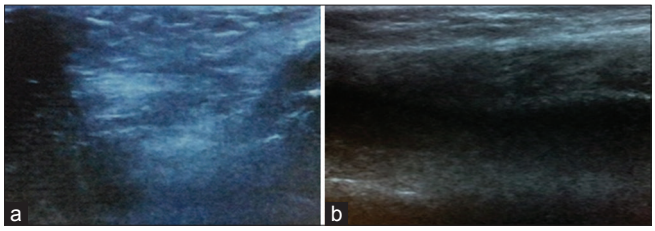


Figure 4: (a) Affected side, (b) Contralateral sid

Chandak *et al.,*[4] showed, out of 35 cases, 30 swellings were finally diagnosed as inflammatory swellings due to odontogenic origin by carrying out USG and surgical interventional investigations. Clinically diagnosed abscess cases shows highest percentage (60%) followed by edema cases (24%) and cellulitis (16%). USG diagnosed pre abscess cases shows highest percentage (60%) followed by edema cases (24%), cellulitis (8%) and abscess (8%). In 56% cases aspiration was positive and in 44 % aspiration was negative. Results showed that USG can be considered to be a valuable addition in diagnosis of inflammatory swellings of odontogenic origin. It can also demonstrate the stages of infections thus influencing the therapeutic options of antibiotic and or anti-inflammatory medications and surgical drainage.

Baurmash *et al.*,[9] conducted a study on 50 patients, with facial space infections involving the buccal and submandibular spaces. There was no parotid abscess included because of the difficulty of diagnosing the stage of infections. In our study, parotid swellings have been excluded which correlates with the study done by Baurmash *et al.*,[9] whose management can be difficult and destructive because of density of parotid-masseteric fascia, the underlying gland parenchyma, and the proximity of the facial nerve.

Kesse *et al.*,[17] described the technique of ultrasound guide the core biopsy in sum of 54 patients who presented with palpable lesions of parotid gland. Initial diagnostic ultrasound confirmed the presence of focal palpable lesions and identified additional Unpalpable lesions in seven patients. Core biopsy was 100 % accurate in differentiating benign and malignant disease. The diagnosis was accurate in 27 out of 28 patients who were subsequently operated. About26 patients avoided an unnecessary surgical procedure. In our study, a total number of 10 patients with odontogenic origin of inflammatory swellings were included. The age of patients who participated in the study ranged from 10 to 50 years and there were 7 males and 3 females in the study. The condition of the subjects was diagnosed clinically. After clinical examination patient underwent USG investigation.

Bassiony and Yang *et al.*,[20] conducted a study on exploration of USG in assessment of facial space spread of odontogenic infections. The aim of this study was to explore the capability of USG as an alternative imaging modality to MRI in detection of facial space spread of odontogenic infections. The study consists of 42 facial spaces in 16 subjects, clinically diagnosed as odontogenic infections were included in this study. The results were confirmed by MRI and microbiological tests. USG demonstrated 32 of 42 involved facial spaces. There were 100% argument between USG and MRI on 32 superficial facial spaces, including 13 buccal, 10 submandibular, 5 canine, 2 sub-massetric, and 2 sub lingual space involvements. USG was able to stage infection starting from edematous change to cellulitis to complete abscess formation. The results show that USG could be considered to be an effective method in detecting and staging spread of odontogenic infections to the superficial facial spaces. However, it might be difficult to detect deep facial space involvements.

Mallorie *et al.*,[23] conducted a study on 43 patients in which ultrasound had been used to look for evidence of pus collection. The management and treatment outcome of these patients were reviewed and data analyzed. 36 of

43 patients had their swelling incised in theatre and in 92% of these cases. USG and clinical findings corresponded, of the seven not taken to the theatre, four were USG negative and three were USG positive; in all seven cases the swelling resolved with antimicrobial therapy. Sensitivity and specificity of USG imaging to identify pus collections were high, 96% and 82% respectively. The evidence of this study indicates that USG is a very reliable diagnostic tool in the diagnosis of a collection as well as providing evidence that small collections of pus can resolve without surgical drainage.

Praveen *et al.*,[28] conducted a study on 25 patients with facial space infection in maxillofacial region were subjected to USG examination following a detailed clinical and radiological examination. Ultrasound guided needle aspiration was performed. Based on the findings, patients diagnosed with abscess were subjected to incision and drainage and those with cellulitis were subjected to medical line of treatment.

Oeppen *et al.*,[29] studied an overview of the use of ultrasound for facial space infection. Ultrasound is a relatively inexpensive, non-invasive, and readily available technique that is well tolerated by patients. It is particularly useful in the examination of superficial structures where the use of a high frequency linear probe (7.5-12 MHz) produces high definition multi-planar images. The spatial resolution achieved is superior to other methods of cross-sectional imaging.

Rahman and Hamimah *et al.*[30] conducted a study on clinical patterns of oro-facial infections. A total of 409 patients were included in this study. There were 258 (63.1%) males and 151 (36.9%) females. The incidence of oro-facial infections was highest in males rather than females.

A study was performed in 1987 by Siegert *et al.*[31] in which USG scan was done for 394 patients. Of these 87% of patients had soft tissue Swellings due to odontogenic infections. The other swellings originated from a non-odontogenic region. Siegert *et al.*[31] divided USG images into four different classes. Edema (4%), cellulitis (30%), preabscess (5%) and abscess (51%). Siegert stated that the sensitivity for diagnosing an abscess was the same for the clinical (93%) and the USG (95%) examinations. However, when only the specific diagnosis of abscess was considered, USG seemed to be slightly higher (82%) in sensitivity than the clinical diagnosis (69%). In the diagnosis of inflammatory swellings, USG seemed to be superior to the clinical diagnosis.

Kothrashetti *et al.*,[32] conducted a study on 25 patients with facial space infections in maxillofacial region of odontogenic origin.

Topazian *et al.*[33] conducted a study on the etiology of the facial space infections and came to a conclusion that dental caries is the underlying cause of most of inflammatory swellings which occurs either in or around the jaws.

CONCLUSION

This study was conducted in the division of oral and maxillofacial surgery, Rajah Muthiah Institute of Health Science, Annamalai University.

Ten cases of superficial facial space infections were chosen in the age group of 10-80 years. USG was done to detect the spread of infection, extent of infection and presence of any pus collection and to diagnose whether the inflammatory swelling is abscess or cellulitis.

Based on the study, following conclusions were made:

- USG is a safe investigation method in diagnosing superficial facial space infections
- USG is an inexpensive method of investigation in superficial facial space infections
- USG is an alternative modality of investigation method to reduce the radiation exposure as in case of radiographs and CT
- USG helps in diagnosing whether the inflammatory swelling is abscess or cellulitis
- USG helps to evaluate the extension of the swelling
- USG helps to subject the inflammatory swellings of the maxillofacial region before medical or surgical intervention
- USG findings help to evaluate the usefulness in the management of superficial facial space infections
- USG is an easier method of investigation, as in case of not able to position the patient, especially with cervical spine injury and pregnant women
- USG is an effective method of investigation in diagnosis of superficial facial space infections.

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Original Article

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Evaluation of Potential Drug-Drug Interactions in Patients of Emergency Medicine Department at a Tertiary Care Teaching Hospital: A Prospective Study

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Abstract

Background: Emergency medicine physicians have the responsibility to recognize and prevent drug-drug interactions (DDI) as they can lead to adverse outcomes. Using current DI resources can ease this seemingly overwhelming DDI burden greatly.

Objectives: To evaluate potential DDIs, nature and mechanism of these DDI and to identify common drug groups involved in these DDI in patients of all age groups admitted in emergency medicine department (ED) of a tertiary care teaching hospital.

Materials and Methods: Data of the patients admitted to ED was collected prospectively for 48 h from the time of admission over 2 months. Data was analyzed for potential DDIs by online Medscape DI checker software.

Results: A total of 156 patients were included in the study (M:F ratio 1.89:1). More than 95% patients had potential for DDI. The total number of potential DI was 1191 with a mean number of DDI of 7.63 ± 3.53. Pharmacodynamic DDIs were most common constituting 73%, followed by pharmacokinetic DDIs 24%. Significant DDIs were most common constituting 61.29% followed by serious DDIs (8.22%), contraindicated DDIs (0.58%) and minor DDIs (29.89%). The Most common involved drug groups in interactions were antimicrobials (8.74%), antiplatelets (4.19%), and steroids (4.19%).

Conclusion: Safeguards need to be introduced to prevent patients from receiving medications that have the potential to cause adverse DIs in the ED.

Key words: Drug-drug interactions, Emergency medicine, Potential

INTRODUCTION

Adverse drug reactions and drug-drug interactions (DDIs) present a growing concern in the health care setting. A number of studies have found that the incidence of drug interactions (DIs) ranges from 3%[1] to 30%.[2] DDI can lead to a variety of adverse events, and it has been suggested that preventable adverse events are the eighth leading cause of death in the United States.[3] While the beneficial effects of medication are manifold, medication use also implicitly involves a risk of DIs, side effects and other drug-related problems. Medicines are often used concomitantly with other drugs, and some degree of DDI occurs with concomitant use. The overall prevalence of DIs is 50-60% in the USA. It is estimated that DIs cause up to 3% of all hospitalizations.[4,5] This translates to nearly 2, 50,000 hospitalizations per year in the USA at a cost of $1.3 billion.[6]

However, most studies have used a variety of screening criteria and evaluate between 300 and 400 patients. The incidence of DDI or adverse events in an unselected emergency department population is unclear.[7] DDI are associated with significant morbidity, mortality, impaired

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quality of life and are primary drivers of hospital admissions.[8] A DDI is defined as a pharmacokinetic or pharmacodynamics influence of drugs on each other, which may result in desired effects, reduced efficacy, and effectiveness or increased toxicity.[9]

Many emergency medicine department (ED) patients are at risk for DIs because they are elderly receiving multiple medications. These interactions can vary from insignificant to potentially lethal. Because of the potential to cause adverse effects, it would be optimal for health care providers to routinely evaluate patient's medication lists to identify and resolve DDIs during each patient care encounter. Recognizing DIs is a daily challenge for physicians and remembering all potential interactions has become virtually impossible.[10]

The clinical reality, however, is that few emergency physicians have the time and training to systematically screen patients for DDIs. The ED represents a patient treatment area where new DDIs could easily be caused. A lack of routine screening for DDIs bypasses the screening that would otherwise detect DIs among inpatients. In addition, as many as 47% of patients admitted to the ED are already taking interacting medications.[11] New medications are added for the patient's benefit in the ED.

Although many DDIs exist, only a small part of these DDIs is clinically relevant.[12] Several factors have been identified that increase a patient's risk of DDIs. The highest risk for DDIs occurs in those patients with advanced age, those taking more than four medications, or those taking medications with a narrow therapeutic index, or requiring therapeutic drug monitoring.[13] According to previous studies, the number of medications used by patients is the best predictor for DDIs.[13] It is therefore not surprising that older patients, who often take many medications, are at the highest risk.

Patients with risk factors warrant extra caution when health care providers add new medications to their regimens. A European study of 1601 ambulatory elderly patients, taking an average of seven different drugs, found that 46.0% were at risk for at least one clinically important potential DDI.[14] Furthermore, it has been reported that about 40% of hospitalized patients had at least one potential drug-disease interaction.[15]

Emergency medicine physicians have the responsibility to recognize and prevent DDI as they can lead to adverse outcomes. Using current DI resources can ease this seemingly overwhelming DDI burden greatly. Overall, data on the occurrence and consequences of DDI alerts within hospitals are scarce. The underlying rationale for the study was to characterize DDIs among ED inpatients likely to have DDIs, in order to assess the potential need for the development of an intervention to monitor and detect DDIs, while the patient is being treated in the ED.

Therefore, our study objectives were,
1. To evaluate potential DDIs
2. To identify nature and mechanism of DDIs
3. To identify common drug groups involved in DDIs

MATERIALS AND METHODS

A prospective observational, cross-sectional study was carried out over a period of 2 months in the ED after obtaining written approval by Institutional Review Board and from head of ED. All patients admitted to ED were enrolled in the study after taking written informed consent from the patient/legal guardian. Patients with very critical condition as per the clinician's opinion were excluded from the study. Demographic data like name initials, age, gender, occupation, address were recorded. The complete prescription was recorded in case record form for first 48 h. Patient admitted in the ED of our institute were transferred to their respective specialty after 48 h of initial stabilization. Hence, data was collected for the first 48 h. Confidentiality of all the patients' data were maintained. Data analyzed for potential DDI by using online Medscape DI checker software, textbooks, and reference books.[16,17] DIs judged by the Medscape DI checker software to be of serious, significant, contraindicated and minor varieties. Fischer exact test and Pearson correlation coefficient test were used to assess the relationship between quantitative variables.

Statistical Analysis

Data analyzed by Microsoft excel 2010®, Microsoft Corporation Pvt. Ltd, USA and statistical software SPSS 21.0.

RESULTS

In our study, prescriptions of 156 patients admitted in the ED were collected for first 48 h and analyzed.

Age

The mean age was 53.38 ± 16.84 years. About 37 (23.71%) patients presenting to ED were 61-70 years of age followed by 30(19.23%) patients belonged to 51-60 years of age group. Male: Female ratio was 1.9:1.

Co-morbid Conditions

Most frequent co-morbid condition were hypertension 59 (37.82%), diabetes mellitus 35 (22.43%), ischemic heart

disease 33 (21.15%) and chronic obstructive pulmonary disease 11 (7.05%).

Drugs Use Pattern

Total 156 patients received 1635 drugs, number of drugs prescribed per patient being 9.99 ± 2.55 (mean ± SD).

DDI

A total of 149 (95.51%) prescriptions had potential for DDIs out of 156 prescriptions. The total number of potential DDIs was 1191 with a mean number of DDIs 7.63 ± 3.53. Demographic variables and nature of potential DDIs are illustrated in Table 1. The association between DDIs, male gender ($P = 0.04$) and age >40 years, $P = 0.05$) was statistically significant using Fischer exact test. The association between DDIs and number of drugs prescribed more than 5 was statistically extremely significant ($P < 0.0001$) using Fischer exact test (Table 2).

Nature and Mechanism

Pharmacodynamic DDIs were most common constituting 73%, followed by pharmacokinetic DDIs 24% and unknown 3%. Significant DDIs were most common constituting 61.3% followed by serious DDIs (8.22%), contraindicated DDIs (0.58%) and minor DDIs (29.9%). Contraindicated DDIs were seen with linezolid and dopamine/norepinephrine in 5 patients. Minor DDIs were not analyzed. Examples of serious and significant pharmacodynamic DDIs are shown in Table 3. Examples of serious and significant pharmacokinetic DDIs are shown in Table 4.

Common Drug Groups

The most common involved drug groups were antimicrobials (8.74%), steroids (4.19%), antiplatelets (4.19%), diuretics (3.59%), anticoagulants (3.23%), angiotensin converting enzyme (ACE) inhibitors + AT_1 antagonists (2.87%) and β blockers (2.75%) (Figure 1). The number of drugs prescribed were in correlation with increasing age of the patient ($r = 0.85$, $P = 0.05$) using Pearson correlation coefficient test. The number of potential DDIs were correlated with the number of drugs prescribed ($r = 0.74$, $P < 0.0001$) using Pearson correlation coefficient test (Figure 2).

Table 1: Demographic variables and nature of potential DDIs (*n*=156)

Demographic variable	Mean±SD (range in years)	Total (%)
Age	53.38±16.84 (12-85)	156 (100)
Male	50.78±13.83 (12-91)	(59.71)
Female	54.93±15.13 (16-85)	(40.29)
Number of drugs prescribed	9.99±2.55 (4-16)	1635 (100)
Potential for DDI	7.63±3.53 (0-34)	1191 (100)
Mechanism of potential for DDI		
Pharmacodynamic interaction (pd)	5.57±4.24 (0-29)	869 (72.96)
Pharmacokinetic interaction (pk)	1.82±0.70 (0-9)	284 (23.85)
Unknown mechanism of interaction	0.24 (0-2)	38 (3.19)
Clinical types of potential for DDI		
Serious drug interaction	0.62±0.70 (0-5)	98 (8.22)
Significant drug interaction	4.68±4.24 (0-21)	730 (61.30)
Contraindicated drug interaction	0.04 (0-2)	7 (0.58)
Minor drug interaction	2.28 (0-12)	356 (29.90)

DDI: Drug-drug interactions, SD: Standard deviation

Table 2: Different variables and DDIs

Variables	Patients without DDIs on their prescription	Patients with DDIs on their prescription	*P* value*
Gender			
Male	2	100	0.04
Female	5	49	
Age range (years)			
≤40	4	32	0.05
More than 40	3	117	
Number of drugs prescribed			
≤5	4	3	<0.0001
≥5	3	146	
Co-morbid condition			
Diabetes	0	35	0.35
Non-diabetes	7	114	
Hypertension	1	58	0.25
Non-hypertensive	6	91	
Ischemic heart disease	0	33	0.34
Non-IHD	7	116	
COPD	0	11	1
Non-COPD	7	138	

*Using Fischer's exact test *P* value significant for gender, age and number of drugs prescribed, IHD: Ischemic heart disease, COPD: Chronic obstructive pulmonary disease, DDI: Drug-drug interactions

DISCUSSION

Drug-related adverse events have been identified as a major source of morbidity and mortality in the United States, and DDIs are significant source of these events. Frequency of potential DDIs and the risk factors has widely been investigated in the hospital of modern countries,[18,19] but it has not been considered a lot in developing countries. In the present study, we calculated the frequency with which potential DDIs would be highlighted by computer-based online Medscape DI checker software.

In our study, the mean age was 53.38±16.84 years with the majority of male patients (M:F - 1.9:1). The average number of medications/patient administered in the study population was 9.99 ± 2.55 indicating polypharmacy which was a major risk factor for DDI. A study by Glintborg *et al*, reported median number of drugs 8 (1-24).[20] These patients were likely to have more medical complications and at a higher risk of drug-related interactions.[11,21,22] In our study, average potential DDI was 7.63 ± 3.53 per prescription

Table 3: Serious and significant potential pharmacodynamics DDIs

Potential effect	Effect of DDI	Drugs	Number
Serious			
↑ Bleeding tendency	Anticoagulant effect enhanced	Heparin+Streptokinase	17
Additive cardiotoxicity	QTc interval prolonged	Azithromycin+Ondansetron	10
		Levofloxacin+Ondansetron	10
↑ Bleeding tendency	Anticoagulant effect enhanced	Ceftriaxone+Heparin	9
Arrhythmia	Hypomagnesemia+digoxin toxicity	Pantoprazole+Digoxin	8
Significant			
↑Bleeding tendency	Hemorrhage	Aspirin+Clopidogrel	53
		Heparin+Clopidogrel	39
		Heparin+Aspirin	36
↓ Therapeutic effect, renal function deterioration	Antihypertensive	Ramipril+Aspirin	30
Altered S. K+	Fluctuation of K+	Aspirin+Furosemide	29

DDI: Drug-drug interactions

Table 4: Serious and significant potential pharmacokinetic DDIs

Mechanism	Potential effect	Drugs	Number
Serious			
Absorption	↑ Digoxin	Omeprazole+Digoxin	3
	↑ Digoxin	Ranitidine+Digoxin	2
Metabolism	↑ Heparin	Azithromycin+Heparin	2
	↓ Clopidogrel	Omeprazole+Clopidogrel	2
	↑ Theophylline	Ciprofloxacin+Theophylline	1
Significant			
Metabolism	↑ Midazolam	Metronidazole+Midazolam	9
	↓ Midazolam	Budesonide+Midazolam	8
Absorption, renal clearance	↑ Digoxin	Carvedilol+Digoxin	5
Metabolism, renal clearance	↑ Digoxin	Spironolactone+Digoxin	5

DDI: Drug-drug interactions

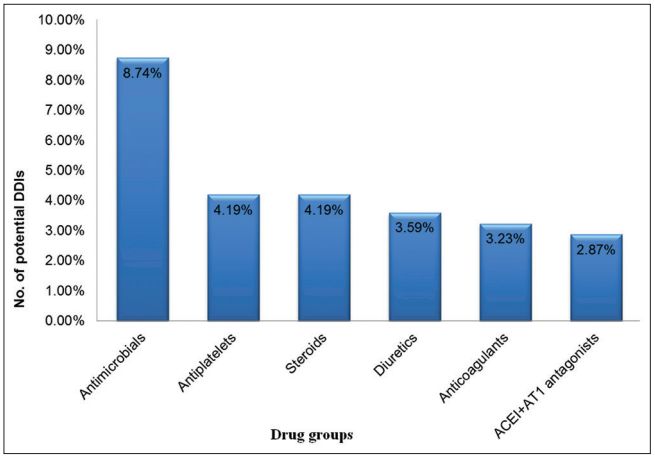

Figure 1: Drug groups involved in potential drug-drug interactions

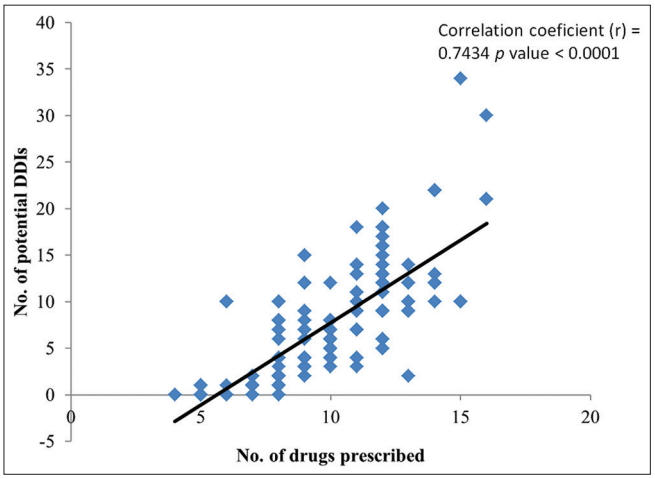

Figure 2: Potential drug-drug interactions with number of drugs prescribed

which was higher than that reported by Zwart-van Rijkom *et al.* with the average of 3.4 DDIs.[23]

The most frequent classes of medications implicated in potential DDIs were antimicrobials (8.74%), steroids (4.19%), antiplatelets (4.19%) diuretics (3.59%) anticoagulants (3.23%), ACE inhibitors + AT_1 antagonists (2.87%) and β blockers (2.75%). This was comparable to study by Goldstein *et al.* in which the most frequent classes of medications implicated in potential DDIs were NSAIDs, beta-blockers, steroids, ACE inhibitors, and anticoagulants.[7] A study by Hohl *et al.* reported that the most frequent implicated drugs were nonsteroidal anti-inflammatory drugs, antibiotics, and anticoagulants.[24] Goldberg *et al.* expressed medication-related DIs by relative risk, and found the greatest relative risk with digoxin, ranitidine, and furosemide.[19] Beers *et al.* reported in 1990 that 89% of DDIs were accounted for by opioid analgesics, nonsteroidal anti-inflammatory agents, benzodiazepines, antacids, and diuretics.[25] Gaddis *et al.* reported most common drugs associated with a DI digoxin, warfarin and aspirin.[11] These differences in causes of DDIs may be due to institution-specific bias in prescribing habits, patient population and screening systems utilized or changes in prescribing habits.[26,27]

Many of these DIs can be monitored and avoided, by means of serum dosage adjustments or by means of clinical or laboratory control. The easiest way to reduce the frequency of DDI is to decrease the number of medicines prescribed. Nevertheless, sometimes it's difficult to reduce the number of drugs prescribed for patients with multiple chronic conditions; therefore, to lower the frequency of potential interactions it would be necessary to make a careful selection of therapeutic alternatives, and in cases without other options, patients should be continuously monitored to identify adverse events.[28]

The association between patients with DDI and male gender was considered to be statistically significant ($P = 0.04$) by Fischer exact test. The association between patients with DDIs and number of drugs prescribed more than 5 was considered to be statistically extremely significant ($P < 0.0001$) by Fischer exact test. The number of drugs prescribed were in correlation with increasing age of the patient ($r = 0.85$, $P = 0.05$). The number of potential DDIs were correlated with the number of drugs prescribed ($r = 0.74$, $P < 0.0001$). So, old age and polypharmacy were important risk factors for causing DDIs in our study. This was comparable to the study by Gaddis *et al.* where DDIs were higher in older age (>60 years) and in patients with more than 6 drugs per prescription.[11] A study by Goldberg *et al.* reported that emergency department patients taking three or more medications and patients older than 50 years of age taking two or more medications are at substantial risk for adverse DDIs and drug-disease interactions.[19]

The most frequent serious pharmacodynamic DDIs were heparin + streptokinase (17). Both increases anticoagulation and can lead to hemorrhage. The most frequent significant pharmacodynamic DDIs were aspirin + clopidogrel (53). Both increases anticoagulation and can lead to hemorrhage. The contraindicated DDIs were linezolid and dopamine/norepinephrine (5). Linezolid increases effects of dopamine/norepinephrine by pharmacodynamics synergism leading to acute hypertensive episode.

Numbers of authors have suggested that computer-aided order entry and prescription writing can reduce the number of medication errors.[29,30] Use of computerized order entry for inpatients, in which all medications are entered and cross-checked for interactions, has been shown to decrease medication errors and adverse drug-related events and to generate cost savings as well.[29] Our data suggest there may be a great deal of added value in translating a similar system to the ED. While a number of potential interactions have been identified, not all are clinically relevant. Patient safety may be improved by decreasing the frequency of preventable adverse drug events.[23]

Limitation

In this study, we did not gather the information to assess the actual relevance of the potential DDI; this may be the topic of our further research.

CONCLUSION

More than 95% patients had potential for DDIs. Close monitoring of patients with drugs groups involved in potential DDIs is required. Safeguards need to be introduced to prevent patients from receiving medications that have the potential to cause adverse DIs (antimicrobials, steroids, antiplatelets, diuretics, anticoagulants, ACE inhibitors + AT_1 antagonists, and β blockers) in the ED. Actual interactions are relatively few. Physicians should be vigilant for potential DDIs, especially among the most high-risk patients taking multiple medications. Further research is needed to investigate the clinical relevance of these DDIs.

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Original Article

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Intraocular Pressure Changes with the Use of Difluprednate: An Observational Study

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Abstract

Introduction: Steroids are the mainstay in the treatment of ocular inflammation and in post-surgical cases. While these agents effectively treat and prevents inflammation, their use is also associated with risks, including ocular hypertension. A clinically significant intraocular pressure (IOP) increase is defined as an observed value >21 mmHg and/or change from baseline ≥10 mmHg. It has been noted in a few studies that difluprednate 0.05% ophthalmic emulsion has a likelihood of increasing the IOP.

Purpose of the study: To study the time of onset magnitude of IOP rise and to study the response of the raised IOP to treatment using topical and oral antiglaucoma medication and withdrawal of difluprednate, on IOP changes.

Methodology: Total of 49 cases of post-operative cataract surgery and a case of allergic conjunctivitis treated with difluprednate 0.05% 3 times a day on monitored at weekly intervals for 6 weeks. During such monitoring patients underwent visual acuity recording and complete ophthalmic examination including evaluation of IOP.

Results: Out of 50 patients, the 4 of the patients from the post-operative group and a case of allergic conjunctivitis treated with difluprednate showed marked increase in IOP, associated with corneal edema, rapid loss of vision and pain.

Conclusion: The patients on treatment with difluprednate can show marked raise in IOP which can be the cause for acute presentations of gross fall of vision and pain, this can be an ocular emergency.

Key words: Corneal edema, Difluprednate, Intraocular pressure, Ocular emergency

INTRODUCTION

Intraocular pressure (IOP) may occur with application topical ocular preparations like corticosteroid drops or ointment applied to the skin of the eyelids. The risk of IOP rise increases with duration of use and may be directly correlated to its anti-inflammatory effect.[1] Difluprednate is the US- Food and Drug Administration (FDA) approved for post-operative pain, and has good ocular penetration good ocular penetration. It is used as an anti-inflammatory and in post-operative cases for pain relief and to prevent inflammatory reactions. This drug is available freely in the market as diflucor and others.

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Pharmacology of Diflupednate

Difluprednate (difluoroprednisolone butyrate acetate, or DFBA) is a synthetic difluorinated prednisolone derivative (Figure 1).[1] Originally developed for dermatologic applications; the molecule derives its potency from fluorination at the C6 and C9 positions. Its anti-inflammatory activity is further augmented by replacing the 17-hydroxyl group with butyrate while its lipophilicity and hence, corneal penetration is enhanced by substituting the 21-hydroxyl group with acetate.[2,3]

On June 24, 2008, the U.S. FDA approved difluprednate, a strong topical steroid, for the treatment of post-operative ocular inflammation and pain. The first steroid to be indicated for pain associated with ocular surgery. The approved dosing for difluprednate is one drop in the

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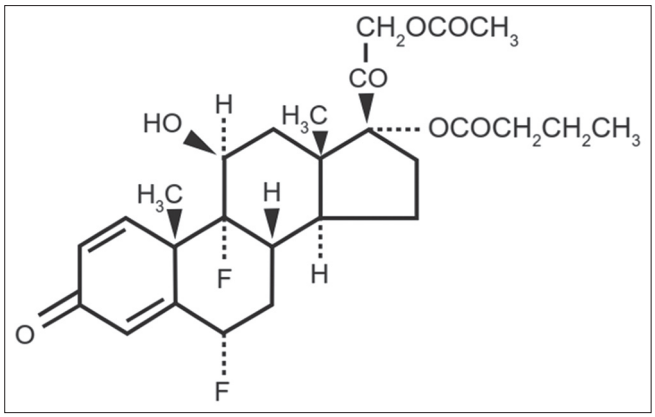

Figure 1: Difluprednate molecule

affected eye(s) 4 times daily beginning 24 h after surgery and continuing for 2 weeks, followed by twice-daily dosing for a week, and then tapering based on the patient's response.[4]

Difluprednate ophthalmic emulsion 0.05% is also being studied in other ocular inflammatory diseases, including the U.S. Phase 3 study evaluating difluprednate for the treatment of anterior uveitis.[5]

This is a relatively newly developed topical anti-inflammatory steroid with high efficacy and is available as 0.05% ophthalmic emulsion. The stable oil-in-water emulsion formulation has an advantage of producing dosage consistency as the other formulations in suspension are needed to be shaken by the patient before instilling the drop for homogeneity of dosage. It has good tissue penetration and better bioavailability, along with fast local metabolism.[6]

Pharmacokinetics

Once instilled, difluprednate emulsion is rapidly deacetylated in the aqueous humor to difluoroprednisolone butyrate (DFB), the drug's active metabolite, which has a similar corticosteroid activity profile. Endogenous tissue esterases then metabolize DFB to the inert metabolite hydroxyfluoroprednisolone butyrate, which limits systemic exposure to the active compound.[7,8]

Two multicenter, randomized, placebo-controlled phase 3 (registration) trials in 438 subjects with significant postoperative ocular inflammation (defined as more than 11 AC cells) demonstrated that both 4-times-daily and 2-times-daily difluprednate, beginning 24 h after surgery, effectively reduced inflammation and pain compared with placebo.[9]

Purpose of the Study

Difluprednate ophthalmic emulsion has been shown to be associated with raised IOP when used for durations less than for other steroids, in this study we aim to study the time of onset, magnitude of IOP rise. And response to treatment using topical and oral antiglaucoma medication and withdrawal of difluprednate on IOP changes.

METHODOLOGY

A sample of 49 patients who had undergone small incision cataract surgery operated at a tertiary care hospital - KIMS Hospital and Research Centre, a case of allergic conjunctivitis who came to the ophthalmology outpatient department of KIMS Hospital. All the cases were operated and were started on medication after written consent. Helsinki Guidelines were followed for treatment of all patients. All patients were given difluprednate 0.05% ophthalmic emulsion (DIFLUCOR) manufactured by Ajantha Pharma, the patients were followed up over 6 weeks.

IOP was within normal limits before starting the drug and on further visits. The IOP was recorded using a rebound tonometer (icare) and a Perkins applanation tonometer. All patients underwent slit lamp examination, visual acuity testing at each visit.

RESULTS

Out of 50 patients treated with difluprednate 0.05% 3 times a day, 5 patients showed significant increase in IOP from 2 days to 4 weeks, the range of IOP rise was 35-67 mmHg which is a clinically significant IOP increase, The earliest presentation was 2nd day and other case was 5th day, remaining 3 cases presented with raised pressures between 2nd and 4th week, as the IOP rise was marked, and was associated pain, loss of vision and corneal edema patients presented early. This helped to treat glaucoma and do the follow-up with concomitant medication.

All cases responded to the withdrawal of difluprednate and topical anti-glaucoma medication. Around 1% of cases are found to have a rapid rise in IOP.

Case 1

Female aged 55 years underwent cataract surgery without complications. Recovered 6/9 vision by the end of 4 weeks, anterior segment was normal. The patient was started on topical difluprednate (0.05%) three times daily post-operatively.

Early in the 5th week, patient presented with a headache and inability to see with the operated eye. On examination we found ground glass cornea (oedematous), IOP measured 67 mm of Hg, vision was PL, the other eye showed IOP of 35 mm of Hg.

The patient was treated with anti-glaucoma drugs, timolol maleate (0.5%) and brimonidine. IOP became normal within 2 days in both the eyes.

Difluprednate (0.05%) was then restarted and the subject developed rise in IOP up to 60 mm of hg within 1-week in the operated eye and 25 mm of Hg in the other eye.

A provisional diagnosis of steroid-induced glaucoma was made, and the difluprednate (0.05%) was withdrawn and anti-glaucoma drugs (brimonidine and timolol) continued for another 2 weeks when the IOP normalized all anti-glaucoma drugs are withdrawn and patient's follow-up was uneventful.

Case 2

Female aged 65 years underwent cataract surgery without complications. Vision recovered to 6/24 by 2nd week, but by 3rd week subject developed corneal edema and gross drop in the vision to PL, IOP measured 48 mm of Hg and the other eye had IOP of 25 mm of hg.

The patient was continued with difluprednate (0.05%) and topical anti-glaucoma drugs timolol maleate (0.5%) and brimonidine (0.2%) combination, hyperosmotic agents, and cycloplegic therapy. Patient did not respond to the management the possibility of endothelial decompensation was thought of as the eye was not showing any inflammatory reactions, all the treatment withdrawn except anti-glaucoma drugs (timolol maleate 0.5% + brimonidine 0.2%) 2 times daily.

On follow-up after 2 months the cornea had become clear, uncorrected vision was 6/24 IOP measured 13 mm of hg in both the eyes. The timolol maleate + brimonidine 0.2% was withdrawn and the case was followed up weekly for 3 months and showed no recurrence of corneal edema and rise in IOP.

Case 3

Male aged 48 years underwent uneventful cataract surgery. Post-operative unaided vision acuity was 6/6 distant and $n = 12$ near acuity on the 2nd week.

In 4th week, patient presented with total blurring of the vision. On examination IOP was 44 mm of hg and the other eye 22 mmHg.

The suspicion of steroid-induced glaucoma was made; difluprednate was withdrawn and started on timolol maleate 0.5% + brimonidine 0.2% 2 times daily.

By the end of 1-week, cornea became clear, and IOP measured 14 mmHg in both the eyes. Further follow-up of patients without anti-glaucoma drugs showed normal IOP of 16 mmHg and uncorrected vision 6/6.

Case 4

Female patient aged 52 years underwent an uneventful cataract surgery in her left eye. The patient was started on difluprednate and moxifloxacin eye drop combination on 1st post-operative day.

The patient came back on the second post-operative day with pain, watering and blurring of vision in the operated eye. On examination cornea was hazy, descemets folds were seen. IOP was 40 mmHg measured with I care tonometer.

The patient was started on tab acetazolamide 250 mg tid and timolol maleate (0.5%) bd. Difluprednate eye drops was stopped, and patient was started on fluorometholone (0.1%) e/d and moxifloxacin e/d 6 times/day. The patient was followed up after 2 days with pressure down to 18 mmHg. The patient was continued on fluorometholone (0.1%) and tapered till 6 weeks later surgery.

Case 5

Male aged 26 years came with severe allergic conjunctivitis with visual acuity of 6/6 vision on both the eyes and was started on difluprednate eye drops 3 times a day.

The patient came back after 5 days with history of cloudy vision, and allergy symptom had disappeared. On examination cornea was hazy with IOP of 35 and 38 mmHg on the right and left eye respectively. Visual acuity was dropped to 6/12 vision in both the eyes.

Difluprednate eye drops were stopped and timolol maleate 0.5% twice a day started along with olopatadine 0.1% eye drops twice a day.

Patient was followed up after 1-week and the pressure was 18 and 19 mmHg in right and left eye, respectively, and the vision had improved to 6/6 in both the eyes and timolol maleate stopped after 3 weeks.

These observations were recorded within 6 months period among 60 patients treated with difluprednate (0.05%). This shows the possibility of incidence of steroid-induced glaucoma in patients receiving difluprednate (0.05%). This may probably be due to higher bioavailability of the drug in the eye as proven by studies and literature. These observations need to be substantiated by comparative studies with other steroid drugs and close monitoring of all cases on difluprednate (0.05%) for glaucoma and corneal changes at frequent intervals and if so proven the dosage and strength,

frequency and safety of difluprednate drug needs to be re-evaluated.

DISSCUSSION

There are several reports of difluprednate induced raised IOP.

The IOP-increasing potential of difluprednate investigated by Cable[10] in a retrospective chart review. Data from 100 consecutive, uncomplicated phacoemulsification patients treated with difluprednate ophthalmic emulsion 0.05% twice daily post-operatively were analyzed. Five percent of patients, all with a history of open-angle glaucoma, responded with ocular hypertension. The average increase in IOP among responders was 17.8 mmHg, considerably higher than the accepted value for a clinically significant increase (≥10 mmHg). Moreover, 60% of IOP elevations were noted on post-operative day 1 and a further 40% on post-operative day 7. The authors concluded that difluprednate administered twice daily could cause significant and early elevations in IOP.

The present study showed marked IOP change probably because the cases were treated with difluprednate thrice daily as this product particulate can clog the trabecular meshwork. The incidence is low in our study as all the cases who showed raised IOP were normotensives before treatment. All patients who had raised IOP presented with acute manifestations. These patients may be strong steroid responders and treatment with difluprednate was stopped. They were started on loteprednol etabonate 0.5% eye drops and anti-glaucoma medications.

Meehan has reported raising of IOP within 2 weeks of initiating difluprednate treatment, resulting in an IOP increase from 9 mmHg to 48 mmHg with subsequent micro cystic edema.[11]

A significant IOP response (IOP increase of ≥10 mmHg from baseline and IOP ≥24 mm Hg) was seen in 50% of eyes (13/26) and in 50% of patients (7/14) in patients treated with difluprednate in paediatric uveitis; 3 eyes of 2 patients required glaucoma surgery.[12]

CONCLUSION

All patients are receiving topical ocular steroids, especially difluprednate have to be followed regularly and should be cautioned of acute raised of IOP causing pain and drop in vision. Once raise in IOP is observed, the drugs should be withdrawn and treated as early as possible with adjuvant medications. These cases may be high steroids responders. They should be branded as difluprednate responders. Future use should be prevented and if steroid use is necessary, safer steroids should or other alternatives should be preferred.

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Original Article

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Comparison of Efficacy of Methylprednisolone and Triamcinolone in Osteoarthritis of the Knee: A Prospective, Randomized, Double-Blind Study

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Abstract

Background: Osteoarthritis is a degenerative joint disease and a common complaint among the elderly patients. Intra-articular steroids have a promising role in not only providing a better analgesia but also delay the surgical intervention in knee arthropathy. We organized a double-blind comparative study to evaluate the efficacy of Methylprednisolone and Triamcinolone for reduction of pain in cases of knee osteoarthritis.

Materials and Methods: We enrolled 60 patients from our Department of Orthopaedics and conducted a randomized, double-blind comparative study in patients complaining of knee pain. The patients were divided into two groups: Group I (30 patients) - Inj. Methylprednisolone 80 mg/ml and Group II (30 patients) - Inj. Triamcinolone 40 mg/ml. Our patients were instructed to regularly visit the out-patient department of our institute every 15 days for the next 12 weeks. During 3 months, patients were evaluated (symptoms and physical examination) every 4 weeks and asked to fill up the Visual Analog Scale (VAS), Western Ontario MacMaster (WOMAC), and Knee Society Score (KSS).

Results: On observing 100 mm VAS score, while walking 20 m, a statistical difference was found during inter-group comparison of VAS scores after 8-week duration of intra-articular injection ($P = 0.01$). On observing the WOMAC score after 8 weeks of intra-articular injection ($P = 0.001$), a statistically significant difference was observed between Group I (96.23 ± 27.59) and Group II (123.31 ± 25.56). On observing KSS score, 8-week duration; Group I (59.25 ± 8.72) and Group II (53.34 ± 8.90) revealed a statistically significant difference among them ($P = 0.01$).

Conclusion: Both intra-articular corticosteroids (Methylprednisolone and Triamcinolone) possess a safer profile, but the use of Methylprednisolone provides more immediate and prolonged improvement in pain, stiffness, and improves joint function.

Key words: Intra-articular steroids, Methylprednisolone, Osteoarthritis, Triamcinolone

INTRODUCTION

Osteoarthritis is a very common orthopedic complaint of elderly and imparts great physical and mental stress to the patient. It is a joint degenerative disorder affecting the joint cartilage leading to joint pain, stiffness, swelling, and disability.[1] It carries a multi-factorial etiology (age, obesity, trauma, mal-alignment, and genetics).[2] The most common joint affected by osteoarthritis is knee and a recent literature search revealed that more than 10% males and more than 13% females are suffering from this joint degenerative disease.[3]

Various treatment modalities had been proposed over 50 years of knee research. Non-pharmacological techniques comprised of weight loss, patient education, and regular exercise are recommended in treatment guidelines. The combined role of non-pharmacological and pharmacological (aspirin, acetoaminophen, NSAIDS, etc.) techniques has shown to be most convincing.[4-7] However, the pharmacological drugs are having side effects and exposing the major systems of the body to dreadful conditions.

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Intra-articular steroids have been also practiced since a long time, but extensive Medline/Cochrane search revealed a very little convincing result regarding the proper choice of drug. Intra-articular steroids are a good alternative for the patients with Osteoarthritis. These agents have a better and safer profile as compared to oral drugs in terms of adverse effects/contraindications of the later. Moreover, Intra-articular steroids impart a better pain relief by delivering and also delays any surgical intervention thereby improving the patient's quality of life.[8]

Corticosteroids are the most extensive used over the years by many researchers for intra-articular injection. Data regarding the comparison between hyaluronic acid with corticosteroids has revealed that the intra-articular administration of the former drug causes better and long term pain relief in the patients with knee osteoarthritis.[9-16] However, the recent studies and the meta-analysis comparing the efficacy of hyaluronic acid in knee osteoarthritis showed that there was no significant differences observed among the use of intra-articular corticosteroid/hyaluronic acid receiving patients even at 3 or 6 months follow-up.[16]

The above controversial role of corticosteroids advocates more extensive research regarding its use in osteoarthritis. Based on this, we organized a study to compare the efficacy in pain relief of two steroidal agents (Methylprednisolone and Triamcinolone) administered by intra-articular route in patients of knee osteoarthritis.

MATERIALS AND METHODS

We conducted a randomized, double-blind comparative study in the Department of Orthopedics, TMMCRC, Moradabad, India, during July-December 2014.

The American College of Rheumatology graded Osteoarthritis, knee patients with the age of 30-65 years, having joint pain, pain score of more than 40 mm on 100 mm Visual Analog Scale (VAS), bony crepitus, joint swelling, radiological grading of 3/4 on Kellgren Lawrence Scale and joint damage were included in the study. We excluded the pregnant patients, drug using patients (aspirin, paracetamol, opioids, and non-steroidal anti-inflammatory drugs), patients with secondary osteoarthritis, any chronic renal/liver disease.

We enrolled 60 patients and they were randomized using computer-generated randomization. And they were divided into two groups: Group I (30 patients) - Inj. Methylprednisolone 80 mg/ml and Group II (30 patients) - Inj. Triamcinolone 40 mg/ml.

They were instructed to visit regularly to the out-patient department of our institute every 15 days for the next 12 weeks. In the 3 months period, patients were evaluated (symptoms and physical examination) for every 4 weeks and asked to fill up the VAS Scale, Western Ontario MacMaster (WOMAC) and Knee Society Score (KSS). After completing the questionnaire, the individual scores were added and finally total score was determined. Moreover, we also examined the presence or absence of osteoarthritis problems (joint swelling, crepitation, and tenderness).

Statistical Analysis

All the parametric data were analyzed using Student's *t*-test and non-parametric data were using Chi-Square/Fisher test whichever is applicable. Data were analyzed using statistical package for social sciences (SPSS) version 19.0. A $P < 0.05$ was considered as statistically significant.

RESULTS

We enrolled 60 patients in our study, but 4 of them refused to be a part of the study as they could not turn out for the routine follow-ups. So, the study was conducted on 56 patients (28 patients in each group). The demographic characteristics were observed to be comparable ($P > 0.05$) between the groups (Table 1).

On observing the 100 mm VAS score while walking 20 m, the patients were found to be comparable on baseline parameters in both the groups (Table 2). There was no statistical difference in Group I (7.56 ± 1.09) and Group II (7.12 ± 1.34) on observing the VAS score for 4 weeks after drug administration ($P = 0.17$). However, a statistical difference was found during inter-group comparison of

Table 1: Demographic characteristics (mean±SD)

Variables	Group I (*n*=28)	Group II (*n*=28)	*P* value
Age (years)	58.78±7.63	59.92±6.21	0.52
Sex (M:F)	12:18	9:21	0.27
Weight (kg)	66.47±8.35	68.26±7.93	0.39
Height (m)	1.58±0.09	1.60±0.07	0.34

SD: Standard deviation

Table 2: Baseline assessment scores using VAS, WOMAC and KSS score (mean±SD)

Variables	Group I (*n*=28)	Group II (*n*=28)	*P* value
100 mm VAS score	8.78±1.31	8.27±0.98	0.09
WOMAC pain score	32.86±7.56	35.57±6.35	0.13
WOMAC stiffness score	10.79±2.42	11.65±3.07	0.24
WOMAC function score	102.46±8.41	105.32±10.52	0.25
WOMAC total score	147.32±17.83	150.69±19.33	0.49
KSS score	37.79±10.62	39.76±8.71	0.43

VAS: Visual Analog Scale, WOMAC: Western Ontario MacMaster, KSS: Knee Society Score, SD: Standard deviation

VAS scores after the 8-week duration of intra-articular injection ($P = 0.01$) (Table 3). Again after 12 weeks, Group I (4.47 ± 1.16) and Group II (4.98 ± 1.23) had comparable results of VAS scores ($P = 0.11$) (Table 3, Graph 1).

WOMAC score comprises of three subgroups: pain, stiffness, and function. The individual subgroup WOMAC score and the total WOMAC score was found to be comparable in the patients received Methylprednisolone or Triamcinolone (Table 2). At 4-weeks of duration after intra-articular Methylprednisolone injection, the patients had the total WOMAC score of 130.67 ± 20.95 while those patients who received Triamcinolone had a WOMAC score of 139. 41 ± 22.74 ($P = 0.12$) (Table 4, Graph 2). However, a statistically significant difference was observed between Group I (96.23 ± 27.59) and Group II (123.31 ± 25.56) after 8 weeks of intra-articular injection ($P = 0.001$) (Table 4). On inter-group total WOMAC score analysis after 12 weeks of intra-articular steroids, the results were observed to be comparable ($P = 0.52$) (Table 4).

On observing KSS score, there was no statistical difference between the inter-group baseline/after 4-week parameters (Table 5). However, on observing the KSS score at 8-week duration; Group I (59.25 ± 8.72) and Group II (53.34 ± 8.90) revealed a statistically significant difference among them ($P = 0.01$) (Table 5, Graph 3). Similarly, the statistical significant data were obtained from Group I (80.54 ± 8.27) and Group II (57.76 ± 10.38) after 12 weeks of intra-articular steroid injection ($P = 0.001$) (Table 5).

Table 3: VAS score after 20 m walk (mean±SD)

Week	Group I (*n*=28)	Group II (*n*=28)	*P* value
0	8.78±1.31	8.27±0.98	0.09
4	7.56±1.09	7.12±1.34	0.17
8	5.61±1.12	6.30±1.03	0.01*
12	4.47±1.16	4.98±1.23	0.11

*$P<0.05$. VAS: Visual Analog Scale, SD: Standard deviation

Table 4: Total WOMAC score (mean±SD)

Week	Group I (*n*=28)	Group II (*n*=28)	*P* value
0	147.32±17.83	150.69±19.33	0.49
4	130.67±20.95	139.41±22.74	0.12
8	96.23±27.59	123.31±25.56	0.001*
12	80.45±23.38	84.19±21.78	0.52

*$P<0.05$. SD: Standard deviation, WOMAC: Western Ontario MacMaster

Table 5: KSS (mean±SD)

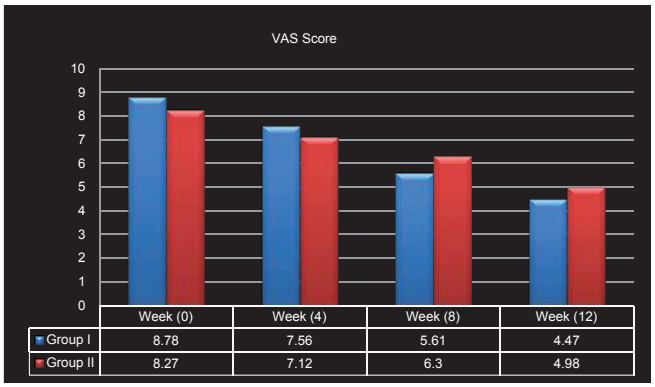
Week	Group I (*n*=28)	Group II (*n*=28)	*P* value
0	37.79±10.62	39.76±8.71	0.43
4	44.47±11.34	45.53±9.86	0.70
8	59.25±8.72	53.34±8.90	0.01*
12	80.54±8.27	57.76±10.38	0.001*

*$P<0.05$. SD: Standard deviation, KSS: Knee Society Score

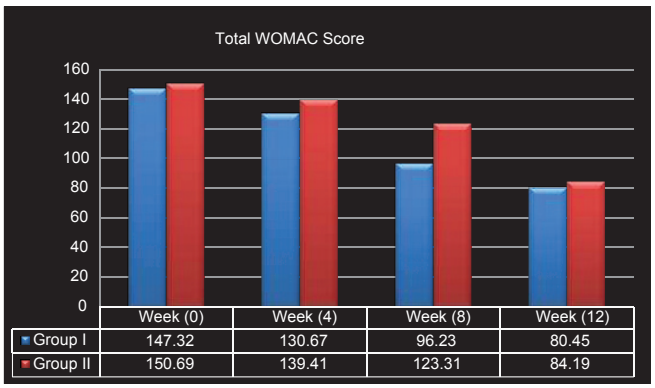
None of the patients reported any adverse events during the study.

DISCUSSION

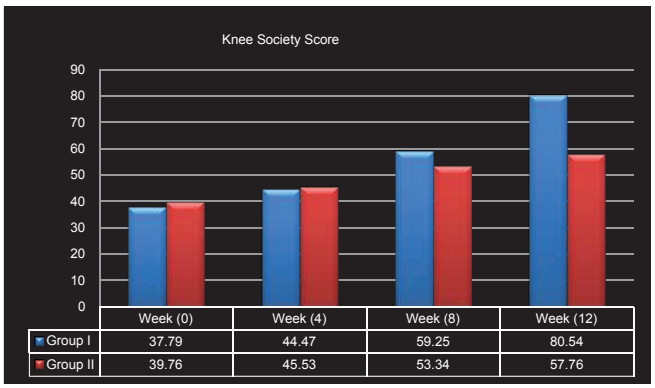
Intra-articular steroids have been extensively used by the doctors for more than five decades. A study conducted by Dieppe *et al.*[17] observed that patients were more satisfied who received corticosteroids as an intra-articular injection in osteoarthritis, compared to placebo receiving group. However, this study was supported by other researchers who similarly observed a short-term beneficial



Graph 1: Visual Analog Scale score



Graph 2: Total Western Ontario MacMaster score



Graph 3: Knee Society Score

effect of corticosteroids in patients with knee and hip osteoarthritis.[18-20] In a study done by Valtonen[21] using multiple injections of Triamcinolone, beneficial effects was observed in knee osteoarthritis patients. Based on these findings, we organized this double-blind study to evaluate the analgesic efficacy of Triamcinolone and Methylprednisolone for knee osteoarthritic patients.

In our study, we observed the VAS score by asking the patients to walk for 20 m. We observed no statistical difference between Methylprednisolone and Triamcinolone receiving patients after 4 weeks of intra-articular injection. However, the significant statistical difference was found during inter-group comparison of VAS scores after the 8-week duration of intra-articular injection ($P = 0.01$). Our findings suggest that both intra-articular steroid injection have beneficial efficacy for analgesia, but Methylprednisolone has been proven have a better analgesic profile in patients with knee osteoarthritis. Our findings are supported by Pyne *et al.*[22] who also compared the analgesic effects of Triamcinolone and Methylprednisolone and concluded that there was no significant difference between the drugs at the 3rd and 8th week of follow-up. Similar findings were observed by Gaffney *et al.*[23] and Bellamy *et al.*[24] who also demonstrated the significant reduction in pain by intra-articular corticosteroids. A similar study done by Shikhar *et al.*[25] observed a statistically significant effect on VAS scores after 4 weeks on comparing between intra-articular Methylprednisolone and Triamcinolone.

In our study, we observed that the total WOMAC score which is explained under three heads: pain, stiffness, and function. We observed the statistical significant difference between Methylprednisolone and Triamcinolone study groups after 8 weeks of intra-articular injection ($P = 0.001$). Our finding was further supported by Shikhar *et al.*[25] who also observed the statistical significant difference between intra-articular Triamcinolone and Methylprednisolone receiving patients. However, the total WOMAC score at 12 weeks follow-up was comparable between the groups in our study which is contradictory to the study performed by Shikhar *et al.*[25] Smith *et al.*[26] observed an improvement in all the WOMAC subgroup scores in patients given intra-articular Methylprednisolone. Raynauld *et al.*[27] performed a study for evaluating the safety and analgesic efficacy of Triamcinolone in patients suffering from knee osteoarthritis using WOMAC scale. They observed significant improvement in the osteoarthritic knee stiffness and pain in patients given intra-articular steroid. The above findings advocate that intra-articular steroid causes a reduction in knee pain particularly if patients were given Methylprednisolone as this agent proves to provide early onset and prolong the duration of analgesia.

The uniqueness of our study is that we have compared two most used routinely steroidal agents for intra-articular injection. Most of the researchers had compared an intra-articular steroid with a placebo.

Although, lot of patients visit for knee pain in our hospital but despite that we managed only 56 patients for our study. A lot of people refused to be a part of the study because of their busy schedule and appointments. However, we followed a strict protocol for proper inclusion and exclusion of the patients for our study. To decrease the number of drop outs and to improve the compliance we enrolled the candidates who are within a 10 km radius from our hospital, even after all these efforts our four patients did not revert back to the hospital.

During our study course, no adverse events except for local irritation which subsided on its own were observed. The patients responded well with local steroid intra-articular injections.

This study has a limitation that we could have prolonged our study time frame of follow-up to even 6 or 12 months. But due to busy schedule of the patients we could not apply it in our study, otherwise most of the patients would have refused to be a part of the study.

CONCLUSION

From our study, we conclude that the use of intra-articular corticosteroids (Methylprednisolone and Triamcinolone) possess a safer profile and are also proven to be beneficial in providing short/long-term analgesia from osteoarthritis knee. Moreover, the use of Methylprednisolone provides more immediate and prolonged improvement in pain, stiffness, and improves joint function.

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Original Article

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Serum Cotinine Concentration and Serum Lipid Profile: Risk for Cardiovascular Disease in Smokeless Tobacco Users

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Abstract

Background: The objective of the study is to find out the effect of long time oral nicotine consumption on serum lipid profile in exclusive smokeless tobacco consumers and compare the findings with healthy tobacco non-users.

Materials and Methods: This case-control study was performed in 100 subjects in which 50 were exclusively smokeless tobacco consumers (cases) and 50 were age and sex matched tobacco non-users (controls). Age group was 30-50 years, Individuals if found to be a smoker, have any associated co-morbid illness or taking regular medication including vitamin/mineral supplements/herbal/native medicines were excluded. Enzymatic methods were used to estimate serum lipid parameters including total cholesterol level, high-density lipid (HDL) cholesterol level and triglycerides (TGL) level using commercial kits. Low-density lipid (LDL) cholesterol level was then calculated. Serum cotinine (CTN) level was estimated using enzyme linked immunosorbent assay kit.

Results: In the present study, mean serum CTN level was found to be raised in smokeless tobacco users as compared to non-users. Also, the lipid parameters were also deranged in cases as compare to control group. A significant association between raised mean serum CTN levels and raised cholesterol, low HDL, raised LDL, TGL, and LDL/HDL ratios was observed ($P < 0.001$) in cases. A strong positive correlation was observed between serum CTN level and deranged lipid profile.

Conclusion: Thus, the present study shows that people who are smokeless tobacco users for the long duration have accumulated more nicotine metabolites as compared to tobacco non-user subjects. Long-term use of smokeless tobacco results deranged lipid profile which is an independent marker for cardiovascular disease.

Key words: Cotinine, Enzyme-linked immunosorbent assay, High-density lipid, Low-density lipid, Smokeless tobacco

INTRODUCTION

Tobacco addiction is a major health concern in our country. The most recognized health risk associated with any tobacco product is the carcinogenic side-effect. However, tobacco has other deleterious effects including its adverse effect on lipid profile.[1,2]

Nicotine is the major addicting substance in tobacco and is thought to be responsible for most of the adverse effects associated with its use. Smokeless tobacco extract has been shown to increase oxidative stress as a result of reactive oxygen free radicals. Overall increased oxidative stress may promote lipid peroxidation and increased deposition in vessel wall. This can lead to atherosclerosis in future.[3,4]

Nicotine is the major addicting substance in tobacco is metabolized in the liver by cytochrome P450 enzymes (mostly cytochrome P450 Type 2A6, and also by Type 2B6). A major metabolite is cotinine (CTN), concentration of which can be measured in urine and serum.[5] Since half-life of CTN is more than nicotine, the level of CTN is used to assess the tobacco exposure.

Because of the pharmacological properties of nicotine and other constituents of smokeless tobacco there is concern that smokeless tobacco products may lead to

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cardiovascular disease or death from cardiovascular causes.[6] In short, nicotine modifies cell structure in a way that facilitates migration and invasion of cells that line the blood vessels. This enables a change in structures called podosomes, which lead to poor vessels and can cause the formation of plaque. Over time, plaque can cause arteries to harden, a form of heart disease called atherosclerosis. It can also block blood flow to the heart or brain, keeping oxygen from reaching those organs and causing heart attack or stroke.[7]

As per global adult tobacco survey India Report, Khaini is the most common smokeless tobacco product in use in India, and also the most common smokeless tobacco in use by men. This is followed by gutkha. The use of smokeless tobacco in India is peculiar as there are large no. of smokeless tobacco products in use e.g. paan with tobacco, paan masala with tobacco, Gul, Mawa, Mishri, Bajjar, Gudakhu etc.

In view of all these facts, this study is designed to assess the effect of smokeless tobacco (mainly gutkha) on lipid profile.

MATERIALS AND METHODS

A case-control study was designed. Ethical clearance was taken from Institutional Ethics Committee before the start of the research. An informed consent was taken from each subject on prescribed consent form obtained from research cell. A total of 100 subjects age group of 30-50 years, were included in the study of which 50 smokeless tobacco consumers (cases) and 50 age and sex matched tobacco non-users (controls) were enrolled. Individuals if found to have any associated co-morbid illness or taking regular medication including vitamin/mineral supplements/herbal/native medicines, was excluded.

Inclusion Criteria

1. Subjects of 30-50 years of age having history of tobacco chewing and gutkha eating (only smokeless tobacco)
2. Control group was comprised of age and sex matched subjects who did not use tobacco in any form.

Exclusion Criteria

1. Age <30 and >50 years
2. Smokers (cigarettes, beedi, hookah etc.)
3. Smokeless tobacco chewers but smokers too
4. Chronic systemic disease
5. Diabetes mellitus
6. Obese persons (World Health Organization Criteria: Body mass index)
7. Family history of hypertension and diabetes mellitus
8. Pregnancy
9. Oral carcinoma.

A working proforma (case sheet) was filled for every subject. It included demographic data (particulars of a subject such as a name, age, sex, address, contact number), past history, and family history of chronic illness. Further addiction history was taken which included type, amount, and duration of consumption of smokeless tobacco.

Blood Sample Collection

After overnight fasting, 5 ml of blood samples were collected in a syringe from all the subjects in the morning. Serum was separated by centrifugation at 3000 rotation per minute.

Biochemical Investigation

Lipid profile

Lipid profile was done the same day in the molecular lab by autoanalyzer.

A total of 6 parameters *viz*. total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglyceride (TGL), very LDL (VLDL) and LDL/HDL ratio were assessed. The criteria for determination of derangement was shown in Table 1.[8]

Serum CTN Level

Exposure to tobacco can be detected by measuring nicotine and its metabolites. Nicotine has a short half-life and is not used as a marker for tobacco exposure. CTN due to its longer half-life has been used in research as a reliable marker of tobacco exposure.

Serum CTN levels were measured by CTN enzyme-linked immunosorbent assay (ELISA) kit (Blue Gene Biotech), catalogue number E01C0050.

Principle of the Assay

CTN ELISA kit applies the competitive enzyme immunoassay technique utilizing a monoclonal anti-CTN antibody and a CTN-high reactive protein (CTN-HRP) conjugate. The assay sample and buffer are incubated together with CTN-HRP conjugate in the pre-coated plate for the one hour. After the incubation period, the wells are decanted and washed five times. The wells are then incubated with a substrate for HRP enzyme. The product of the enzyme-substrate reaction forms a blue colored complex. Finally, a stop solution is added to stop the reaction, which will then turn the solution yellow. The intensity of the color is measured spectrophotometrically at 450 nm in a microplate reader. The intensity of the color is inversely proportional to the CTN concentration since CTN from samples and CTN-HRP conjugate compete for the anti-CTN antibody binding site. Since, the number of sites is limited, as more

sites are occupied by CTN from the sample, fewer sites are left to bind CTN-HRP conjugate. A standard curve is plotted relating the intensity of the color (optical density) to the concentration of standards. The CTN concentration in each sample is interpolated from this standard curve. In a non-smoker mean serum CTN concentration is <12 ng/ml. Higher value is expected in passive smokers. The statistical analysis was done using Statistical Package for Social Sciences Version 15.0 statistical Analysis Software.

OBSERVATIONS AND RESULTS

The present study was carried out with an aim to find out the association of serum CTN level with lipid profile in smokeless tobacco users. Comparison of two groups for mean value of lipid parameters has been shown in Table 2 (Group 1-cases, Group 2-controls).

None of the subjects in Group II had total cholesterol and serum TGL levels >200 mg/dl and >150 mg/dl respectively as against 56% and 58% of subjects in Group I, thus showing a significant difference between two groups ($P < 0.001$). Proportion of subjects with low HDL was significantly higher ($P < 0.001$) in Group I (72%) as compared to that in Group II (26.0%). A total of 49 (98%) subjects in Group I and 7 (14.0%) in Group II had serum LDL levels >100 mg/dl, thus showing a significant difference between two groups and a total of 40 (80%) of Group I and 2 (4.0%) of Group II subjects had LDL/HDL ratio >3. For all the lipid parameters, the differences between two groups were significant statistically ($P < 0.001$) (Table 3).

Serum CTN levels ranged from 56.9 to 210.5 ng/ml in Group I and from 23.1 to 68.7 ng/ml in Group II. Mean serum CTN level in Group I was 146.89 ± 33.21 ng/ml and 38.66 ± 10.66 ng/ml in Group II. On comparing the data statistically, the differences between two groups were found to be significant statistically ($P < 0.001$). (Table 4).

A significant association between raised mean serum CTN levels and raised cholesterol, low HDL, raised LDL, TGL, and LDL/HDL ratios was observed ($P < 0.001$) (Table 5).

Table 1: Criteria for determination of deranged lipid profile values[8]

Parameter	Derangement criteria
Total cholesterol (mg/dl)	>200
HDL (mg/dl)	<40
LDL (mg/dl)	>130
VLDL (mg/dl)	>30
TGL (mg/dl)	>150
LDL/HDL	>3.5

Source: National cholesterol education program-Adult treatment panel-III, LDL: Low-density lipid, HDL: High-density lipid, VLDL: Very low-density lipid, TGL: Triglyceride

Table 2: Comparison of lipid parameters in two groups

Lipid parameters	*n*=50				Significance of difference	
	Group I		Group II			
	Mean	SD	Mean	SD	*t*	*P*
Total cholesterol	200.88	15.63	148.12	16.22	16.642	<0.001
HDL	39.44	2.29	50.50	8.09	9.315	<0.001
LDL	131.07	13.66	75.90	19.96	16.182	<0.001
Triglycerides	151.91	11.63	108.64	16.12	15.443	<0.001
VLDL	30.38	2.33	21.73	3.22	15.443	<0.001
LDL/HDL ratio	3.33	0.38	1.59	0.64	16.691	<0.001

For all the parameters except HDL, mean value in Group I was significantly higher as compared to that in Group II (*P*<0.001), LDL: Low-density lipid, HDL: High-density lipid, VLDL: Very low-density lipid, TGL: Triglyceride

Table 3: Comparison of derangement of lipid parameters in two groups

Lipid parameters	*n*=50				Significance of difference	
	Group I		Group II			
	No.	%	No.	%	"χ^2"	*P*
Total cholesterol >200 mg/dl	28	56.0	0	0	38.889	<0.001
HDL (<40 mg/dl in males, <50 mg/dl in females)	36	72.0	13	26.0	21.168	<0.001
LDL>100 mg/dl	49	98.0	7	14.0	71.591	<0.001
TGL>150 mg/dl	29	58.0	0	0	41.494	<0.001
LDL/HDL ratio>3	40	80.0	2	4.0	59.78	<0.001

LDL: Low-density lipid, HDL: High-density lipid, VLDL: Very low-density lipid, TGL: Triglyceride

Table 4: Comparison of serum cotinine levels (ng/ml) between two groups

Variable	Group I (*n*=50)	Group II (*n*=50)
Minimum	56.9	23.1
Maximum	210.5	68.7
Mean	146.89	38.66
SD	33.21	10.66

t=22.14, *P*<0.001, SD: Standard deviation

Table 5: Association of serum cotinine levels with different lipid parameters (overall) (*n*=100)

Variable	No. of cases	Mean serum cotinine	SD	Significance of association
Total cholesterol				
Normal	72	73.16	56.23	*t*=6.046; *P*<0.001
Deranged	28	141.99	34.41	
HDL				
Normal	51	67.54	53.50	*t*=4.725; *P*<0.001
Deranged	49	118.46	54.79	
LDL				
Normal	44	40.41	21.27	*t*=12.534; *P*<0.001
Deranged	56	133.90	46.22	
Triglyceride				
Normal	71	69.94	53.57	*t*=7.313; *P*<0.001
Deranged	29	147.60	31.10	
LDL/HDL ratio				
Normal	58	59.02	48.67	*t*=8.829; *P*<0.001
Deranged	42	138.91	38.73	

HDL: High-density lipid, LDL: Low-density lipid, SD: Standard deviation

DISCUSSION

Effect of smokeless tobacco use on serum CTN levels and its association with cardiovascular risk factors were analyzed.

The 100 subjects were enrolled in the study of which 50 subjects were exclusive smokeless tobacco users (study group), and remaining 50 subjects were age and sex matched controls (non-tobacco users).

Statistically, no significant difference was found between the two groups for any demographic characteristic.

Smokeless tobacco (gutkha) remains in contact of buccal mucosa for a longer duration, and a large amount of nicotine is absorbed into the blood stream. Nicotine then binds to acetylcholine receptors present on endothelial cells; it is metabolized in the liver by cytochrome P450 enzymes. A major metabolite is CTN which has a much longer half-life than nicotine, the reason for it being used as a biochemical marker of average daily intake of nicotine.

In the present study, a high mean serum CTN level was found in cases (146.89 ± 33.21 ng/ml) as compared to controls (38.66 ± 10.66 ng/ml) (Figure 1).

Longer duration of ST exposure resulted in high level of serum CTN levels. CTN is found in blood, serum, urine, and saliva. It is accumulated in hair, brain, and probably other parts of body.[3]

In the control group mean serum CTN level was 38.66 ± 10.66 ng/ml. Maximum level was 68.7 ng/ml, and minimum level was 23.1 ng/ml. Since our controls were not using tobacco in any form, it is assumed that the level above the expected value was due to passive exposure of tobacco smoke.

In the present study, raised mean serum CTN level was found to be significantly associated with many parameters of dyslipidemia.

Dyslipidemia in ST users has been reported by many past studies like Khurana *et al.*[9] and Gupta *et al.*[10] On contrary, in some other studies of healthy baseball players and firemen, smokeless tobacco users demonstrated no significant differences in total cholesterol levels, LDL and HDL levels compared with non-users.[5,11]

In the present study, the control group had lower total cholesterol (mean 148.12 ± 16.22 mg/dl) than cases (mean 200.88 ± 15.63 mg/dl) and this difference was statistically significant ($P < 0.001$). Tucker[12] found higher cholesterol level in ST users (>240 mg/dl).

The HDL cholesterol level in the control group was higher (mean 50.50 ± 8.09 mg/dl) than those in study group (mean 39.44 ± 2.29 mg/dl) and the difference was statistically significant ($P < 0.001$). Khurana *et al.*[9] also found similar HDL level in ST users (38 mg/dl) (Figure 2 and 3).

The LDL cholesterol in the study group was higher (mean 131.07 ± 113.66 mg/dl) as compared to control group (mean 75.90 ± 19.96 mg/dl) and the difference was statistically significant ($P < 0.001$).

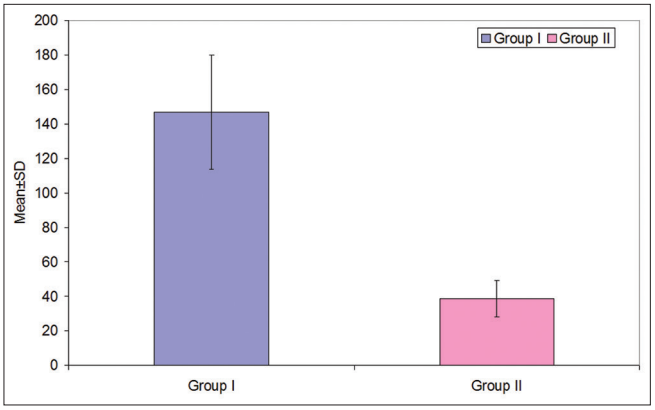

Figure 1: Comparison of serum cotinine levels (ng/ml) between two groups

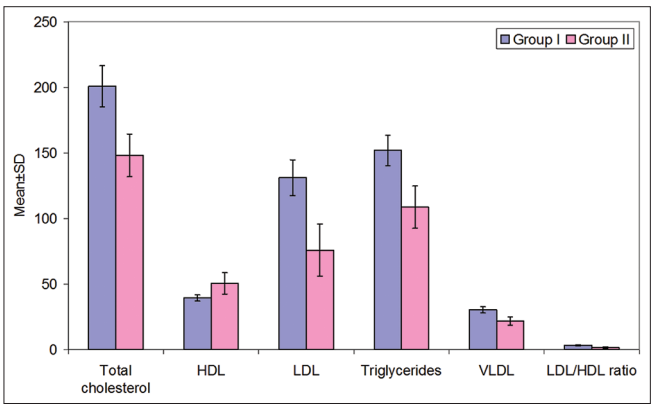

Figure 2: Comparison of lipid parameters in two groups

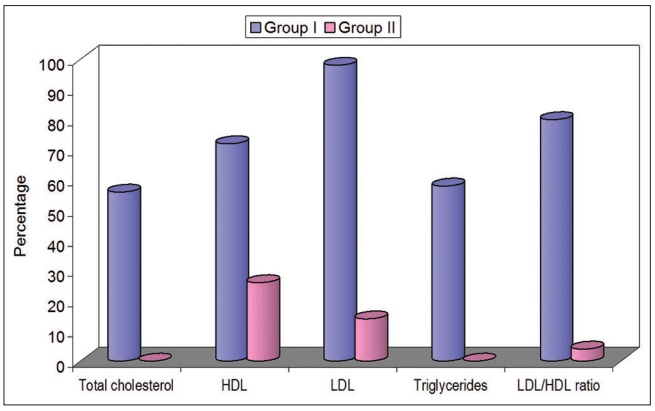

Figure 3: Comparison of derangement of lipid parameters in two groups

TG levels in the study group were also higher (mean 151.91 ± 11.63 mg/dl) than levels in control group (mean 108.64 ± 16.12 mg/dl) and the difference was statistically significant ($P < 0.001$). Similar TGL levels were obtained by Khurana *et al*.[9] They found TGL level of 160 mg/dl in ST users and 96 mg/dl in controls.

Similarly, VLDL levels were also higher in the study group (mean 30.38 ± 2.33 mg/dl) as compared to control group (mean 21.73 ± 3.22 mg/dl) and difference was statistically significant ($P < 0.001$).

LDL/HDL ratio also follows the above trend and shows higher value in study group (mean 3.33 ± 0.38) than in controls (mean 1.59 ± 0.64) and the difference was statistically significant ($P < 0.001$).

In ST users and non-users the deranged lipid profile were significantly associated with high mean serum CTN level. Hence, long-term consumption of ST probably results in deranged lipid profile.

Above findings could be explained by the fact that nicotine after absorption binds to acetylcholine receptors on the endothelial cell surface where it promotes atherogenesis thrombotic and vascular occlusion by promoting formation of plaque in vessel wall. It causes direct injury to endothelial cells which act as a nidus for plaque formation. Nicotine also affects lipid peroxidation which results in dyslipidemia.[13]

These sympathoadrenergic and hemostatic mechanisms affect vascular system most importantly coronary system and could lead to stroke.[14]

A significant association was observed between serum CTN levels with duration of its use and not with daily consumed amount. Hence, duration of use of tobacco seems to be a better predictor of risk outcome than the amount of tobacco consumed.

LDL/HDL ratio shows a higher mean value in gutkha consumers as compared to non-consumers - an independent risk factor for cardiovascular diseases.

Therefore, consumption of gutkha on a long-term basis imposes a serious threat to overall health precisely to cardiovascular health.

CONCLUSION

High serum CTN level in smokeless tobacco consumers probably results in deranged lipid profile which is an independent marker for cardiovascular disease. Intense education program about adverse health events of smokeless tobacco should be under taken through all means including audio-visual media to the public and to students through their curriculum. Hence, national policy makers must be enlightened by the findings and efforts to curb the use of smokeless tobacco by the society must be their priority.

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Original Article

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Correlation of CD4 Count and Severity of Dry Eye in Human Immunodeficiency Virus Positive Patients

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Abstract

Introduction: Ocular lesions occur in 70% of patients with human immunodeficiency virus (HIV)/AIDS. More than 50% of HIV infected patients have anterior segment manifestations. Keratoconjunctivitis sicca has been reported as one of the most common anterior segment manifestations in these patients.

Purpose: To evaluate the dry eye status in HIV-positive patients and correlate it with CD4 count.

Materials and Methods: Sample size: A total of 50 patients (100 eyes), patients attending the outpatient and inpatient department, Department of Ophthalmology, and the ART center at a tertiary care center diagnosed with HIV who fulfill the inclusion and exclusion criteria were selected randomly. All patients were investigated for dry eye with Schirmer's test (significant if <10 mm), tear film break up time (significant if <10 s), and slit lamp examination with Rose Bengal stain.

Results: Relative frequency of eyes with significantly decreased aqueous tear production (<10 mm Schirmer's test) 53.0%, decreased lipid layer (<10 s TBUT) 20%, decreased mucin layer (positive Rose Bengal) 20% in 100 eyes.

Conclusion: The aqueous tear production is affected in our study group, but increased frequency of decreased tear production is not associated with the level of CD4+ count.

Key words: CD4 lymphocyte count, Dry eye syndromes, Human immunodeficiency virus

INTRODUCTION

Dry eye is a clinical condition characterized by deficient tear production or excessive tear evaporation. It causes ocular irritation resulting from an alteration of the tear film. The effects can vary from minor inconvenience for most sufferers to rare sight-threatening complications in severe cases.[1]

The common feature of all dry eye syndromes is tear film instability, a result of disease or dysfunction of one or more component of lacrimal functional unit. Some of the many factors involved in the causation of dry eye include age, hormonal deficiencies, medications, surgery, and systemic autoimmune disease. All these can cause dysfunction of the lacrimal functional unit that is associated with ocular surface inflammation and eventually the signs and symptoms of dry eye. The symptoms that the patient complains of are heaviness of the lids, foreign body sensation, burning, stinging, itching, photophobia, dryness, soreness, and ocular fatigue.[2]

Human immunodeficiency virus (HIV) is a global pandemic causing morbidity and mortality at the rate of millions. India has the world's third-largest population suffering from HIV/AIDS. The NACO 2012-2013 annual report stated that in 2011, 20.9 lakh people are living with HIV/AIDS in India and about 1.16 lakh new cases of HIV infection are detected annually.[3]

Ocular manifestations of HIV infection typically occur late in the course of disease when there occurs profound

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CD4+ T-lymphocyte depletion (<200 cells/mm^3), or the development of opportunistic infections or unusual neoplasms. Anterior segment is affected in up to 20% of the ocular complications associated with HIV infection, and yet remain unrecognized or undertreated in many patients. Keratoconjunctivitis sicca or dry eye occurs in later stages of the disease in 10-20% of the patients. An abnormal Rose Bengal staining and Schirmer's test is invariably detected in these patients. The cause of dry eye in HIV patients is complex. Combined effects of HIV-mediated inflammation and destruction of the lacrimal and salivary glands and direct HIV infection of the conjunctiva is the proposed mechanism.[4]

Dry eye by itself may be of a small consideration in view of the other more serious sequelae of HIV infection. However, when considering the importance of tear film in maintaining the ocular surface integrity, it becomes apparent that treatment of dry eye is important to prevent the sight-threatening complications such as secondary corneal ulcers or infections. Dry eye In HIV-positive patients can be managed by the usual methods of tear substitutes.[5]

With the increasing global burden of HIV, there is an increasing need to identify, treat and hence reduce the cause of morbidity and mortality. The causes of ocular morbidity are well documented in ophthalmic literature. Several studies have been done on the various ocular manifestations of HIV and their correlation with the level of CD4 count.[6,7]

According to the literature, dry eye is the most common anterior segment manifestation of HIV infection. But, no study has been done to correlate the severity of dry eye with the CD4 count.[8,9]

The present study has endeavored to correlate the level of CD4 count with the severity of dry eye in HIV seropositive patients.

MATERIALS AND METHODS

This explorative study was conducted at the Department of Ophthalmology, KR Hospital, Mysore between January 2014 and June 2014.

This study included 50 patients (100 eyes) who were diagnosed with HIV infection in the ART center at K.R Hospital, Mysore irrespective of whether they were on ART or not at the time of our evaluation. Data was collected using a piloted proforma meeting the objectives of the study after an informed consent. A detailed history of each patient was obtained regarding the age, gender, address, occupation, duration of the disease, duration since start of ART, history of any other illness. All patients were investigated for dry eye with Schirmer's test, Tear film break up time and slit lamp examination with Rose Bengal stain. Patients with history of certain systemic illnesses such as primary Sjogrens's syndrome, autoimmune diseases like rheumatoid arthritis and systemic lupus erythematosus, sarcoidosis, neuroparalytic keratitis, anterior and posterior blepharitis and contact lens wearers were excluded from the study as these could independently cause dry eye.[1]

Schirmer's test was performed using Schirmer's strips (5 mm × 35 mm filter paper), which was placed in the inferior fornix at the junction of medial two-third and lateral one-third of the lid. The amount of wetting of the strip was noted. It was considered to be negative if the value was >10 mm, mild dry eye between 5 and 10 mm and severe when <5 mm. Tear film break up time was assessed by staining the eye with 2% fluorescein strips and the eye was examined under cobalt blue filter with the slit lamp. The time taken for the first random dark spot to appear was noted and considered positive when <10 s. Rose Bengal stains healthy epithelial cells if a normal amount of mucin does not overlie the cell surface. Hence, in patients with dry eye Rose Bengal stains the conjunctiva and/or cornea.[1,10]

Statistics

Chi-square test and contingency coefficient analysis were used for statistical analysis of the data collected.

RESULTS

The Schirmer's Test was significantly less in 53% of all patients. However, in patients with CD4 count of 101-500 cells/mm^3 it was <10 mm in 25 out of 44 eyes (56.82 %). In patients with 0-100 cells/mm^3 and >500 cells/mm^3 20 out of 34 eyes (58.81%) and 8 out of 22 (36.36%) eyes had dry eye. This however was not found to be statistically significant (P = 0.2) (Table 1 and Figure 1).

Tear film break up time <10 s only in 20% of all eyes. In patients with CD4 count of 101-500 cells/mm^3 the tear film break up time was <10 s only in 12 eyes (27.27%). In patients with 0-100 cells/mm^3 and >500 cells/mm^3 only 20.59% and 4.5% of the eyes had dry eye. This was not found to be statistically significant (P = 0.09) (Table 2 and Figure 2).

In Rose Bengal test in the count of 0-100 cells/mm^3, only 7 eyes were positive for Rose Bengal staining which constitutes 20.59% and in 101-500 cells/mm^3 only 29.55% eyes were positive. But, with count of >500 cells/mm^3 100% were negative (P = 0.018) (Table 3).

Table 1: Results of Schirmer's test

CD4 count (cells/mm^3)	Schirmer's strip wetting			Total
	<5 mm	5-10 mm	>10 mm	
0-100				
Count (%)	4 (11.77)	16 (47.07)	14 (41.19)	34 (100)
101-500				
Count (%)	7 (15.90)	18 (40.90)	19 (43.20)	44 (100)
>500				
Count (%)	0 (0.0)	8 (36.36)	14 (63.64)	22 (100)
Total				
Count (%)	11 (11.0)	42 (42.0)	47 (47.0)	100 (100.0)

Table 2: Tear film break up time results

CD4 count (cells/mm^3)	Time		Total
	<10 sec	>10 sec	
0-100			
Count (%)	7 (20.59)	27 (79.41)	34 (100)
101-500			
Count (%)	12 (27.27)	32 (72.73)	44 (100)
>500			
Count (%)	1 (4.5)	21 (95.5)	22 (100)
Total			
Count (%)	20 (20)	80 (80)	100 (100)

Table 3: Results of Rose Bengal stain

CD4 count (cells/mm^3)	Rose Bengal staining		Total
	Negative	Positive	
0-100			
Count (%)	27 (79.41)	7 (20.59)	34 (100)
101-500			
Count (%)	31 (70.45)	13 (29.55)	44 (100)
>500			
Count (%)	22 (100)	0 (0.0)	22 (100)
Total			
Count (%)	80 (80)	20 (20)	100 (100.0)

There was no significant difference in dry eye between those on ART and those who were not on ART.

No significant difference was found between males and females in our study.

DISCUSSION

Ocular lesions occur in 70% of patients with HIV/AIDS[6] and affect almost all the structures of the eye.[11] In addition to the posterior segment lesions such as cytomegalovirus retinitis, the anterior segment, and ocular surface lesions can be vision threatening.[12] More than 50% of HIV infected patients have anterior segment manifestations. Kerato-conjunctivitis sicca has been reported as one of the most common anterior segment manifestations.[13] Various studies conducted on normal population show that the prevalence of dry eye ranges between 10% and 20%.[14,15]

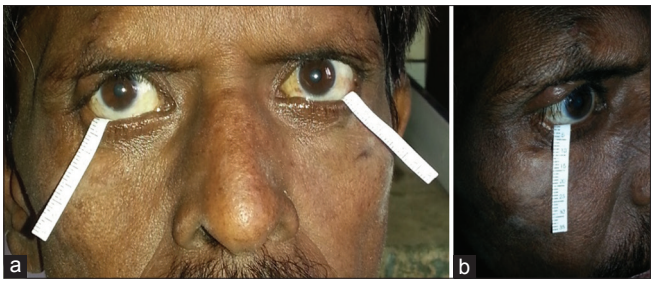

Figure 1: (a and b): Schirmer's test being performed in a patient whose CD4 count was 98 and Scirmer's test was OD - 5 mm, OS - 8 mm at the end of 5 min

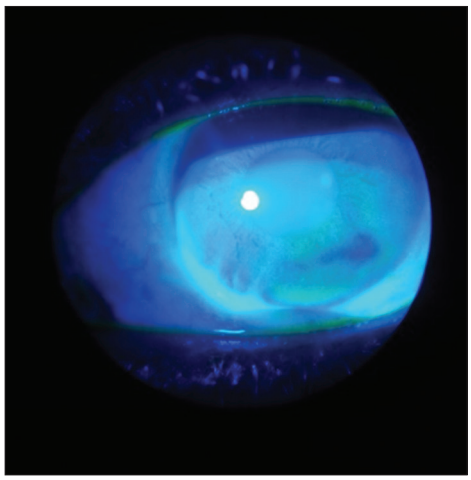

Figure 2: Tear film break up time (7 s) in a patient

The prevalence of dry eye is HIV seropositive patients is found to be higher than in normal population. However, there is a paucity of studies to determine the correlation between CD4 count and dry eye.

The demographic pattern in our study is similar to the Indian statistics, higher prevalence in males (64%) than females (36%) and in the age group of 20-50 years.[3] There was a significant decrease in the aqueous layer of the tear film assessed by Schirmer's test in more than half the eyes examined (53 out of the 100). This however was not statistically significant.

The Schirmer's test was positive 58.8% of eyes in patients with CD4 count of 0-100 cells/mm^3 and significantly lower in count of 101-500 cells/mm^3 (18.16%). This shows that the aqueous layer was deficient in the lower CD4 count. The tear film break up time showed dry eye in 29.1% of eyes (7 out of 34) in patients with CD4 count of 0-100 cells/mm^3, which was slightly higher than in a count of 101-500 cells/mm^3 (27.2%, 12 out of 44) and a lesser prevalence was noted among the higher count (4.5% in patients with >500 cells/mm^3). The Rose Bengal stain test was negative in 100% cases of CD4 count over 500 cells/mm^3, which could indicate that higher CD4 count may have a lesser prevalence of dry eye.

In all the three tests conducted for dry eye, we observe that the higher CD4 count had a lesser prevalence of dry eye than the lower CD4 count. This indicates that as the disease progresses dry eye prevalence increases. Whether the use of ART can halt this or not is inconclusive. The Schirmer's test was positive in 53% of the study population whereas tear film break up time and Rose Bengal staining was positive in 20% each. This signifies that the aqueous layer of the tear film is affected more than lipid and mucin in our study. The lacrimal gland may be affected due to the disease leading to a decrease in its secretion.[16]

Although, the results of the tests are statistically insignificant in our study, the fact that more than half the patients were positive for dry eye cannot be looked down upon. Further studies are needed with higher sample size to evaluate a relationship between CD4 count and dry eye.

The ocular involvement may often precede systemic manifestations in HIV infection,[14] hence the role of an ophthalmologist in the management of HIV-positive patients is becoming increasingly important.[6,12,17]

In a study, Sicca syndrome in patients infected with HIV conducted by Geier *et al.* data show that decreased tear production occurs in approximately 20-25% of patients with HIV infection. This increased frequency of decreased tear production is not associated with the CD4+ count or related to the severity of HIV disease, respectively.[18]

However, our study shows decreased tear production in around 50% patients. Although the association with CD4 count is inconclusive.

The limitations of our study was the small sample size. The role of ART on dry eye was not assessed in our study. But, a subset of literature has shown no such association between dry eye and ART. However, further studies with larger sample size may be needed to overcome these limitations.

CONCLUSION

In all the three tests that we conducted we found that there is decreased tear production. The aqueous tear production as evaluated by Schirmer's test is affected in our study group in 50% of patients. Tear film break up time and Rose Bengal staining is positive in only 20% each. However, increased frequency of decreased tear production is not associated with the level of CD4+ count.

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Original Article

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Role of Intra-operative Cytology in the Diagnosis of Ovarian Neoplasm's

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Abstract

Background: Intraoperative cytology (IOC) has been widely used nowadays for establishing an early diagnosis of ovarian neoplasms. It is a simple, inexpensive and a rapid diagnostic test which can be performed in a short duration of time. We organized a study to compare the diagnostic utility of IOC with the histopathological examination (gold standard technique) in ovarian benign and malignant neoplasms.

Materials and Methods: We conducted a prospective study on 68 suspected ovarian neoplasms and samples were collected using touch, imprint, scrape or crush technique. The samples were fixed by 95% ethyl alcohol and stained with hematoxylin and eosin stain. An experienced cytopathologist diagnosed and interpreted the cytology slides of ovarian neoplasm and correlated the histopathological diagnosis with cytological interpretation. Based on the data the sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were determined.

Results: Among the 68 cases, the standard histopathological diagnosis confirmed 24 as benign, 6 as borderline and 38 as malignant lesions. The diagnostic concordance between cytological and histopathological study was observed in 65 of the 68 cases. We observed a satisfactory diagnostic accuracy of the intraoperative imprint cytology (95.60%) in our study. The sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were 97.7, 91.37, 95.56, 95.65, and 95.60% respectively in our study.

Conclusion: The diagnostic utility of cytological examination for ovarian masses is really appreciable on comparison with the histological diagnosis.

Key words: Cytological diagnosis, Histopathological diagnosis, Ovarian neoplasm

INTRODUCTION

Ovarian tumors are classified on the basis of their microscopic findings. The macroscopic features of the different ovarian cancers possess very much similarity.[1] Therefore, histopathologic findings helps in not only making a definitive diagnosis of the ovarian neoplasms but also helps in proper planning and management of the tumors.

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Intraoperative cytology (IOC) is performed by taking imprint smears from the cancerous tissue and establishing an early diagnosis at the operation site.[2] In the past, frozen section was used traditionally but now imprint cytology has been proved to be an acceptable and easily reproducible technique as it is performed on other body organs also.[3-7] IOC is easy to perform, inexpensive, less tissue traumatic, and preservation of cell details.[8] IOC has also helped surgeons to establish the diagnosis at the operating site and after examining the cellular details of the tumor, they can plan proper marginal resection accordingly.

The diagnosis of ovarian neoplasms by Fine needle aspiration cytology (FNAC) is difficult to establish as the ovaries are a deep, structured organ and it causes difficulty for the needle to access the tumor site.[9] However, the

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imaging technique is required to make the pre-operative diagnosis by FNAC of ovarian tumours.[10] Moreover, excessive needling of the neoplastic tissue leads to spilling and seeding of the cancerous cells to the peritoneum.[9] But, IOC enables a prompt diagnosis without the fear of tumor dissemination.

The diagnosis of ovarian tumors by histopathological examination has been established as the gold standard technique. Based on the above advantageous role of IOC and limited literature availability of this technique for establishing the diagnosis of ovarian tumors, we planned to formulate a study comparing the diagnostic correlation of ovarian tumors between imprint cytology and histopathology.

MATERIALS AND METHODS

We conducted a prospective study on 68 suspected ovarian neoplasms in Department of Pathology Teerthanker Mahaveer Medical College and Research Centre, Moradabad, India from January 2014 to December 2014. We included all the samples for our study which are solid/cystic-solid in consistency. Preoperatively, samples were collected using touch, imprint, scrape or crush technique. We employed touch and imprint technique most common whereby, the glass slide was touched with various representative areas. The samples from lesions of somewhat harder consistency were taken by scrape method. While performing scrape method, the tissue was scraped by the edge of one slide and smeared on another slide. The friable lesions were crushed and smeared gently between the two slides. The samples were fixed by 95% ethyl alcohol and stained with hematoxylin and eosin stain. Mucin was demonstrated by using Periodic-acid Schiff's or Alcian Blue stain. An experienced cytopathologist diagnosed and interpreted the cytology slides of ovarian neoplasm under the heads of types, pattern, and morphology of cells.

Since, histopathological diagnosis is considered as a gold standard of diagnosing the type of ovarian neoplasm, so we correlated the histopathological diagnosis with cytological interpretation.

Statistical Analysis

The benign tumors were taken as negative control and malignant/borderline tumors as a positive control. True positives were cytology/histology positive tumors; true negatives were cytology/histology negative tumors; false positives histology negative and cytology positives; false negative was histology positive and cytology negative cases. The cases where pathologist felt difficulty in establishing a diagnosis were labeled as inconclusive. Statistical analysis of data was performed by using SPSS version 20 software. Based on above parameters, positive predictive value, negative predictive value, and diagnostic accuracy were determined together with 95% confidence interval (CI).

RESULTS

We successfully enrolled 68 cases, in our study. The cellularity and morphology of the cell structures were found to be better preserved with imprint/scrape smears. The age of the patients varied between 12 and 64 years, the mean age being 44 years. Among the 68 cases, the standard histopathological diagnosis confirmed 24 as benign, 6 as borderline and 38 as malignant lesions (Figures 1 and 2). Table 1 reveals the diagnostic concordance between cytological and histopathological study in 65 of the 68 cases. We observed prompt results by using hematoxylin and eosin staining technique. The better cytological and nuclear details were observed within 2 min.

We observed a satisfactory diagnostic accuracy of the intraoperative imprint cytology (95.60%) in our study. However, the imprint cytology does not correlated with 4.40% cases with the histological diagnosis. One case of mucinous cystadenoma on imprint cytology was diagnosed as a borderline mucinous tumor on histology, thus giving

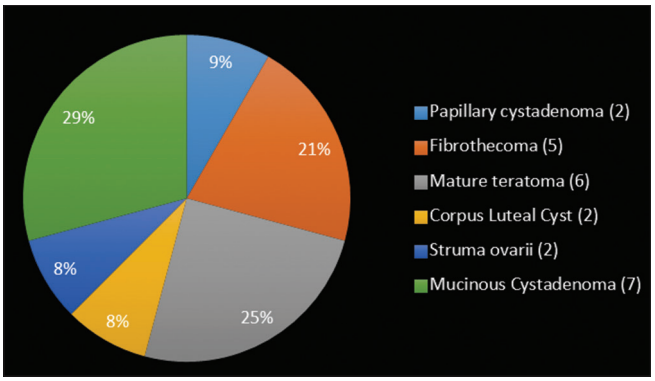

Figure 1: Benign ovarian tumors

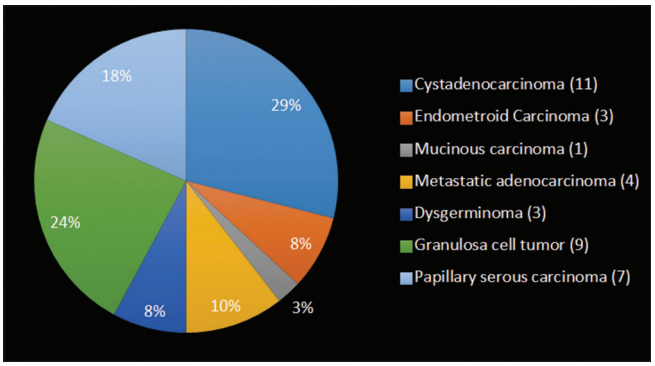

Figure 2: Malignant ovarian tumors

Table 1: Cyto-histopathological correlation of ovarian neoplasms

Cytological diagnosis	Number of cases	Histopathological diagnosis	Correlation (%)
Papillary cystadenoma	2	Papillary cystadenoma	2/2 (100)
Fibrothecoma	5	Fibrothecoma	5/5 (100)
Cystadenocarcinoma	11	Cystadenocarcinoma	11/11 (100)
Endometrioid Carcinoma	3	Endometrioid Carcinoma	3/3 (100)
Borderline mucinous tumor (5) mucinous cystadenoma (1) [FN]*	6	Borderline mucinous tumor	5/6 (83.3)
Mucinous carcinoma	1	Mucinous carcinoma	1/1 (100)
Mucinous Cystadenonoma (5) borderline mucinous tumour (2) [FP]*	7	Mucinous cystadenonoma	5/7 (71.4)
Metastatic adenocarcinoma	4	Metastatic adenocarcinoma	4/4 (100)
Dysgerminoma	3	Dysgerminoma	3/3 (100)
Granulosa cell tumor	9	Granulosa cell tumor	9/9 (100)
Mature teratoma	6	Mature teratoma	6/6 (100)
Papillary serous carcinoma	7	Papillary serous carcinoma	7/7 (100)
Corpus luteal cyst	2	Corpus luteal cyst	2 (100)
Struma ovarii	2	Struma ovarii	2 (100)
Total	68		65/68 (95.6)

*FN: False negative, *FP: False positive

one false negative case in our study. Moreover, two cases of mucinous cystadenoma were misdiagnosed as a borderline Mucinous tumor on cytological examination. This implies the two false positive cases.

Based on the above data, we derived the following parameters;

a. Sensitivity: True positive/true positive + false negative = 97.7% (87.98% - 99.9%, 95% CI).
b. Specificity: True negative/false positive + true negative = 91.37% (73.00% - 98.97%, 95% CI)
c. Positive predictive value: True positive/true positive + false positive = 95.56% (84.85% - 99.46%, 95% CI)
d. Negative predictive value: true negative/false negative + true negative = 95.65% (78.05% - 99.89%, 95% CI)
e. Diagnostic accuracy: 65/68 = 95.60%.

DISCUSSION

The intraoperative cytological examination was first introduced by Dudgeon and Patrick in 1927.[11] Since, then it has gained wide applicability and importance around the globe. By the help of this method, smears can be taken and examined and the diagnosis and management of various tumors can be made within a short period of time. We had performed Hematoxylin and Eosin staining and we were able to diagnose the smears in 2 min. Our findings were supported by Mair *et al.*[5] who also performed IOC within the same time frame of 2 min. Shahid *et al.*[8] further supported our study by performing IOC within 2 min and 23 s. However, Eltabbakh *et al.*[12] had taken 13 min for the same. Although, frozen section had been considered a gold standard for making diagnosis of ovarian malignant tumors but because of ovarian tumors large size, different pathological patterns, and more time consuming, it has been gradually replaced by IOC.[13]

Of all the 68 cases observed, 24 were non-neoplastic lesions. Out of these 24 benign tumors, we observed most of the cases (7) of mucinous cystadenoma on histological examination. On cytological examination, two cases were misdiagnosed as a borderline mucinous tumor. Our findings were supported by Shahid *et al.*[8] who also found one false positive case while examining mucinous cystadenoma. This result was found, as we observed very minimal nuclear atypia with increased nuclear: cytoplasmic ratio. One case of Borderline mucinous tumor was misdiagnosed as mucinous cystadenoma on cytological examination. However, we were able to interpret mucinous carcinoma on both cytological and histological examination accurately.

In our study, we were able to diagnose papillary benign and malignant tumors accurately on both cytological and histopathological examinations. Our study was also supported by Vijayakumar[14] who demonstrated 100% correlation between cyto-/histological findings of papillary cystadenoma and papillary cysadenocarcinoma.

On examining the germ cell tumors, 9 cases of granulosa cell tumors, 3 cases of dysgerminoma and 6 cases of mature teratoma was accurately diagnosed by cytological examination. Our findings were supported by Shahid *et al.*[8] and Khunamornpong and Siriaunkgul[15,] who also found 100% diagnostic accuracy of cytological examination in detecting germ cell tumors. In our study, endometrioid carcinoma was observed to be cytologically similar to serous tumours but we had successfully correlated our three cases of endometrioid carcinoma.

The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy were 97.7, 91.37, 95.56, 95.65 and 95.60%, respectively in our study. Shahid *et al.*[8] in their cytological and histological ovarian tumours correlated study observed sensitivity, specificity and

diagnostic accuracy of 95.8, 96.0 and 95.8% respectively. However, they did not observe the positive and negative predictive values in their study. They also observed 2% of the results as inconclusive, however, no inconclusive results were observed in our cases. In a study conducted by Nagai *et al.*[16] between malignant/borderline/benign ovarian tumours they observed the sensitivity, specificity and diagnostic accuracy as 89.5, 90.3 and 83.6% respectively. Ganjei[10] compared the benign and malignant ovarian cysts by aspiration cytology and observed the sensitivity (75%), specificity (100%) and diagnostic overall accuracy (96%) in their study. Kjellgren *et al.*[17] observed a sensitivity, specificity and diagnostic accuracy of 90, 85, and 93-95% in their study on ovarian tumours by fine needle aspiration biopsy.

The frozen section had been considered as a gold standard for establishing the diagnosis of ovarian neoplasms. One of our limitations in our study is that we should have compared frozen section with IOC smears. But a recent meta-analysis of 18 studies compared the sensitivity and specificity of ovarian neoplasms between frozen section and histopathology and observed similar observations as ours.[18] Other limitation of IOC is that it is difficult to make a proper diagnosis of ovarian tumours with borderline malignant potential and in such cases we advocate that the diagnosis should be relied upon the histopathological findings.

CONCLUSION

From our study, we conclude that the diagnostic accuracy of cytological examination of ovarian masses is really appreciable. Moreover, in a developing country like ours where the facility of frozen section techniques is not available, cytological examination plays a key role in making an early and accurate diagnosis. IOC is a simple, rapid, inexpensive, and easy to perform the procedure and thus helpful in making an early preliminary diagnosis of ovarian tumors thereby helpful in the timely start of patient treatment.

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Original Article

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Supracondylar Osteotomy of Femur for Management of Deformities around Knee Joint: A Camp Experience in Chhattisgarh

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Abstract

Background: Genu recurvatum secondary to paralytic poliomyelitis is disabling and difficult to treat. In our country, 10% population is disabled. Deformities around the knee joint are common disability in patients such as flexion contracture of knee joint, genu valgus, genu varus, and genu recurvatum. To assess the results of supracondylar osteotomy as corrective surgery for deformities around knee joint with patients of flexion contracture deformity, genu valgus, genu varus, genu recurvatum with different diseases and accidental disorders at free disabled surgical camps.

Materials and Methods: In our study, 50 patients were included with 70% male and 30% female, with 10-24 years of age group. Maximum patients had single lower limb knee joint deformity and 8 patients had bilateral lower limb knee joint deformity such as genu valgum and genu varum. Nearly all patients were neglected for long time. All patients were operated in different free disabled surgical camps. Our period of study was 36 weeks (1st May 2004-31st April 2007). Improvement in functional ability and locomotion of all operated patients was assessed by physical examination.

Results: All patients operated in our study showed significant improvement in functional abilities and locomotion after surgery. All patients who came for subsequent follow-up were maintaining functional ability at follow-up duration of 1-year (12 months). At the end results in our study buttonhole and anterior wedge, osteotomy proved to be with excellent results.

Conclusion: Our study shows excellent results that can be achieved in patients with severe neglected knee joint deformities of lower limb with supracondylar osteotomy bony corrective surgeries. It's the team work of devoted surgeon, paramedical and rehabilitation staff at free disabled surgical camps which facilitates services in remote areas with frequent follow-up and maximum achievements of good results in minimum expenditures.

Key words: Genu valgum, Osteotomy, Varus

INTRODUCTION

Genu valgum is a common orthopedic problem in children. The vast majority of cases are physiologic variants, which resolve normally.[1] Frontal plane knee deformity may be congenital, idiopathic, and secondary to trauma or might be due to rickets or osteomalacia. An angular correction by wedge corrective osteotomy is the standard treatment.[2] Pediatric femoral shaft fractures are known to produce growth arrest at the proximal tibia, probably caused by compression injuries of the proximal tibial physis, most often in the area of the tibial tubercle, producing late onset genu recurvatum deformities.[3]

Genu recurvatum secondary to paralytic poliomyelitis is disabling and difficult to treat.[4] In our country, 10% population is disabled. Deformities around knee joint is a common disability in patients such as flexion contracture of knee joint, genu valgus, genu varus, and genu recurvatum. It

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is caused by poliomyelitis, hemiparesis, cerebral palsy, rickets, developmental congenital disorders, and accidental disorders. It's a big challenge for surgeons to improve their locomotor system and making patient independent. A measurable varus angle or a valgus higher than 11° during this period should be considered abnormal.[5] Due to a big load of trauma cases in higher centers in our state, and country these disabled patients are neglected and refused everywhere for the management (corrective surgeries). So small satellite free disabled surgical camps organized by the help of NGOs, Akhil Bharatiya Viklang Chetna Parishad, GOVT agencies and life line express are very helpful for these disabled patients.

Supracondylar osteotomy for the correction of deformities around knee joint not only corrects the deformity but also improves personal hygiene, gait and independent ambulation with or without assistive devices. This treatment should be planned with patient needs. In our study to complete the evaluation of the knee, we have taken different radiographic views, including the standard lateral and the axial views of the patellofemoral joint.[6]

This retrospective study of 50 patients with deformities around knee joint were operated in free disabled surgical camps at different districts of Chhattisgarh state in institutions with helping NGOs, GOVT agencies, and life line express.

MATERIALS AND METHODS

In our study, out of 50 patients included, 70% were male and 30% were female with 10-24 years in age group. Almost all were neglected for a long time for corrective surgeries, some were operated but not achieved good results.

Patients were admitted and operated at different free disabled camps in different institutions in different districts of Chhattisgarh over the period of 3 years (1st May 2004-31st April 2007). Choice of patients was mild to moderate and severe deformities around the knee joint, standing or walking with some or other gait with or without support. Deformities around knee joint and condition of the lower limb of patients were assessed with a physical and radiological examination at the time of admission. Deformities around knee joint such as flexion contracture, genu valgus, genu varum, genu recurvatum, and gait pattern were noted in all patients clinically.

SCHEDULE OF CAMPS

Day 1

- Registration and screening of patients suitable for surgery.
- Preoperative preparation, routine investigations, and medication of patient and X-rays of the knee joint and lower limbs.
- Meticulous asepsis and arrangement in the operation theater.
- The inaugural ceremony of camp organized by NGOs (Figure 1).

Day 2

Operation theater was prepared at the site of camp as shown in Figure 1. Surgery was done for the whole day. We ran four OT tables simultaneously. Post-operatively application of cast and slab was done at the site only for which a dedicated team of paramedical staff was available as shown in Figure 2.

Day 3-5

- Daily morning and evening rounds are taken.
- Care for hematoma soakage, fever, extreme pain, loss of toe movements, discoloration of skin, and neurovascular deficit.

Day 6

- The closing ceremony, discharge of patients with medicine and proper instructions.

First Follow-up

- After 1 month to see any complications and for measurement of assistive devices.

Figure 1: Operation theater prepared at the site of camp

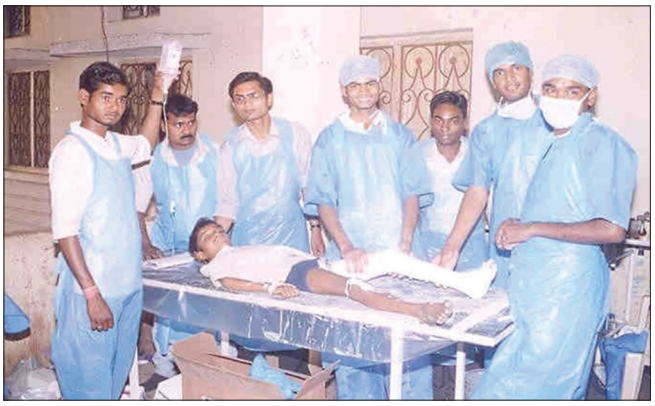

Figure 2: Post-operative plaster cast application in the camp

Second Follow-up

- After 2.5-3 months for removal of the pop cast, stitches, k wires
- Calipers and shoes are provided
- Parallel bar walking and physiotherapy explained to patient and relatives
- Advised regular follow-up every 2 months for at least 2 years.

SURGICAL PROCEDURES

If correction is not satisfactory after soft tissue release surgery for deformities around the knee joint, the patient needs supracondylar osteotomy of the femur. Supracondylar osteotomy is a big answer to many problems around the knee joint.

TYPES OF OSTEOTOMIES

- Anterior wedge osteotomy for flexion contractures of knee joint as shown in Figure 3.
- Side to side (medial or lateral) for genu valgus and genu varum deformity of the knee joint. Distal femoral medial closing wedge osteotomy is performed from the medial side, just proximal to the adductor tubercle, and the anterior margin of the femoral articular surface[4] (Figure 4).
- Posterior wedge for genu recurvatum deformity of the knee joint was done. The pre-operative, and post-operative case is shown as in Figures 5 and 6.
- Mixed wedge for mixed deformity of knee joint (rotational deformity of the leg) as shown in Figure 7.

Approaches for Osteotomy

The anterior, lateral, or medial are the approaches for osteotomy at the lower third of the thigh. The lateral approach is for thin build patients and osteoporotic bones.

The advantage of the lateral approach is soft tissue release of a lateral side can be done simultaneously, and there is no quadriceps stiffness.

The anterior approach is for thick build and stout bones.

Anterior wedge osteotomy: Indication is flexion contracture deformity of knee joint

Degree of flexion contracture	Size of wedge
Up to 10°	1 cm
11°-20°	2 cm
21°-30°	3 cm

Buttonhole (Cuneiform) Osteotomy

The approach is the lateral side of the lower third of thigh and indication is for rigid knee flexion deformities without any soft tissue contracture and with hand on knee gait with quadriparesis.

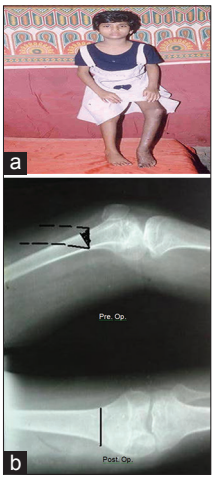

Figure 3: (a and b) Radio graphical evaluation of the patient pre and post-operatively in buttonhole anterior wedge osteotomy in case of flexion contracture deformity

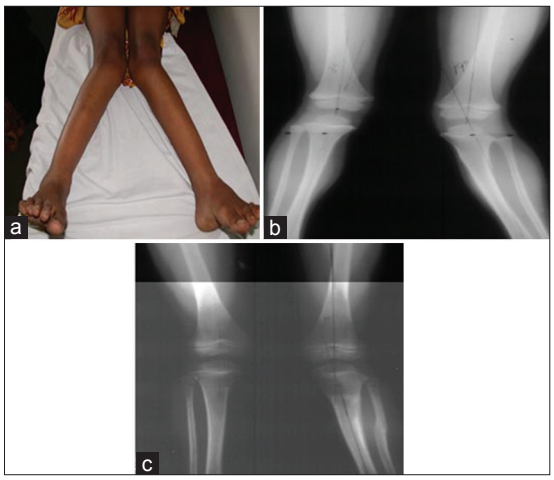

Figure 4: (a-c) Case of genu valgum pre and post-operative radiographic evaluation

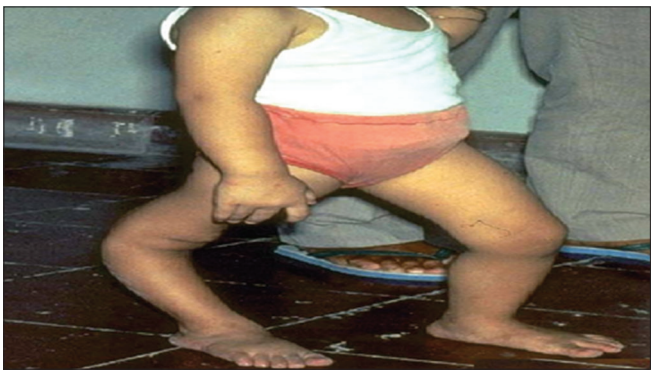

Figure 5: Case of genu recurvatum

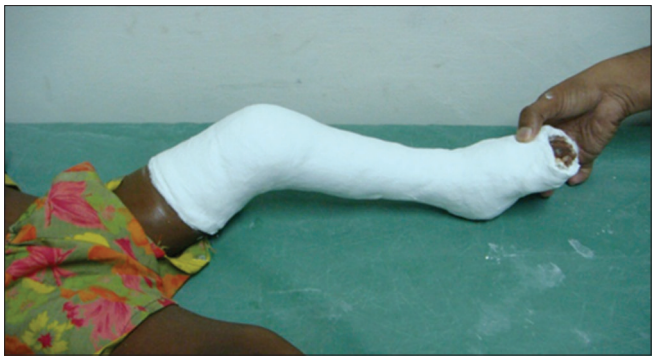

Figure 6: Plaster cast after posterior wedge osteotomy for genu recurvatum

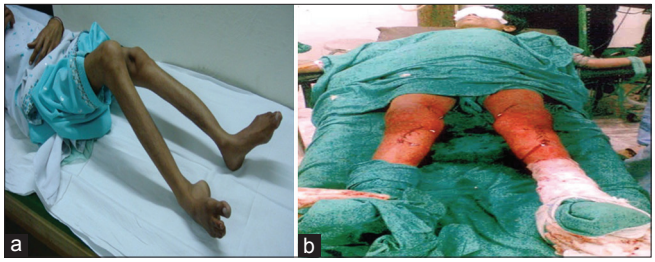

Figure 7: (a and b) Mixed deformities flexion contracture, genu valgum and rotational deformity pre and post-operatively

TECHNIQUE

Bone deep small incision given over lateral aspect and lower third of the thigh. Than periosteum separated, bone lever introduced anterior to femur, than osteotomies anterior 3/4 cortex, side to side movements of osteotomy to create small wedge, collapse it by gradual pressure over fracture site and elevate heel unless wedge is impacted, spring movements of knee joint confirms good reduction. 5° hypertension of knee joint is achieved to lock knee during walking and weight bearing.

Advantage

It's a minimal invasive surgery, less hematoma and infections, and no quadriceps stiffness.

It facilitates early mobilization, physiotherapy, rom and discarding calipers after few months and walking without aid and hand on knee gait.

Medial wedge osteotomy: Indication is genu valgum deformity.

Lateral wedge osteotomy: Indication is for genu varum deformity.

Posterior wedge osteotomy: Indication is for genu recurvatum deformity.

The degree of deformity and size of the wedge is same as anterior wedge osteotomy. Gradual reduction and achieving anatomical alignment of the limb are the main aim of these supracondylar osteotomy surgeries.

Key Points

Controlled sustained pressure and counter pressure during hammering is mandatory.

Use of sharp instruments to avoid subluxation, use of a tourniquet, cautery and drain for the bloodless field. Only corticotomy without removal of bone marrow if possible, that facilitates minimal hematoma and soakage.

COMPLICATIONS

Early

Intraoperative: Posterior subluxation of proximal fragment.

Immediate post-operative: Extreme pain, soakage, fever, discoloration of the skin, loss of toe movements, and sensation, i.e., impending neurovascular deficits.

Late

Infection, subluxation, pin track infection, neurovascular complication, and compartment syndrome.

Management of Complications

Intraoperative: Posterior subluxation of the proximal fragment is managed by telescopic reduction into a distal fragment that gives stable anatomical reduction with or without k wire fixation.

Post-operative: For neurovascular deficits and compartment syndrome

- Remove pop cast completely
- Bring original anatomical position of limb
- Active knee movements and elevation of foot end
- Change pop cast and dressing

POST-OPERATIVE PROTOCOL

For patients with anterior, medial, lateral and mixed wedge osteotomy, toe to groin cast applied at the time of surgery with knee 5-10° flexion for 2-3 months with or without k wire fixation.

For posterior wedge osteotomy, patients toe to groin cast applied at time of surgery with 45-90* flexion of the knee joint for 2-3 months with or without k wire fixation.

Patient discharged with the pop cast with analgesics, antibiotics, symptomatic, and supportive medicines with proper instructions and advised to review after 1-month and as and when required at the same camp institution for any complication. They are again advised to review

after 2.5-3 months for second follow-up, when pop cut, stitches, and k wires removed, and shoes and calipers provided, parallel bar walking and physiotherapy explained to patients.

RESULTS

Criteria for excellence results were when bony union achieved in 2 months with no post-operative complications without neurovascular deficits, patients walk without any support more than 1 km. It was termed as good results when bony union achieved in 2.5 months with minimal post-operative complications, soakage and neurovascular deficit, patient walk 1 km with calipers. The patients were termed as having fair results when bony union achieved in 3 months with moderate post-operative complications, soakage and neurovascular deficit, patient walk 0.5 km with calipers.

100% cases came up to second follow-up, but 60% cases came for subsequent follow-up.

A number of cases for buttonhole and anterior wedge osteotomy for flexion contracture deformity of the knee joint were 30, where excellent results in 23 cases, good in 5 cases and fair in 2 cases.

The number of cases for side to side wedge osteotomy was 10, where excellent results in 6 cases, good in 3 cases and fair in 1 case.

The number of cases for mixed wedge osteotomy was 6, where excellent results in 4 cases and one each with good and fair results.

The number of cases for posterior wedge osteotomy was 4, where excellent results in 2 and one each with good and fair results (in our study button hole and anterior wedge osteotomy proved to be with excellent results) (Table 1).

Table 1: Result of different osteotomy procedures

Type of wedges	No. of cases	Excellent	Good	Fair
Buttonhole and anterior	30	23	5	2
Side to side	10	6	3	1
Mixed	6	4	1	1
Posterior	4	2	1	1
Total	50	35	10	5

DISCUSSION

Before planning of the treatment for the patients with deformity especially when etiological factor being cerebral palsy emphasis has to be given to tone. As claimed by Bobath tone is more complex and comprises both neural and non-neural elements.[7] Progressive correction of the knee flexion by serial casting or skeletal traction requires a long time in hospital. It is associated with high morbidity such as pain, pin site infection like pressure sore and posterior subluxation of the knee and usually does not correct the deformity entirely.[8] Few has opinion that restoration of the mechanical axis of the limb should be the principal goal of the treatment.[9] It is observed that most of the patients tries conservative management before taking steps toward surgical intervention. Ilizarov technique is one of the corrective method of the genu recurvatum.[10] Shim *et al.* reported opening wedge high tibial osteotomy below the tibial tubercle should be recommended in relatively young patients with genu varum.[11] Studies also recommended use of temporary hemiepiphysiodesis using tension band plates for correction of genu varus and valgus.[12]

Zhang *et al.* reported Proximal opening high tibial osteotomy performed in conjunction with the special rigid locking plate yielded good results for symptomatic genu varum.[13] The present study has evaluated anterior, posterior, medial, and lateral wedge osteotomies in the different patients as per the need, management by Butonhole osteotomy gained achievement of the mechanical axis and correction of the knee flexion. From the results and performance output on the basis of activities of daily living, gait pattern and other parameters we observed the more excellent result in buttonhole osteotomy.

CONCLUSION

Supracondylar osteotomy is a big answer for correction of many problems around knee joint, minimal exposure and operative time with satisfactory results and smile of patient are effective steps to correct disability and making patient independent, earning and minimizing burden of society. Small free disabled surgical camps facilitate services in remote areas with frequent follow-up, and good results proves minimum expenditures and maximum achievements. We acknowledge the support and encouragement of Dean CIMS Bilapur and Civil Surgeon for successful organization of these camps.

We can conclude from the present study that buttonhole osteotomy is one of the better option when it comes to camp approach in corrective surgeries.

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Original Article

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Efficacy and Safety of Intra-operative Posterior Sub-Tenon's Triamcinolone Injection in Cataract Surgery Associated with Diabetic Retinopathy

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Abstract

Background: Diabetes mellitus increases the probability of developing cataract. There is growing evidence that diabetic retinopathy (DR) progresses more rapidly after cataract surgery.

Purpose: To study the effect of single posterior sub-Tenon's triamcinolone acetonide on occurrence and progression of macular edema and visual outcome following cataract surgery in diabetic patients.

Materials and Methods: This is a prospective interventional comparative study conducted on 36 eyes of 26 patients with DR and cataract. Patients were randomly assigned to Group I, triamcinolone acetonide (TA) (triamcinolone group) receiving a single posterior sub-Tenon's TA injection 1 ml (40 mg), at the end of small incision cataract surgery and Group II (control group) who underwent only cataract surgery. Best corrected visual acuity (BCVA) and intra-ocular pressure (IOP) were recorded at baseline and at each follow-up. Fundus fluorescein angiography and optical coherence tomography were done at baseline and 3 months postoperatively.

Results: The macular thickness in the control group increased by 71 microns (30.45%) at 3 months post-operatively and was statistically significant (P = 0.006). However, there was no statistically significant difference in the foveal thickness between the groups either at baseline (P = 0.07) or at 3 months (P = 0.63). At 6 months, there was no significant difference in the mean change in foveal thickness between the 2 Groups. There were no statistically significant differences between the groups in BCVA at 1 month (P = 0.38) and 6 months (P = 0.66) post-operatively.

Conclusions: The results of our study suggest that a sub-Tenon's injection of triamcinolone reduced the incidence of cystoid macular edema after cataract surgery in diabetic patients. In addition, it reduced the central macular thickness and improved visual acuity in the short term However, sub-Tenon's injection of TA did not affect DR progression or visual acuity at 6 months post-operatively which was determined by the pre-operative metabolic status.

Key words: Cataract, Macular edema, Macular thickness, Sub-Tenon's triamcinolone, Visual acuity

INTRODUCTION

The probability of developing early cataract is more in patients with diabetes mellitus.[1] This also increases the risk of reduced visual outcome.[2] Cataract and diabetic retinopathy (DR) are the leading causes of blindness.[1] DR is the progressive dysfunction of the retinal vasculature due to chronic hyperglycemia. Macular edema is an important cause of poor post-operative visual gain following cataract surgery. Patients with DR are more prone to develop post-operative macular edema following cataract surgery than normal subjects. This is because cataract surgery facilitates inflammation and breakdown of blood-retinal barrier, especially in patients with DR with dysfunctional retinal vasculature.[3]

Poor visual outcome of cataract surgery in diabetic patients is linked to severity of retinopathy and maculopathy existing prior to cataract surgery.[4-6] DR progression after

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cataract surgery is known to be influenced by the severity of pre-operative DR, duration of diabetes, and the adequacy of glycemic control.

Diabetic macular edema (DME) is defined as retinal thickening from the accumulation of fluid within one disc diameter of the center of the macula. DME can be classified as focal, diffuse, ischemic, and mixed types. Macular edema can be treated with macular photocoagulation, intra-vitreal/peribulbar steroids or anti-vascular endothelial growth factor (VEGF) agents.[7-9] Based on the observations of early treatment DR group (ETDRS), focal or grid laser photocoagulation is the gold standard treatment for DME.[3] However in the ETDRS, only 17% of the eyes had an improvement in visual acuity and <3% had a visual improvement of three or more ETDRS lines following laser. Moreover, a significant number of patients with DME, especially the DME of the diffuse type, remain refractory to focal or grid laser treatments. Among alternative treatments, pharmacotherapeutic agents such as triamcinolone acetonide (TA), a long-acting synthetic corticosteroid, when given by the intravitreal route or posterior sub-Tenon's route has been reported to be efficacious.[9-12]

The effect of cataract surgery on the progression of DR remains an issue of debate. Krepler *et al.*,[13] in a prospective study on 42 eyes showed that cataract surgery seems to have no influence on the progression of DR. A visual improvement is achieved in the majority of patients with non-proliferative DR (NPDR), but poorer visual outcome is observed in patients developing macular edema. Mittra *et al.*[14] showed that NPDR and surgical inexperience resulted in an increased rate of retinopathy progression.

Kato *et al.*[15] found that diabetic patients who did not have preoperative DR were more susceptible to postoperative DR progression after surgical intervention. Moreover, cataract surgery may facilitate inflammation and breakdown of the blood-retinal barrier, especially in patients with DR.

TA for ophthalmic use is available as a suspension. TA is a corticosteroid that in addition to its anti-inflammatory effects, causes down-regulation of VEGF.[16] Intravitreal triamcinolone may be associated with various complications such as glaucoma, cataract, endophthalmitis, retinal detachment, and scleritis.[17]

Peribulbar injection of corticosteroids appears a good alternative way of delivering the drug intravitreally. This route appears a less invasive approach than intravitreal injection and may deliver equivalent therapeutic concentrations to the retina.

Aim

To study the effect of single posterior sub-Tenon's triamcinolone acetonide on occurrence and progression of macular edema and visual outcome following cataract surgery in diabetic patients. The objectives are:

a. To compare the change in the central macular thickness (CMT) between the 2 Groups.
b. To compare the best corrected visual acuity (BCVA) scores between the 2 Groups.
c. To study steroid related complications.

MATERIALS AND METHODS

This is a prospective interventional comparative study conducted on 26 patients with DR and cataract who attended vitreo-retina outpatient development at Sarojini Devi Eye Hospital, from April 2012 to November 2013.

Inclusion Criteria

1. Diabetes with NPDR/mild PDR
2. Uneventful cataract surgery
3. In the bag placement of IOL.

Exclusion Criteria

1. DR with high-risk characters
2. Diabetes with other macular pathologies such as ARMD and macular holes
3. Patients with glaucoma
4. Intraoperative complications of cataract surgery such as posterior capsular rupture and iris damage.

Diagnosis, prognosis, various treatment options, and possible complications were explained to the patients and their informed consent was taken before enrolment. All the patients underwent a comprehensive ophthalmological examination.

BCVA and intraocular pressure (IOP) were recorded at baseline and at each follow-up. Fundus fluorescein angiography (FFA) and optical coherence tomography (OCT) were done at baseline and 3 months postoperatively. Patients were investigated for blood and urine sugars, glycosylated hemoglobin, Hb%, serum lipids, serum creatinine, and blood urea. Patients with deranged systemic parameters were referred to a general physician for the control before they were taken up for cataract surgery.

Patients were randomly assigned to Group I (TA group) receiving a single posterior sub-Tenon's TA injection 1 ml

(40 mg), at the end of small incision cataract surgery, Group II (control group) underwent only cataract surgery.

Postoperatively, patients were instructed to use topical antibiotic eye drops 4 times a day, steroid eye drop 6 times a day, and cycloplegics 2 times a day for 1-week. After 1-week, only steroid drops were used in tapering doses for 6 weeks, the minimum period of follow-up was 6 months. Patients were re-examined at 1-day, 1-week, 1-month, 3 months, and 6 months after the injection. The data thus collected were subjected to statistical analysis. The data were statistically evaluated using the Wilcoxon signed rank test, Mann–Whitney test, and t-tests wherever applicable. The analysis was performed using SPSS (Version 17) windows software ($P < 0.05$).

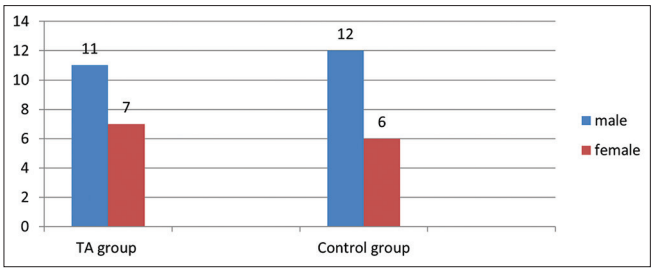
RESULTS

Patients with diabetes are more likely than patients without diabetes to develop macular edema after cataract surgery, the major vision-threatening form of DR in addition to PDR.

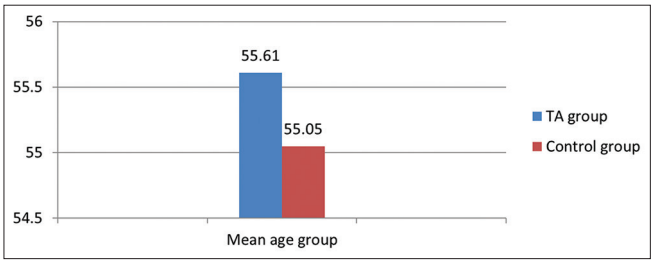
The mean patient age was 55.6 ± 6.2 (range 45-70) in TA group and 55.0 ± 6.5 in the control group. Eleven patients (61.1%) were men and seven patients (38.9%) were women in TA Group and 12 patients (66.7%) were men and 6 patients (33.3%) were women in control group (Graphs 1 and 2).

The mean ± SD value of the duration of diabetes was 11.61 ± 6.11 years in the TA group and 11.50 ± 6.08 years in the control group (Graph 3). The mean glycosylated Hb% was above 9 in both the groups (TA Group - 9.35%, control Group - 9.26%) (Graph 4). Patients with deranged systemic parameters were referred to a general physician for the control before they were taken up for cataract surgery.

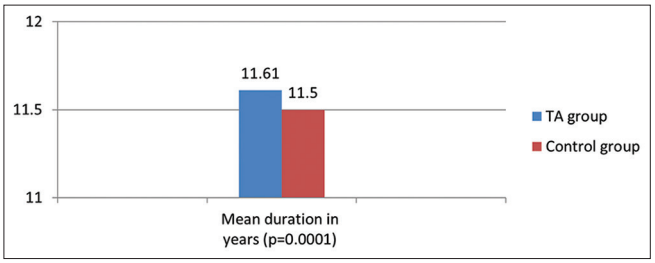
The mean preoperative CMT on OCT was 231.16 ± 40.86 µm in the control group and 288.83 ± 115.87 µm in the TA group ($P = 0.07$) (Graph 5). The mean CMT was 304.33 ± 115.38 µm and 281.50 ± 163.74 µm, respectively ($P = 0.63$), postoperatively, at the end of 3 months. The mean change in CMT at 3 months was statistically significantly greater in the control group ($P = 0.006$) in our study. The macular thickness in the control group increased by 71 microns (30.45%) at 3 months postoperatively and was statistically significant ($P = 0.006$). However, there was no statistically significant difference in the foveal thickness between the groups either at baseline ($P = 0.07$) or at 3 months ($P = 0.63$). At 6 months, there was no significant difference in the



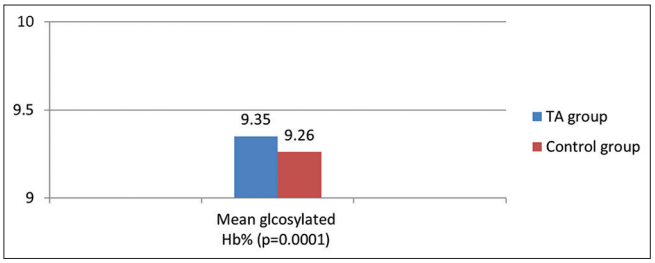
Graph 1: Demographic profile: Gender distribution



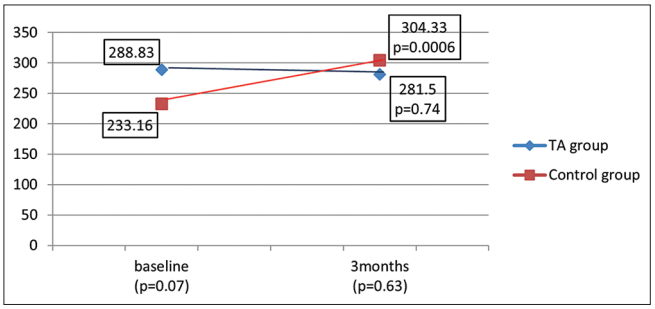
Graph 2: Age distribution



Graph 3: Duration of diabetes



Graph 4: Glycosylated Hb%



Graph 5: Macular thickness comparison

mean change in CMT between the 2 groups. In our study, four (22.2%) eyes in the control group showed CME on OCT and FFA and none in TA group. Patients with good metabolic control showed lesser CMT than the patients with poor metabolic control irrespective of the group, thus emphasizing the importance of good preoperative metabolic control on the occurrence of postoperative macular edema. A case with poor metabolic control is shown in Figure 1a-c with increased foveal thickness and diffused leakage on fluorescein angiography. Post cataract surgery with PST, there is no respite in foveal thickness and diffuse leakage on FFA, at 3 months (Figure 1d-f). Another case with good metabolic control (Figure 1a-c) shows stable fovea on OCT and no foveal leakage on FFA (Figure 1d-f).

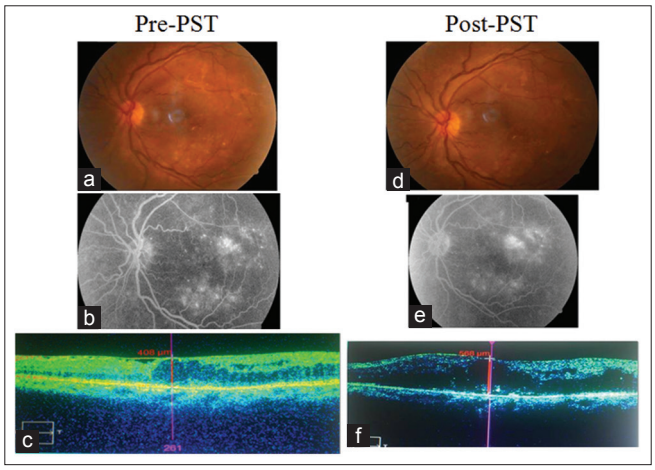


Figure 1: (a-c) Pre-triamcinolone injection with cataract surgery and (d-f) Post injection, show no respite in diffuse leakage on fundus fluorescein angiography and persisting increased foveal thickness on optical coherence tomography, after 3 months

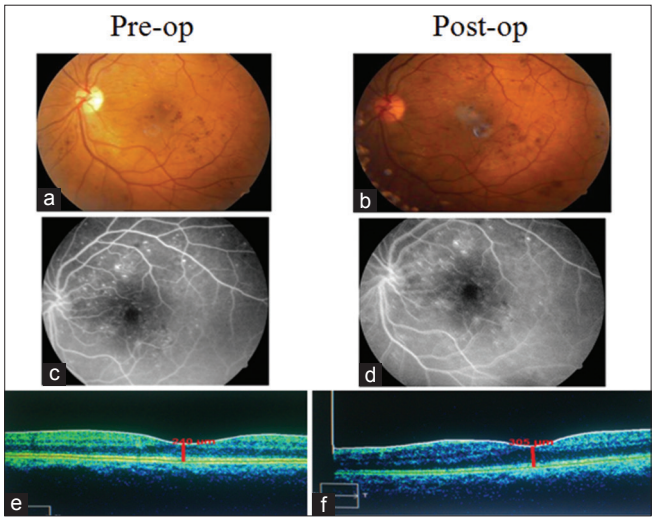


Figure 2: (a,c,e) Control group. Preoperative pictures of a case with good metabolic control, (b,d,f) 3 months post cataract surgery pictures with stable macula, no leakage on fundus fluorescein angiography, and no increase in foveal thickness on optical coherence tomography

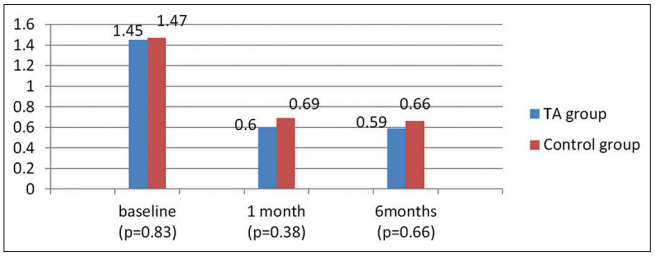
The mean change in BCVA at 1-month postoperatively was greater in TA than in control group. There were no statistical significant differences between the groups in BCVA at 1-month (P = 0.38) and 6 months (P = 0.66) postoperatively (Graph 6).

The IOP rise from baseline to 1-month postoperatively was greater in TA group than in control group but the rise was not statistically significant (P = 0.12) (Graph 7).

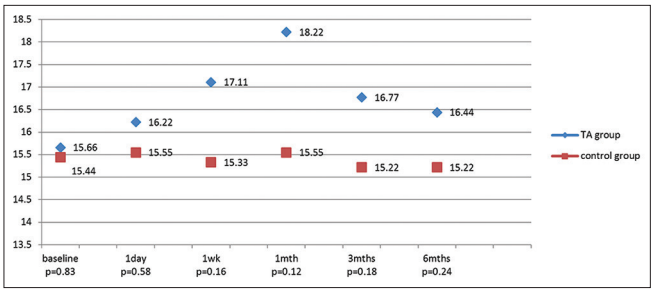
DISCUSSION

This study shows that the average CMT in the control group increased by 71 microns at 3 months and this was statistically significant, but there was no statistically significant difference between the 2 Groups. In a similar study by Kim *et al.*[18] reported in their study that the mean preoperative CMT on OCT was 204.93 ± 39.08 μm in the control group and 228.24 ± 43.34 μm in the triamcinolone group (P = 0.130). One month postoperatively, the mean CMT was 273.93 ± 91.00 μm and 238.76 ± 48.20 μm, respectively (P = 0.469). The mean change in CMT at 1-month was statistically significantly greater in the control group (P = 0.015), but the difference was not statistically significant at the end of 6 months.

In our study, we observed that mean change in visual acuity (log MAR) in TA group was 1.45 log MAR (P = 0.0001), 0.6 log MAR (P = 0.0001), and 0.59 log MAR (P = 0.0001)



Graph 6: Best corrected visual acuity (log MAR) comparison



Graph 7: Intraocular pressure rise comparison

at baseline, 1, and 6 months, respectively. While in the Control group it was 1.47 log MAR ($P = 0.0001$), 0.69 log MAR ($P = 0.0001$), and 0.64 log MAR ($P = 0.0001$) at baseline, 1, and 6 months, respectively. The mean change at 1-month postoperatively was greater in TA than in control group. There were no statistically significant differences between the groups in BCVA at 1-month ($P = 0.38$) and 6 months ($P = 0.66$) postoperatively. Kim *et al.*[18] reported that there were no statistically significant differences between the groups in BCVA at 1-month and 6 months postoperatively ($P > 0.05$). The mean change in the lines of BCVA (log MAR) from baseline to 1-month postoperatively was significantly greater in the TA group than in the control group ($P = 0.045$). However, mean change at 6 months was not statistically significant between the groups. In a study by Ahmadabadi *et al.*,[19] intravitreal injection of TA reduced the amount of central point thickness after phacoemulsification in eyes of diabetic patients. It also reduced the incidence of cystoid macular edema but it had no effect on visual acuity gain.

Potential side effects of injecting TA into the posterior sub-Tenon's capsule include IOP elevation, globe perforation (rare), occlusion of the central retinal artery, blepharoptosis, and infection. In our study, we did not encounter any complication in the TA group.

In our study, IOP rise from baseline to 1-month postoperatively was greater in TA group than in control group but the rise was not statistically significant ($P = 0.12$). IOP rise in between the groups was never statistically significant with $P = 0.12$, 0.18, 0.24 at 1, 3, and 6 months, respectively, in our study.

Chew *et al.* (DRCR Net)[20] reported that anterior peribulbar triamcinolone injections were associated with an increased risk of IOP elevation and cataract development compared to posterior sub-Tenon's triamcinolone injections.

The limitation of this study is that the number of patients was relatively small. Further study with a larger sample size will be necessary to elucidate our results.

CONCLUSION

The results of our study suggest that a sub-Tenon's injection of triamcinolone reduced the incidence of cystoid macular edema after cataract surgery in diabetic patients. In addition, it reduced the CMT and improved visual acuity in the short term. However, sub-Tenon's injection of TA did not affect DR progression or visual acuity at 6 months postoperatively which was determined by the preoperative metabolic status.

Rate of DR progression after cataract surgery is influenced by the severity of pre-operative DR, duration of diabetes, adequacy of glycemic control, and other associated systemic factors such as hypertension and hyperlipidemia.

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Original Article

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Anthropometry: A Comparative Study of Right and Left Sided Foramen Ovale, Jugular Foramen and Carotid Canal

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Abstract

Introduction: The sphenoid bone contains numerous foramina and fissures, which accommodate several vessels and nerves. One of these is the foramen ovale. Normally the foramen ovale is located in the greater wing of the sphenoid bone, posterior and lateral to the foramen rotundum, the jugular foramen (JF) is formed by the edge of the occipital bone forming the jugular notch, and the petrous temporal bone is excavated to form jugular fossa, carotid canal is the passage way in the temporal bone. The canal starts on the inferior surface of the temporal bone at the external opening of the carotid canal also called as the carotid foramen.

Materials and Methods: In this study, the distance of the foramen ovale, JF and external opening of the carotid from the midline, the anteroposterior diameter, the transverse diameter and the area of the foramina were measured.

Observation and Results: When compared to right and left sides for the individual foramen showed no statistical significance. The mean combined area (CA) of the foramen ovale was found to be 35.5 mm^2 and 22.4 mm^2 in males and females, respectively. The mean CA for JF was 170.89 mm^2 and 125.5 mm^2 in males and females, respectively, and the mean CA for the carotid canal was 59.55 mm^2 and 43.25 mm^2 in males and females, respectively. The CA of the foramen ovale and external opening of the carotid canal were used to find the limiting points (LP). The LP is 47.5 mm^2 and 31 mm^2 for foramen ovale and external opening of the carotid canal. The skulls are having CA lesser than the LP were classified as female skulls. Of the 100 skulls studied 83 skulls were classified as male skulls, 12 skulls were classified as female skulls and the remaining 5 skulls had overlapping values of the LP, and therefore, unclassified.

Conclusion: The need for familiarity with the detailed Anatomy of the foramina under study and their variations are very much essential in microsurgical techniques as many extracranial and intracranial lesions including intrinsic anomalies may affect the foramina.

Key words: Carotid canal, Foramen ovale, Jugular foramen, Morphometry, Skull base foramina

INTRODUCTION

The sphenoid bone contains numerous foramina and fissures, which accommodate several vessels and nerves. One of these is the foramen ovale, which serves as a passage for the mandibular nerve, accessory meningeal artery and the lesser petrosal nerve. Normally, the foramen ovale is located in the greater wing of the sphenoid bone, posterior and lateral to the foramen rotundum.[1,2]

The foramen ovale is important in functional cranial anatomy and neurosurgeries as it enables access to the trigeminal nerve.

It is situated in the transition zone between intracranial and extracranial structures. Therefore, it is used for various invasive surgical, as well as diagnostic procedures. Electroencephalographic analysis of seizure by an electrode

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placed at foramen ovale is done. Foramen ovale electrode technique provided good neurophysiological information in a candidate for selective amygdalohippocampectomy.

The jugular foramen (JF) is formed by the edge of the occipital bone forming the jugular notch, and the petrous temporal bone is excavated to form jugular fossa, which accommodates the superior bulb of internal jugular vein. The JF may be partially or completely divided into three compartments by small spicules of bone.

The anteromedial compartment transmits inferior petrosal sinus and meningeal branch of ascending pharyngeal artery, middle compartment contains tympanic branch of glossopharyngeal nerve (Jacobson's nerve), the auricular branch of Vagus nerve (Arnold's nerve) and eleventh cranial nerves (CN) and the cochlear aqueduct.[3] Although the large posterolateral compartment transmits the sigmoid sinus on its way to become the jugular vein and meningeal branch of occipital artery.[4]

Different pathologic conditions involve the JF and may result in the lower CN deficits. The lower CN deficits leading to dysphagia, breathing difficulty, hoarseness, and pneumonia due to aspiration are potential dangerous problems. Understanding the relationship of the compartments of JF to the lower CN, and its measurements are essential if neural preservation is desired.

The carotid canal is the passage way in the temporal bone through which the internal carotid artery enters the middle cranial fossa from the neck. The canal starts on the inferior surface of the temporal bone at the external opening of the carotid canal also called as the carotid foramen. The canal ascends at first vertically, and then, making a bend, runs horizontally forward and medially. The canal opens in the lateral wall of foramen lacerum.

The carotid canal transmits the internal carotid artery along with the carotid plexus of nerves into the cranium, sympathetic to the head from superior cervical ganglion also pass through the carotid canal.

The carotid canal is considered as an important landmark by the neurosurgeons as the canal is most vital and easily visualized structure on magnetic resonance imaging angiography and digital subtraction angiography.

The detailed knowledge of the normal and variant position of the carotid canal is important for radiologists, neurosurgeons, and anatomists as identification of the skull base anatomy is of great importance in cases of aneurysms and clival tumors.

MATERIALS AND METHODS

A total of 100 adult human skulls were collected. The samples for the study were collected randomly independent of the sex and origin of the skull. The skulls were collected from the bone bank of department of anatomy, Navodaya Medical College, Raichur and from the students of Navodaya Medical College Raichur, Navodaya Dental College, Raichur and Khaja Bandanawaz Institute of Medical Sciences, Gulbarga.

After collection of the skulls sample randomly, sex of the skull is determined based on the non-metrical parameters, these skulls were further assessed with the metrical parameters using vernier calipers. The non-metrical parameters[5] taken were size and overall architecture of the skull, zygomatic bone presenting marginal tubercle in the posterior of the frontal process and ridges on its lower edge in males, size and ridges of the mastoid process, roughness in the occipital bone. According to the non-metrical parameters 84 skulls were male skulls, and 16 skulls were female skulls.

Only fully ossified adult skulls were included in the present study. Skulls are showing wear and tear, any fracture or pathology was excluded.

Parameters taken under Study are

1. Distance of the foramina from the midline
2. Number of foramina on right and left side
3. Diameters of the foramina. Anteroposterior diameter and transverse diameter
4. Area of the foramina
5. Male and female sexing of the skull by morphometrical analysis of the foramina.

Observations

The foramen ovale, JF, and external opening of the carotid canal of 100 skulls are studied and observed on the right and left sides. The following observations were made.

- Position of the foramen: The distance of the medial edge of the foramen from the median plane were observed and compared to both sides
- Number of the foramen: The number of foramen on both sides was observed and compared, any bony growths around the margins of the foramen due to ossified ligaments or any septations dividing the foramen into the compartments as in case of JF were also studied
- Diameters of the foramen: The anteroposterior diameter and the transverse diameter of the foramen were observed and compared to both sides
- Area of the foramen (A): The area of the foramen was calculated using the formula $A=\frac{\pi\times APD\times TD}{4}$, the areas of both the foramina were compared

- Combined area (CA) is calculated by adding areas of the foramina of both sides, which is used further to determine the sex of the skull.

For the above-mentioned parameters the range, mean, and standard deviation (SD) of the measurements are calculated. The means of both sides are compared statistically using "*t*" test. The identification point (IP) for the CA is calculated from the range of CA of each foramen, the demarcating points (DP) are determined from the calculated range,[6] and from the DP the limiting point (LP) is determined by multiple trial and error method.[7] These values are calculated to determine the sex of the skull.

Position of the foramen: As seen in Figure 1, it is observed that the mean of the distance of foramen ovale are 22.98 mm on the right side and 22.79 mm on the left side. The comparison of the position of the foramina on right and left sides showed no statistical significance ($P > 0.05$). The mean of the position of JF is 23.9 mm on the right side and 24.04 mm on left side JF. The comparison of the position of JF on the right and left sides showed no statistical significance ($P > 0.05$), and the mean of the distance of the external opening of carotid canal is 26.14 mm on the right side and 26.02 mm on left side.

The comparison of the position of the external opening of the carotid canal on right and left sides showed no statistical significance ($P > 0.05$).

Number of foramen: As seen in Figures 2 and 3, it is observed that with each of the 100 skulls only 1 foramen ovale is present on the right side and 1 foramen ovale on the left side, with no duplication of the foramina on either side, 1 JF is present in 96 skulls on the right side and 92 skulls on the left side, whereas, 91 skulls showed a single JF on both sides. 2 jugular foramina are observed in 1 skull only on the right side, and 2 jugular foramina are observed in 5 skulls only on the left side, whereas 3 skulls showed doubled jugular foramina on both sides and 1 carotid canal is present on the right side and 1 carotid canal on the left side, with no duplication of the external opening of the carotid canal on either side.

Anteroposterior diameter of the foramen: As seen in Figure 4, it is observed that the range of the anteroposterior diameter of foramen ovale is 3-7.5 mm on the right side and 2-7 mm on the left side, with a mean of 5.255 mm on the right side and 4.84 mm on the left side. The comparison of the anteroposterior diameter of the foramen ovale on the right and left sides is found to be statistically significant ($P < 0.05$), with a diameter of the right side being greater than the left side. JF is 6-13.5 mm on the right side and 5-10 mm on the left side, with a mean of 9.885 mm on the

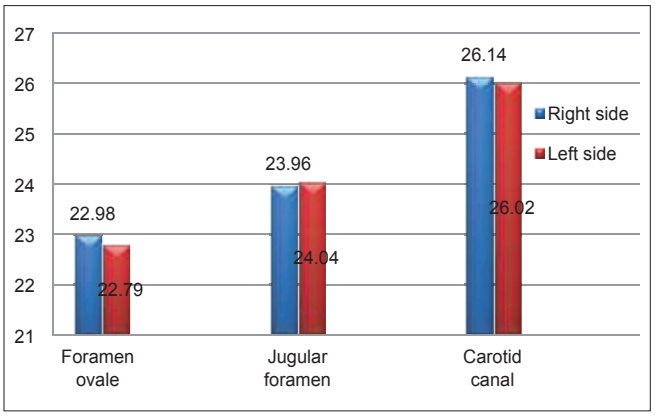

Figure 1: Position of the foramen from the midline

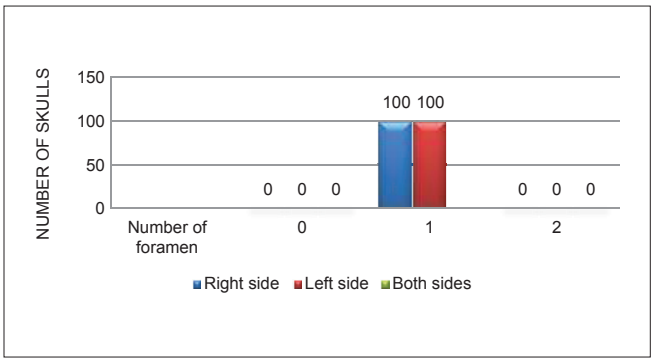

Figure 2: Number of foramen ovale and carotid canal opening on the right and the left sides

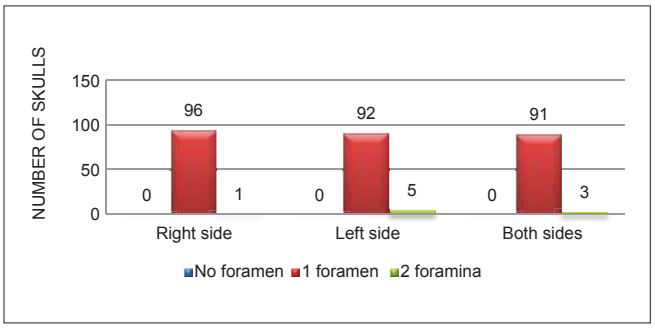

Figure 3: Number of jugular foramen on the right and the left sides

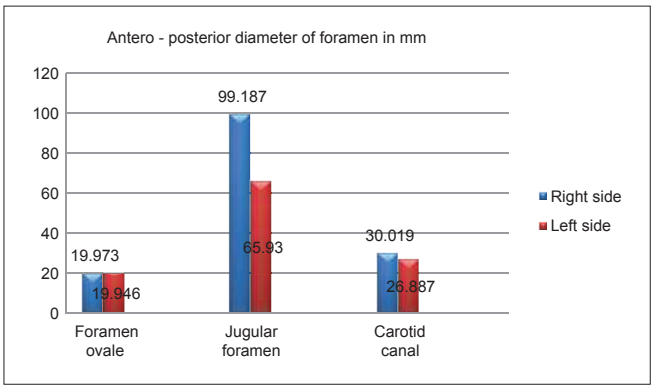

Figure 4: Comparison of anteroposterior diameters of foramen ovale, jugular foramen, and carotid canal on the right and the left sides

right side and 7.475 mm on the left side. The comparison of anteroposterior diameter of JF on the right and left sides is found to be statistically very highly significant ($P < 0.001$), with diameter of right side being greater than left side and external opening of carotid canal is 5-8.5 mm on the right side and 5-8 mm on the left side, with a mean of 6.795 mm on the right side and 6.285 mm on the left side. The comparison of anteroposterior diameter of the external opening of carotid canal on right and left sides is found to be statistically highly significant ($P < 0.001$), with diameter of the right side being greater than the left side.

Transverse diameter of the foramen: As seen in Figure 5, it is observed that the range of the transverse diameter of foramen ovale is 2-6 mm on the right side and 3.5-7 mm on the left side, with a mean of 4.87 mm on the right side and 5.185 mm on the left side. The comparison of the transverse diameter of foramen ovale on the right and the left sides is found to be statistically significant ($P < 0.05$), with a diameter of the right side being greater than the left side. The range of the transverse diameter of JF is 9-16 mm on the right side and 8.5-14 mm on the left side, with a mean of 14.665 mm on the right side and 14.39 mm on the left side. The comparison of transverse diameter of foramen ovale on the right and the left sides is found to be statistically very highly significant ($P < 0.001$), with diameter of the right side being greater than the left side, and the range of the transverse diameter of carotid canal is 4-7.5 mm on the right side and 4-7 mm on the left side, with a mean of 5.54 mm on the right side and 5.27 mm on the left side. The comparison of transverse diameter of external opening of carotid canal on the right and the left sides is found to be statistically significant ($P < 0.05$), with diameter of the right side being greater than the left side.

Area of the foramen: As seen in Figure 6, it is observed that the mean area of foramen ovale is 19.993 mm^2 on the right side and 19.946 mm^2 on the left side. The comparison of the area of foramen ovale on the right and the left sides is found to be statistically not significant ($P > 0.05$). The mean area of JF is 99.187 mm^2 on the right side and 65.93 mm^2 on the left side. The comparison of area of JF on the right and the left sides is found to be statistically highly significant ($P < 0.01$), with the area of the right JF greater than the left JF, and the mean area of external opening of carotid canal is 30.0193 mm^2 on the right side and 26.887 mm^2 on the left side. The comparison of the area of external opening of the carotid canal on the right is greater than the left carotid canal.

CA of the foramen: CA of the foramen is compared and is used to determine the sex of the skull. In the present study, to determine the sex of the skull, the CA of the foramen ovale, as seen in Table 1 and external opening

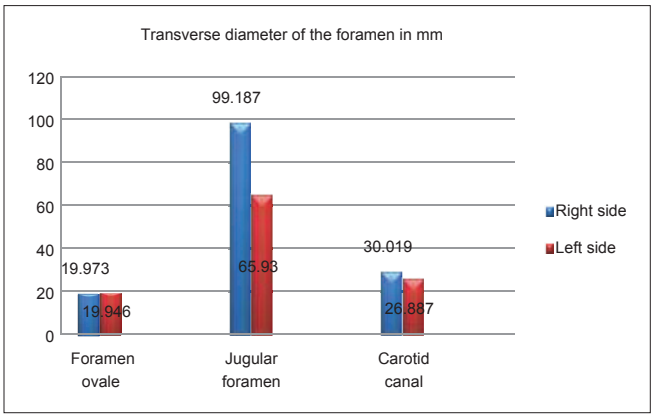

Figure 5: Comparison of transverse diameter of foramen ovale, jugular foramen, and carotid canal on the right and the left sides

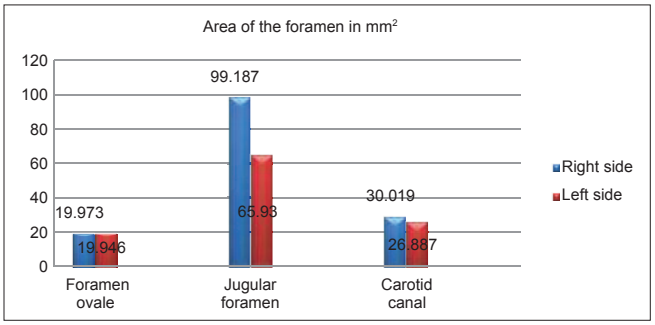

Figure 6: Comparison of area of foramen ovale, jugular foramen, and carotid canal on the right and the left sides

of the carotid canal, as seen in Table 2, are used. The CA are used to determine the LP, the skulls having CA greater than the LP are classified as male skulls and skulls with CA lesser than the LP are classified as female skulls. As seen in Table 1, the CA of foramen ovale with male range are 34.5-56.4 mm^2 and female range 14-31.6 mm^2, values 34.5 mm^2, and 31.6 mm^2 were the IP, for females and males, respectively. Any skull with CA reading less 34.5 mm^2 is regarded as a female skull and >31.6 mm^2 is regarded as the male skull. Alternatively stated, for CA of each foramen, if the measurement is conducted on the skulls of known sex was in range of 34.5-56.4 mm^2 for male skulls, then any skull of unknown sex with a value of the CA of the foramen <34.5 mm^2 is considered as female and thus 34.5 mm^2 is regarded as IP of female skulls. Similarly, if for female skulls of known sex, the measurement ranged between 14.0 and 31.6 mm^2 then any skull of unknown sex showing the measurement of the CA of the foramen >31.6 mm^2 is regarded as male skull. 31.6 mm^2 is regarded as IP for males. Mean and standards deviations are calculated for each range of the CA of the foramina for both the sexes. The male calculated range is 28.67-42.327 mm^2 and female calculated range is 3.092-41.708 mm^2, 28.67 mm^2, and 41.708 mm^2 are chosen as DP,[6,8,9] for females and males, respectively. Skulls with

measurements <28.67 mm^2 are identified as female skulls and >41.708 mm^2 as male skulls. Although IP and DP can identify sex accurately, only 15-20% of skulls can be sexed based on these, as most of the remaining skulls show the measurements in the overlapping neutral zone. Therefore, an LP is chosen in this study using multiple trial and error method. The LP is an absolute value found within both male and female ranges of the CA. It is so chosen that the vast number of male skulls showed values greater than it and bulk of female skulls showed values lesser than the chosen LP. Hence, as compared to IP and DP, the percentage of skulls that could be identified are far larger with LP.[10] Female skulls showed values lesser than the chosen LP. Hence, as compared to IP and DP, the percentage of skulls that could be identified are far larger with LP.[10] In case of foramen ovale the LP is 31 mm^2.

In the present study, with external opening of carotid canal, as seen in Table 2, CA with male range are 43.1-93.9 mm^2 and female range 39.2-49.6 mm^2, values 43.1 mm^2 and 49.6 mm^2 were the IP, for females and males, respectively. Any skull with CA reading less 43.1 mm^2 is regarded as a female skull and >49.6 mm^2 is regarded as the male skull. Alternatively stated, for CA of each foramen, if measurement is conducted on the skulls of the known sex were in range of 43.1-93.9 mm^2 for male skulls, then any skull of unknown sex with a value of the CA of the foramen <43.1 mm^2 is considered as female, and thus, 43.1 mm^2 is regarded as IP of female skulls. Similarly, if for female skulls of known sex, the measurement ranged between 39.2 and 49.6 mm^2, then any skull of unknown sex showing the measurement of the CA of the foramen >49.6 mm^2 is regarded as male skull 49.6 mm^2 is regarded as IP for males.

The male calculated range is 21.75-97.35 mm^2 and female calculated range is 31.32-55.18 mm^2, 21.75 mm^2, and 55.18 mm^2 are chosen as DP,[6,8,9] for females and males, respectively. Skulls with measurements <21.75 mm^2 are identified as female skulls and >55.18 mm^2 as male skulls. Although IP and DP can identify sex accurately, only 15-20% of skulls can be sexed based on these, as most of the remaining skulls show the measurements in the overlapping neutral zone. Therefore, an LP is chosen in this study using multiple trial and error method. The LP is an absolute value found within both male and female ranges of the CA. It is so chosen that a vast number of male skulls showed values greater than it and bulk of female skulls showed values lesser than the chosen LP. Hence, as compared to IP and DP, the percentage of skulls that could be identified is far larger with LP.[10]

In case of external opening of the carotid canal the LP is 47.5 mm^2.

The LP (47.5 mm^2) of the carotid canal and LP (31 mm^2) of foramen ovale combined are further utilized for the determining the sex of the given skull.

As seen in Table 3 and Figure 7, 83% of skulls were classified as male skull, and 12% of skulls were classified as female skulls, and the remaining 5% of the skulls were unclassified.

Table 1 shows the range, mean, calculated range. DP, SD, IP, and LP for determining the sex of the skull by using CA of foramen ovale.

Table 2 shows the range, mean, calculated range. DP, SD, IP, and LP for determining the sex of the skull by using CA of external opening of the carotid canal.

Table 3 shows the sexing of the skulls based on the CA of foramen ovale and CA of external opening of the carotid canal.

Table 1: Foramen ovale CA in mm^2

Details of measurement	Male	Female
Range	34.5-56.4	14-31.6
Mean	35.5	22.4
SD	±6.827	±6.43
IP	>31.6	<34.5
Calculated range mean±3 SD	28.67-42.32	3.09-41.7
DP	41.7	28.67
LP	>31	<31

CA: Combined area, IP: Identification point, SD: Standard deviation, DP: Demarcating points, LP: Limiting points

Table 2: Carotid canal CA in mm^2

Details of measurement	Male	Female
Range	43.1-93.9	39.2-49.6
Mean	59.55	43.25
SD	±12.6	±3.97
IP	>49.6	<43.1
Calculated range mean±3 SD	21.75-97.35	31.32-55.18
DP	55.18	21.75
LP	>47.5	<47.5

IP: Identification point, DP: Demarcating points, LP: Limiting points, CA: Combined area, SD: Standard deviation

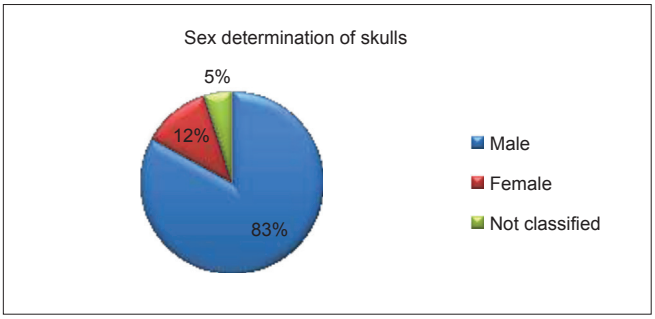

Figure 7: Sex determination of skulls by metrical parameters

DISCUSSION

The present study is compared with other studies. As seen in Table 4, the position of foramen ovale is in the range of 20-27 mm on the right side and 20-29 mm on the left side, the mean were 22.98 mm on the right side and 22.79 mm on the left side foramen ovale. The comparison of the position of foramina on the right and the left sides showed no statistical significance ($P > 0.05$). These findings correlate with a study done by Lang *et al.*[10] and Sharma and Garud.[11] The position of external opening of the carotid canal, as seen in Table 5 is in the range of 20-30 mm on the right side and 20-29 mm on the left side, the mean were 26.14 mm on the right side and 26.02 mm on the left side foramen. The comparison of the position of foramina on the right and the left sides showed no statistical significance. $t = 0.30$ and $P > 0.05$. The present study values correlate with study done by Sharma and Garud.[11]

As seen in Table 6, 1 JF is present in 96 skulls on the right side and 92 skulls on the left side, whereas, 91 skulls showed a single JF on both sides. Two jugular foramina are observed in 1 skull only on the right side, and 2 jugular foramina are observed in 5 skulls only on the left side, whereas, 3 skulls showed doubled jugular foramina on both sides. The present study correlates with the study done by Sturrock.[12]

In the present study, as seen in Table 7, the range of the area of foramen ovale is 8.6-28.2 mm^2 on the right side and 5.4-30.2 mm^2 on the left side, with a mean of 19.993 mm^2 on the right side and 19.946 mm^2 on the left side. In this studies were done by Somesh *et al.*[14] the mean area of foramen ovale was calculated as 30.808 ± 7.545 mm^2 and 31.310 ± 8.262 mm^2 on the right side and the left sides. As seen in Table 8, the range of the area of JF is 44.7-166.3 mm^2 on the right side and 35.3-102 mm^2 on the left side, with a mean of 99.187 mm^2 on the right side and 65.93 mm^2 on the left side. This study demonstrated a statistically significant asymmetry in the areas of right and left sided JF, with the area of the right foramina being more than the left foramen. Wysocki *et al.*[15] reported the surface area of the jugular foramina in males, left side as 51.11 mm^2 ranging from 21 to 126.2 mm^2, and on the right side as 57.53 mm^2, with a range of 12.5-94.9 mm^2. In females, the surface area on the left side as 53.83 mm^2, with a range of 15.8-1122.7 mm^2 and on the right side as 59.84 mm^2 with a range of 40.5-221.1 mm^2. The present study correlated with the study done by the author. As of external opening of the carotid canal, as seen in Table 9, the CA of external opening of the carotid canal is 59.55 mm^2 in males and 43.25 mm^2 in females.

The present study shows the mean distance of the foramen ovale on the right and the left side from the midline. It

Table 3: Sex determination using metrical parameters LPs of foramen ovale and external opening of carotid canal

Sex	Number of skulls	Percentage
Male	83	83
Female	12	12
Not classified	5	5

LPs: Limiting points

Table 4: Comparison of findings of the present study of the distance of foramen ovale from the midline with the other studies

Foramen ovale	Distance of the foramen from midline mean (mm)	
Investigators	Right side	Left side
Lang *et al.*[10]	20.9	22.5
Sharma and Garud[11]	22.13	21.71
Present study	22.98	22.79

Table 5: Comparison distance of the medial edge of the carotid canal with the other studies

Carotid canal	Position of the carotid canal from midline mean (mm)	
Investigators	Right side	Left side
Sharma and Garud[11]	25.31	24.88
Present study	26.14	26.02

Table 6: Comparing number of JF (septations) with the other study

JF	Percentage of skulls showing septations in JF (%)		
Investigators	Right side	Left side	Both sides
Sturrock[12]	1.3	10.9	3.2
Hussain *et al.*[13]	20.8	21	0
Present study	1	5	3

JF: Jugular foramen

Table 7: Comparing area of foramen ovale with other studies

Foramen ovale	Area of the foramen mean (mm^2)	
Investigators	Right side	Left side
Somesh *et al.*[14]	30.808	31.310
Present study	19.973	19.946

Table 8: Comparing area of the JF with the other studies

JF	Area of the foramen, mean (mm^2)	
Investigators	Right side	Left side
Wysocki *et al.*[15]	57.53	51.11
Present study	99.187	68.93

JF: Jugular foramen

Table 9: Comparing CA of the carotid canal with other studies

Carotid canal	CA of carotid canal (mm^2)	
Investigators	**Males**	**Females**
Chimalgi *et al.*[7]	38.51	29.28
Present study	59.55	43.25

CA: Combined area

is seen that the mean distance of foramen ovale from the midline is found to be 22.8 mm on the right side and 22.79 mm on the left side.

The distance of the medial edge of Carotid canal in the present study is found to be 26.14 mm on the right side and 26.02 mm on the left side.

The number of jugular foramen showing the presence of septations or bony spurs, in the present study was around 1% on the right side, 5% on the left sided foramen and 3% on both sided foramina.

The mean area of foramen ovale in the present study is found to be 19.973 mm^2 on the right side and 19.946 mm^2 on the left side foramen.

The mean area of jugular foramen in the present study is found to be 99.187 mm^2 on the right side and 68.93 mm^2 on the left side.

The mean CA of carotid canal in the present study is found to be 59.55 mm^2 in males and 43.25 mm^2 in females.

The CA of the foramina under study is calculated to determine the sex of the skull; it is calculated by adding the area of the right side and the left side foramen.

The CA used in the study is the CA of foramen ovale and external opening of the carotid canal. A LP is determined in the study for foramen ovale and carotid canal, which is used combined to differentiate male skulls from female skulls, in the present study the LP are 31 mm^2 for foramen ovale and 41.5 mm^2 for carotid canal. The skulls differentiated using these CA are 83% male skulls and 12% female skulls, however, the remaining 5% of the skulls cannot be differentiated because the CA of both foramina (foramen ovale and carotid canal) are overlapping with each other for male and female values.

CONCLUSION

The need for familiarity with the detailed anatomy of the foramina under study and their variations are very much essential in microsurgical techniques as many extracranial and intracranial lesions including intrinsic anomalies may affect the foramina. Pathological processes affecting the foramina include paragangliomas, schwannomas, metastatic lesions, and infiltrative inflammatory processes from surrounding structures such as the middle ear. Surgical resection is the treatment of choice in the majority of these cases. Advances in microsurgical techniques have made possible the removal of advanced lesions of the foramina, which were once assumed inoperable. A neurosurgeon becomes bolder in approaching the region with the anatomical and variational knowledge of these foramina.

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Original Article

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Clinico - Microbiological Profile of Necrotizing Fasciitis in a Tertiary Care Hospital

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Abstract

Introduction: Necrotizing fasciitis (NF) is a rare, rapidly progressive inflammatory infection of the fascia, with secondary necrosis of subcutaneous tissues. It is a surgical emergency which requires high degree of suspicion, early diagnosis, and treatment to reduce disease-associated morbidity and mortality.

Aim: This retrospective study was done to analyze NF; its clinical presentation, predisposing factors, and microbiological characteristics. This study also emphasizes on surgical management and prognosis of this condition.

Methodology: This is a retrospective study which included all the 30 patients admitted and treated for NF in Victoria hospital, Bengaluru between July 1, 2014 and June 30, 2015.

Results: There were 30 patients admitted and treated with NF during the study period. The mean age of occurrence was 48 years, who were predominantly male agriculturists. Most common site affected was calf. Various risk factors were identified with the major contributor being diabetes mellitus and main etiology being soft tissue infection. The patients presented with an array of physical findings, with tenderness present in almost all patients. Microbiologically half of the culture yielded growth, with polymicrobial being the most common type isolating *Pseudomonas*, *Staphylococcus*, *Klebsiell*a as organisms causing it. Mono microbial cultures mainly yielded *Escherichia coli* and *Streptococcus*. The majority of them responded well to antibiotics and surgical debridement with few patients needing amputation, all being diabetics. The mortality rate in our study was 13.3%.

Key words: Culture, Diabetes mellitus, Necrotizing fasciitis, Surgical debridement

INTRODUCTION

Necrotizing fasciitis (NF) is a rapidly spreading, inflammatory infection of the deep fascia, associated with secondary necrotic changes of subcutaneous tissue.[1] It is perhaps the most aggressive form of necrotizing soft tissue infection[2] and can spread rapidly to entire limb within hours.[3]

The first description of NF was given in the fifth century B.C by Hippocrates.[4] In 1921, Wilson coined the term "NF" which aptly describes its pathologic process.[5] Many other terminologies are used to describe same disease process such as Fournier's gangrene (perineum), phagedena gangrene, bacterial synergistic gangrene, and Meleney's gangrene (abdominal wall).

At the initial stages of presentation, it has a paucity of clinical signs and is difficult to differentiate it from cellulitis. A high index of suspicion is needed to diagnose it.

According to the microbiological characteristics, NF is classified into Type 1 (synergistic polymicrobial infections including anaerobes) and Type 2 (mono microbial infections), the former being more common.[6,7] The most common mono microbial infection causing organisms include Beta-hemolytic *Streptococcus*, *Staphylococcus aureus*, and *Clostridial* species. Common polymicrobial synergistic infection causing organisms includes *S. aureus*, *Staphylococcus pyogenes*, *Enterococci* species, *Escherichia coli*, *Pseudomonas* species, and anaerobic organisms such as *Bacteroides*.[8,9]

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The Precise pathogenesis of NF is unclear. Inoculation of microbes can occur through minor trauma, snake or insect bite, surgical incisions, etc., Under favorable environmental conditions such as immune compromised states, liver failure, renal failure, and diabetes organisms multiply to cause disease process. It can occur in any part of the body, but more commonly in some anatomic areas such as extremities, abdomen, groin, and perineum.

NF first starts in deep tissue plane, so superficial skin signs may not be evident initially. This usually leads to a delayed diagnosis of this condition. Many patients present with toxic features due to sepsis without any underlying signs. Later, they may develop edema, tenderness, vesicle, bullae, and crepitus.

This condition is usually diagnosed by clinical features, but other investigations may help to confirm it. Plain X-ray may show subcutaneous gas. Computed tomography scan and magnetic resonance image may show asymmetrical fascial thickening, fat stranding, and gas tracking along fascial planes. Tissue biopsy is the diagnostic test which reveals necrosis, polymorph nuclear infiltration and thrombosis of vessels.

The management includes initial resuscitation, supportive care, adequate control of risk factors such as blood sugars; intravenous antibiotics, extensive debridement, and occasionally radical procedures such as amputations.

The mortality rates of this disease have remained alarmingly high with reported mortality rates ranging from 6% to 76%.[10] Multiple studies have shown that delay in the diagnosis and consequently delayed operative debridement which has caused increase in the mortality.[11]

The purpose of this study is to analyze NF, its clinical presentation, predisposing factors, and microbiological characteristics. This study also emphasizes on surgical management and prognosis of this rare surgical emergency.

METHODOLOGY

The authors conducted a retrospective study that included the 30 patients admitted and treated at Victoria hospital, Bengaluru between July 1, 2014 and June 30, 2015 for NF. Only those patients with diagnosis confirmed by histopathological examination were included in the study.

Clinical microbiological profile of the patient was studied with respect to age, sex, clinical features, site/location of infection, risk factors, etiological factors, microbiological characteristics, and the treatment outcome.

RESULTS

The minimum age of appearance of NF was 22 years, and the maximum being 84 years (mean age = 48).

There were 28 males (93.3%) and only 2 females (6.7%). About 66.6% of the people were agriculturists by occupation.

The majority of the patients had involvement of calf region (70%). The various sites affected are shown in Table 1.

Among the risk factors Type 2 diabetes mellitus was present in 21 (70%) cases. Totally, 8 (26.6%) had hypertension, 3 (10%) had renal failure, HIV positive status in two (6.6%) patients. In 8 (26.6%) patients, no risk factor could be identified and 6 (20%) were aged more than 60 years.

Figure 1 bar diagram shows the risk factors associated with NF.

Etiological factors were soft tissue infection in 16 (53.3%), trauma in 8 (26.6%), snake bite in 2 (6.7%), post-operative status 2 (6.7%), and unknown etiology in 2 (6.7%).

Figure 2 pie chart shows the different etiological factors of NF.

Table 1: Different sites of involvement of necrotizing fasciitis

Lower limb	
Foot	1
Calf	21
Thigh	2
Foot+calf	1
Calf+thigh	1
Upper limb	2
Abdomen	2

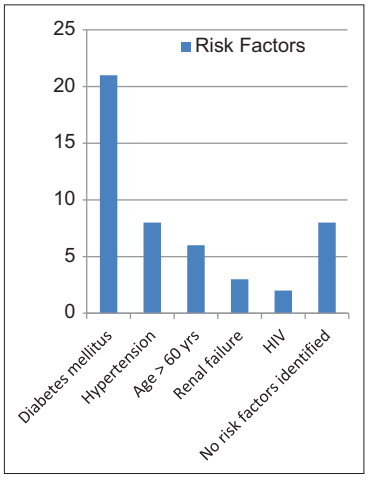

Figure 1: Various risk factors associated with necrotizing fasciitis

Physical findings were varied. Tenderness was the most common and was seen in 28 patients (97.9%), followed by edema in 26 (91.5%), erythema 15(50%), skin vesicles/bullae 5 (16.6%), soft tissue crepitus 10 (33.3%), hypotension 6 (20%), fever 8 (26.6%), tachycardia 16 (53.2%), and altered mental status 4 (13.3%).

Figure 3 bar diagram is showing an array of physical findings.

After culture 15 (50%) showed no growth and 15 (50%) showed growth. 40% mono microbial and 60% were polymicrobial (Figure 4). Of all the cultures, 80% were aerobic, 6.6% anaerobic and 13.3% mixed. The most common organism isolated was *Pseudomonas aeruginosa* (33%) followed by *S. aureus* (20%) and *Klebsiella* (13.3%) in poly microbial culture. Beta-hemolytic *Streptococcus* and *E. coli* were found to be the important cause of mono microbial infection (40%) in NF.

Figure 4 pie diagram is showing culture growth patterns.

Mean number of surgical debridement was 2.5. Amputation was done in 3 patients (10%) with two below knee amputation, one above knee and all were diabetic.

4 (13.3%) patients died, 26 (87.7%) recovered.

DISCUSSION

NF is a rapidly spreading infection involving the skin, superficial fascia, and subcutaneous fat. It is a surgical emergency that requires a high degree of suspicion, early diagnosis, and aggressive debridement to prevent sepsis and mortality. The mortality rate in our study was 13.3% which is lower when compared to other literature.[6,12]

NF has affected wide age group, but the mean age of presentation was 48 years with most of them being male and with agriculture as their occupation. The most common site of involvement was the calf.

Above results can be explained by the fact that it commonly affects the working age group who are barefoot walkers, frequently encountering trauma to exposed parts, especially lower limbs. There are various risk factors which predisposes to this condition such as diabetes, hypertension, HIV status, and chronic renal failure among which diabetes was the most common risk,[13] which was present in more than two-third of the patients. Above finding was consistent with other studies. Increased blood sugars predispose to the environment of low oxygen tension and acts as a good substitute for bacterial growth. Etiological factors included soft tissue infections, trauma, snake bite, postoperative

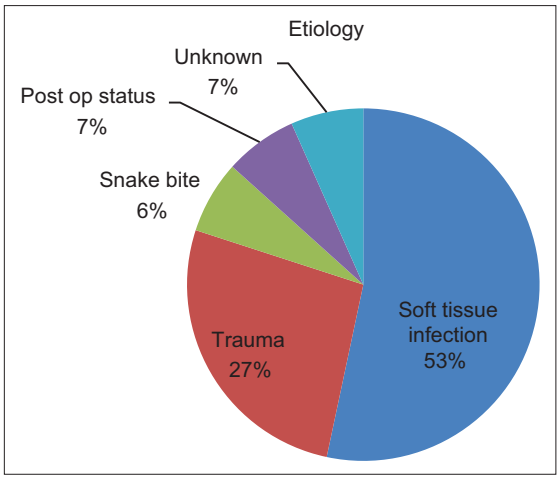

Figure 2: Various etiology for necrotizing fasciitis

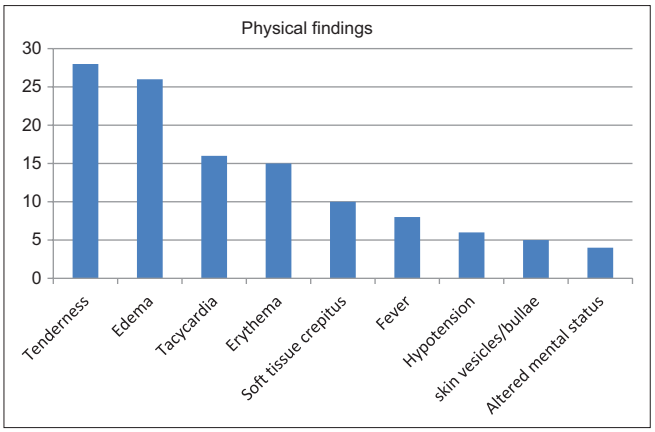

Figure 3: Various physical findings in cases of necrotizing fasciitis

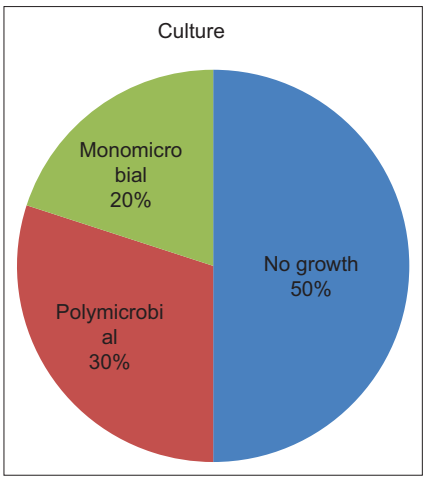

Figure 4: Culture growth pattern

status, with soft tissue infection being the prime cause. Above observation can be explained by the fact that most of them presented and were admitted as cellulitis in whom later involved deeper tissues, in diagnose later as NF. The patients presented with a wide range of clinical features

such as tenderness, edema, erythema, skin vesicle/bullae, soft tissue crepitus, hypotension, fever, tachycardia, and altered mental status in decreasing order of their frequency. In our study, tenderness and edema were the consistent physical findings, which suggest that these may be the early signs of NF. Soft tissue crepitus, which is the characteristic finding, was an inconsistent presentation seen in only 33.3% of the patients.

In our study, 50% of cultures yielded growth, out of which polymicrobial was the leading cause. The most common organism isolated was *P. aeruginosa*, followed by *S. aureus* and Klebsiella. Beta-hemolytic *Streptococcus* and *E. coli* were found to be the important cause of mono microbial infection.

Most of the patients recovered with appropriate antibiotics and surgical debridement, with 10% requiring amputation, all of them being diabetic, which suggests the aggressiveness of this disease in diabetics.

CONCLUSION

NF is relatively rare but dreaded surgical emergency. Arriving at the diagnosis is one of the challenging tasks in treating patients, which requires a high index of suspicion. The outcome is influenced by prompt early diagnosis, the timing and extent of surgical debridement and even radical procedures such as amputation, when necessary to prevent mortality.

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Original Article

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Enthesophytes and Tubercles of the Calcaneum: An Anatomical and Clinical Understanding of the Relationship between Calcaneal Spurs and Plantar Heel Pain

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Abstract

Background: Calcaneus is the largest of all the bones that constitute the skeleton of the foot. It is also the largest tarsal bone and plays a pivotal role in weight transmission, weight bearing, gait, and posture. In professions involving long durations of standing and in disorders such as obesity there may be growth of abnormal bone tissue at the site of tendinous attachments known as enthesophytes or spurs. Radiologically these spurs may differ from the naked eye and clinical examinations. The apices of these spurs are often embedded in the plantar fascia of the foot.

Aim: The aim of the present study was to observe the enthesophytes and tubercles of dry adult human calcanei.

Materials and Methods: One hundred dry adult human intact calcanei were obtained from the four different medical colleges in the state of Bihar and observed in detail. Bones were of unknown, age and sex and were supposedly from cadavers of Bihar origin.

Results: The incidence of calcaneal spurs was reported to be 22% with laterality of 14 and 8 in right and left sides, respectively. Our findings have been compared with those of other researchers. Medial tubercle was larger than lateral tubercle, and all enthesophytes were observed to be originating from the medial tubercle only.

Conclusion: Calcaneal enthesophytes or spurs may be related to the nature of work or orthopedic pathology. Probable other factors that may increase the incidence of spur formation are uncontrolled weight gain, advancing age, and constant use of uncomfortable footwear.

Key words: Calcaneus, Enthesophytes, Pain, Spurs, Tubercles

INTRODUCTION

The foot extends from the point of the heel to the roots of the toes. Superior and inferior surfaces of the foot are referred to as dorsum and plantar, respectively. The foot is divided into tarsus and metatarsus. The tarsus is the posterior half formed by the tarsal bones, which are arranged in two rows. The proximal row consists of talus and calcaneus, whereas the distal row consists of cuboid, navicular, and cuneiform. The largest of the tarsals, the calcaneus forms an irregular block of bone.[1] It is also referred to as heel bone and forms a major component of the skeleton of the hindfoot and prominence of the heel.[2] The calcaneus is the longest, strongest, and largest of all the tarsal bones.[3] It is the first bone in the foot to ossify and is also the most frequently injured tarsal bone. It transmits the weight of the body to the ground. This bone also provides leverage for the action of the posterior calf muscles attached to its broader and non-articular posterior surface.[4] Very rarely, the calcaneum may also present itself with a set of accessory bones.[5,6] Being irregularly cuboidal in shape,

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it presents six surfaces and a shelf-like bony projection the sustentaculum tali which as the name implies sustains the head of the talus and also bears the greatest weight per area. The calcaneus bears four tubercles, anterior, lateral, and medial which are present on the inferior or plantar surface and a small peroneal tubercle on the lateral surface. Occasionally, an enthesophyte has been observed growing anteriorly along the calcaneal tuberosity along the entire width of the bone. Plantar fasciitis is the most common cause of plantar heel pain. Clinically, the etiology and pathophysiology of enthesophyte formation in calcaneum has not yet been clearly understood. In spite of different treatment modalities of a heel spur, the association of incidence of calcaneal spur with clinical and functional parameters in nonconclusive. It has been suggested that longitudinal traction or vertical compression may be the causative factors. Enthesophyte formation usually occurs at the site of ligamentous and tendinous insertions into the bone. An enthesophyte tends to grow in the direction of natural pull of ligaments and tendons involved.[7] The lateral and medial tubercles of calcaneus provide sites for the origin of muscles of the various layers of the sole. The medial tubercle gives origin to abductor hallucis, flexor digitorum brevis, and abductor digiti minimi. The lateral tubercle gives origin to abductor digiti minimi and lateral head of flexor digitorum accessorius. The anterior tubercle provides attachment to the short plantar ligament, and the long plantar ligament is attached to the rough strip between the three tubercles. The peroneal tubercle lies between the tendons of peroneus brevis above and peroneus longus below. Variations in the gross morphology of the calcaneus have been reported in the literature with reference to sex, race, and occupation; but there are few citable references regarding the observation on tubercles and incidence of calcaneal enthesophytes. The most enthesophytes are encountered radiographically or clinically during surgical procedures, but our study focuses on observing the incidence of enthesophytes in dry bone by naked eye examination.

MATERIALS AND METHODS

One hundred dry intact adult human calcanei were observed in details for enthesophytes. The bones were supposedly of Bihar origin. Sex of the bone was not taken into consideration. Specimens that showed signs of damage or previous fracture were discarded from the study. Naked eye examination of all the bones was performed, and incidence of spurs was recorded. Handheld magnifying lens was used for observing the peroneal tubercle (Figures 1-4).

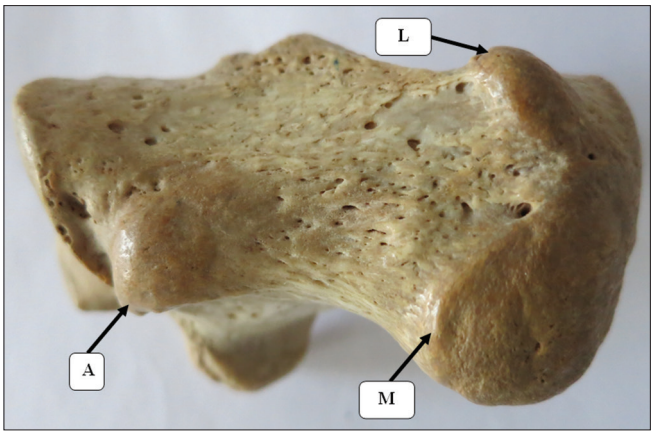

Figure 1: Plantar surface of a normal calcaneus showing the normal morphology of three tubercles (A) anterior (M) medial (L) lateral. The medial tubercle is larger than all other tubercles. Concavity present between the three tubercles in a normal calcaneus is smooth. Peroneal tubercle is not shown in this figure

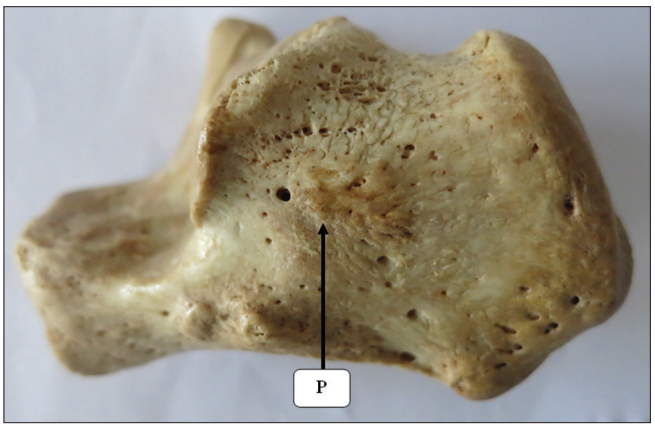

Figure 2: Lateral surface of a normal calcaneus showing the normal morphology of the peroneal tubercle (P). Concavities present both above and below the tubercle are for the tendons of peroneus brevis and peroneus longus, respectively

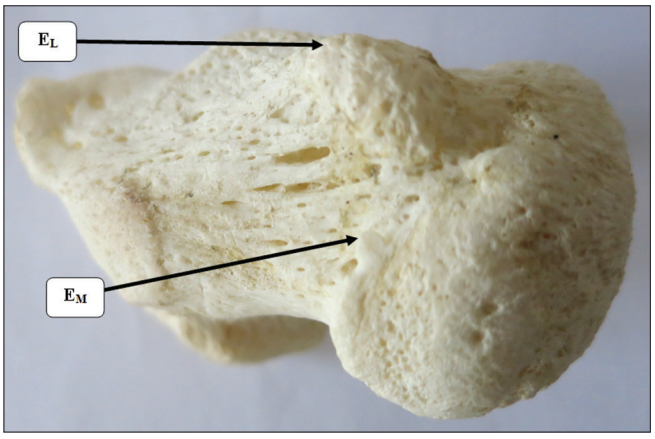

Figure 3: Specimen of calcaneus showing small enthesophytes arising from both lateral and medial tubercles. E_M and E_L denote the enthesophytes arising from the medial and lateral tubercles, respectively

Inclusion Criteria

- Bones belonging to cadavers of Bihar origin
- Bones with intact gross morphology and tubercles
- Bones belonging to adult
- Bone which were available in pairs.

Exclusion Criteria

- Bones which were unpaired
- Bones with abnormal morphology and tubercles
- Bones belonging to children
- Bones which showed signs of previous fracture.

Observation

Of 100 calcanei observed (n = 100) enthesophytes were observed in 22 specimens. All the specimens studied presented with four tubercles. Medial tubercles were larger in all specimens. The total incidence in this study was 22% out of which fourteen were on the right side, and eight were on the left side, respectively (Tables 1-4).

Figure 5 shows the incidence of enthesophytes in the present study.

Figure 6 shows a pictorial representation of laterality of incidence of enthesophytes in the present study. On the right side, enthesophytes were observed in 14 out of 22 calcanei. On the left side, enthesophytes were observed in 8 out of 22 calcanei.

Table 1: Incidence of enthesophytes in this study

Total number of calcanei observed	Incidence of enthesophytes
n=100	22%

Table 2: Number of tubercles in each calcaneus observed

Total number of calcanei observed	Tubercles present in each calcaneus
n=100	A/P/L/M

A: Anterior, P: Peroneal, L: Lateral, M: Medial

Table 3: Largest of all the tubercles in each calcaneus observed

Total number of calcanei observed	Largest tubercle
n=100	Medial tubercle

Table 4: Incidence of laterality of enthesophytes in this study

Incidence of enthesophytes	Laterality of incidence
22%	R=14/22 (64%) and L=08/22 (36%)

DISCUSSION

Enthesophytes were observed in 22 out of 100 bones examined in this study. In this study, we observed that there was no spur formation from either of the anterior, lateral, and peroneal tubercles of any specimen. Only in three specimens, we observed enthesophytes originating

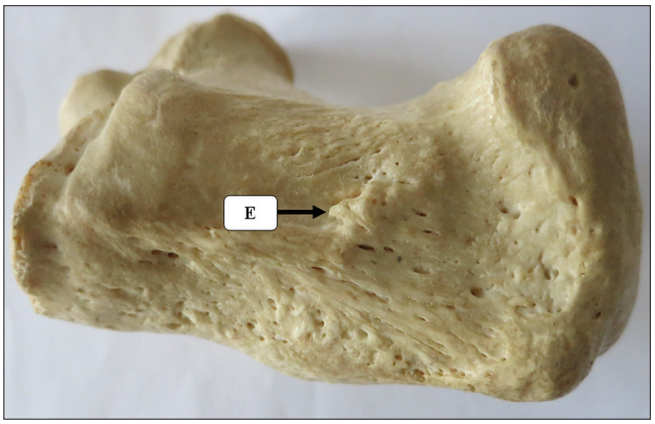

Figure 4: Specimen of calcaneus showing an enthesophyte arising from the concavity of the plantar surface of the anterior, medial, and lateral tubercles. Location of the enthesophyte is indicated in figure by an arrow (E)

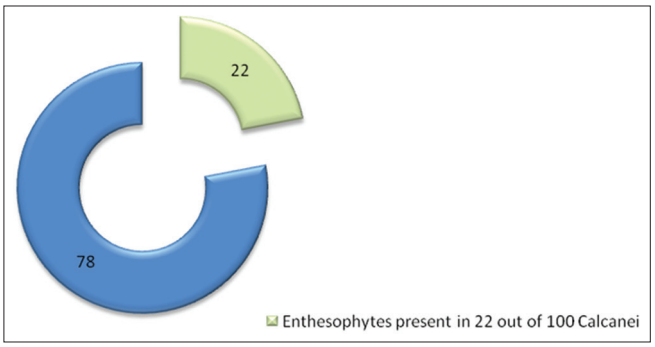

Figure 5: Incidence of enthesophytes. Enthesophytes were observed in 22 out of 100 calcanei studied with an incidence of 22%

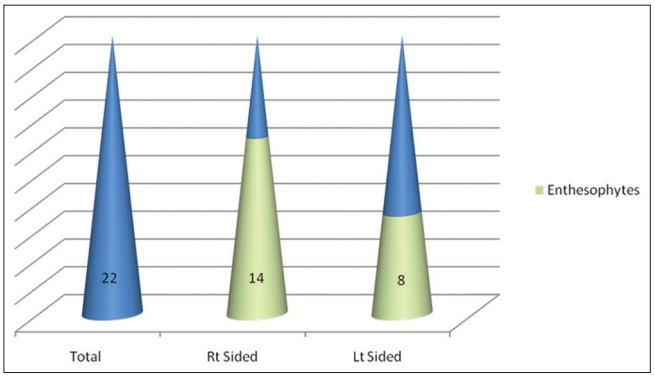

Figure 6: Pictorial representation of laterality of incidence of enthesophytes

Table 5: Comparison of incidence of calcaneal enthesophytes in different studies

Researcher	Year	Sample size (*n*)	Incidence (%)
Resnick[14]	1977	Not available	22
Prichasuk and Subhadrabandhu[15]	1994	Not available	15.5
Riepert[16]	1995	Not available	15.7
Menz *et al*.	2008	216	55.1
Perumal	2013	218	56
Kullar *et al*.	2013	200	26.5
Omar	2015	100	22

from both medial and lateral tubercles. These findings have been pictorially represented in Figures 1 and 2. Such enthesophytes may occur on the plantar surface of the bone due to deposition of calcium salts and on the fibrous tissue attached to the tubercles. Many such related studies have highlighted this occurrence of enthesophyte formation based on radiological data of the western population. The formation of spurs was due to compression force exerted on the bone due to weight bearing.[8] Irrespective of their origin calcaneal spurs result in heel pain and interfere with daily activities. Calcaneal spurs have also been reported in young individuals.[9] Intra-articular incongruity, varus and valgus misalignment of the heel, widened heel due to lateral bulge, shorter heel height, decreased ankle dorsiflexion, and elevated Achilles tendon insertion leading to weakening of the gastrocnemius-soleus complex can result in enthesophyte formation in the calcaneus. The attachment of the plantar fascia to the calcaneus may become ossified, or a similar spur may occur related to the insertion of the tendo Achilles. Spurs are usually seen in the middle age or later and are usually asymptomatic.[10] All enthesophytes observed had a hook or semi-hook like appearance from the lateral aspect. It could be due to an increased axial load or obesity.[11] Calcaneal enthesophytes appear to be multifactorial in origin and in our study it is evident that all enthesophytes are extending from the medial tubercle. A detailed analysis of patterns of anterior talar articular facets in a series of 401 Indian calcanei revealed four types. Type I (67%) showed one continuous facet on the sustentaculum extending to the distomedial calcaneal corner; Type II (26%) presented two facets, one sustentacular and one distal calcaneal; Type III (5%) only a single sustentacular facet; and Type IV (2%) showed confluent anterior and posterior facets.[12] In this study, the incidence of calcaneal enthesophytes was lower than Menz *et al*.,[13] Anand[8] and Kullar *et al*.[2] gender may be a cofactor leading to heel pain.[2] We have compared to our findings with those of previous researchers in Table 5. A higher frequency of calcaneal spur formation in individuals with abductor digiti minimi has also been reported.[5] As sex and age of the bones were not considered it was not possible to comment on the gender and age group having higher or lower incidence of calcaneal enthesophytes. A further study with these parameters may be performed in the future. Our findings shall serve as a guide for podiatrists with who deal with calcaneal enthesophytes.

CONCLUSION

Calcaneal enthesophytes are bony outgrowths of the calcaneus that are common findings on radiographic examinations of the foot and ankle. Such outgrowths can extend on the whole extent of the calcaneus. Anatomical knowledge of calcaneal enthesophytes is clinically relevant as these spurs affect the normal alignment of the calcaneus. Misalignments lead to instability and are a frequent cause of heel pain. Enthesophyte formation usually occurs in the medial tubercle of calcaneum and is probably due to biomechanical reasons. The factors that aggravate the incidence of spurs are increasing weight, obesity, advancing age, and concurrent orthopedic diseases. Ethnic and developmental variations must also be considered. Theoretically, calcaneal enthesophytes may be an adaptive response to vertical compression of the heel. Regular wearing of uncomfortable or improper footwear can also be a causative factor.

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Original Article

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Side Effects Encountered in Treatment of Multidrug-resistant Tuberculosis: A 3-Year Experience at First Dots Plus Site of Chhattisgarh

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Abstract

Background: The emergence of strains of *Mycobacterium tuberculosis* that are resistant to anti-mycobacterial agents is a worldwide problem.

Materials and Methods: We included patients who are admitted to the Institute between 2011 and 2015 with an intention to report frequency of side effects in cases of multi-drug resistant tuberculosis (MDR-TB), as a part of pharmacovigilance program. A questionnaire-based study of 150 patients who received MDR-TB treatment under directly observed treatment, short-course plus program.

Results: One or more side effects developed in 125/150 (83.33%) of patients. Gastrointestinal side effects (76%); psychiatric (44.7%); arthralgia and hyperuricemia (31.3%); central nervous system (22.7%); ototoxicity (22%); peripheral neuropathy (18.7%); menstrual disturbances (4.7%); hepatitis, visual disturbances, nephrotoxicity (4% each); and hypothyroidism (0.6%).

Conclusion: Timely management of side effects helps in retaining patients that lead to the success of treatment, despite the high occurrence of side effects.

Key words: Chhattisgarh, Directly observed treatment short-course, Multidrug-resistant tuberculosis, Side effect

INTRODUCTION

The emergence of strains of *Mycobacterium tuberculosis* that is resistant to antimycobacterial agents is a worldwide problem.[1] Multidrug-resistant tuberculosis (MDR-TB) has been an area of growing concern and is posing a threat to the control of TB. A project by the international union against TB and lung diseases started in 1994-1997 for global drug resistance surveillance with the help of World Health Organization (WHO). The global TB report 2014 estimated that a 3.1% of newly diagnosed and 20.5% of previously treated cases had MDR-TB. It has been estimated that 480,000 cases emerged, and 210,000 deaths occurred due to MDR-TB globally in 2013. In India, estimates showed that the prevalence of MDR-TB among new and previously treated patients was 2.2% and 15%, respectively. It is estimated that 99000 cases of MDR-TB emerge every year out of which 62000 were among notified cases of TB in 2013. MDR-TB is usually a man-made problem and results mainly due to mismanagement of the disease. Serious side effects have been observed in many studies.[2]

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The most cost-effective public health measure for the control of TB is the identification and cure of infectious TB cases, i.e., patients with smear-positive pulmonary TB. Nevertheless, National TB Programs provide for the identification and cure of all patients with TB. These guidelines cover the treatment of patients, both adults and children, with smear-positive pulmonary TB, smear-negative

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pulmonary TB, and extrapulmonary TB.[3] Adequate timely early diagnosis, optimal treatment, and proper compliance are needed to curb the epidemic. The last part compliance is very important because the lack of compliance in previous treatment is usually a cause of MDR-TB. The long 2-year course of MDR-TB treatment with reserve antitubercular drugs is full of side effects, which many times add to the agony of patients, and they leave treatment. These reserve drugs are having a lot of side effects. To know the frequency of side effects, the present study was done.

Definition of MDR-TB

MDR-TB is defined as disease due to *M. tuberculosis* that is resistant to isoniazid and Rifampicin with or without resistance to other drugs (the culture and drug susceptibility test results being done from an accredited laboratory).[4] MDR-TB, is an important obstacle to TB control. In 2013, MDR-TB represented 480,000 incident TB cases worldwide and, as denoted by global experts including the WHO.[5]

Studies claim that medications used in the treatment of MDR-TB are less potent and associated with a greater number of side effects.[6] Rapid and early diagnosis of MDR-TB improve survival and are of a public health benefit.[7]

MATERIALS AND METHODS

This study was done at first directly observed treatment, short-course (DOTS) plus the site of Chhattisgarh state established in the department of Chest and TB Chhattisgarh institute of medical sciences, Bilaspur (Chhattisgarh). We included patients who are admitted to the Institute between 2011 and 2015. First, MDR suspects were identified here and all linked districts. These suspects were screened by gene expert and confirmed by intermediate reference laboratory (i.e., reference lab) Raipur under DOTS-plus program. All patients who were resistant to rifampicin (R) and isoniazid (H) were diagnosed as MDR-TB. All rifampicin resistant (monoresistance) patients were also treated for MDR-TB. After diagnosis patients were admitted and screened as per DOTS-plus framework. All HIV-positive patients were excluded from the study. All patients having other preexisting diseases were also excluded from the study. We did not include transferred outpatients. Side effects observed during the course of 18-24 months of treatment were included. Doses of drugs given were according to weight band as per revised national TB control program. Dosages and weight (in kg) band recommendations are as shown in Table 1. All patients had tab pyridoxine 100 mg. All patients were hospitalized for an initial period of 7 days. After discharge monitoring was done monthly by recalling the patients or by the help of DOTS-plus supervisors. All patients who completed at least 6 months of treatment were included. All new side effects which occurred after initiation of MDR-TB treatment were listed and evaluated. Their side effects which appeared at any time during treatment were recorded (i.e., intensive/continuation phase). Monthly meetings of senior treatment supervisors also contributed to data collection. Among the 200 plus patients registered in our DOTS-plus site, 150 patients met the above criteria and included in the study. An investigation done were as per DOTS-plus program. Additional investigations such as audiometry were done when needed. The DOTS-plus regime employed was kanamycin, ethambutol, pyrazinamide, cycloserine, ethionamide, levofloxacin, and pyridoxine; sometimes para-aminosalicylic acid (PAS) was used. If patient's weight changes, his doses were also changed according to weight band with his next supply of drugs.

OBSERVATION AND RESULTS

We registered 150 patients for this study. Among them, 108 were male (72%) and 42 (28%) were females with the overall mean age of 34.8 years. Injection kanamycin was administered in IP, i.e., first 6 months, on all weekdays except Sundays.

The side effects are summarized in Table 2. The side effects of varying degree were observed in 125/150 patients (82.33%), although most of the side effects were mild in nature and subsided with pharmacotherapy and counseling. Gastrointestinal (GI) side effects were the most common 114/150 (i.e., 76% of total patients) nausea, vomiting, loss of appetite were the most common. These symptoms were responded to counseling, food and drug intake advice. In severe cases, we had to treat with pantoprazole 40 mg + domperidone 30 mg. None of the patients left treatment due to these side effects. Most of these side effects occurred during first 6 months of treatment.

Ototoxicity was also a common side effect with the hearing loss of varying degree. We did audiometry in all patients complaining of hearing loss. This ototoxicity appeared in 33/150 patients (22%). The majority of patients treated were with increased hydration, ginko biloba, and counseling. This side effect mostly occurred during first 6 months. Our three patients went almost deaf during treatment and in five patients' kanamycin were stopped. Central nervous system symptoms were observed in 34 patients (22.7%). The most common was dizziness tremors and insomnia. They responded to symptomatic treatment, one patient of convulsions also responded to symptomatic treatment. No patient left treatment due to complications.

Arthralgia and hyperuricemia occurred in 47 cases (31.3%), and most cases occurred during first 6 months. Symptoms of

most patients were very trivial and did not need any treatment, while although etoricoxib 120 mg was used in some patients. Hyperuricemia was treated with febuxostat 40 mg BID or 80 mg BID, and all patients responded. Although morbidity was there, but it did not cause any disruption in treatment.

Slight nephrotoxicity observed in 6 patients (4%), i.e., elevation of 0.5 mg serum creatinine from base level but did not cause any problem in management, visual disturbances occurred in six patients (4%) who were treated symptomatically, and counseling, five patients had refractory error which was corrected.

Hepatitis occurred in six patients (4%), and we have to stop hepatotoxic drugs for 10-14 days. The patients responded to symptomatic management.

Most patients with dermatological complications complained of itching (21/150, i.e. 14%) which responded to symptomatic treatment with cetirizine 10 mg. Two patient developed rashes which were managed by a dermatologist. No patient left the treatment.

One patient developed hypothyroidism (although he was not taking PAS), which responded to oral thyroxine, gynecomastia was developed in two cases counseling was done for that. Menstrual irregularity occurred in 7 patients (4.7%), which did not cause any change is treatment. All female patients were counseled for family planning.

Psychiatric disturbances occurred in 67 patients (44.7%); most patients suffered from anxiety and mild depression who responded to counseling and in some cases treated with drugs such as clonazepam and escitalopram. More severe cases were treated by a psychiatrist with olanzapine 10 mg, suicidal tendencies developed in 2 patients and 5 patients suffered from severe psychosis. Two patients continued treatment by stopping cycloserine, but 5 patients left the treatment in the continuation phase.

Peripheral neuropathy developed in 28 patients (18.7%). This side effect increased with the duration of treatment. Most patients responded by increasing the dose of pyridoxine and by adding methylcobalamin and sometimes pregabalin. One patient developed severe neuropathy and cycloserine was replaced by PAS, and dose of ethionamide was reduced; however, she continued treatment under cover of other medicines.

DISCUSSION

Chan *et al.* (2004) stated improvement was statistically significant for surgery and among older patients for fluoroquinolone therapy.[8] The side effects of varying degree occurred in 125/150 patients (83.33%) but the majority of these are very trivial and responded to symptomatic treatment and counseling, GI side effects were the most common but responded to treatment. Most important side effects we observed were ototoxicity (22%) and psychiatric (44.7%). These side effects were more disturbing and caused the threat of losing our patients. We should keep track of these two side effects. Gatell *et al.* 1987 analyzed risk factors predisposing to auditory toxicity of aminoglycosides from records of 187 patients enrolled in three prospective randomized trials comparing the toxicity of netilmicin, tobramycin, and amikacin.[9] Ototoxicity is more important in initial 6 months and psychiatric disorders increase with length of treatment. In these two disorders, high familial support is required so patient and his family members to be counseled properly. There two are the most common reason of default in our study. Timely intervention, treatment, and counseling are the key to success. The

Table 1: Dosage and weight band recommendations

Drug	16-25 Kg	26-45 Kg	>45 Kg
Kanamycin (mg)	500	500	750
Levofloxacin (mg)	250	750	1000
Ethambutol (mg)	400	800	1200
Pyrazinamide (mg)	500	1250	1500
Cycloserine (mg)	250	500	750
Ethionamide (mg)	375	500	750
PAS (mg)	5	10	12
Pyridoxine 50 (mg)	50	100	100

PAS: Para-aminosalicylic acid

Table 2: Distribution of side effects

Side effects	First 6 month	After 6 month	Total
GI: Diarrhea, vomiting, abdominal pain, loss of appetite, metallic taste, sulfurous belching, and excessive salivation	93	21	114
Ototoxicity	31	2	33
CNS symptoms: Dizziness, vertigo, convulsions, slurred speech, tremors, and insomnia	21	13	34
Arthralgia and hyperuricemia	35	12	47
Nephrotoxicity	5	1	6
Visual disturbances	4	2	6
Hepatitis	3	3	6
Skin rash and pruritus	15	6	21
Psychiatric	31	36	67
Hypothyroidism and goiter	1	-	1
Gynecomastia and menstrual disturbances	4	3	7
Peripheral neuropathy	8	20	28

CNS: Central nervous system, GI: Gastrointestinal

frequency and early occurrence of ototoxicity may be due to the extended exposure to aminoglycosides during or prior to MDR-TB treatment. It is worth noting that 38.3% of patients had previous exposure to streptomycin. This is consistent with the finding from Moore *et al.*, who showed an association between ototoxicity and cumulative duration of aminoglycosides. We did not find nephrotoxicity due to aminoglycosides that much high as ototoxicity and was similar to observation of other workers. Psychiatric disorders were also very frequent in our study. Many patients under treatment suffered from some of depression, and this was partly attributable to a loss of confidence due to long-suffering, previous treatment failures and long treatment need. Hence, there is need of good counseling by doctors and other staff to win the trust and confidence of the patient. The main culprit of psychiatric disorders was cycloserine, and we have to stop or replace drug in some patients because we were not able to manage patient with counseling and pharmacotherapy. A headache was attributed to quinolones in some patients and responded to pharmacotherapy and counseling. Hypothyroidism was very few because very few patients were on PAS. In one female patient severe disturbing peripheral neuropathy occurred, and we had to stop cycloserine and ethionamide dose were reduced. Hence, ototoxicity, psychiatric, and neurological complications are more important and of concern. Prasad *et al.* opined that the primary objective in the control of MDR-TB is to prevent its development in the first place. This can be done by DOTS, which is the most cost-effective method of treatment and prevention of MDR-TB.[10]

CONCLUSION

There was a high rate of side effects in the treatment of MDR-TB. However, a high rate of side effects does not prevent care of these patients. We conclude by saying that effect should be made to continue treatment in the face of side effects as long as they fall short of being life-threatening. The timely and aggressive management of side effects and good counseling is, therefore, important in keeping patients in treatment.

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Original Article

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Carpal Tunnel Syndrome: Prevalence and Association with Occupation among Presenting Cases in a Tertiary Care Hospital in North East Bihar

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Abstract

Background: Carpal tunnel syndrome (CTS) is a disorder that causes pain and weakness in the hand and wrist. It usually develops from compression of median nerve when it passes deep to the flexor retinaculum through the carpal tunnel in the wrist. It is characterized by the presence of both sensory and motor presenting features in the peripheral distribution of the nerve. A number of etiological factors have been suggested for the onset of CTS including repetitive prolonged hand activities, recurrent exposure to vibration, extremes of temperatures and mechanical stress. Evolution of the pathophysiology of CTS is not clearly understood, but it appears that the median nerve is compressed when the tissues of the hand surrounding the nerve swell in response to trauma or inflammation. It is often very difficult to determine the precise cause of onset of CTS. Older people are at a higher risk due to degenerative neuropathy.

Aim: The aim of this study was to observe the prevalence of CTS and its association with the occupation.

Materials and Methods: Patients attending the outdoor clinics of Katihar Medical College and presenting with complaints of tingling, burning, numbness, and pain in the hands were referred to the Department of Orthopedics for further clinical examination, diagnosis and management. Cases were categorized into two groups. The first group comprised persons engaged in heavy manual work and the second group consisted of persons engaged in light manual work.

Result: Prevalence of CTS was higher in the first group as CTS is usually triggered in cases with occupation consisting of prolonged heavy manual work.

Conclusion: CTS has a direct relation with occupation and some medical conditions may increase the susceptibility towards developing CTS. Early diagnosis, rest and conservative approach are preferred for the management of CTS.

Key words: Carpal tunnel syndrome, Compression, Median nerve, Occupation

INTRODUCTION

The flexor retinaculum is a strong fibrous band which acts as a tie-beam and converts the anterior concave surface of the carpus into an osseo-fibrous carpal tunnel. Through this tunnel pass the digital flexor tendons and the median nerve. The median nerve is the chief nerve of sensation in the hand as it supplies the palmar surfaces of the digits the most common employed for feeling and for precision grip. In addition, it is motor to the thenar eminence musculature. The median nerve enters the hand by passing deep to the flexor retinaculum. The median nerve may be compressed in the carpal tunnel due to continued swelling of the synovial sheaths. This is known as the carpal tunnel syndrome (CTS) and is manifested by weakness and wasting of thenar muscles with the loss of power of opposition, and loss

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of cutaneous sensations of the palmar surface involving lateral three and a half of the digits.[1] Upon emerging from the carpal tunnel, the median nerve ramifies. A muscular branch innervates the thenar muscles. Remaining branches terminate in the palmar digital nerves for the thumb, index, middle, and ring fingers. A communicating branch usually links the nerve to the ulnar nerve. The median nerve is prone to compression in the carpal tunnel.[2] The CTS provides an instructive demonstration of the distribution of the median nerve. Only by knowing its anatomy, it is possible to distinguish this condition from other syndromes that cause paresthesias and muscle atrophy in the hand. The condition is more common in women and often there is no identifiable cause. The syndrome may be precipitated by arthritis of the wrist or intercarpal joints, dislocation of the lunate, tenosynovitis, tumor or acromegaly. Irritation of the nerve may cause a tingling sensation and twitching of the thenar muscles. Due to nerve paralysis, the thenar muscles atrophy and there is anesthesia in the sensory distribution area of the nerve. Movements of fingers and thumb are not seriously impaired. Division of the flexor retinaculum at the wrist relieves symptoms and signs of the compression syndrome. In long-standing cases, nerve regeneration may not take place.[3] CTS is a common problem with an estimated annual incidence rate of 0.5-5.1 per 1000.[4] Certain occupations involving wrist activities materially increase the risk of CTS. This syndrome can also produce nocturnal symptoms including hand or arm pain and numbness. CTS was first reported 1947 by brian among six cases of CTS in repetitive work.[5] It is the most common compressive neuropathy of the upper limb and an increasingly recognized cause of work disability.[6] CTS belongs to a ménage of disorders called cumulative trauma disorders (CTDs) which are caused by the repetitive, sustained, or forceful motions occurring over time, compromising the integrity or functioning of the soft tissues producing inflammation of the tendons or compression of the peripheral nerves.[7] Higher prevalence rates have been observed in certain groups with repetitive hand movements especially flexion at the wrist joint and extension at the shoulder and elbow joints. Diagnosis of CTS is based on characteristic complaint confirmed preferably by abnormal electrophysiological tests.[8] In the United States, occupational CTS is a major cause of loss of working days for workers and carpal tunnel release is the most common preferred operation on the hand, accounting for approximately two hundred, thousand procedures each year incurring direct medical costs in excess of one billion dollars annually. More rigorous study of treatment for CTS will be enhanced by better measures of outcome.[9] CTS is reported to be more common in women.[10] No tests are yet available to target the causative factor.

MATERIALS AND METHODS

A cross-sectional study which evaluated the prevalence of CTS and its association with occupation among the general population was undertaken in a tertiary care center in North East Bihar. Ethical committee clearance was obtained prior to the study. 80 cases of CTS which attended the outdoor Orthopedic Clinic of Katihar Medical College were observed in this study. Cases were categorized into two Groups A and B. Group A consisted of cases engaged in heavy manual work and Group B consisted of cases engaged in light manual work.

Inclusion Criteria

1. Adult males
2. Adult females
3. Cases with intact surgical anatomy of wrist and joint
4. Cases with no past history of nerve injury or pre-existing diseases.

Exclusion Criteria

1. Geriatric males
2. Geriatric females
3. Cases presenting with fracture repair of distal radius, distal ulna or any of the carpus
4. Cases presenting with hormonal conditions and arthritis.

RESULTS

All 80 cases were adults and no pediatric case of CTS was observed. There were 60 cases in Group A of which all were persons involved in occupations concerned with heavy manual work. Twenty cases observed in Group B were involved in occupations concerned with light manual work. In Group A out of 60 presenting cases the occupations of the cases are as follows; drill machine operators (22), construction laborers (16), drivers (12), automotive garage mechanics (5), butchers (3), and railway station porters (2). In Group B out of 20 presenting cases the occupations of the cases are as follows; chefs (6), computer operators (4), tailors (3), gardeners (3), office clerks (2), billboard painters (2). Out of 80 presenting cases, irrespective of group the prevalence among males and females were 53 out of 80 (66.25%) and 27 out of 80 (33.75%) respectively (Table 1-4).

DISCUSSION

CTS is considered an inflammatory disorder caused by repetitive stress, physical injury or a medical condition. CTS is the most common clinical entity seen by the

health surgeons with some reporting that the condition affects up to 10% of the general population.[11] It is often very difficult to determine the precise cause. The most important problem associated with this occupational exposure is the complexity of exposure assessment at the workplace. No tests are yet available to target the causative factor. Except in patients with certain underlying diseases, the biological mechanisms leading to CTS are unknown. Some studies suggest that more than half of CTS cases are associated with workplace factors, though there is no strong evidence of cause and effect relationship. CTS is felt to be induced or aggravated by any process that compresses the median nerve as it passes through the narrow carpal canal. Repetitive flexion and extension of the wrist and grasping motions of the hand are thought to repeatedly compress the median nerve between the tendons and carpal bones, leading to nerve injury. Such recurring movements at the wrist joint also make a person prone to develop tendonitis and tenosynovitis. Repetitive heavy manual work or light manual work both can trigger CTS. In this study, we observed 80 cases of CTS which were associated with occupation (Table 1). Prevalence of CTS in relation with occupation and among different genders has been illustrated in Figures 1 and 2. Distribution of cases of CTS among heavy and light workers has been represented n Figures 3 and 4. Heavy manual workers are more prone to developing onset of CTS. As pregnancy was an exclusion criteria in this study we observed that males were more vulnerable to CTS (Table 2). With relation to the occupation in Group A, we observed drill machine workers are more susceptible to CTS due to prolonged use of heavy vibration tools (Table 3). Prolonged vibration exposure resulting in CTS has been documented by Leclerc *et al*.[12] In Group B, we observed that chefs are more vulnerable to CTS due to repetitive and prolonged use of the wrist joint in all stages of cooking, being seconded by professional computer operators (Table 4). Studies now strongly suggest that CTS is primarily associated with medical conditions such as diabetes mellitus, osteoarthritis, hypothyroidism and rheumatoid arthritis. Prevalence of CTS in the general population ranges from 1% to 25% which is comparatively very low.[13] This syndrome also tends to occur in people with certain genetic or risk factors including obesity, smoking and alcohol abuse. In pregnant women, hormonal fluctuations may trigger CTS due to fluid retention. CTS is typically worse at night and with repetitive activity.[14] Pain or muscle weakness may prevent a person a person from doing important day-to-day tasks and also affect a person's hobbies. Individuals with CTS are unable to oppose the thumb and have difficulty buttoning a shirt or blouse as well as gripping things such as a comb. As the condition progresses sensory changes radiate to the forearm and axilla.[15] Workers may be compelled to opt for another occupation. It is advisable to begin early conservative treatment to avoid surgical intervention. The most common type of conservative treatment is corticosteroid injections

Table 1: Number of cases in each group

Number of presenting cases	Group A	Group B
n=80	60	20

Prevalence among cases in Group A is more than that of Group B

Table 2: Prevalence of CTS among males and females observed in this study

Number of presenting cases	Prevalence among males (%)	Prevalence among females (%)
n=80	53 (66.25)	27 (33.75)

Group has not been considered in this table. CTS: Carpal tunnel syndrome

Table 3: Occupation specific distribution of cases in Group A

Group A (*n*=60)	Occupation
22 cases	Drill machine operators
16 cases	Construction labourers
12 cases	Drivers
5 cases	Automotive garage workers
3 cases	Butchers
2 cases	Railway station porters

Table 4: Occupation specific distribution of cases in Group B

Group B (*n*=20)	Occupation
6 cases	Chefs
4 cases	Computer operators
3 cases	Tailors
3 cases	Gardeners
2 cases	Office clerks
2 cases	Billboard painters

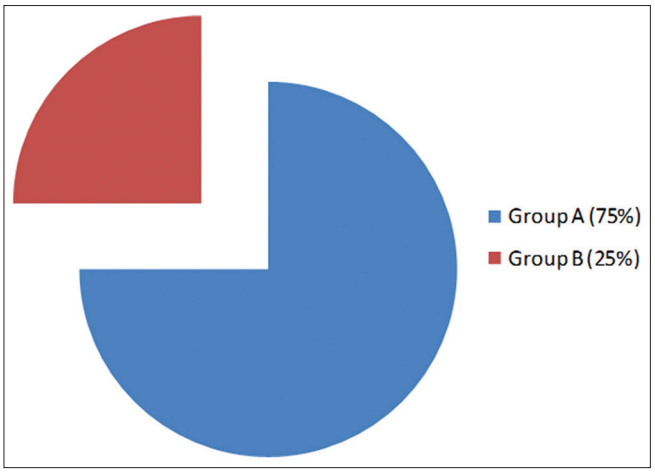

Figure 1: Prevalence of carpal tunnel syndrome in relation with nature of occupation. Group A contains 60/80 (75%) cases and Group B 20/80 (25%) cases observed in this study

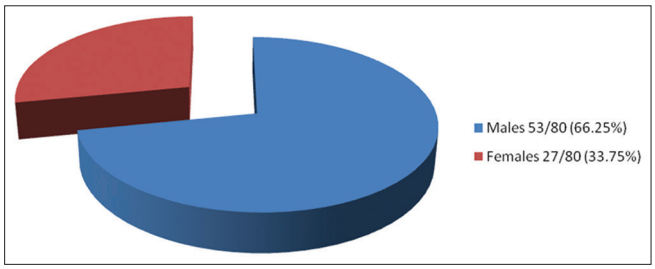

Figure 2: Prevalence of carpal tunnel syndrome (CTS) among males and females. Group to which the male or female belongs has not been considered in this figure. Result shows that prevalence of CTS among males is higher than that among women

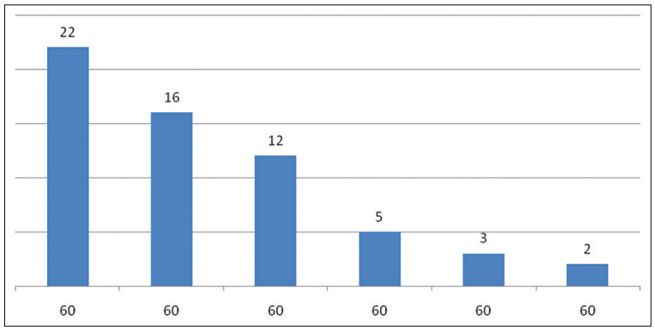

Figure 3: Distribution of cases presenting with carpal tunnel syndrome in Group A

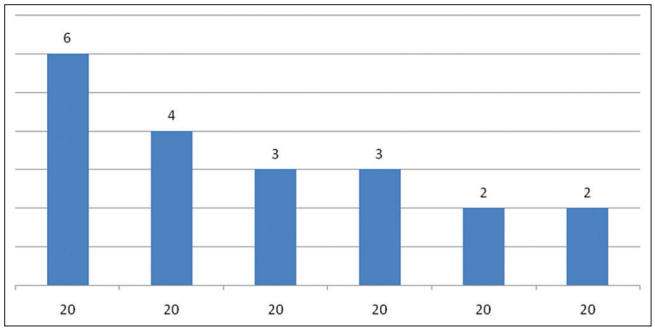

Figure 4: Distribution of cases presenting with carpal tunnel syndrome in Group B

that are quite successful in mild cases of CTS. In all the cases we encountered, rest and physiotherapy was advised with considerable results. In a follow-up, we observed that the inflammation of adjacent tissues had subsided, and compression symptoms of the median nerve were substantially relieved.

CONCLUSION

Anatomical knowledge of the carpal canal and clinical knowledge of CTS are both crucial for assessing the prognosis of median nerve entrapment neuropathy. CTS exhibits female predilection due to smaller wrists and lower carpal tunnel volumes. Heavy manual workers using heavy-duty vibration tools are vulnerable to CTS. Experts have suggested that people who are physically fit have a lower risk for developing CTS. Regular regimen involving resistance training strengthens the muscles of the girdles and the limbs.

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Original Article

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Comparative Study on Combination of Microdermabrasion with 35% Glycolic Acid Peel versus 35% Glycolic Acid Peel Alone for Facial Melanoses of Indian Skin Types

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Abstract

Background: Facial melanoses (FM) include a group of disorders where hyperpigmentation is predominantly present on the face and neck and are a common presentation in Indian patients. The treatment includes skin lightening agents, chemical peeling, dermabrasion, and lasers. They are used either alone or in combination.

Objective: The objective of the study was to compare the therapeutic effect of combined microdermabrasion (MDA) and 35% glycolic acid peel (GA Peel) versus 35% GAP for FM.

Materials and Methods: This study was carried out in 40 patients with FM aged 18 years above, divided into two, 20 patients each. The patients were recruited from those attending the outpatient Department of Dermatology. Detailed history and clinical examinations were done. Pigmentation was assessed by extent of involvement, depth and photography taken. Pregnant females were excluded from the study. The Group I patients were treated by MDA followed by 35% GAP and Group II patients were treated with 35% GAP alone.

Results: Our results revealed a significant decrease in the pigmentation in Group I compared to Group II.

Conclusions: As per the present study, MDA is more efficacious to decrease pigmentation when combined with GA 35% peel for epidermal melasma, post-inflammatory following acne and photodamage in three sittings. However, long-term studies are required to document complete resolution of FM with combination procedural treatments.

Key words: Chemical peels, Facial melanoses, Glycolic acid peel, Melasma, Microdermabrasion

INTRODUCTION

Facial melanoses (FM) include a group of disorders with multifactorial etiology where diffuse or patchy hyperpigmentation present on the face and neck and is commoner in older woman.[1] Hyperpigmentary skin disorders may be broadly classified into two groups – Epidermal and dermal depending on the location of the pigment.

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Epidermal hyperpigmentation is characterized by brown pigmentation exclusively due to melanin pigment. Dermal pigmentation characterized by blue pigmentation or ceruloderma may be either due to melanin or non-melanin pigment.[2]

The etiopathogenesis[3] of hyperpigmentation varies according to the etiology. Dermal hyperpigmentation is usually due to damage to the dermo-epidermal junction, resulting in pigment incontinence and deposits of melanophages in the upper dermis.

Epidermal pigmentation is caused by increased melanization in the melanocytes. The causes of facial pigmentation can be genetic or acquired. Genetic causes include ephelides, lentigines, nevus of ota, pigmentary demarcation lines, periorbital melanosis, and dyschromatosis.

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Acquired causes of FM include melasma, lichen planus pigmentosus (LPP), Riehl's melanosis, erythema dyschromicum perstans (EDP) and post-inflammatory[4] melasma (chloasma).

Melasma (Chloasma)

Melasma is derived from Greek word melas (black) while chloasma is derived from the word chloazein (green), and since the pigmentation is brown black, melasma is the preferred term.[5]

The exact etiology of melasma is not known but several factors have been implicated. Ultraviolet (UV) radiation (UVA and UVB) and visible light cause peroxidation of lipids in cellular membranes, leading to generation of free radicals, which stimulate melanogenesis. Elevated levels of estrogens and progesterone (as occurring in pregnancy) are important. Melasma also develops with estrogen and progesterone containing pills used for prostatic cancer.[6] Melasma begins as well as worsens during pregnancy as also after profound emotional stress. Genetic factors, drugs, and cosmetics are commonly implicated.

Melasma is characterized by symmetrical hyperpigmented macules (Figure 1a), which may be blotchy, irregular, arcuate, or polycyclic and rarely have a linear or a starburst distribution.

The face is the most common site affected though rarely the pigmentation may extend on to V of the neck or may be confined to the forearms. On the face, three patterns of melasma are recognized:

- Centrofacial: The most frequent (63%) pattern, with pigmentation on cheeks, forehead, upper lip, nose, and chin
- Malar: Constituting 21%, with pigmentation present only on cheeks and nose
- Mandibular: The least common (16%), with pigmentation on ramus of the mandible.

Treatment is difficult, prolonged and recurrences are common.

Lichen Planus Pigmentosus (LPP)

Though the exact etiology of LPP is not known, cosmetics including fragrances, hair dyes, and mustard oil have been incriminated.[7]

LPP is characterized by generally asymptomatic (sometimes itchy), diffuse (less frequently reticular, blotchy, or perifollicular) hyperpigmented dark brown to slate gray to black macules (Figure 2a) present mostly on the exposed areas and flexures. The lesions lack the erythematous border of EDP. Histopathology is typical of lichen planus (pigmentary incontinence and lymphocytic infiltrate seen).

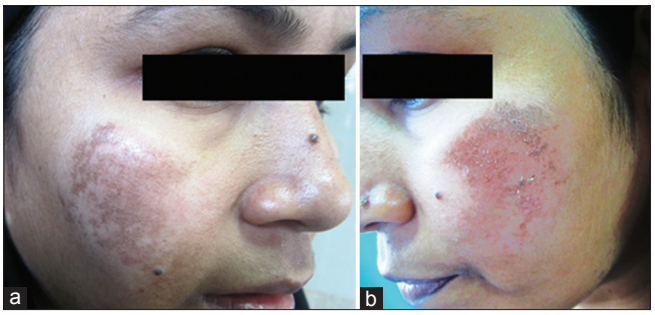

Figure 1: (a) Melasma, (b) melasma after microdermabrasion with 35% glycolic acid peel - Erythema and scaling are noticed

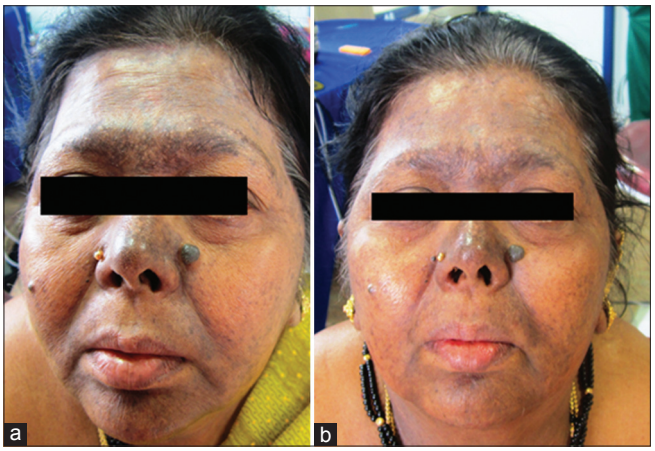

Figure 2: (a) Lichenplanus pigmentosus (LPP), (b) LPP after treatment with microdermabrasion with 35% glycolic acid peel

Riehl's Melanosis (RM) (Pigmented Cosmetic/Contact Dermatitis [CD])

RM is probably a pigmented CD to antigens present in cosmetics and textiles with anecdotal reports of airborne CD to musk ambrette and other plants.[8,9]

RM is characterized by diffuse/patchy/rarely reticular pigmentation, often with satellite perifollicular pigmented macules and scaly follicular hyperkeratosis. Pigmentation is brown seen on lateral cheeks and sides of the neck with relative sparing of shaded areas.

Erythema Dyschromicum Perstans (Ashy Dermatosis of Ramirez, EDP)[10,11]

It is an acquired asymptomatic idiopathic, macular, ashy gray or blue pigmented macules with raised reddish margins present on the face, trunk, and limbs. Some consider EDP as a variant of macular lichen planus.

Post-inflammatory

Post-inflammatory hyperpigmentation is a frequent occurrence following any inflammatory reaction, particularly in dark skin individuals. The various causes are Trauma, allergic disorders (Figure 3a), infections, sun exposure (Figure 4a), drug eruptions, inflammatory diseases, and therapeutic interventions.

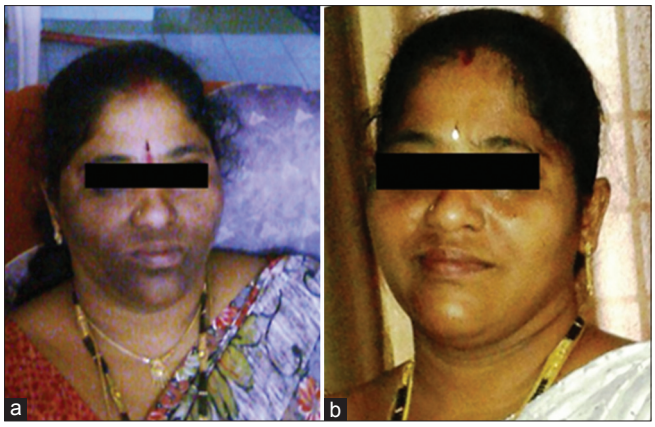

Figure 3: (a) Post-inflammatory pigmentation, (b) post-inflammatory pigmentation after treatment with 35% glycolic acid peel

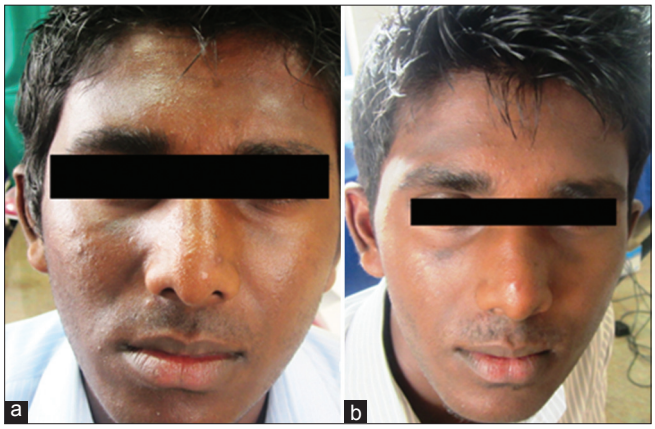

Figure 4: (a) Post-inflammatory pigmentation following acne, (b) post-inflammatory pigmentation following acne after treatment with 35% glycolic acid peel

Clinically the pigmented macules are discrete but have hazy, feathered margins roughly corresponding to the configuration of the inflammatory lesion.[2]

The treatment of FM[12] includes removal of aggravating factors, vigorous photoprotection and some form of active pigment reduction either with topical agents or physical modes of treatment. Topical agents include hydroquinone (HQ), which is the most common used agent, often in combination with retinoic acid, corticosteroids, azelaic acid, kojic acid, and glycolic acid (GA). Physical modes of treatment include chemical peels, dermabrasion, and lasers.

Epidermal melasma responds best, and patients who continue topical therapy after the peel, maintain improvement better than those who do not.[13] Medium depth peels should be performed with great caution, especially in dark-skinned patients, and deep peels are not recommended for Indian skin because of high risk of prolonged or permanent pigmentary changes.[14]

Objective of Study

The objective of the study was to compare the therapeutic effect of combined microdermabrasion (MDA) and 35% GA peel (GAP) versus 35% GAP for FM.

MATERIALS AND METHODS

This study was carried out in 40 patients with FM aged 18 years above, divided into two groups, 20 patients each (Table 1). The patients were recruited from those attending the outpatient Department of Dermatology. Detailed history and clinical examinations were done. Pigmentation was assessed by extent of involvement, depth and photography taken. Pregnant females are excluded from the study (Table 2).

The Group I patients (Table 1) were treated by MDA followed by 35% GAP and Group II patients (Table 1) were treated with 35% GAP alone.

Procedure

The participants in both groups were primed 2 weeks before the procedure with a triple regimen (HQ, tretinoin, corticosteroid) or glyco 6 night time and sunscreen day time. Two days prior to the procedure, the patients of both groups are advised to stop night creams.

Table 1: The detailed statistics of the patients for the both the groups with respect to age and sex

Description	Group I (20 patients)		Group II (20 patients)	
	Number of patients	%	Number of patients	%
Sex				
Males	8	40	10	50
Females	12	60	10	50
Age group				
18-25 years	7	30	6	30
26-35 years	6	30	8	40
36-45 years	6	35	4	20
46-60 years	1	05	2	10

Table 2: Etiology of facial melanoses of participating groups

Description	Group I (20 patients)		Group II (20 patients)	
	Number of patients	%	Number of patients	%
Melasma	12	70	8	40
Epidermal	5		3	
Mixed	7		5	
Post-inflammatory	8	30	12	60
LPP	1		-	
Acne	4		10	
Photo-melanoses	3		2	

LPP: Lichenplanus pigmentosus

Group I Patients - Treatment

Combination of MDA followed by 35% GAP

After cleaning and degreasing with alcohol, MDA was done on the pigmented areas. Later the aluminum oxide crystals are removed with gauze and then 35% GAP is applied. After 3-5 min, the peel is neutralized with water or peel neutralizer depending on the skin sensitivity. Then the participants were applied mild corticosteroid creams for 2 days and sunscreens continued. Night creams followed after 2 days.

Procedure done every 2-3 weeks for 12 weeks. At the end of 12 weeks, results and side effects were noted.

Group II Patients - Treatment

35% GAP

After cleaning and degreasing with alcohol on the pigmented areas, 35% GAP is applied. After 3-5 min, the peel is neutralized with water or peel neutralizer depending on the skin sensitivity. Then the participants were applied mild corticosteroid creams for 2 days and sunscreens continued. Night creams followed after 2 days. Procedure done every 2-3 weeks for 12 weeks. At the end of 12 weeks, results and side effects were noted.

The patients were strictly instructed to follow the post procedure treatment including the application of sunscreens and night creams.

RESULTS

On the basis of patients and observer assessment changes were noted by visual inspection and with woods lamp during each sitting. The final results were recorded through photographs and knowing the total satisfaction. The abstract of results are tabulated at Table 3.

DISCUSSIONS

Facial Melanoses, most commonly caused by melasma, other conditions being post-inflammatory due to acne, photodamage and LPP (Table 2).

The observations made during the study are post-inflammatory pigmentation following acne is more common in 18-30 years age group, photomelanoses occured most commonly in males, melasma commonly seen in 30-45 years age group, LPP commonly noticed in females, melasma of recent on set regressed after two sittings (2 patients), males have predominantly epidermal melasma - 80% reduction seen in epidermal melasma after three sittings, Only 40-50% reduction noted in mixed melasma at the end of 3 months (Figure 1b), complete resolution not seen, 50% reduction seen for LPP (Figure 2b), photomelanosis regressed after two sittings (Figure 4b), 60% reduction is seen in post-inflammatory pigmentation following acne at the end of 3 months. Post-inflammatory pigmentation following CD resolved completely after two sittings with 35% GAP (Figure 3b), short contact time is noticed after application of peel following MDA. With 35% glycolic peel alone only 25-50% reduction is seen at the end of 3 months, patients satisfaction is more with MDA with 35% glycolic peel (Table 3, Figure 2b).

FM causes cosmetic disfigurement with significant emotional impact. Its treatment includes removal of provocating factors, vigorous photo protection, and some form of active pigment reduction either with topical agents or physical modes of treatment. There is no universally effective specific therapy - existing agents have varying degrees of efficacy and relapses are frequent. In our present study, MDA is combined with 35% GAP gives significant results. The findings were based on the visual observation (Table 3).

MDA is an FDA approved process first introduced in 1985 and is a popular method used to treat scars, acne and other cosmetic-dermatologic conditions like pigmentation.[15] MDA, popularly known as body polishing,[16] is a simple and safe, office cosmetic procedure. In this procedure, aluminum oxide crystals are blown onto the face and then vacuumed off, using a single handpiece. MDA peels the stratum corneum there by forming channels for deeper penetration of chemicals. Local side effects are uncommon and transient but include pain, burning, photosensitivity, diffuse hyperpigmentation (Table 4).

GA is a superficial peeling agent that is made from sugar cane. It is often considered the most active and beneficial of the alpha-hydroxy-acids. At higher concentrations it causes epidermolysis, decreases melanin production by direct inhibition of tyrosinase, it also acts as a humectant.[12]

Both procedures are easy to perform and manual control is possible. The results with hydroxy acids are time

Table 3: Results of participating groups

Brief description	Group I (total 20 patients) (MDA+GAP35)	Group II (total 20 patients) (GAP35)
Improvement %		
0-25	2 patients	5 patients
26-50	9 patients	11 patients
50-75	7 patients	4 patients
100	2 patients	0 patients

MDA: Microdermabrasion, GAP35: Glycolic acid peel 35%

Table 4: Side effects noticed in participating groups

Side effects	Group I (total 20 patients) (MDA+GAP35)	Group II (total 20 patients) (GAP35)
Burning	Noticed in all patients	12 patients
Erythema	Noticed in all patients	15 patients
Swelling	Noticed in all patients	-
PIH	6 patients	4 patients
Scaling	12 patients	-
Complication encountered with significant scaling (Figure 5)	1 patient	-

MDA: Microdermabrasion, GAP35: Glycolic acid peel 35%, PIH: Post-inflammatory hyperpigmentation

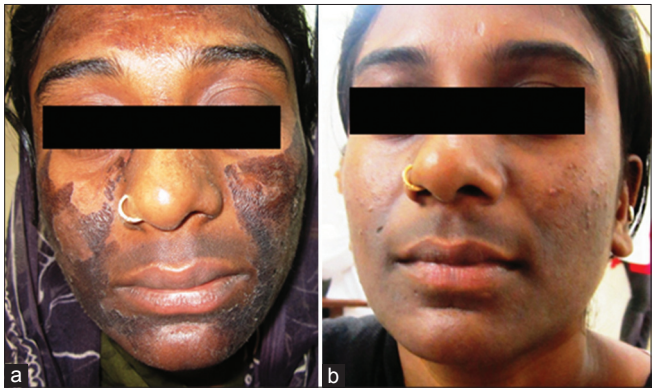

Figure 5: (a) Complication encountered during microdermabrasion with 35% glycolic acid peel (scaling and pigmentation), (b) post-treatment with mild steroids and moisturizers – (after 4 days)

dependent.[17] Appearance of erythema is the end point of neutralization of the peel. The most common observed side effect in our study is intense burning, erythema followed by pigmentation which are usually transient.

The post peel reactive hyperpigmentation, scaling, and erythema can be tackled by judicious use of mild topical steroids for 2 days and continuation of sunscreens (Figure 5a and b). MDA is safer when compared to mechanical dermabrasion. Scarring and hypopigmentation are rare with MDA. The pigment clearance achieved should be maintained by regular use of sunscreens.

In a study by Kunachak *et al.*[18] from Thailand 533 patients with resistant melasma were treated by mechanical dermabrasion, they achieved 97% clearance for the follow-up period of 5 years. They observed complications such as hypertrophic scars and permanent hypopigmentation.

According to study by Grover and Reddu,[19] New Delhi GAP is useful especially in superficial scarring and melasma, moderately successful in acne patients with no response in dermal pigmentation.

According to study by Rashmi Kumari and Thappa D.M., JIPMER[20] found 20-35% GAP and 10-20% TCA peel are found to be equally effective for epidermal and mixed melasma.

In our study, combining MDA with GA 35% found to be effective for epidermal melasma, solar melanoses and post-inflammatory pigmentation for acne with mixed results for dermal melasma (Table 3).

CONCLUSION

FM is a disfiguring and disturbing cosmetic disability. Melasma, post-inflammatory hyperpigmentation, are most common. In the present study, MDA is more efficacious to decrease pigmentation when combined with GA 35% peel for epidermal melasma, post-inflammatory following acne and photodamage in three sittings. However, long-term studies are required to document complete resolution of FM with combination procedural treatment.

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Original Article

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High-Resolution Computed Tomographic Evaluation of Pulmonary Diseases in Human Immunodeficiency Virus Positive Patients: A Study of 30 Cases

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Abstract

Background: The association between tuberculosis (TB) and human immunodeficiency virus (HIV) presents an immediate and grave public health and socio-economic threat, particularly in the developing world.

Purpose: The aim of given study was to utilize high resolution computed tomography (HRCT) for the detection of pulmonary disease in HIV patients coming with suspected pulmonary complications, and then to arrive at a conclusive or differential diagnosis on the basis of HRCT finding.

Materials and Methods: The cases were selected based on all patients referred to the Department of Radiology, Gauhati Medical College with proven HIV/acquired immunodeficiency syndrome (AIDS) infection which was clinically suspected of pulmonary infections. HRCT was done.

Results: Total 30 cases of HIV/AIDS with suspected pulmonary disease were studied. Out of which 21 were male and 9 were female. Out of which 60% of patients were diagnosed as having pulmonary TB, followed by bacterial infection in 16.6% cases and *Pneumocystis carinii* pneumonia in 10% patients, while 13.3% of our study did not reveal any significant abnormality. Nodular opacities in HRCT were the most common findings in patients with pulmonary TB (77.7%).

Conclusion: Various findings such as pulmonary TB being the most common infection and most common HRCT finding in pulmonary TB were nodular opacity can be obtained from the present study. HRCT is a highly sensitive tool for detecting parenchymal abnormalities and allows better characterization of the lesions, with better reproducibility and less interobserver difference.

Key words: Bronchiectasis, Enzyme-linked immunosorbent assay, Miliary tuberculosis, Mortality, Pulmonary tuberculosis

INTRODUCTION

Human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) is a major world health concern and is a major cause of morbidity and mortality.[1]

It is a serious disorder of the immune system in which the body's normal defenses against infection breakdown, leaving it vulnerable to a host of life-threatening infections/conditions including unusual malignancies. The persons with severe opportunistic infections (OIs) and unusual malignancies are at the one end of the spectrum of disease, while healthy seropositive (for HIV) individuals are at the other end.[2]

The association between tuberculosis (TB) and HIV presents a major public health and socio-economic threat, particularly in the developing world including India.[3]

The estimated adult HIV prevalence in India is to be 0.27% according to National AIDS Control Organization's (NACO) 2013 report which is the third highest burden in the world. India is the highest TB burden country in the world with an estimated 2.2 million new TB cases

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occurring annually. While TB is commonest OIs in HIV-infected individuals, HIV infection is an important risk factor for acquiring TB infection and its progression to active TB. HIV/TB together is a fatal combination with extremely high death rates (15-18%) reported among HIV-infected TB cases notified under Revised National TB Control Program. Overall, TB is estimated to cause about 25% of all deaths among HIV infected cases in India. Early detection of HIV/TB cases and timely administration of anti-retroviral treatment (ART) and anti-TB treatment are key interventions to reduce mortality rates significantly.[4]

Imaging plays a vital role in the diagnosis and management of lung of complications associated with HIV. Accurate diagnosis is based on an understanding of the pathogenesis of the processes involved and their imaging findings.[1]

High-resolution computed tomography (HRCT) combines the use of thinly collimated CT slices that are 1-1.5 to 2 mm in thickness, with a high spatial frequency algorithm that enhances edge detection. Thin collimation decreases partial volume averaging and improves the ability of the CT to demonstrate small pulmonary lesions. HRCT allows delineation of the lung parenchyma down to the level of the secondary pulmonary lobule. Advantage of HRCT over radiograph is that it there is better delineation and characterization of the lesion and less observer variance. HRCT helps in revealing pulmonary parenchymal changes before they are evident on chest radiograph and also helps in better characterization of the lesions and thus helps in differential diagnosis of pulmonary complications seen in these patients.[1]

Empowered with an advanced modality like the HRCT, it was deemed essential to undertake a study on the HRCT evaluation of the pulmonary diseases in HIV/AIDS patients with the following aims and objectives in view:

1. To utilize HRCT for the evaluation of pulmonary parenchyma in HIV patients coming with suspected pulmonary complications.
2. To detect and categorize the pattern of involvement of the pulmonary parenchyma with the help of HRCT findings and then to arrive at a conclusive or differential diagnosis on the basis of HRCT findings.
3. Post-treatment follows up of HIV/AIDS patients.

MATERIALS AND METHODS

The present study was carried out in the Department of Radiology, Gauhati Medical College and Hospital, Guwahati from May 2013 to April 2014.

The cases were selected from ART center of Gauhati Medical College and Hospital based on their HIV-positive status and suspicion of pulmonary disease. The cases were evaluated by using the HRCT.

The age group the patients ranged from 8 to 52 years. Both sexes had their share of cases.

The primary clinical features were of weight loss, fever, and cough both productive and non-productive, and dyspnea.

Methods

A thorough clinical history of all the HIV positive patients presenting with suspicion of pulmonary disease was taken. The history mainly comprised of cough whether productive or non-productive, fever whether low grade or high grade, weight loss, and dyspnea duration of symptoms was also recorded. Then, a meticulous record of all the available laboratory investigations including HIV status, CD4 counts, routine blood examination, sputum examinations, pleural fluid analysis, fine needle aspiration cytology, and other available investigations was kept. Then, chest X-rays of the patients were studies for the presence of any abnormality.

General and systemic examinations of all the patients were done. HRCT scan of the thorax was done in all the cases taken up in the study.

Preparation of the Patient

The procedure and objectives of performing the high-resolution scans were explained to the patients and written consent of the patient or the attendant were taken. The patient was explained and demonstrated the procedure of breath holding during the acquisition of HRCT scans.

CT Protocol

The machine used is PHILIPS MX16 (16 SLICE CT) scanner. CT scan was performed using the following protocols:

1. Positioning: Patients were scanned in the supine position with their arms above their heads. Scans were performed in the axial axis from cephalic to caudal levels.
2. Scanning: After positioning the patient, the topogram or scanogram was taken. Spiral scanning were done with following protocols:
   - Collimation = 1 mm
   - Feed = 10 mm
   - Scan time = 1 sec
   - KVp = 120-140
   - mA = 240
   - Matrix size = 512 × 512

RESULTS AND OBSERVATIONS

Age and Sex Distribution

In the present study of 30 patients with HIV/AIDS with suspected pulmonary disease, 21 patients were male and 9 patients were female. So, males accounted for 70% and females accounted for 30% of cases.

In the present study, a maximum number of cases are seen between 31 and 40 years age group (46.6%), followed by 9 cases in 21-30 years (30%) (Table 1).

So, the most common pulmonary disease in the present study is pulmonary TB (60%) followed by bacterial infection (16.6%) (Table 2).

So, the most common presenting symptom in our present study is weight loss seen in 80% of cases followed by cough with expectoration seen in 70% of cases (Table 3).

So, the most common mode of HIV transmission in the present study is sexual (90%) (Table 4).

Pathological Investigations

1. Enzyme-linked immunosorbent assay (ELISA): All patients had undergone 2 or more ELISA tests and are found to be positive.
2. CD4 counts: Are available in all the patients. The range of CD4 counts varied from 21 to 382 with a mean count of 159.8 cells/cumm.

Pulmonary TB

A total of 18 patients in the preset study are diagnosed to be suffering from pulmonary TB.

So, the most common clinical symptom in patient with pulmonary TB were cough with expectoration (88.9%) followed by weight loss (83.3%) (Table 5).

CD4 Counts in Patient with Pulmonary TB

The CD4 count in these patients varied from 21 to 382 cells/cumm, with a mean count of 170.6 cells/cumm. Six patients had CD4 count >200 cells/cumm, while 12 patients had CD4 counts < 200 cells/cumm (Table 6).

So, sputum positive cases in the present study are 33.3% (Table 7).

Other Investigations

All 18 patients have high ESR counts (counts >20 acid fast bacilli [AFB]), a total of 7 patients has pleural effusion, and in six of these patients pleural analysis reveal findings suggestive of pulmonary TB.

Table 1: Age distribution

Age	No. of patients	Percentage
<10	1	3
11-20	0	0
21-30	9	30
31-40	14	46.66
41-50	5	16.66
>50	1	3

Table 2: Different pulmonary disease noted

Pulmonary disease	Number of patient	Percentage
Pulmonary tuberculosis	18	60
Bacterial infection	5	16.6
Pneumocystis carinii	3	10
No abnormality	4	13.3

Table 3: Clinical findings

Clinical findings	Number of patients	Percentage
Weight loss	24	80
Cough with expectoration	21	70
Non-productive cough	5	16.6
Low grade fever	20	66.6
High grade fever	6	20
Dyspnea	4	13.3

Table 4: Mode of HIV transmission

Mode of transmission	Number of patient	Percentage
Sexual (heterosexual)	27	90
IV drug users	2	6.6
Vertical infection (mother to child)	1	3.3

IV: Intravenous

Table 5: Clinical symptoms in patients with pulmonary tuberculosis

Clinical symptoms	No. of patients	Percentage
Cough with expectoration	16	88.9
Dry cough	1	5.5
Fever low grade	14	77.7
Fever high grade	1	5.5
Weight loss	15	83.3
Dyspnea	1	5.5

Table 6: CD4 counts

CD4 count (cells/cumm)	No. of patients	Percentage
>500	0	0
200-500	6	33.3
<200	12	66.7

Table 7: Patient with sputum positive for AFB

Sputum for AFB	No. of patients	Percentage
Positive	6	33.3
Negative	12	66.7

AFB: Acid fast bacilli

Imaging Findings

Chest radiographs are done in all 18 patients. All patients have some radiograph abnormality detectable in the radiograph. HRCT are done in all the cases (Table 8).

So, the most common HRCT finding in pulmonary TB in present study is nodular opacities seen in 77.7% cases followed by consolidation seen in 50% cases, bronchiectasis in 44.4% cases, pleural effusion in 38.8% cases, lymphadenopathy in 33.3% cases, Cavitations seen in 22.2% cases and miliary TB in 16.6% cases (Figures 1-6).

So, centrilobular nodules are seen in maximum cases (Table 9).

Bacterial Infections

A total of 5 patients in the present study are diagnosed to be suffering from bacterial infections.

Table 8: HRCT findings in pulmonary tuberculosis

HRCT findings	No. of patients	Percentage
Nodular opacities	14	77.7
Consolidation	9	50
Pleural effusion	7	38.8
Lymphadenopathy	6	33.3
Cavitation	4	22.2
Miliary tuberculosis	3	16.6
Bronchiectasis	8	44.4
Septal thickening		
Interlobular	6	33.3
Intralobular	3	16.6
Pleural thickening	5	27.7

HRCT: High-resolution computed tomography

Table 9: Classification of nodules in pulmonary tuberculosis

Nodules (distribution)	No. of patients
Centrilobular	9
Tree in bud	6
In clusters	4
Random	5

So, the most common clinical manifestation in the present study is high grade fever and cough with expectoration both in 80% cases (Table 10).

CD4 Counts in Patient with Bacterial Infections

The CD4 count in these patients varied from 121 to 366 cells/cumm with a mean count of 189.4 cells/cumm.

Other Investigations

Sputum culture is done in one patient and it reveals presence of pneumococcus.

None of the patients has AFB in their sputum.

Imaging Findings

Chest radiographs are done in all 5 patients. Four patients have some radiograph abnormality detectable in the radiograph.

So, the most common HRCT finding in bacterial infection is lobar consolidation seen in 60 % cases (Table 11 and Figure 7).

Pneumocystis carinii Pneumonia (PCP)

A total of 3 patients in present study are diagnosed to be suffering from PCP.

So, the most common clinical symptoms in patients with PCP are dry cough, weight loss and dyspnea in 100% cases (Table 12).

CD4 Counts in Patients with PCP

The CD4 count in these patients varied from 24 to 47 cells/cumm, with a mean count of 32.7 cells/cumm, i.e., all these patients are severely immunocompromised (Table 13).

Imaging Findings

Chest radiographs are done in all 3 patients. All patients have some radiograph abnormality detectable in the radiographs.

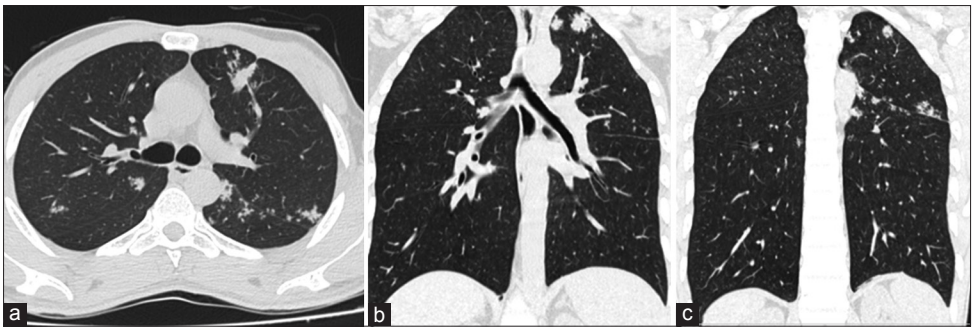

Figure 1: Case of tuberculosis - human immunodeficiency virus (a) Axial, (b and c) coronal HRCT images reveal multiple nodules some are conforming to tree-in-bud nodules

So, the most common HRCT finding in patients with PCP are diffuse ground glass opacities in mosaic pattern of distribution noted in 100% cases, followed by crazy paving noted in 66.6% cases (Table 14 and Figure 6a).

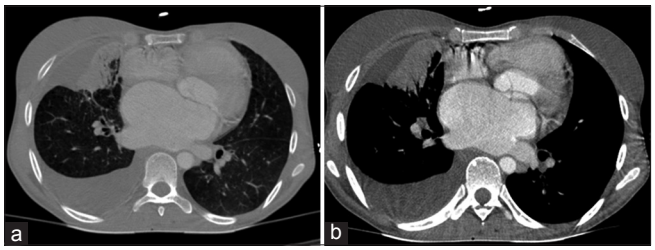

Figure 2: (a) Axial HRCT and (b) Corresponding mediastinal window showing consolidation in the right middle lobe with pleural effusion and in a case of pulmonary tuberculosis

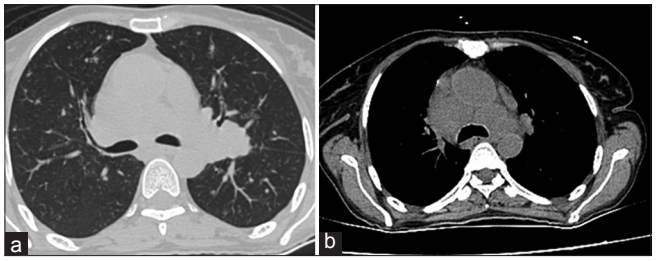

Figure 3: (a) Axial HRCT images reveal multiple discrete nodules in bilateral lung fields. (b) Mediastinal window showing mediastinal lymphadenopathy

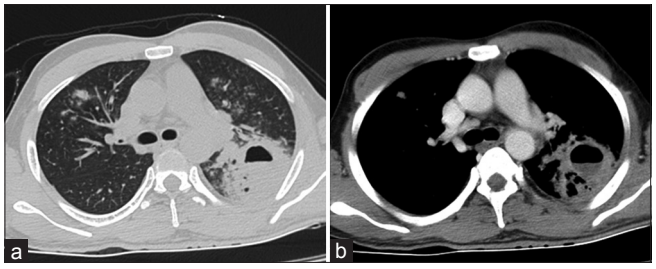

Figure 4: (a) Axial HRCT and (b) corresponding mediastinal window showing cavitary lesion with air fluid level and multiple nodules in a patient with pulmonary tuberculosis

Follow up

Two out of three patients with PCP are followed up after treatment, one patient shows complete resolution of abnormalities, while in another patient radiological resolution lagged behind clinical resolution.

Table 10: Clinical symptoms in patients with bacterial infections

Clinical symptoms	No. of patients	Percentage
Cough with expectoration	4	80
Dry cough	0	0
Fever low grade	1	20
Fever high grade	4	80
Weight loss	3	60
Dyspnea	0	0

Table 11: HRCT findings in bacterial infections

HRCT findings	No. of patients	Percentage
Lobar consolidation	3	60
Bronchiectasis	1	20
Nodules	1	20

HRCT: High-resolution computed tomography

Table 12: Clinical symptoms in patients with PCP

Clinical symptoms	No. of patients	Percentage
Cough with expectoration	0	0
Dry cough	3	100
Fever low grade	2	66.7
Fever high grade	1	33.3
Weight loss	3	100
Dyspnea	3	100

PCP: *Pneumocystis carinii* pneumonia

Table 13: CD4 counts

CD4 counts	No. of patients	Percentage
<200 cells/cumm	3	100
>200 cells/cumm	0	0

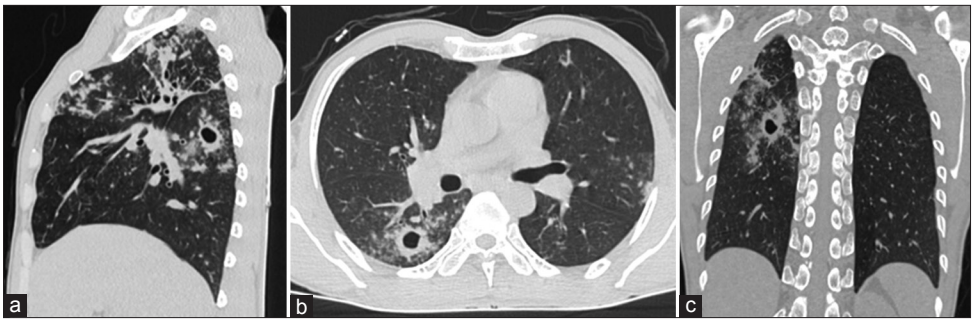

Figure 5: (a) Sagittal, (b) axial and (c) coronal HRCT images reveal cavitary lesion and tree in bud nodules in a case of pulmonary tuberculosis

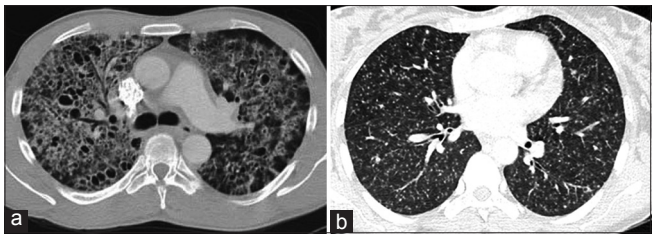

Figure 6: (a) Axial HRCT image reveals ground glass attenuation with crazy paving pattern and multiple cysts in bilateral lung fields which is classic of *Pneumocystis carinii* pneumonia. (b) HRCT image reveals miliary tuberculosis in bilateral lung fields in a different case

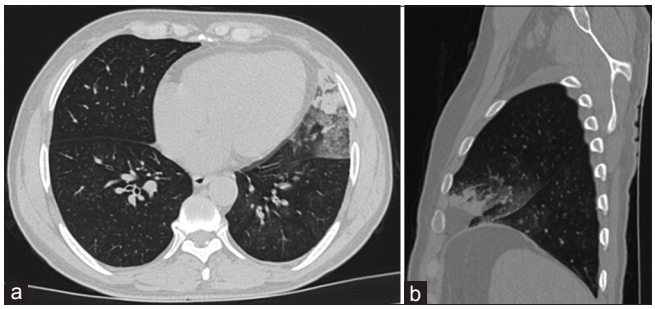

Figure 7: (a) Axial and (b) Sagittal HRCT images showing consolidation in the left lingular segment in case of bacterial infection

Table 14: HRCT findings of PCP

HRCT findings	No. of patients	Percentage
Diffuse ground glass opacity	3	100
Mosaic attenuation	3	100
Crazy-paving	2	66.6
Consolidation	1	33.3

HRCT: High-resolution computed tomography, PCP: *Pneumocystis carinii* pneumonia

DISCUSSION

In present study, maximum number of cases was seen between 31 and 40 years age group numbering 14 cases, followed by 9 cases in 21-30 years of age group. Hence, a maximum number of cases in the present study are also noted in the age group 21-40 years comprising about 76.7% of cases. This correlates well with study by Sharma *et al.*[5] who reported that most of the HIV-positive patients were in the age group 21-40 years.

In the present study, out of 30 patients, 21 patients are male and 9 patients are female. So males accounted for 70% and females accounted for 30% of cases. In a nation-level statistics of the HIV/AIDS cases reported to the NACO,[4] 74% were males. Kumarasamy *et al.*[6] reported a male preponderance with 72.9% cases being males.

In the present study, most common presenting symptom was weight loss seen in 80% of cases, fever (low grade) seen in 66.6% of cases and high grade fever in 20% of cases; cough with expectoration seen in 80% of cases. The cumulative data published by NACO[4] in 5204 AIDS patients indicates that 89% patient had weight loss, 88% had fever and cough was seen only in 68%.

As per NACO[4] recommendation HIV infection is diagnosed on the basis of 3 ELISA/rapid single blood tests using different antigen preparations. AIDS is diagnosed on the basis of 2 ELISA/rapid tests and presence of AIDS-related OI. All patients have undergone 2 or more ELISA tests and are found to be positive. Hence, all patients in the present study matched the NACO[4] recommendation.

The range of CD4 counts varied from 21 to 382 with a mean count of 159.8 cells/cumm. Hence, maximum numbers of patients are in advanced stage of immunosuppression in the present study.

In present study of 30 patients, 18 patients are diagnosed as having pulmonary TB accounting for 60% of cases, 5 patients are diagnosed as having bacterial infection accounting for 16.6% of cases and 3 patients are diagnosed as having PCP (10%).

An analysis of various OIs reported to NACO[4] from different parts of the country shows that about 64% of the AIDS cases were found to be suffering from pulmonary TB, bacterial infection in 7.6% cases, and PCP in 3% cases. Lanjewar and Duggal.[7] in an autopsy study to evaluate pulmonary pathology in patients with AIDS identified the cause of be TB in 59% cases, bacterial pneumonia in 18% cases, and PCP in 5% cases. Hence, the present study fairly correlates with the above-mentioned studies.

Pulmonary TB

A total of 18 patients in the present study are diagnosed to be suffering from pulmonary TB and are the most common disease noted. Worldwide, TB is the most common OI affecting HIV-seropositive individuals and it remains the most common cause of death in patients with AIDS.[8] Mohar *et al.*[9] stated that it is also possible that TB masked the recognition of other OIs.

Kumar *et al.*[10] reported cough and expectoration in 97.6% patients, while 90.4% of the patients had a low- grade fever, and significant weight loss was observed in 78.6% of the patients. In the present study, most common clinical manifestation is cough with expectoration (89%), followed by weight loss (83%), and low-grade fever (78% cases). Slight variation in present study could be attributed to small sample size.

The CD4 count in these patients varied from 21 to 382 cells/cumm with a mean count of 170.6 cells/cumm.

6 patients has CD4 count >200 cells/cumm, while 12 patients has CD4 count <200 cells/cumm.

Kumar *et al.*[10] reported that direct smear examination for AFB in sputum specimens was positive in 21.4% patients. In the present study, 33.3% has AFB in their sputum.

The most common HRCT finding in pulmonary TB are nodular opacities seen in 77.7% cases, followed by consolidation in 50%, pleural effusion in 38.8%, lymphadenopathy in 33.3%, and cavitation in 22.2% cases. Laissy *et al.*[11] also noted that nodular opacities, mainly centrilobular in distribution were the most common finding seen in 72% cases.

In present study 50% patients with pulmonary TB has consolidation visible on HRCT scans and it most commonly involved the right middle lobe and right lower lobe which correlated with study by Leung *et al.*[12] who noted consolidation in 43% cases and it was predominantly right sided.

In present study ground glass opacity are noted in 22% of patients which correlated well with study by Hartman *et al.*[13] who noted presence of ground glass opacity in 19% of cases.

Leung *et al.*[12] detected cavitation in 19% of patients with pulmonary TB. In present study, cavities are seen in 22% patients. Laissy *et al.*[11] noted that 24% patients with pulmonary TB demonstrated presence of cavitation. Furthermore, cavitation are more common in patients who had CD4 counts >200 cells/cumm. The mean CD4 count in these 24% patients is 254.2 cells/cumm.

Hartman *et al.*[13] noted pleural effusions in 38% patients with pulmonary TB. Relkin *et al.*[14] reported an increased prevalence of pleural effusion in AIDS - related TB compared with the TB in HIV - negative patients. In present study, pleural effusions are seen in 38.8% patients with pulmonary TB.

Kumar *et al.*[10] observed lymphadenopathy in 16.8% cases with pulmonary TB. In present study, lymphadenopathy is noted in 33.3% patients with pulmonary TB.

Leung *et al.*[12] noted that miliary disease was more frequent in HIV seropositive patients with 17% their cases showing miliary pattern. In present study, miliary patterns are noted in 16.7% patients. Mcguinness *et al.*[15] mentioned that bronchiectasis and bronchial wall thickening is common in HIV patients occurring in both primary and reactivation disease. In present study, bronchiectasis is noted in 44.4% patients.

Bacterial Infections

A total of 5 patients in present study are diagnosed to be suffering from bacterial infections.

Brecher *et al.*[16] noted that patients with bacterial infection typically present with a relatively rapid onset of clinical symptoms such as a productive cough, fever, shaking chills, pleuritic chest pain, and dyspnea. The most common clinical manifestation in present study is high grade fever (80%) and cough with expectoration (80%).

Hirschtick *et al.*[17] observed that although bacterial pneumonia often occurs in the early stages of HIV infection, the risk of bacterial infection increases steadily with declining CD4 lymphocyte counts. In present study, the CD4 counts varied from 121 to 366 cells/cumm with a mean count of 189.4 cells/cumm.

Boiselle *et al.*[18] and Magnenat *et al.*[19] reported that focal consolidation was observed in approximately 45-60% of patients with pyogenic infection. In present study, lobar consolidations are seen in 60% cases with bacterial infection.

Boiselle *et al.*[18] noted that bacterial infections may also present as solitary or multiple lung nodules. In present study, nodules were noted in 20% patients. The nodules are randomly distributed; some are associated with cavitation.

McGuinness *et al.*[15] noted that HIV-infected patients are at increased risk for developing infectious airways disease, with bronchiectasis being noted to develop in a relatively short time after an episode of pulmonary pyogenic infection. In present study, bronchiectasis is noted in one out of five patients with bacterial infections and it is associated with presence of air fluid level.

PCP

A total of 3 patients in present study are diagnosed to be suffering from PCP.

Thomas and Limper[20] mentioned that common symptoms of PCP include the subtle onset of progressive dyspnea, non-productive cough, and low-grade fever. In present study, most common clinical manifestation are dyspnea (100%), and then cough without expectoration (66.6%), low grade fever (66.6%), and high grade fever (33.3%).

Phair *et al.*[21] noted that PCP occurs more frequently when the CD4 count level falls below 200 cells/cumm. In present study, CD4 counts in all patients with PCP are <200 cells/cumm, with a mean count of 32.7 cells/cumm.

Hartman *et al.*[13] noted ground glass opacities in 92% of patients with PCP. Kuhlman *et al.*[22] noted that PCP

classically results in a ground-glass infiltrate, often in a geographical distribution. In present study, ground glass opacity is noted in 100% patients with PCP. Here the ground glass opacities extended from the apical to basal regions bilaterally. In addition to diffuse disease, a distinct mosaic pattern can be identified in all three patients.

Bergin *et al.*[23] noted crazy-paving pattern in 50% of patients with PCP. In present study, 66.7% patients demonstrated crazy-paving pattern. Slight variation in present study could be attributed to small sample size.

Hartman *et al.*[13] noted consolidation in 38% patients with PCP. In the present study, consolidation is seen in 33.3% cases.

CONCLUSION

From our present study of 30 HIV-positive patients coming with suspected pulmonary disease the following conclusions can be drawn:

The most common HRCT finding in pulmonary TB were nodular opacity, lobar consolidation in bacterial infection and diffuse ground glass opacities in mosaic pattern of distribution in PCP.

The diagnosis of HIV/AIDS patients presenting with pulmonary disease remains a challenge as the signs and symptoms are non-specific and tend to be atypical.

HRCT is a highly sensitive modality for detecting parenchymal abnormalities, and it allows better delineation and characterization of the lesions. Hence, HRCT should be incorporated into the management protocols of HIV/AIDS patients coming with suspected pulmonary complications.

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Original Article

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Comprehensive Study on Lobular Capillary Hemangioma of Nose in Tertiary Care Centre: A Retrospective Study

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Abstract

Background: Lobular capillary hemangioma (LCH) is a benign vascular lesion of unknown origin, the diagnosis of which can be confusing with other vascular lesions of the nose.

Materials and Methods: We retrospectively studied a cohort of 20 confirmed cases of LCH treated over 5 years period. Data regarding symptoms, possible etiologic factors, demographic profile, imaging patterns, histopathological features, and treatment modalities are reviewed.

Results: Nasal obstruction (80%) and epistaxis (60%) were the chief symptoms. The size of the lesions ranged from 1 to 10 cm. LCH was predominantly seen in females. In 70% of the patients, the mass was seen arising from the caudal end of the septum, in 20% from the anterior end of middle turbinate and in 10% from the anterior end of the inferior turbinate. All patients were operated endoscopically under general anesthesia. At mean follow-up period of 1 year no recurrence was noted.

Conclusion: Endoscopic resection of LCH in nasal cavity is associated with relatively minimal morbidity, no recurrence and better visualization of the tumor with no need for preoperative embolization.

Key words: Cohort, Epistaxis, Endoscopy, Lobular capillary hemangioma, Nasal obstruction

INTRODUCTION

Lobular capillary hemangioma (LCH) is a benign vascular growth of the skin and mucus membrane commonly affecting the head and neck.[1] Most mucosal LCH of the head and neck arise in the oral cavity, but nasal cavity involvement is rare.[2] When it is seen in the nasal cavity, the anterior portion of septal mucosa and tip of inferior turbinate are the most common involved areas.[2,3] To date there have been no reported case of malignant transformation.[2] LCH was first described by Poncet and Dor in 1897 where they referred to these tumors as small vascular tumors in the fingers of four patients.[4] LCH are commonly seen in females and usually in the third decade.[1] The exact etiology is still unknown.[5] Recurrent nose picking or nose packing may play a role in the development of LCH resulting in the overgrowth of granulation tissue.[6] Other plausible etiologies that have been proposed include viral oncogenes, microscopic arterial venous malformations and over production of angiogenic growth factors.[1] We hereby report a series of 20 cases of LCH of the nose which were managed by endoscopic guided electro-cauterization. This is one of the biggest retrospective study next to study done by Puxeddu *et al.*[1]

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MATERIALS AND METHODS

This is retrospective study wherein clinical records of 20 patients confirmed to be having LCH treated

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over a period of 6 years (June-2009 until May-2014) at Sri Siddhartha University Hospital were reviewed. Patients were individually informed about the study and their informed consent was taken to include them and their hospital records in the study. They were also informed that their images will be included in the publication in future for which they agreed. Institutional ethical clearance was taken for the study.

Inclusion Criteria

All patients confirmed by histopathology to have LCH of the nose.

Exclusion Criteria

Patients with bleeding diathesis, and other comorbidities.

Information regarding symptoms, possible etiologic factors, demographic profile, imaging patterns, histopathological features, and treatment modalities were reviewed.

RESULTS

Under endoscopic guidance, the mass was excised with electrical diathermy. Minimal bleeding was encountered for which anterior nasal packing was done with Merocel, which was removed after 24 h. Excised specimens were sent for histopathological examination, which showed the lobular arrangement of capillaries at the base. The lobules consisted of discrete clusters of endothelial cells and lumina varying from indistinct to prominent. In some, there were additional changes like capillary dilation, inflammation, stromal edema and granulation tissue reaction. The patients were followed up for a period of 1 year with no recurrence noted during this time.

Out of 20 patient, 16 (80%) were females, and 4 (20%) were males (Table 1). All 16 female patients (80%) were in the third decade, of these 10 had a history of oral contraceptive pills intake. Of the 4 male patients, 2 were in the first decade, and 2 in the third decade. Main clinical symptoms were a unilateral nasal obstruction (80%) and epistaxis (60%) which was unprovoked or with trivial trauma (Table 2). In 14 (70%) patients the mass was seen arising from the caudal end of the septum, in 4 patients (20%) from the anterior end of the middle turbinate and in 2 patients (10%) from the anterior end of inferior turbinate (Table 3). The lesions varied from 1 to 10 cm. The above findings were confirmed endoscopically.

Computed tomography (CT) scan with contrast was done in all patients, and there was almost a uniform pattern of lobulated, irregular intensely enhancing lesion.

Table 1: Sexwise distribution

Sex	*n*=20	Percentage
Male	4	20
Female	16	80

Table 2: Clinical symptoms

Symptoms	*n*=20	Percentage
Nasal obstruction	16	80
Epistaxis	12	60

Table 3: Origin of LCH in nose

Site of origin of LCH	*n*=20	Percentage
Septum	14	70
Anterior end of middle turbinate	4	20
Anterior end inferior turbinate	2	10

LCH: Lobular capillary hemangioma

DISCUSSION

LCH, also called as pyogenic granuloma was first described in 1940 by Frank and Blahd M. In 1980 Mills *et al.* termed pyogenic granuloma as LCH due to its characteristic microscopic features.[7] Although the etiology of LCH has not been clearly identified micro trauma and female hormonal factors have been suggested has predisposing factors of LCH because these lesions usually occur after trauma or during pregnancy.[8] This tumor occurs at all ages, but more frequent seen in middle-aged adults and in females than in males.[1,2] This was similar to our study where more than 3/4th of the patients were females. In nasal cavity anterior portion of the septal mucosa and tip of inferior turbinate are the most common involved areas.[1-3,8] In the present study the mass was seen to be arising from the caudal end of the septum in the majority (70%) of the patients. Epistaxis is the most common mode of presentation of LCH. However as the lesion increase in size, it may cause symptomatic unilateral nasal obstruction.[2] This was in contrast to our study wherein the nasal obstruction was the predominant (80%) presenting complaint which can be attributed to late medical attention. CT imaging findings of LCH are non-specific, LCH should be considered as a possible diagnosis whenever a well-defined soft tissue mass with mild diffuse homogenous enhancement or marked central enhancement of the mass with a peripheral isodense area on the enhanced CT scans is seen in the nasal cavity.[9] In our study all patients, CT scan showed lobulated irregular intensely enhancing picture. Endoscopic surgery is the treatment of choice even for large lesions, preoperative embolization warranted very rarely.[1]

All 20 patients in our study underwent endoscopic excision with cauterization of base of the lesion under general anesthesia with minimal morbidity. Cauterization of the base of the tumor is associated with good hemostasis and low rate of recurrence.[6,10,11]

CONCLUSION

With this experience, we advocate trans nasal endoscopic resection of LCH in nasal cavity using electrocautery, as it is associated with relatively minimal morbidity, low rate of recurrence and better visualization of the tumor. However, this being a single center study this needs to be replicated in other centers.

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Original Article

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Immunophenotyping in Acute Leukemia: A Clinical Study

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Abstract

Background: Acute leukemia area a group of neoplastic disorders characterized by proliferation and accumulation of immature hematopoeitic cells in bone marrow, blood, and other tissues. The present study was conducted to have a detailed understanding of immunophenotyping profile, the morphologic and immunophenotypic discrepancy and importance of immunophenotyping in diagnosis of acute leukemia.

Objectives: To study immunophenotyping profile in acute leukemia (acute myeloid leukemia [AML], acute lymphoid leukemia, and mixed lineage leukemia) and to study its importance in diagnosis.

Materials and Methods: This study was performed in Medical College, Jabalpur. 160 patients diagnosed morphologically with AML, acute lymphoblastic leukemia and mixed lineage leukemia seen were included in the study.

Results: Only in 73% cases of acute leukemia did find similarity in morphological appearance and immunophenotyping. In remaining 27% cases morphological findings did not correlate with immunophenotyping expression. Diagnosis in these 27% patients changed after immunophenotyping.

Conclusions: It is imperative and absolutely essential to ascertain the lineage of leukemia by immunophenotyping before starting on treatment as more than 25% of patients would not respond or later relapse if treatment is initiated on morphological diagnosis.

Key words: Cytogenetics, Leukemia, Lineage leukemia, Immunophenotyping

INTRODUCTION

Acute leukemia area group of neoplastic disorders characterized by proliferation and accumulation of immature hematopoeitic cells in bone marrow and blood and other tissues.

Velpeau in 1827 reported the first accurate description of case of leukemia. In 1845, Bennet published a report of series of patients who died with enlarged spleen and changes in color and consistency of blood. He coined the term "Leukocythemia." Virchow introduced the term "leukemia" which he derived from Greek meaning white blood. Neumann in 1869 described that white blood cells (WBC) were made in bone marrow. Moser in 1869 described aspiration of bone marrow as the means to diagnose acute leukemia. Negalia in 1900 described myeloblast and divided leukemia into acute lymphocytic leukemia (ALL) and acute myeloid leukemia (AML). The development of histochemical stains, cytogenetics, immunologic, molecular, and biochemical markers have helped to define the lineage of acute leukemia.[1]

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Acute leukemia is diagnosed on doing morphologic evaluation of bone marrow based on suspicion created by altered hematological profile. The malignant cells are called blasts. The normal percentage of blasts in marrow is <5%. For diagnosis of acute leukemia the percentage of blasts in marrow is >20%. Morphologically that is how blasts appear under microscope, leukemia are classified into two types AML and ALL. AML is subclassified into M0-M7 and ALL has three subtypes L1-L3. After

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diagnosing acute leukemia morphologically the cells are subjected to cytochemistry.[2]

Every blood cell expresses certain cytoplasmic and surface proteins which are called cluster differentiation (CD) antigens. Every level of differentiation has a unique set of expression of CD antigens. Immunophenotyping is the identification and quantification of cellular antigens through flourochrome labeled monoclonal antibodies. The immunophenotypic identification and classification of cells began in late 1970 with revolution in immunology by the discovery of T- and B-cells.[3] The technology then expanded to the analysis of other cells as myeloid cells in various stages of maturation. As a result of the progress in the understanding of molecular biology and cytogenetics of acute leukemia, WHO again classified leukemia from morphologic classification to immunological and cytogenetic classification in 1985. Morphological classification of acute leukemia may not always be correct and hence clinically immunophenotype analysis since then has become critical part of initial diagnosis and classification of acute leukemia.[4] In addition, immunophenotyping provides prognostic information not available by other techniques provides a sensitive means to monitor the progress of patients after chemotherapy and aids in detection of minimal residual disease.

The present study was conducted to have a detailed understanding of immunophenotyping profile, the morphologic and immunophenotypic discrepancy and importance of immunophenotyping in diagnosis of acute leukemia.

Aims and Objectives

To study the immunophenotypic profile in acute leukemia (AML, ALL and mixed lineage leukemia) and to study its importance in diagnosis.

MATERIALS AND METHODS

The 160 patients diagnosed morphologically with AML, acute lymphoblastic leukemia and mixed lineage leukemia seen were included in study.

Eligibility Criteria

1. Patients of all age groups were eligible
2. Only previously untreated patients were included
3. The requirement for the diagnosis
   - Presence of >20% blasts in bone marrow aspirate with appropriate clinical syndrome
   - The morphological diagnosis to be supplemented by immunological diagnosis
   - If possible, the diagnosis to be supplemented by cytogenetic studies.
4. No cases of chronic leukemia were eligible.

Investigations to be Completed on Patient Entry

1. Clinical information
2. Nutritional status assessed based on Indian Academy of Pediatric classification (weight for age)
3. Routine laboratory investigations
4. Hematology: Hemoglobin, total leukocyte count, differential leucocyte count, peripheral smear red blood cell indices, platelet counts
5. Biochemistry: Renal function test, liver function tests, serum electrolytes, serum uric acid and serum lactic acid dehydrogenase
6. X-ray chest
7. Bone marrow aspirate and sample evaluation for cytochemistry with periodic acid-Schiff (PAS) and Sudan black B stains, immunophenotyping and cytogenetics
8. Other laboratory and imaging as par clinical indications
9. Diagnosis was based on immunological classification rather morphologic classification. Immunophenotyping was primarily performed by three color flowcytometric analysis of bone marrow aspirate or peripheral blood. After mononuclear cell enrichment by centrifugation over histopaque 1077, the peripheral blood and bone marrow specimens were studied for surface antigen expression using panel of monoclonal antibodies. Blasts were gated for the analysis with the use of CD45 antigen expression and right angle light scatter as described by Borowitz. The antigens detected and antibodies used were CD45, human leukocyte antigens (HLA) DR, CD34, CD13, CD33, CD117, CD54, CD56, CD41, CD61, CD2, CD3, CD4, CD5, CD7, CD8, PAN T, CD10, CD19, CD22, CD79, and PAN B. For all the above markers, blasts were considered positive if 20% or more expressed an antigen. For myeloperoxidase (MPO), it was considered to be positive when more than 3% of blasts reacted positively with anti-MPO.
10. Treatment of patient was according to immunologic diagnosis. ALL patients were kept on NCI MCP 841 or BFM 90 ALL protocol. AML patients were treated with standard 7 + 3 protocol (cytosine arabinoside 100-200 mg/m^2 × 7 days + daunorubicin 45-60 mg/m^2 × 3 days) or 5 + 2 protocol (cytosine arabinoside 100-200 mg/m^2 × 5 days + daunorubicin 45-60 mg/m^2 × 2 days) depending on age and performance status of patients
11. ALL patients were evaluated on day 8 for assessing the cytoreduction and response to chemotherapy. The peripheral blood smear on day 8 was assessed for the

presence or absence of blasts. If blasts were seen their percentage and absolute count was recorded

12. AML patients were evaluated 21-28 days after induction chemotherapy for demonstration of morphological remission. This was followed by 2-3 courses of intermediate dose (2 g/m^2 q12 hourly × 3 days) cytosine arabinoside as post induction consolidation therapy after achieving morphological remission
13. If AML patient failed to achieve morphologic remission after 1st course of 7 + 3 therapy, he was reinduced by 2nd course of induction 7 + 3 chemotherapy regimen in same dose
14. All patients were periodically assessed for any complication, mortality and response of treatment.

Support Measures and Management of Tumor Lysis

Neutropenic patients with absolute neutrophil count <500 with fever >100°F were hospitalized and immediate intravenous (IV) antibiotics to be started. Patients managed according to standard febrile neutropenia guidelines.

Patients with platelet counts <15,000/uL or overtly bleeding received platelet rich plasma transfusions. Irradiated blood products were administered. To the possible extent single donor platelets were transfused.

All patients were hydrated and given allopurinol (10 mg/kg for 7 days, then 5 mg/kg) during initial induction therapy. IV fluids at 3 L/m^2 preferably half normal salione without added potassium (unless hypokalemia) were given until WBC count was below 10,000/cmm, lymphadenopathy and organomegaly were reduced in size by 75%.

Patients of ALL with WBC of >1 Lakh/cmm were treated with prednisolone 10 mg/m^2 twice a day until the WBC count falls below 50,000/cmm prior to commencing induction protocol. If no response to prednisolone occurs within 24 h, induction protocol was started under careful surveillance of electrolytes and urine output.

Observations

There were 160 cases of acute leukemia in the study.

The distribution of cases was according to imunophenotyping profile into AML (83 cases: 51%), ALL (66 cases: 42%) and mixed lineage leukemia (11 cases: 7%).

AML

There were 83 cases (51%) of AML in the study.

Bone marrow profile of AML patients

Marrow was hypercellular in all cases.

In cytochemistry PAS stain was positive in 18 (22%), inconclusive in 5 (6%) and negative in 51 (60%) cases of AML. Sudan black was positive in 55 (66%), inconclusive in 5 (6%) and negative in 20 (24%) patients. Bone marrow blasts ranged between 14% and 95% and average percentage of blasts in marrow was 38%. Auer rods were seen in 15 (18%) of cases and absent in 68 (81%) of cases.

Bone marrow profile in various subtypes of AML

Marrow was hypercellular in all cases.

PAS was positive in 2 (25%) of AML M0, 5 (27%) cases of AML M1, 13 (40%) of AML M2, 3 (42%) of AML M3, 1 (12%) of AML M4, 2 (25%) of AML M5, and in no case of AML M6. PAS was inconclusive in 1 (4.4%) of AML M1, 2 (6%) cases of AML M2, and 1 (13%) cases of AML M5. PAS was negative in 5 (75%) of AML M0, 22 (68%) of AML M1, 17 (53%) of AML M2, 3 (57%) of AML M3, 8 (88%) of AML M4, 5 (62%) of AML M5, and 1 (100%) of AML M6.

Sudan black was positive in 6 (100%) of AM M0, 13 (63%) cases of AML M1, 22 (66%) of AML M2, 5 (86%) of AML M3, 6 (66%) of AML M4, 4 (50%) of AML M5, and in 1 (100%) cases of AML M6. Sudan black was inconclusive in 1 (9%) of AML M1, 1 (3%) of AML M2, 1 (11%) of AML M4, and 1 (13%) cases of AML M5. Sudan black was negative in 2 (27%) of AML M1, 10 (30%) of AML M2, 1 (13%) of AML M3, 2 (23%) of AML M4, and 3 (37%) of AML M5.

Bone marrow blasts ranged from 14% to 95%. Average number of blasts was 66.7% in AML M0, 71.2% in AML M1, 67.6% in AML M2, 82% in AML M3, 74% in AML M4, 73.1% in AML M5, and 65% in AML M6.

Auer rods were seen in 100% cases of AML M0, 3 (13%) cases of AML M1, 5 (20%) cases of AML M2, 5 (91%) cases of AML M3, 3 (33%) cases of AML M4, and were not seen in 17 (86%) of AML M1, 28 (80%) of AML M2, 1 (9%) of AML M3, 6 (66%) of AML M4, 8 (100%) of AML M5, and 1 (100%) of AML M6.

Immunophenotyic profile of AML patients

The expression of HLA-DR was highest in AML MO - 3 (50%). It was positive in 6 (33%) of M1 MI, 4 of ML M2, 4 (44%) of AML M4, and 3 (33%) of AML M5 and was absent in AML M3 and AML M6.

The expression of CD34 was highest in AML M1 - 6 (33%). It was positive in 2 (7%) of AML M2 and 1 (12%) of AML

M5 and was absent in AML M0, AML M3, AML M4, and AML M6.

The expression of CD 13 was highest in AML M6 - 1 (100%). It was positive in 1 (11%) cases of AML M0, 9 (43%) of AML M1, 3 (10%) of AML M2, 3 (42%) of AML M3, and 7 (77%) of AML M4, and 3 (37%) of cases of AML M5.

The expression of CD 33 was highest in AML M4, AML M5 and AML M6, - 100%. It was positive in 75% cases of AML M0 and AML M1, 28 (86%) of AML M2 and 3 (57%) of AML M3.

The expression of CD117 was highest in AML M6 - 1 (100%). It was positive in 3 (50%) cases of AML M0, 8 (40%) of AML M1, 10 (31%) of AML M2 2 (28%) of AML M3, and 7 (75%) of AML M4, and 3 (37%) of cases of AML M5.

MPO was expressed in all cases of AML M0, AML M1, AML M2, AML M4 and AML M6. It was positive in 5 (85%) cases of AML M3 and 6 (75%) cases of AML M5.

Lymphoid antigens CD22 and CD79 were seen in 1 (1%) of AML patients (AML M2).

In the present study positive lymphoid markers were CD22 and CD79 positive in 1 patient of AML M2.

The high lymphoid antigen expression was not observed in our study as we have included cases expressing both myeloid and more than one lymphoid antigen in multiple lineage leukemia.

Acute Lymphoblastic Leukemia

Bone marrow profile of ALL patients

Marrow was hypercelular in all cases.

In cytochemistry PAS stain was positive in 42 (62%), inconclusive in 2 (3%), and negative in 19 (28%) cases of ALL. Sudan black was positive in 3 (4.4%), inconclusive in 2 (3%) and negative in 62 (91%) patients. Bone marrow blasts ranged between 43% and 99% and average number of blasts in marrow was 85.2%.

Morphological diagnosis in ALL patients

Morphologically 60% (89%) marrow were suggestive of ALL, 3 (4%) suggestive of AML and 4 (6%) were suggestive of acute undifferentiated leukemia.

Immunophenotypic profile of ALL patients

B lymphoid antigens

CD10: 38 (67%) and CD22: 34 (60%) were the most common B lymphoid antigens expressed. HLA-DR was expressed in 22 (34%), CD34 in 21 (32%), CD79 in 17 (30%), CD19 in 24 (42%) and PAN B was expressed in 31% of all B-cell ALL cases.

T lymphoid antigens

CD3 7 (78%) was the most commonly expressed T-cell antigen. CD2 was expressed in 3 (33%), CD5 in 5 (56%), CD7 in 5 (56%) and PAN T was seen in 4 (44%) of all T-cell ALL cases.

There were a total of 57 (83%) cases of B-cell ALL and 9 (17%) cases of T-cell ALL.

Mixed Lineage Leukemia

Bone marrow profile of mixed lineage leukemia (MLL) patients

Marrow was hypercelular in all cases.

In cytochemistry PAS stain was positive in 3 (27%), inconclusive in 0 (0%) and negative in 8 (72%) cases of ALL. Sudan black was positive in 3 (27%), inconclusive in 1 (9%) and negative in 7 (63%) patients. Bone marrow blasts ranged between 65% and 90% and average number of blasts in marrow was 83.1% Auer rods were absent in all 100% of cases.

Immunophenotypic profile of MLL patients

Myeloid antigens

HLA-DR was present in 9% (1) cases, CD34 in 9% (1) cases, CD33 in 63% (7) cases CD117 in 18% (2) cases and MPO positive in 81% (9) cases.

B lymphoid antigens

PAN B (54%) was the most common B lymphoid antigens expressed. VCD 10 in 9%, CD22 in 9% and CD79 in 9% were other B lymphoid antigens expressed.

T lymphoid antigens

PAN T 45% was the most common expressed T-cell antigen. CD3 in 18% CD5 in 9% CD7 in % and CD8 in 9% cases were the other T lymphoid antigens expressed.

When biphenotyping score was calculated, off the total 11 cases, 4 (36%) patients had biphenotypic leukemia and 7 (64%) patents had bilineage leukemia.

DISCUSSION

There were 160 cases of acute leukemia in the study.

The distribution of cases was according to imunophenotyping profile into AML (83 cases: 51%), ALL (66 cases: 42%) and mixed lineage leukemia (11 cases: 7%).

AML

Distribution of AML patients according to FAB subtype is shown in Table 1.

According to one of the study conducted,[1] MPO activity is present in the primary (azurophilic granules) of both myeloid and monocytic precursors. In cytochemistry PAS stain was positive in 18 (22%), inconclusive in 5 (6%) and negative in 51 (60%) cases of AML. Sudan black was positive in 55 (66%), inconclusive in 5 (6%) and negative in 20 (24%) patients. Bone marrow blasts ranged between 14% and 95% and average percentage of blasts in marrow was 38%. Auer rods were seen in 16 (19%) of cases and absent in 67 (81%) of cases (Table 2).

Morphologically 61 (73%) marrow were suggestive of AML, 15 (18%) suggestive of ALL, 3 (3%) were reported as chronic myeloid leukaemia blastic phase, 1 (1%) was suggestive as acute undifferentiated leukemia, biphenotypic leukemia, myelodysplastic syndrome, and bilineage leukemia (Table 3).

Hoffbrand *et al.*,[5] San Miguel *et al.*,[6] Griffin *et al.*[7] in their studies have shown that the morphological diagnosis is not very reliable in conclusively diagnosing acute leukemia. Immunophenotyping is mandatory for establishing the confirmed diagnosis of acute leukemias and their subtypes. In up to 25% cases the immunophenotyping for cell antigen marker change the lineage of leukemia similar to that seen in our study.

Marrow was hypercellular in all cases (Table 4).

Positive staining with Sudan black B stains intracellular lipids which are found in secondary granules of both myeloid and monocyte precursors.

Griffin *et al.*[7] observed MPO positive in >95% cases of AML and PAS positive in 70% cases and negative in 8% cases.

Ghosh *et al.*[8] have found MPO positive in 97% AML.

Estey *et al.*[9] in their study of 180 acute leukemia cases found MPO to be very specific marker for myeloid antigen, the overall positivity of anti MPO in AML was 92%. Anti MPO

Table 1: Distribution of AML according to FAB subtypes

FAB subtype	Number of patients (%)
AML M0	5 (6)
AML M1	20 (24)
AML M2	33 (39)
AML M3	6 (7.2)
AML M4	9 ((10.8)
AML M5	8 (9.6)
AML M6	1 (1)
AML M7	0

AML: Acute myeloid leukemia , FAB: French american british classification

Table 2: Bone marrow profile of AML patients

Cytochemistry (%)						Blasts (%)		Auer rods	
PAS			Sudan			Mean	Range	Present	Absent
Positive	Incon	Negative	Positive	Incon*	Negative				
18 (22)	5 (6)	51 (61)	55 (66)	5 (6)	20 (24)	32	14-95	16 (19)	67 (81)

PAS: Periodic acid-Schiff, AML: Acute myeloid leukemia

Table 3: Morphological diagnosis of AML patients

Total number	Morphological diagnosis (%)						
	AML	ALL	AUL	CML (BP)	Biphenotypic	MDS	Bilineage
83	61 (73)	15 (18)	1 (1)	2 (3)	1 (1)	1 (1)	1 (1)

AML: Acute myeloid leukemia, ALL: Acute lymphocytic leukemia, CML: Chronic myeloid leukemia, AUL: Acute undifferentiated leukemia, MDS: Myelodysplastic syndrome

Table 4: Bone marrow profile of AML patients according to FAB subtype

FAB subtype	Number of cases	Cellularity	Cytochemistry (%)						Blasts (%)		Auer rods (%)	
		Hyper (%)	PAS			Sudan			Mean	Range	Present	Absent
			Positive	Incon*	Negative	Positive	Incon*	Negative				
M0	4	4 (100)	1 (25)	-	3 (75)	4 (100)	-	-	66.7	45-91	4 (100)	-
M1	22	22 (100)	6 (27)	10 (4.4)	15 (68)	14 (63)	2 (9)	6 (27)	71.2	22-95	3 (13)	19 (86)
M2	33	33 (100)	13 (40)	2 (6)	17 (53)	22 (66)	1 (3)	10 (30)	67.6	14-95	7 (20)	26 (80)
M3	7	7 (100)	3 (42)	-	4 (57)	6 (86)	-	1 (13)	82	67-90	6 (91)	1 (9)
M4	9	9 (100)	1 (12)	-	8 (88)	6 (66)	1 (11)	2 (23)	74	41-90	3 (33)	6 (66)
M5	8	8 (100)	2 (25)	1 (13)	5 (62)	4 (50)	1 (13)	3 (37)	73.1	56-93	-	8 (100)
M6	1	1 (100)	-	-	100%	100%	-	-	65	65	-	100
M7	-	-	-	-	-	-	-	-	-	-	-	-

PAS: Periodic acid-Schiff, AML: Acute myeloid leukemia, FAB: French american british classification, Incon: Inconsequential

was negative in all but two ALL which later was classified as biphenotypic leukemia.

Table 5: Immunophenotype profile of AML patients

FAB subtype	HLA-DR (%)	CD34 (%)	CD13 (%)	CD33 (%)	CD117 (%)	MPO (%)
MO	3 (50)	0 (0)	1 (11)	5 (75)	3 (50)	6 (100)
M1	7 (33)	6 (30)	9 (43)	15 (57)	8 (40)	20 (100)
M2	10 (13)	2 (7)	3 (10)	28 (86)	10 (31)	33 (100)
M3	0 (0)	0 (0)	3 (42)	3 (57)	2 (28)	5 (85)
M4	4 (44)	0 (0)	7 (77)	9 (100)	7 (75)	9 (100)
M5	3 (33)	2 (12)	3 (37)	8 (100)	3 (37)	6 (75)
M6	0 (0)	0 (0)	1 (100)	1 (100)	1 (100)	1 (100)

HLA: Human leukocyte antigens, AML: Acute myeloid leukemia, MPO: Myeloperoxidase

Table 6: Lymphoid antigen expression in AML patients

FAB subtype	CD10	CD19	CD22	CD79	CD2	CD3	CD4	CD5	CD7	CD8
M0	-	-	-		-	-	-	-	-	-
M1	-	-	-		-	-	-	-	-	-
M2	-	-	1 (3%)	1 (3%)	-	-	-	-	-	-
M3	-	-	-	-	-	-	-	-	-	-
M4	-	-	-	-	-	-	-	-	-	-
M5	-	-	-	-	-	-	-	-	-	-
M6	-	-	-	-	-	-	-	-	-	-

AML: Acute myeloid leukemia

Table 7: Comparison between the immunophenotyping observations of presentation of lymphoid markers in AML all figures represent % of patients having positive antigen

Subtype	CD10	CD19	CD2	CD3	CD5	CD7
M0	0/0*	0/0*	0/0*	0/0*	0/0*	29/0*
M1	0/0*	7/0*	7/0*	7/0*	0/0*	20/0*
M2	5/0*	21/0*	5/0*	0/0*	5/0*	14/0*
M3	0/0*	14/0**	29/0*	0/0*	0/0*	0/0*
M4	0/0*	0/0*	9/0*	20/0*	0/0*	0/0*
M5	0/0*	0/0*	17/0*	17/0*	17/0*	17/0*
M6	0/0*	0/0*	0/0*	0/0*	0/0*	0/0*

AML: Acute myeloid leukemia

Blasts with L1 or L2 morphology showing block PAS positivity will be classified as lymphoblasts; therefore, a combined MPO RAS staining has relevance in developed countries.

Considering the significance of cytogenetics and immunopnenotyping in the diagnosis, treatment decision and prognosis of acute leukemia, consensus panel of WHO proposed a new revised classification for acute leukemia.[10]

Immunophenotypic observations in our study (Table 5) were similar to those observed by Khalidi *et al.*[11] and Ghosh *et al.*[8] and in their study. Similarly, the expression of lymphoid antigens (Table 6) in AML was similar to the observations of by Ghosh *et al.*[8]

Acute Lymphoblastic Leukemia

Comparison between the immunophenotyping observations of presentation of lymphoid markers in AML all figures represent % of patients having positive antigen. (Table 7).

In cytochemistry PAS stain was positive in 41 (62%), inconclusive in 2 (3%) and negative in 18 (28%) cases of ALL. Sudan black was positive in 3 (4.4%), inconclusive in 2 (3%) and negative in 62 (91%) patients (Table 8). Morphologically 60% (89%) marrow were suggestive of ALL, 3 (4%) suggestive of AML and 4 (6%) were suggestive of acute undifferentiated leukemia.

Data from India varies from center to center. In general there is a relatively high incidence of T-cell ALL. This was particularly high in the series by Kamat *et al.*[12] (43%). Similar data from Naeem and Hayee from Lahore reported 36% T-cell ALL.[13]

B lymphoid antigens

CD10: 38 (67%) and CD22: 34 (60%) were the most common B lymphoid antigens expressed. HLA-DR

Table 8: Bone marrow profile of ALL patients

Cytochemistry (%)						Blasts (%)		Auer rods (%)	
PAS			Sudan			Mean	Range	Present	Absent
Positive	Incon*	Negative	Positive	Incon*	Negative				
41 (62)	2 (3)	18 (28)	3 (4)	2 (3)	61 (93)	85.2	43-99	0 (0)	66 (100)

PAS: Periodic acid-Schiff, AML: Acute myeloid leukemia

Table 9: Immunophenotypic profile of ALL patients

Stem cell (%)		B-cell (%)					T-cell (%)				
HLA DR	CD34	CD79	CD22	CD10	CD19	PAN B	CD3	CD2	CD5	CD7	PAN T
22 (34)	21 (32)	17 (30)	34 (60)	38 (67)	24 (42)	20 (31)	7 (78)	3 (33)	5 (33)	5 (56)	4 (44)

ALL: Acute lymphocytic leukemia, HLA: Human leukocyte antigens

was expressed in 22 (34%), CD34 in 21 (32%), CD79 in 17 (30%), CD19 in 24 (42%) and PAN B was expressed in 31% of all B-cell ALL cases.

T lymphoid antigens

CD3 in 7 (78%) was the most common expressed T-cell antigen. CD2 was expressed in 3 (33%), CD5 in 5 (56%), CD7 in 5 (56%), and PAN T was seen in 4 (44%) of all T-cell ALL cases (Table 9).

There were a total of 57 (83%) cases of B-cell ALL and 9 (17%) cases of T-cell ALL.

Pui *et al.*[14] have reported incidence of Sudan black to be positive in 2.7% cases of ALL Therefore, Sudan black B used alone to differentiate lymphoid from myeloid leukemia may be misleading. Arber has found MPO positive in 23% cases of ALL.

Data from the western series indicate a high incidence of pre B (80-87%) immunophenotype.

In the present study the immunophenotypic diagnosis of pre B ALL was seen in 83% and T-cell ALL was seen in 16% cases (Table 10) which was similar to observations of Shanta *et al.*[15] and Magrath *et al.*[16] but less than the observations of Schrappe *et al.*,[17] and Tsuchida *et al.*[18] This difference in the incidence of distribution of various subtypes of ALL may have some regional influences which needs further evaluation.

Mixed Lineage Leukemia

Marrow was hypercelular in all cases.

In cytochemistry PAS stain was positive in 3 (27%), inconclusive in 0 (0%) and negative in 8 (72%) cases of ALL. Sudan black was positive in 3 (27%), inconclusive in 1 (9%) and negative in 7 (63%) patients. According to one of the study conducted[19] in their series observed PAS positivity in 50% of cases and remaining 50% were PAS negative in. Sudan B was positive in 25% and negative in 75% of cases. The findings were comparable to the present study.

Table 10: Distribution of ALL cases according to lineage

B-cell ALL (%)	T-cell ALL (%)
57 (83)	9 (16)

ALL: Acute lymphocytic leukemia

Myeloid antigens

HLA-DR was present in 9% (1) cases, CD34 in 9% (1) cases, CD33 in 63% (7) cases CD117 in 18% (2) cases and MPO positive in 81%(9) cases.

B lymphoid antigens

PAN B (54%) was the most common B lymphoid antigens expressed. VCD 10 in 9%, CD22 in 9% and CD79 in 9% were other B lymphoid antigens expressed.

T lymphoid antigens

PAN T 45% was the most common expressed T-cell antigen. CD3 in 18% CD5 in 9% CD7 in % and CD8 in 9% cases were the other T lymphoid antigens expressed (Table 11).

When biphenotyping score was calculated, off the total 11 cases, 4 (36%) patients had biphenotypic leukemia and 7 (64%) patents had bilineage leukemia (Table 12).

Kantarjian *et al.*[20] observed the following immunophenotype in their study.

T-cell markers: CD2 - 42%; CD3 - 0%; CD4 - 24%, CD5 - 14%; CD7 - 57%; CD8 - 0. B-cell markers: CD10 - 14%; CD19 - 28%; CD20 - 28%; SLG - 0%.

Myeloid markers: CD11b - 0%; CD13 - 57%; CD14 - 0%; CD154 - 28%; CD33 - 57% MPO – 100%.

Non lineage restricted markers: HLA-DR - 85%; CD34 - 57%.

The observations of Kantarjian *et al.* are comparable to the observations seen in the present study.

CONCLUSION

Only in 73% cases of acute leukemia did find similarity in morphological appearance and immunophenotyping. In remaining 27% cases morphological findings did not correlate with immunophenotyping expression.

Table 11: Immunophenotypic profile of mixed lineage leukemia patients

Myeloid (%)						Lymphoid (%)										
HLA DR	CD34	CD13	CD33	CD117	MPO	CD10	CD19	CD22	CD79	CD3	CD4	CD5	CD7	CD8	PAN B	PAN T
1 (9)	1 (9)	-	7 (63)	2 (18)	9 (81)	1 (9)	-	1 (9)	1 (9)	2 (18)	-	1 (9)	1 (9)	1 (9)	6 (54)	5 (45)

HLA: Human leukocyte antigens, MPO: Myeloperoxidase

Table 12: Immunophenotypic classification of mixed lineage leukemia patients

Number of patients	Biphenotypic leukemia (%)	Bilieneage leukemia (%)
11	4 (36)	7 (64)

Diagnosis in these 27% patients changed after immunophenotyping.

It is therefore imperative and absolutely essential to ascertain the lineage of leukemia by immunophenotyping before starting on treatment as more than 25% of patients would not respond or later relapse if treatment is initiated on morphological diagnosis.

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Original Article

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Morphological Changes of Placenta in Cases of Pre-eclampsia and Perinatal Outcome

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Abstract

Background: Hypertensive disorder of pregnancy is most common medical problem complicating 3-8% of pregnancies. As pathophysiology lies in placenta most attention is drawn on placenta. In recent years it acts as valuable indicator for maternal and fetal diseases.

Objectives: The objective of study was to assess the morphological changes of placenta and to correlate the findings with severity of disease and with fetal outcome.

Materials and Methods: Total of 400 placentae of which 200 placentae from cases of pre-eclampsia (PE) (100-mild, 100-severe) and 200 placentae from normal cases were studied in labor room Vijayanagara Institute Medical Sciences, Bellary. The morphometric parameters of placenta like weight, volume, thickness, diameter, shape, number of cotyledons were recorded. Gross features like infarctions, calcifications, retro placental (RP) hematoma were noted and fetal parameters like fetal weight and Apgar score at 1st and 5th min recorded.

Results: There was a significant correlation between placental weight and weight of baby and neonatal intensive care unit admission $P < 0.001$. Placental morphometric features like mean weight, volume, thickness, diameter, number of cotyledons values were significantly less in severe PE group compared to mild PE group with $P < 0.001$ and compared to control group all parameters are significantly less in study group ($P < 0.001$). There was significant correlation between infarction and fetal birth weight ($P < 0.001$). There were 5 still births 4 in severe PE and 1 in mild PE. The placentae of this still birth were having calcifications, infarctions and RP clots. Mean fetoplacental (F/P) ratio was higher in study group compared to control group ($P < 0.001$).

Conclusion: In present study the placental morphometric features like placental weight, volume, diameter, thickness were low with increasing grades of hypertension compared to control group. There was an increased F/P weight ratio in the hypertensive group. The study of morphological changes of placenta in cases of PE may help us to plan the treatment plan for better outcome of mother and newborn. Serves as important medico legal record.

Key words: Apgar score, Morphology, Placenta, Perinatal outcome, Pre-eclampsia

INTRODUCTION

Placenta is discoid, haemochorial and a decidual structure developed during pregnancy and is the organ of exchange between the fetus and mother for the purpose of physiological exchange. It is considered as the accurate record of prenatal experiences. Hypertensive disorder of pregnancy along with hemorrhage and infection form one of the deadly triad that greatly contributes to maternal mortality and morbidity. Pre-eclampsia (PE) has been described as the disease of theories. One of the leading theories is that there is a maternal immunological response to the fetal immune system, resulting in abnormal transformation of the spiral arteries these leads to a high-resistance blood flow to the placenta. The turbulence of the blood flow and hypoxia in the placenta then give rise to a destruction of placental tissue and release of factors, such as soluble vascular endothelial growth factor receptor-1,

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syncytio-trophoblast membrane micro particles, fetal RNA and DNA, which might injure maternal endothelium and be responsible for the maternal symptoms in PE.[1-6] In addition it has its effect on fetal growth restriction, prematurity, contributing largely to perinatal mortality and morbidity. Morphologically placentae of hypertensive disorders of pregnancy are lighter in weight, lesser in diameter and thickness. Abnormal shape, cord insertion and with diminished fetoplacental (F/P) ratio. There is higher incidence of infarction, retro placental (RP) hematoma, sub-chorionic fibrin. These placental changes are directly proportional to the duration of the disease and its severity. Decrease of fetal weight is significantly larger than placental weight loss. Most obstetricians and pediatricians would agree that the examination of placenta often helps to explain an abnormal neonatal outcome. As in our country still many unbooked patients visit the hospital only for delivery, it may be possible to decide whether the pathological condition that endangered the well-being of the fetus was an acute or a chronic process. Conditions with the risk of recurrence can be recognized, resulting in counseling and management of subsequent pregnancies. Despite the understanding and appreciation of placental disease, great resistance still exists in performing placental examination routinely. So the detail study of placentae morphologically done in cases of PE to know significant changes compared to normal and its fetal outcome.

MATERIALS AND METHODS

After taking ethical clearance from the institute study of a total of 200 placentae from cases of PE (100-mild, 100-severe) and 200 placentae from normal cases attending the Vijayanagara Institute Medical Sciences, Obstetrics and Gynecology Bellary, Labor room were studied from December 2011 to September 2013.

Inclusion Criteria

All pregnant women admitting to the labor room with gestational age >34 weeks irrespective of age and parity were included.

Exclusion Criteria

Twin pregnancy, Rh negative pregnancy, pregnancy with - gestational diabetes, heart diseases, autoimmune disorders, chronic hypertension; placenta previa and eclampsia were excluded.

Samples were grouped into three groups as Group A, Group B, Group C.

Group A: This group comprised of pregnant women with mild PE.
Group B: This group comprised of pregnant women with severe PE.
Group C: This group comprised of pregnant women without PE.

The criteria adopted for grouping of the cases were defined according to the Working Group of National High Blood Pressure Education Programme (2000).

Detailed obstetric and medical history was taken for all cases, clinical examination done and they were subjected to following investigations:

1. Urine: Sugar, albumin, microscopy
2. Blood: Hemoglobin%, blood grouping and Rh typing, HIV, hepatitis B surface antigen. Blood urea and uric acid, serum creatinine
3. Platelet count liver enzymes, fundoscopy.

Just after delivery all the placentae were collected in a clean tray. The membranes and cord at their attachment to the placenta was cut off. The placenta was gently expressed so as to remove its blood content and mopped with dry cotton pad. The following parameters of placenta were used for comparison among various study groups. Weight measured by weighing machine, with help of graduated metallic scale mean of two maximum diameters taken at right angles. Thickness measured by using thick needle which was inserted at 5 points and volume by water displacement method. Gentle pressure was put on the fetal surface to make the cotyledons prominent and cotyledons counted. RP hematoma, infarction, calcification. All parameters were measured using methods same as study done by Kishwara *et al*.[7] At the time of delivery fetal conditions like birth weight, Apgar score at 1 min and 5 min were noted. Babies admitted to neonatal intensive care unit (NICU) were followed up. F/P ratio calculated.

Statistical Analysis

Comparison of various parameters between study groups will be analyzed by ANOVA and by Student's test. Categorical data will be analyzed by Chi-square test.

RESULTS

Highest study subjects were from age group 21 to 30 years (64.5%) followed by <20 years (32.8%). Out of 400 study subjects 245 (61.3%) were primigravida and 155 (38.8%) were multigravida. 300 (75%) had spontaneous

vaginal delivery, 20 (5%) had induced vaginal delivery and 80 (20%) delivered by caesarean section. In the present study more number of preterm delivered cases belonged to the hypertensive group. Pre-term delivery 19 (9.5%) in normal cases, 11 (11.1%) mild PE, 20 (20.8%) severe PE. Most common shape of the placenta in our study was circular in both cases and controls about (90.2%). In severe PE the occurrence was 81 (91.0%) in mild PE it was 91 (91.0%). Compared to controls we observed more oval shaped placenta in cases. In severe PE 19 (19.0%), mild PE 7 (7.0%) and in controls 9 (4.5%) the findings were statistically significant ($P < 0.001$). Among both cases and controls central cord insertion was observed most commonly (95.0%). Compared to controls (2.5%) we observed more number of eccentric and marginal cord insertion in mild PE 8 (8%) and severe PE 7 (7%) $P < 0.068$.

We observed more calcification in severe PE group 35 (35.0%) compared to mild PE 13 (13.0%) and controls 5 (5.0%). This observed finding of increased incidence of calcification in severe PE compared to mild PE was significant $P < 0.001$. There was increased incidence of infraction in severe PE group 48 (48.0%), compared to mild PE 25 (25.0%) and controls 5 (2.5%). There was increased incidence of infraction in cases compared to controls 5 (2.5%). This observation of increased incidence of infraction in severe PE compared to mild PE and increased incidence of infarction in cases compared to controls was statistically significant $P < 0.001$ (S). Among study subjects number of cotyledons observed commonly between 16 and 20. We observed in severe PE group about 37% patients had 10-15 cotyledons compared to mild PE 25% and controls 11%. This observation is statistically significant.

As shown in Table 1 morphometric features of placenta like its weight, volume, thickness, diameter values are less in severe PE compared to mild PE and controls from this observation it was observed that morphometric features of placenta highly correlate with the severity of the disease.

Table 1: Placental morphometric study

Placental parameters	Mean±SD		
	Mild PE	Severe PE	Controls
	Group B	Group C	Group A
Weight	399.10±79.112	371.70±85.316	478.80±292.122
Volume	275.80±86.459	238.20±93.197	420.45±140.816
Thickness	1.96±0.197	1.77±0.423	2.02±0.199
Diameter	18.64±1.812	17.94±1.963	20.33±1.446
F/P ratio	6.15±0.757	6.40±0.888	5.89±0.769

P<0.001 (S). SD: Standard deviation, F/P: Fetoplacental, PE: Pre-eclampsia

Findings were statistically significant. F/P ratio increases as the severity of the disease increases.

There were 200 cases in hypertensive group and 200 normal cases. There were 5 still births in total study group and 4 still births in severe PE group, remaining 1 in mild PE group and there were no still births in control groups. These still births are excluded from the cross tabulations and the morphologic changes in placenta of still born babies are explained in respective discussion of each variables. In the study group the incidence of low Apgar was more compared to controls. In the study group incidence of still birth was more when placental weight 200-300 g with $P < 0.001$. Significant relation was noted between placental weight and neonatal death and NICU admission in study group. In the control group, incidence of low birth weight, stillbirth, neonatal death and NICU admission was more when placenta weighed between 200 and 300 g. There was significant correlation between infarction and fetal birth weight <0.001. These observations can be seen in Tables 2 and 3.

DISCUSSION

Placenta is a vital organ maintaining pregnancy and promoting fetal development, which functions as fount upon which developing fetus derives its nutritional substance and obtains its metabolic and immunological requirements. Gross placental measures can best assess the time of onset and cumulative placental effects of a suboptimal intrauterine environment. Maternal morbidity remains great with PE, which continues to be one of the leading causes for the admission of pregnant women to intensive care units. Furthermore, fetal mortality and morbidity is considerable, related to the effects of the disease on the fetus as well as prematurity. In present study morphometric parameters of placenta like, weight, volume were significantly reduced in pre-eclamptic group as compared to normal group ($P < 0.01$). This study had similarities to the study conducted by Majumdar *et al*.[8] and Virupaxi *et al*.[9] The placentae of PE patients were significantly smaller in diameter than the normal. The absolute volume of placenta was significantly lowered in the pre-eclamptic group than the control group.[10] It has also been reported by Nazmeen (2006) that weight and volume of the placenta was less in PE cases. As severity of hypertension increases, placental mean volume, diameter, thickness decreases this finding correlates with our study and study of Udainia and Jain,[11] Majumdar *et al*. Londhe and Mane.[12] We observed mean fetal weight of 2.24 g in severe PE 2.49 g in mild PE and 2.64 g in

Table 2: Comparison of placental weight

Placenta	Cases						
	Birth weight (%)		APS 1 (%)		APS 5 (%)		NICU
	<2.5 kg	>2.5 kg	<7	>7	<7	>7	Yes
Placental weight							
200-300 (44)	41 (93.2)	3 (6.8)	14 (31.8)	30 (68.2)	5 (11.4)	39 (88.6)	21 (47.7)
301-400 (89)	84 (94.4)	5 (5.6)	23 (25.8)	66 (74.2)	10 (11.2)	79 (88.8)	23 (25.8)
401-500 (58)	22 (37.9)	36 (62.1)	9 (15.5)	49 (84.5)	1 (1.7)	57 (98.3)	7 (12.1)
>500 (4)	0	4 (100)	0	4 (100)	0	4 (100)	0
	P=0.001		*P*=0.155		*P*=0.154		*P*=0.001
Calcifications							
Present (44)	39 (88.6)	5 (11.4)	15 (34.1)	29 (65.9)	6 (13.6)	38 (86.4)	20 (45.5)
Absent (151)	108 (71.5)	43 (28.5)	31 (20.5)	120 (79.5)	10 (6.6)	141 (93.4)	31 (20.5)
	P=0.020		*P*=0.062		*P*=0.136		*P*=0.02
Infarction							
Present (69)	62 (89.9)	7 (10.1)	20 (29.0)	49 (71.0)	6 (8.7)	63 (91.3)	21 (30.4)
Absent (126)	85 (67.5)	41 (32.5)	26 (20.6)	100 (79.4)	10 (7.9)	116 (92.1)	30 (23.8)
	P=0.001		*P*=0.189		*P*=0.853		*P*=0.314
Haematoma							
Present (27)	25 (92.6)	2 (7.4)	10 (37.0)	17 (63.0)	2 (7.4)	25 (92.6)	11 (40.7)
Absent (168)	122 (72.6)	46 (27.4)	36 (21.4)	132 (78.6)	14 (8.3)	154 (91.7)	40 (23.8)
	P=0.025		*P*=0.076		*P*=0.871		*P*=0.63

APS: Antiphospholipid syndrome, NICU: Neonatal intensive care unit

Table 3: Birth weight and NICU Admission

Placenta	Controls (%)						
	Birth weight		APS 1		APS 5		NICU
	<2.5	>2.5	<7	>7	<7	>7	Yes
Placental weight							
200-300 (10)	9 (90)	1 (10)	4 (40)	6 (60.0)	3 (30)	7 (70.0)	3 (30)
301-400 (49)	42 (85.7)	7 (14.3)	9 (18.4)	40 (81.6)	2 (4.1)	47 (95.9)	1 (2)
401-500 (115)	50 (43.5)	65 (56)	8 (7.0)	107 (93)	1 (0.9)	114 (99)	0
>500 (26)	0	26 (100)	1 (3.8)	25 (96.2)	0	26 (100)	0
	P=0.001		*P*=0.001		*P*=0.001		*P*=0.01
Calcification							
Present (10)	4 (40)	6 (60.0)	2 (20)	8 (80)	20 (20)	8 (80.0)	2 (20)
Absent (190)	97 (51.1)	93 (48.9)	20 (10.5)	170 (89.5)	4 (2.1)	186 (97.9)	2 (1.1)
	P=0.496		*P*=0.351		*P*=0.001		*P*=0.001
Infarction							
Present (05)	5 (100)	0	2 (40)	3 (60)	2 (40)	3 (60)	2 (40)
Absent (195)	96 (49.2)	99 (50.8)	20 (10.3)	175 (89.7)	4 (2.1)	191 (97.9)	2 (1.0)
	P=0.074		*P*=0.169		*P*=0.001		
Haematoma							
Present (32)	28 (87.5)	4 (12.5)	7 (21.9)	25 (78.1)	3 (9.4)	29 (90.6)	3 (9.4)
Absent (168)	73 (43.5)	95 (56.5)	15 (8.9)	153 (91)	3 (1.8)	165 (98.2)	1 (0.6)
	P=0.001		*P*=0.032		*P*=0.082		*P*=0.010

APS: Antiphospholipid syndrome, NICU: Neonatal intensive care unit

Table 4: Comparison of mean birth weight of babies in cases and controls in different studies

Study	Mild PE (kg)	Severe PE (kg)	Controls (kg)
Present study	2.49	2.24	2.64
Navbir *et al.* (2012)	2.79±0.42	2.59±0.28	3.27±0.46
Londhe and Mane (2011)	2.26		2.73
Majumdar *et al.* (2005)	2.04±0.48		2.8±0.32
Udainia and Jain (2001)	2.2		2.6

PE: Pre-eclampsia

controls. Findings are compared to other studies; we can observe it in Table 4. The mean F/P weight ratio was more in severe PE 6.15 ± 0.757 group than control group 5.89 ± 0.769. This correlates with Majumdar *et al.* which shows ratio of 5.89 ± 10.04 in control group and 6.23 ± 0.87 in hypertensive cases. Londhe and Mane study showed ratio of 7.23 ± 1.90 in hypertensive group compared to 6.79 ± 2.04 in controls. Zia-ur-rehman *et al.* study findings also show similar results. The same ratio was found less in the hypertensive group than

control group by Garg *et al.*, 1996 and Priya *et al.* 2012.[13] In present study cotyledon numbers were found to be significantly less in hypertensive group which is similar to the findings of the study by Sultana *et al.*, 2007.[14] Study by Majumdar *et al.* showed no significant difference between controls and cases.

In present study most common shape of the placenta observed was circular in severe PE the occurrence was 81 (91.0%) in mild PE it was 91 (91.0%). We also observed increased oval shaped placenta in PE group about 13% which was comparable with study of Kiswara *et al.* who found 40% oval placenta in PE group but most common shape found in study group was discoidal or circular. In a study by Navbir *et al.*[15] they found the shape of the placenta was discoidal in 73.33% of cases in the study group and 83.33% in the control group. Other shapes that were observed were irregular (16.67%) in study group and 10% in control group and bidiscoidal, lobed and diffused (3.33% each) in both study and control group. Shah *et al.* observed no clinical significance in oval or rounded shaped placenta. We observed increased incidence of marginal and eccentric cord insertion in PE group 15% compared to controls 5% this observation holds good with pretorius (1996) 55 who reported cases of marginal insertion of placenta in about 42% cases of pregnancy induced hypertension.

Calcification is regarded as evidence of placental senescence or degeneration. In present study incidence of calcification is increased in severe PE group 35% compared to mild PE 13% and controls 10%. Harsh *et al.* (1989) found frequency of calcification was same in control as well as in hypertensive group.[16] In our study, the overall incidence of calcification is more in severe PE compared to mild PE and controls. This is similar to study by Narasimha and Vasudeva (2011)[17] which showed the overall incidence was 26.9%, 22.2% in mild PE and slightly higher (33.3%) in severe PE. In the present study significant association found between calcification and NICU admission in control group. But we did not found any significance in study group this might be due to exclusion of still births findings from cross tabulation. This is similar to study conducted by Goswami *et al.* (2011)[18] which concluded that fetal outcome in terms of birth weight of newborn to mother having pregnancy induced hypertension and calcification of placentae (grossly and microscopically) was poor as compared to control group.

Infarction was seen in 48% of severe PE compared to 25% of mild PE and 5% of cases. This is in comparison with Masodkar *et al.*'s 40.4%[19] and Udainia *et al.* (2004) who had observed a similar increase in the incidence of placental infarction with severity of toxemia. In the case group the association of stillbirth and low birth weight with infarction was statistically significant, whereas no relation was noted in the low Apgar, NICU admission and presence of infarction. In control group there was statistically significant association between infarction and NICU admission. This is comparable with study by Salgado *et al.* where the difference in the birth weight of the newborns in hypertensive and normotensive groups in relation to placental infarction was statistically significant (2.2 vs. 3.1 kg, $P < 0.001$).

CONCLUSION

The hypertensive disorders of pregnancy adversely influence the morphology of the placenta. The pathological changes observed in placentae of patients with hypertensive disorders of pregnancy like RP hematoma and infarction adversely influence the perinatal outcome. However, none of these pathological changes of placenta are specific to hypertensive disorders of pregnancy but these pathological findings are significantly increased in cases of PE compared to controls.

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Original Article

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Prevalence of Hypothyroidism among Pregnant Women in the Sub Mountain State of Manipur

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Abstract

Background: Hypothyroidism is among the most common endocrine disorder encountered during the pregnancy and reproductive age group. Endemic iodine deficiency and autoimmune disease remain a major cause of hypothyroidism. This study was conducted at Jawaharlal Nehru Institute of Medical Sciences, situated in Manipur, a submountain area of India. The aim of this study was to find out the prevalence of hypothyroidism among pregnant women in Manipur.

Method: All the consecutive 400 first- and second-trimester pregnant women were registered for the study after institutional ethics approval and consent from the study subjects. The pregnant women with diagnosed thyroid disorder and on thyroid medication were excluded from the study. Apart from routine obstetrical investigations, thyroid stimulating hormone (TSH) was done. Test for free T4 was done in patients with TSH level > 3 mIu/L.

Result: The mean (SD) age of study subjects was 26.8 (±8.2) years. About 92 (23%) subjects had TSH values > 3.0 mIu/L, the cut-off value used for the upper limit of normal in this study. Out of these 72 (18%) had normal FT4 value and, therefore, labeled as subclinical hypothyroidism (SCH) and 18 (4.5%) had low FT4, hence termed overt hypothyroidism. Two women had low FT4 values and normal TSH, hence labeled as isolated hypothyroidism.

Conclusion: Prevalence of hypothyroidism in pregnancy was found to be higher, more so the SCH in the present study.

Key words: Autoimmune disease, Endemiclodine deficiency, Overt and subclinical hypothyroidism, Pregnancy, Sub mountain area of Manipur

INTRODUCTION

Thyroid disorder is a common occurrence in pregnancy and reproductive age group next to diabetes mellitus.[1] Endemic iodine deficiency and Hashimoto's disease remain a major cause of hypothyroidism.[2] Pregnancy has a profound impact on the thyroid gland and its functions. During pregnancy, the thyroid gland may enlarge by 10% in iodine-replete countries and by 20-40% in areas of iodine deficiency.[3] Production of thyroid hormones and iodine requirement each increases by approximately 50% during pregnancy.[3] Iodine requirement in pregnancy is increased due to increased renal loss cause by increased renal blood flow, increased glomerular filtration rate and increased renal clearance due to reduced tubular reabsorption of iodine. Throughout pregnancy, maternal thyroxin is transferred to the fetus.[4-7] Maternal thyroxin is important for normal fetal brain development, neural implication, migration and structural organization, thus, future intellectual development especially before the development of fetal thyroid gland.[3] This insult is likely to occur in the first trimester and, therefore, preconceptional optimization of thyroxin therapy is important.[8] Maternal thyroxin contribution remains important sources before 12 weeks of gestation after which fetal thyroid synthesized hormone.[9] The increased demand for thyroid hormone starts very early, reaching a plateau at 16-20 weeks.

Pregnancy is a stress test for the thyroid and the physiological changes may result in hypothyroidism in

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the later stages in women with limited thyroidal reserve with underlying autoimmune disease or iodine deficiency who were euthyroid prior to conception.[3] Serum thyroid stimulating hormone (TSH) level in early pregnancy decline because of weak TSH reception stimulation from massive quantities of human chorionic gonadotropin (hcG) secreted by placental trophoblast during the first trimester. The TSH level is the lowest and FT4 level is the highest when hcG levels peak.[2]

The pregnancy-related changes in thyroid physiology make diagnosis of thyroid disorder difficult, because it can simulate signs and symptoms of physiological changes of pregnancy.[7] Symptoms of heat intolerance, sluggishness, fatigue, and examination findings of tachycardia, edema, hair changes, and weight gain are common to pregnancy and thyroid disease much in same way.[7] The management of therefore based principally on biochemical measures.

Although it is well accepted that overt hypothyroidism (OH) have a deleterious impact on pregnancy, studies are now focusing on potential impact of subclinical hypothyroidism (SCH) on maternal and fetal heath, the association between miscarriage and preterm delivery in euthyroid women positive thyroid peroxidase (TPO) and/or thyroglobulin antibody.[2,3] Undiagnosed SCH is likely associated with some adverse pregnancy outcomes. It may progresses to overt thyroid failure, and the rate of progression is affected by TSH level, age of women, disorder such as diabetes, and presence and concentration of TPO antibody.[2]

The prevalence reports of hypothyroidism during pregnancy in India, a country considered to be a relative moderate iodine deficiency, ranges from 4.8% to 11%.[8] The prevalence of OH and SCH complicating pregnancy has been reported 3% and 9%, respectively.[9] There are few published Indian studies on this topic. Therefore, this study was conducted with sincere effort to throw some light on this topic.

MATERIALS AND METHODS

This study was conducted in the Department of Obstetrics and Gynecology. All consecutive pregnant women who gave consent were included in this study.

Inclusion Criteria

- All pregnancy women registered in the hospital
- Duration of pregnancy: First trimester to the second trimester.

Exclusion Criteria

- Pregnant women with diagnosed thyroid disorder and on thyroid medication
- Multiple gestation
- Diabetes mellitus
- Hypertension
- History of recurrent pregnancy loss.

All subjects were subjected routine ante-natal checkup with an obstetric profile of investigation. TSH was tested in all subjects registered for the study. In patients with deranged TSH, free T4 test were done. The test was carried out by chemi-luminescence immunoassay (vitros 5600).

The reference ranges used in this study was based on the guidelines of American Thyroid Association (ATA) for the diagnosis and management of thyroid disease during pregnancy and postpartum. As per regulation 14.2 of ATA guidelines, if trimester-specific ranges for TSH are not available in the laboratory, the following reference ranges are recommended: first trimester, 0.1-2.5 mlu/L, second trimester, 0.3-3 mlu/L.[3]

RESULT

The patients were divided into the groups as shown in Table 1 according to TSH and FT4 value.

Euthyroid defined as serum level of TSH 0.2-3 mlu/L with FT4 normal level. SCH defined as serum TSH > 3 mlu/L with FT4 normal level. OH defined as TSH > 3 mlu/L with FT4 < 7.5 mcg/dl.

Two hundred sixteen subjects had both TSH and FT4 value within normal limit. About 92 (23%) subjects had TSH value > 3.0 mlu/L, the cut-off value for the upper limit of normal in this study. Out of this 72 (18%) had normal FT4 values and, therefore, labeled as SCH and 18 (4.5%) subjects had low FT4, hence termed OH. Whereas TSH value was normal, 2 (0.5%) had low FT4 and labeled as isolated hypothyroidism (Table 2).

DISCUSSION

Maternal hypothyroidism is defined as the presence of an elevated TSH concentration during gestation. More recently, normative data from healthy pregnant women suggest the

Table 1: The patients were divided into the following groups according to TSH and FT4 value[3]

Groups	TSH (mlu/L)	FT4 (mcg/dl)
Euthyroid	0.2-3.0	N
SCH	>3.0	N
OH	>3.0	<7.5

SCH: Subclinical hypothyroidism, OH: Overt hypothyroidism, TSH: Thyroid stimulating hormone

Table 2: Thyroid dysfunction in pregnant women (*n*=400)

Thyroid dysfunction	*n*	%
Euthyroid	216	54
Hypothyroidism	92	23
SCH	72	18
OH	18	4.5
Isolated hypothyroidism	2	0.5

SCH: Subclinical hypothyroidism, OH: Overt hypothyroidism

upper reference range may approximate 2.5-3 mlu/L.[3] When maternal TSH is elevated, measurement of serum FT4 concentration is necessary to classify the patient's status as either SCH or OH. The distinction of OH from SCH is important because published data relating to maternal and fetal effects attributable to OH are more consistent.[3]

Thyroid dysfunction during pregnancy has an immense impact on maternal and fetal outcomes.[10,11] More importantly, children born to hypothyroid mothers have a poor intellectual function during the latter part of their life.[3] Low IQS in infants of even very mild hypothyroid women have been reported.[5] There is an increased risk of preeclampsia placental abruption, intra-uterine growth restriction, prematurity and intra-uterine fetal demise.[2] Therefore, the majority of the developed countries have national neonatal screening program.[12] The prevalence of hypothyroidism is more in Asian countries compare with the west, it varies from 2.5% from the West to 11% from India.[12-14]

Rao *et al.* found hypothyroidism in 4.2% of recurrent pregnancy less which is statistically significant.[14] Sahu *et al.* have done thyroid function in the second trimester and reported prevalence of thyroid disorder especially OH and SCH 6.47%.[15]

Dhanwal *et al.* from Delhi in 2013 reported hypothyroidism prevalence of 14.3% with cut-off value of 4.5 mlu/L as the upper limit of normal in a cohort of 100 pregnant women.[12,13] In another study from Delhi Nagia AS *et al.* in 2013 reported a prevalence rate of 12% amongst 400 pregnant women.

In the present study, in contrast, has shown the prevalence of hypothyroidism as high as 23% with 4.5% OH and 18% SCH, thus necessitating the need for universal screening for thyroid function during pregnancy.

Various reasons have been proposed for increased prevalence of hypothyroidism in pregnant women especially in sub mountain areas (Kashmir to North East India). Geo-chemical nature in deficiency of iodine and micronutrients, due to glaciations, high rain fall, floods leading to decrease iodine content in soil and water is considered to be the cause of increase prevalence of hypothyroidism in this region.[16,17]

CONCLUSION

The study concludes that there is a high prevalence of hypothyroidism in pregnant women of Manipur majority being SCH. In view of deleterious effects of hypothyroidism in pregnancy routine screening of thyroid dysfunction may be recommended especially in endemic iodine deficiency area.

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Original Article

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Role of Cervical Vasopressin in Vaginal Hysterectomy: A Tertiary Care Level Centre Study

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Abstract

Background: The use of vasoconstrictive drugs like vasopressin in major surgeries like hysterectomy can decrease the morbidity of the patient by controlling the intra-operative blood loss.

Materials and Methods: About 80 patients undergoing elective vaginal hysterectomy were selected for the study. They were divided into two groups, in which vasopressin in diluted form was injected pre-operatively in one group, and another group was taken as control. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) for Windows version 19.0 software, Chicago, SPSS Inc.

Result: The parameters like duration of surgery, change in vitals during surgery and post-operative complications showed no significant difference in two groups. However, significant difference ($P < 0.0001$) was seen in the amount of blood loss in two groups.

Conclusion: Vasopressin is a drug which can play a key role in changing the percentage of post-operative morbidity in the patients undergoing vaginal hysterectomy by bringing drastic change in the amount of blood loss in the surgery.

Key words: Hysterectomy, Morbidity, Vasopressin

INTRODUCTION

Hysterectomy is a surgical removal of the uterus with or without the excision of cervix, ovaries, fallopian tube, and other neighboring structures. It is the most frequent performed gynecological surgery. In 2003, over 600,000 hysterectomies were done in the United States alone.[1]

It is believed that the short-term mortality (within 40 days of surgery) is common after hysterectomy (0.38 cases per 1000) even when done for benign causes. However, risk increases when the reason for surgery is malignant.[2] However, the long-term prognosis of treatment is relatively good. About 35% of women after hysterectomy go through another linked surgery within 2 years.[3]

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The success of any surgery in the medical field is dependent mainly on three factors: (a) Amount of bleeding, (b) rate of infection, and (c) intra and post-operative pain. Less amount of blood loss in surgery is essential because of the related morbidity. Besides this, profound bleeding during surgery can hinder the sight of the operative field, resulting in complications. In particular, surgeries like hysterectomy already have high short-term mortality.[4]

During hysterectomy, the chief blood supply of the region is not ligated until after much of the dissection has been done. So, the intra-operative bleeding is the major problem faced during this surgery.[5] Numerous methods have been used to control blood loss which included hydrodissection with saline and vasoconstrictor injections.[6]

In previous studies, drug which has been used to control the blood loss during surgery are vasopressin and nor-epinephrine. Julian TM *et al.* in 1983, first reported the use of vasoconstrictors in an attempt to lessen the blood loss during hysterectomies.[7]

Vasopressin is a vasoconstrictive drug having a short half-life (20 min) is most preferred drug in gynecological

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surgeries to decrease intra and post-operative bleeding and to improve surgical field visualization. Repeat dose after 45-60 min is safe.[8]

Vasopressin is a synthesized peptide hormones used in the management of diabetes insipidus and gastro intestinal hemorrhage. Three types of vasopressin receptors (V1A, V1B, and V2) are discussed in the literature. All are G protein-coupled receptors. The V1A and V1B receptors increase the intracellular Ca concentration through phosphatidylinositol hydrolysis whereas the V2 receptors operate by increasing the cyclic adenosine monophosphate levels. It causes vasoconstriction through its action on the vasopressin (V1) receptor and acts as antidiuretic drug through its action on V2 receptor in the kidney. The chief mechanism by which vasopressin reduces bleeding is vasoconstriction.[9]

The aim of this study was to analyze the effect of vasopressin in the patients undergoing elective hysterectomy in order to reduce the blood loss during surgery and to decrease the morbidity of the patient.

MATERIALS AND METHODS

In this prospective case-control study conducted at Teerthanker Mahaveer Medical College and Research Centre, Moradabad, India. We examined 80 female patients undergoing elective vaginal hysterectomy. The age of the study population was 30-65 years. Before starting data collection oral consent about the participation in the study was taken from the subjects. Subjects with a history of smoking, hypertension, ischemic heart disease, severe liver disease, peripheral vascular disease, epilepsy, elevated serum creatinine, asthma, and history of recurrent migraines were excluded from the study.

History of the patient (medical and obstetrical) was taken and thorough examination (general and obstetrical) was done. Pre-operative work-up and necessary investigations were done. The patients were taken up for elective surgery after proper pre-anesthetic check-up.

Hysterectomy was planned under sub-arachnoid block. The patients were divided into two groups each consisting of 40 subjects. Dilute 20 unit of vasopressin in 100 ml of normal saline was used for controlling blood loss. In Group A patients (control group), no cervical vasopressin was given. In Group B patients, 30-40 ml solution of vasopressin at the cervicovaginal junction was injected in 2, 4, 8, and 10 'O' clock positions.

Following parameters were observed during surgery:

1. Duration of surgery
2. Blood loss during surgery (mops and gauze pieces used during surgery were weighed before and after the operation)
3. Blood pressure monitored (pre-operatively and intra-operatively)
4. Post-operative febrile morbidity (oral temperature of >101°F)
5. Post-operative per vaginal discharge
6. Post-operative increase in micturition.

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) for Windows version 19.0 software, Chicago, SPSS Inc. Student's *t*-test were used to analyze quantitative parameters while for qualitative parameters Chi-square test was used. A $P < 0.05$ was considered as statistically significant.

RESULTS

Among 70 patients who underwent hysterectomy, maximum number of patients belonged to 30-65 years of age. The mean age in control and study group was 49.74 years and 48.86 years, respectively. Most of the patients were para 3 in both groups (52.71% in control group and 47.29% in study group).

As regards time required for surgery, 47.50% patients in the control group and 40.00% in study group required the time between 55-60 min and 61-65 min, respectively (Table 1 and Figure 1).

From the Table 1 it is calculated that average time required (min) mean ± standard deviation (SD).

Table 1: Distribution of cases according to time required for the surgery

Duration of surgery (min)	Group A (%)	Group B (%)
45-50	7 (17.5)	9 (22.5)
55-60	19 (47.5)	15 (37.5)
61-65	14 (35)	16 (40.0)

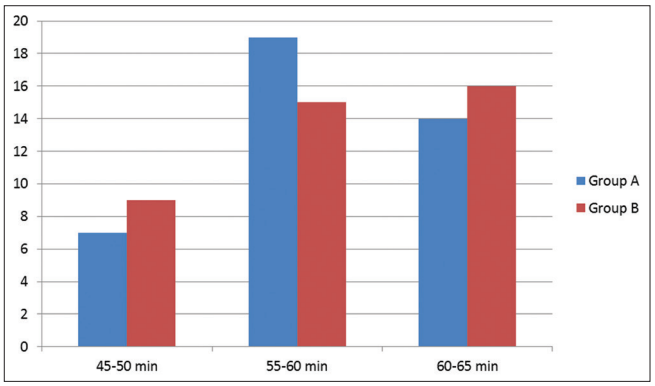

Figure 1: Comparison of duration of surgery in both groups

In control group = 56.79 ± 7.91.
In study group = 53.91 ± 7.32.
P value = 0.09 (not significant).

Maximum number of patients in control group had blood loss between 200 and 250 ml (30.0%) and study group had blood loss between 101 and 150 ml (45.0%) (Table 2 and Figure 2).

From the Table 2 it is calculated that average blood loss (ml) mean ± SD.

In control group = 209.51 ± 21.18.
In study group = 138.21 ± 19.64.
P value = 0.0001 (statistically significant).

After vasopressin infiltration rise in blood pressure was seen. Mean rise was 16.61 mmHg after 5 min of vasopressin in study group as compared to 6.75 mmHg in control group (Table 3).

The difference in the post-operative complications in both control and study group was statistically insignificant (Table 4).

DISCUSSION

Removal of the uterus with or without other organs leads to an inability to bear children and has short- and long-term surgical risks. So, the surgery is usually recommended when other treatment options have failed. However still, is a very common surgery done at different centers as it is the final treatment of many gynecological problems.

In several gynecological procedures, vasoconstrictors have been used to curtail blood loss such as in myomectomy, hysteroscopy, and abdominal hysterectomy.[10] Still vaginal hysterectomy has been performed without any intracervical injection and use of vasopressin in it remains debatable. However, saline injection intracervically has been used to build a mechanical tamponade and to help in creating an easier plane of dissection.[9,11-14]

In our study, there was a significant decrease in mean blood loss in Group B patients. It was also observed that ascend in mean BP was significant intra-operatively at 5 min after drug introduction as compared to raise at 10 min and 15 min and control group. Similar study in 1993 has concluded that vasopressin group had significantly less intra-operative bleeding (296 ± 37 ml) than control group (435 ± 55 ml) ($P < 0.02$).[9] This study supports our findings emphasizing on the fact that use of vasopressin in hysterectomy is useful.

A similar study was done by Holmes *et al.* who found that a decrease in median blood loss from 675 ml in the placebo group to 225 ml in the vasopressin arm ($P < 0.001$) during myomectomy.[15] Still the literature regarding same results of vasopressin in vaginal hysterectomy is lacking.

Other factors like duration of surgery and post-operative complications showed no statistical significance in two study groups.

Thus, this study supports the statement that the use of vasopressin with sensible case selection during vaginal hysterectomy results in significant decrease in blood loss and drop in hemoglobin g% thereby decreasing patient's morbidity and improving prognosis. However, further

Table 2: Distribution of cases according to blood loss during surgery

Amount of blood loss (ml)	Group A (%)	Group B (%)
<100	0 (0)	5 (12.5)
100-150	4 (10.0)	18 (45)
150-200	9 (22.55)	11 (27.5)
200-250	12 (30.0)	6 (15)
250-300	10 (25)	0 (0)
>300	5 (12.5)	0 (0)

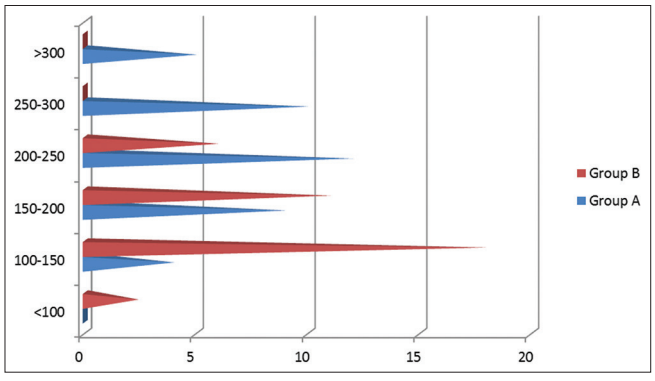

Figure 2: Comparison of blood loss during surgery in two groups

Table 3: Distribution of cases according to pre- and intra-operative blood pressure (mean)

Group	Pre-operative (mmHg)	Intra-operative (mmHg)		
		5 min	10 min	15 min
A	102.56	98.00	96.62	101.37
B	100.49	113.21	111.86	106.53

Table 4: Distribution of cases according to post-operative complications

Complication	Group A	Group B
Fever (>101°F)	2	1
Per vaginal discharge	0	0
Increase micturition	1	0

research work is obligatory to confirm universal role and use of vasopressin in decreasing blood loss during vaginal hysterectomy.

CONCLUSION

No surgical procedure in medical science is more gratifying than one finished successfully with minimal blood loss, with the surgical field as unspoiled at the end as it was at the beginning. Vasopressin has a role in attaining this ideal, but it should be used in dilution and at a low total dosage.

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Original Article

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Accuracy of Fine Needle Aspiration Cytology in Diagnosis of Cyto-Architecture of Thyroid Lesions

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Abstract

Background: The morphological characterization of thyroid swellings is one of the most difficult parts of the treatment protocol. The most diagnostic tests now-a-day to confirm the cyto-architecture is fine needle aspiration cytology (FNAC) which is confirmed by histopathology after surgery. The aim of this study is to analyze the results of FNAC with histopathology and to assess its sensitivity and specificity.

Materials and Methods: The study included 50 patients with thyroid swellings whose observations of FNAC were compared with the histopathology after surgery. The sensitivity, specificity, positive predictive value, and negative predictive value of the test were determined together with 95% confidence interval.

Result: Sensitivity and specificity of the diagnostic test were 96.77%, 50.00%, respectively. Positive predictive value was 98.77%, and negative predictive value was 55.80%.

Conclusion: FNAC plays an important part in the selection of patients in surgical management thus controlling the surgical burden.

Key words: Diagnosis, Fine needle aspiration cytology, Histopathology, Malignancy, Thyroid swelling

INTRODUCTION

Thyroid swelling is a very frequent dilemma in developing countries like India. It is the more common in females as compared to males and is linked with assorted disorders.[1] Thyroid swellings are classified on the basis of cyto-architecture of the growth. Besides it, the treatment and prognosis of disease also depends on the cellular pattern of the swelling (benign or malignant).[2]

It should be mentioned that morphological characterization of thyroid tumors vestiges one of the most difficult parts of the treatment protocol. The variety of histological forms is allied with a big amount of possible sources of the rise of tumors. The cyto-architecture of swelling also helps in knowing the etiology of the disease and helps in deciding the prevention the disease.[3]

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The universally used mode to determine the malignancy of swelling is fine needle aspiration cytology (FNAC). It is a harmless, non-invasive, cheap, and competent time-saving outpatient department procedure, which provides specific, quick diagnosis with nominal complications. It is considered as a good quality diagnostic tool for the evaluation of clinically palpable thyroid lesions.[4]

Although FNAC is not a replacement of conventional histopathology, it is tremendously required in categorizing the diseases. It is used mainly in deciding the treatment protocol of the disease and bridges the gap between clinical evaluation and final treatment thus reducing the unnecessary surgeries. Varied imaging methods, now-a-days have become popular for preoperative diagnosis of clinically palpable thyroid lesions such as radionuclide scanning and high-resolution ultrasonography.[5] However, FNAC and histopathology are still regarded as the better accurate procedures.

The diagnosis of thyroid tumors by histopathological examination has been established as the gold standard technique.[6] However, due to the limited medical facility and availability of the techniques for establishing the diagnosis of thyroid tumors, we planned to formulate a study

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comparing the diagnostic correlation of thyroid tumors between imprint cytology and histopathology.

The aim of this study is to analyze the cyto-architecture of clinically palpable thyroid lesions and compare the results with the histopathological examination and to assess its sensitivity and specificity.

MATERIALS AND METHODS

After obtaining Institutional Ethical approval, we conducted a prospective study in our Department of Pathology from January 2015 to June 2015. We included 50 patients in our study referred from different clinical departments with thyroid swelling. Patients' clinical profile, relevant investigations and informed consent were obtained before commencing the study.

Under strict aseptic precautions, a 23 Gauge spinal needle fitted with a 10 ml syringe was introduced in the swelling. After careful aspiration of the fluid, smears were prepared, dried by air and fixed using alcohol. All slides were fixed using hematoxylin and eosin stain, Giemsa stain, Papanicolaou stain, and Ziehl–Nelson stain. All cases selected for histopathological examination were fixed by 10% formalin. Two pathologists were assigned to perform the histopathological examination to eliminate the observer bias. Moreover, the pathologists performing the histopathological examination were blinded regarding the diagnosis.

Statistical Analysis

True positives were cytology or histology positive tumors; true negatives were cytology or histology negative tumors; false positives (FP) were histology negative and cytology positives; false negatives (FN) were histology positive and cytology negative cases. The cases where pathologist felt difficulty in establishing a diagnosis were labeled as inconclusive. Statistical analysis of data was performed by using SPSS version 20 software. Based on above parameters, the sensitivity, specificity, positive predictive value, and negative predictive value were determined together with 95% confidence interval (CI).

RESULTS

The age of the patients varied between 7 and 65 years, the mean age being 31 years. Male: female ratio was about 22:28 (Table 1). The aspirates of 50 patients showed three patterns clinically, which were gray white (58%), gray white with necrotic tissue (28%), and gray white with hemorrhage (14%) (Table 2). Among 50 cases, the FNAC of six patients presented infective lesions (Table 3). So, histopathology was done only in 44 patients.

The FNAC was compared with the equivalent histopathological diagnosis. Out of 34 benign cases in FNAC, only 31 showed a similar pattern in histopathology. Similarly, only 2 cases out of 10 showed similar results in both techniques (Table 4 and Figure 1).

Based on the above data, we derived the following parameters;

a. Sensitivity: True positive/true positive + FN = 96.77% (83.3−99.92%, 95% CI)
b. Specificity: True negative/FP + true negative = 50.00% (1.26−98.74%, 95% CI)
c. Positive predictive value: True positive/true positive + FP = 98.77% (82.3−97.92%, 95% CI)
d. Negative predictive value: True negative/FN + true negative = 55.80% (1.56−96.74%, 95% CI).

DISCUSSION

Presently, FNAC of the thyroid nodule is the most preferred analytic method for the preliminary evaluation of

Table 1: Demographic characteristics

Demographic profile	Thyroid swelling patients (*n*=50)
Age	7-65 years (median=31 years)
Weight	14-79 kg (median=57 kg)
M:F ratio	22:28

Table 2: Thyroid swelling aspirate on FNAC

Nature of aspirate	Number of cases (*n*)	Percentage
Gray white	29	58
Gray white with necrotic tissue	14	28
Gray white with hemorrhagic tissue	7	14

FNAC: Fine needle aspiration cytology

Table 3: Incidence of infective and malignant lesions on FNAC

Lesions	Number of cases (*n*)	Percentage
Infective	6	12
Malignant	44	88

FNAC: Fine needle aspiration cytology

Table 4: Diagnostic accuracy of FNAC in thyroid lesions

FNAC diagnosis	Total number of FNAC cases	Number of cases with histopathology	Correct FNAC diagnosis	FN	FP
Benign	34	31	30	-	1
Malignant	10	2	1	1	-
Total	44	33	-	-	-

FN: False negative, FP: False positive, FNAC: Fine needle aspiration cytology

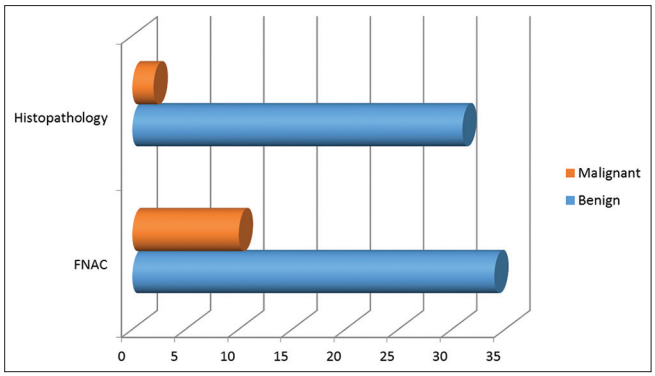

Figure 1: Comparison of the results of fine needle aspiration cytology and histopathology

thyroid nodules. It has decreased the quantity of patients who have undergone surgical management by 25-50%,[7,8] thus increasing the rightness of the treatment decision taken by the consulting team in the hospitals.

However, still in few cases the disparity is seen in the results of FNAC done pre-operatively and histopathology done during or after surgeries. The present study was undertaken to correlate the observations of these two techniques in the same person in order to verify the effectiveness and diagnostic accuracy of FNAC.

The FNAC of the thyroid swelling was performed in 50 cases, out of which histopathological specimen of only 44 patients were compared during the study phase. Different parameters in our present study were compared with previous studies in order to establish the correlation between the two procedures.

In our study, the average age of the subjects was 31 years with most of the patients in the third and fourth decade which is analogous to the previous studies.[9,10]

Females were the more affected than males in this study (M: F = 22:28), which showed concordance with the earlier research.[9-11]

Being a tertiary care center, large population which is a representative of the general population was involved in the study. In addition, this region comes under sub-Himalayan belt or "goiter belt," therefore percentage of benign cases is more as compared to malignant.[12]

In the present study, the similar cytohistological end result rate was achieved in 31 (93.9%) cases whereas 2 cases (FN, FP) showed disconcordance (3.03% of FN and 3.03% of FP). Similar study conducted showed in sub-Himalayan belt showed the percentage of similar end result rate of 97.5% with the percentage of FN and FP as 1.65% and 0.80%, respectively.[13]

Misunderstanding of aspirate from a malignant lesion of the thyroid as benign occurred in only 1 case where a follicular neoplasm diagnosed on FNAC was actually a colloid Goitre on histopathology. The reason might be the aspiration done from the hypercellular areas of colloid nodules resulting in misdiagnosis. A possible solution to this problem is that multiple aspirates from diverse parts of the swelling must be collected to decrease the chances of incorrect diagnosis.[14,15]

FN cases (misunderstanding of benign nodules of the thyroid as malignant) occur due to inaccuracy in the understanding of the cytological material because of overlapping features of different lesions.[16] This is of great fear because it can lead to missing of the malignant lesion and thus endangering the life of the patient.

So, proper sampling from different areas is extremely important for the correct diagnosis. Some pathologists advocate the preparation of 4-6 smears from different sites of the nodule. Ultrasound-guided FNAC is a better alternative for better sample attainment leading to a little rate of non-diagnostic smears.[17]

According to earlier studies,[9,18] the sensitivity and specificity of the thyroid FNAC ranges from 43% to 99% and 72% to 100%, respectively. In the present study, results were analogous with the findings in this sequence.

CONCLUSION

Thus, we conclude from the study that FNAC is an outstanding, harmless, and less invasive diagnostic procedure with a high degree of accuracy. Besides this, in a developing country like India less expertise people are required for FNAC along with less investment as compared with the tissue biopsy. It plays an important part in the selection of patients in surgical management thus controlling the surgical burden.

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Original Article

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Multiorgan Dysfunction in *Plasmodium vivax* Malaria: A Prospective Study

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Abstract

Background: *Plasmodium vivax* is the most widely distributed human malarial parasite with an at risk population of 2.5 billion persons. With an implementation of molecular diagnosis, it has become evident that *P. vivax* mono infection could also result in multiorgan dysfunction and severe life threatening disease as seen in *Plasmodium falciparum* infection.

Aims and Objectives: (1) To study, the clinical profile of *P. vivax* malaria, (2) to study, multiorgan dysfunction in *P. vivax* malaria.

Materials and Methods: A total of 102 patients of documentary *P. vivax* infected patients and fulfilling the criteria for severe malaria according to WHO during study period from September 2012 to September 2014 were taken for this study. Detailed history and examination along with investigations were noted in all patients.

Results: In the present study, maximum patients with severe vivax malaria belonged to 21-30 years followed by 41-50 years. About 62.7% patients are males and 37.3% patients are females with severe *P. vivax* malaria with organ dysfunction. In our study, out of 102 patients of severe *P. vivax* malaria, 44 patients (43.1%) are having multiorgan dysfunction, while 58 patients (56.9%) are having single organ dysfunction. Hematological dysfunction was the most common dysfunction either alone or in combination, presents in 89.2%. Followed renal dysfunction was present in 34.3% and jaundice in 21.6%. 7.8% patients had central nervous system manifestation while respiratory dysfunction (acute respiratory distress syndrome [ARDS]) was seen in only 2%. Most of the patients (56.9%) had presented with single organ dysfunction. 33.3% had two organ dysfunction, whereas 7.8% had three organ dysfunction. Four organ dysfunction were observed in only 2% patients. In our study, 93.1% patients survived and 6.9% patients expired due to severe *P. vivax* malaria with multiorgan dysfunction.

Conclusion: In the present study, similar to severe falciparum malaria as mentioned in past studies multiorgan dysfunction and associated mortality though less common and less severe is seen in severe vivax malaria.

Key words: Falciparum, Malaria, Severe, Thrombocytopenia, Vivax

INTRODUCTION

Plasmodium vivax is the most widely distributed human malarial parasite with an at risk population of 2.5 billion persons. With an implementation of molecular diagnosis, it has become evident that *P. vivax* mono infection could also result in multiorgan dysfunction and severe life threatening disease as seen in *Plasmodium falciparum* infection.[1]

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P. vivax can cause both sequestration related and non-sequestration related complications of severe malaria as defined by WHO, including cerebral malaria (coma persisting for more than 30 min after generalized convulsions), renal failure (24 h urine output <400 ml in adults and serum creatinine level >3 mg/dl), circulatory collapse (systolic blood pressure <80 mm of hg in adults), severe anemia (hemoglobin [Hb] level <5 g/dl), haemoglobinuria (not associated with effects of G6PD deficiency), abnormal bleeding (significant and/or evidence of disseminated intravascular coagulation), acute respiratory distress syndrome (ARDS) (non-cardiogenic pulmonary edema), jaundice (serum bilirubin level >3 mg/dl), and acidosis (arterial pH <7.25 or plasma bicarbonate level <15 mmol/l).[2]

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In such situation assessment of multiorgan dysfunction is required for risk of stratification, prognostication and planning of treatment to prevent the progress of disease and hence morbidity and mortality.

MATERIALS AND METHODS

This prospective study was conducted on patients, who were admitted at our Medical College Hospital to the medicine ward and intensive care unit under medicine department. Clearance was obtained from the Ethical Committee for the study. Patients of age 18 or above with documentation of *P. vivax* infection were included in study. All patients with age <18 years, HIV positive individuals, patients with diseases, such as chronic renal failure, diabetes mellitus with micro vascular and macro vascular complications, rheumatic heart disease, coronary artery disease, and sickle cell anemia, and all patients other than *P. vivax* malaria were excluded from study. The study was carried out on 102 severe vivax malaria patients out of 460 vivax positive patients, admitted during the period of 24 months from September 2012 to September 2014. Peripheral blood smear for malarial parasite (MPQBC) and/or rapid malarial antigen test was done by chromatographic immunoassay for quantitative determination of malaria parasite infection in human blood and to confirm mono infection. Patients were further investigated if they fit the category of severe and complicated malaria as per WHO criteria.

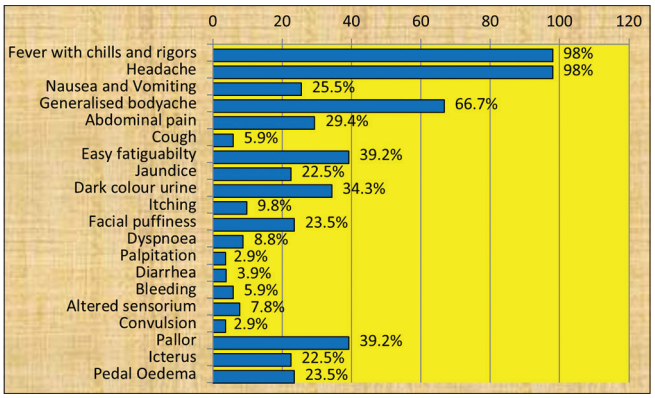
Statistical Analysis

Data were analyzed by statistical product and service solution V-16 (SPSS 16) statistical software. Data were presented in frequency and percent distribution form. Association in between the parameters was tested using Pearson's Chi-square test or Fishers exact test. The significance level was set at $P < 0.05$. $P < 0.05$ was considered as significant.

RESULTS

Out of 460 vivax positive patients 102 (22.1%) were having severe malaria as per WHO criteria. In the 102 cases of severe, *P. vivax* cases 62.75% were male and 37.25% were female. In the 102 cases of severe, *P. vivax* malaria, 11.76% were up to 20 years of age, 23.53% were 21-30 years, and 17.65% were 31-40 years of age group. 20.59% cases were 41-50 years of age and 10.78% were 51-60 years old. Furthermore, 15.69% cases were found above 60 years. Maximum number of patients was in the age group of 21-30 years. Mean age was 39.75 ± 15.66.

Graph 1 shows commonest presenting symptom in severe *P. vivax* malaria was fever with chills and rigors along with headache present in 98% of cases.



Graph 1: The most common presenting symptom in severe *Plasmodium vivax* malaria was fever with chills and rigors along with headache present in 98% of cases

The most common presenting symptom in severe *P. vivax* malaria was fever with chills and rigors along with headache present in 98% of cases. Generalized body ache was the following most frequent symptom. Dry cough was present only in 5.9%, while vomiting was present in 25.5% and abdominal pain was in 29.4%. 22.5% patients had history of jaundice. Dark color urine was present in 34.3% and facial puffiness and pedal edema were present in 23.5%. Patients presented with altered sensorium were only 4.9% and those who were having convulsions were 2.9%. Most of the patients (66.7%) had presented with acute illness of 2-7 days duration of fever, 25.5% the fever was of 8-14 days duration and 5.9% it was >14 days.

Severe anemia with Hb <5 g% was present in 2.8% patients and lowest Hb observed was 3.5 g%. 67.6% patients had normal complete blood count (CBC) value. Majority (83.3%) patients had platelet count in range of 40000-1.5 lacks. 5.9% had platelet count below 40000. Serum bilirubin was raised above 3 in 22.5% patients and highest bilirubin value noted was 7.6. Prothrombin time deranged above 16 was observed in 6.9% patients while acidosis was present in only 6.9%. Serum creatinine raised above 1.5 was seen in 34.8%. Majority (41.2%) of severe vivax malaria patients had Grade 1 (low) parasitemia, while heavy, Grade 4 parasitemia was observed in 10.8%. Splenomegaly was most common finding present, either alone or in combination in 84.3% patients, while hepatomegaly either alone or in combination was present in 62.7%. Isolated splenomegaly was present in 29.4% and isolated hepatomegaly was seen in 7.8%. 54.9% patients had both hepatosplenomegaly.

In the present study out of 102 severe *P. vivax* malaria cases 43.14% had multiorgan dysfunction and 56.86% had single organ dysfunction.

Graph 2 shows, in present study, most of the patients (56.9%) had presented with single organ dysfunction.

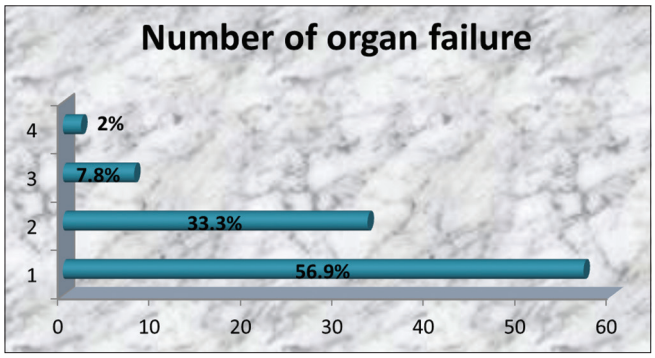
33.3% had two organ dysfunction while 7.8% had three organ dysfunction. Four organ dysfunction were observed in only 2% patients.

Graph 3 shows incidence of organ dysfunction present in vivax malaria.

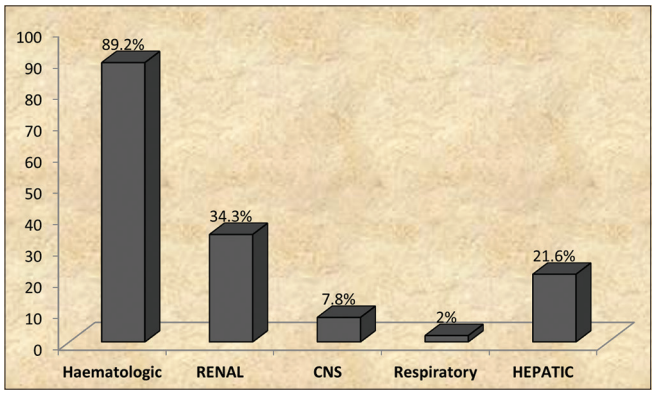
Hematological dysfunction was the most common dysfunction either alone or in combination, presents in 89.2%. Followed renal dysfunction was present in 34.3% and jaundice in 21.6%. 7.8% patients had CNS manifestation while respiratory dysfunction (ARDS) was seen in only 2%.

Hematological dysfunction was the most common dysfunction either alone or in combination, presents in 89.2%. Followed renal dysfunction was present in 34.3% and jaundice in 21.6%. 7.8% patients had central nervous system (CNS) manifestation while respiratory dysfunction (ARDS) was seen in only 2%.

In 2 organ dysfunction hematological along with renal was commonest presentation, seen in 18.6% followed by hematological with hepatic dysfunction present in 10.8%.



Graph 2: In present study, most of the patients (56.9%) had presented with single organ dysfunction. 33.3% had two organ dysfunction while 7.8% had three organ dysfunction. Four organ dysfunction was observed in only 2% patients



Graph 3: Incidence of organ dysfunction present in vivax malaria

Hematologic dysfunction and cerebral vivax malaria in combination was seen in 3.9%.

Hematological dysfunction along with hepatic and renal dysfunction was commonest three organ dysfunction seen in 3.9%.

Four organ dysfunction were observed in only two patients, one had hematological, renal, CNS and hepatic dysfunction and other had hematologic, renal, respiratory and hepatic dysfunction.

In single organ dysfunction, *P. vivax* malaria maximum patients were having lower age groups (below 50 years) while in multiple organ dysfunction patients having *P. vivax* malaria maximum patients were having higher age groups (above 40 years). There was statistically significant ($P < 0.001$) difference with higher percentage patients having multiple organ dysfunction in higher age groups with *P. vivax* malaria.

In multiple organ dysfunction patients 27.3% had 2 plus parasitemia grade, 47.7% had 3 plus grade and 25% had 4 plus parasitemia grade. In single organ dysfunction *P. vivax* malaria patients 72.4% had 1 plus parasitemia and 27.6% had 2 plus. There was statistically significant ($P < 0.001$) that higher parasitemia grade is seen in multiple organ dysfunction patients than in single organ dysfunction patients.

It was found that 6.9% had expired of *P. vivax* malaria patients. Of those *P. vivax* malaria patients up to 60 years ago 95.3% survived and 4.7% expired while those more than 60 years old 18.8% had expired. There was statistically significant ($P < 0.05$) difference of the outcome of *P. vivax* malaria patients at 60 years age difference.

All 7 patients expired had 4 plus parasitemia grade and in 4 plus parasitemia grade 63.6% *P. vivax* malaria patients expired, while all in Grade 3 and lower had survived.

In single organ dysfunction, all patients survived while in multiple organ dysfunction 15.9% expired and 84.1% survived. There was statistical significant ($P < 0.01$) difference of outcome of patients according to organ dysfunction in *P. vivax* patients.

In hematological organ dysfunction 7.7% expired, in CNS dysfunction 25% expired, 20% with renal dysfunction and 100% with respiratory dysfunction expired. All 2 patients with 4 organ dysfunction expired, 50% with 3 and 2.9% with 2 organ dysfunction had expired. No mortality is seen in single organ dysfunction.

15.9% of multi organ dysfunction plasmodium malaria needed Quinine, while it was none in single organ dysfunction patients. While, artesunate was needed in 74.1% and chloroquine in 25.9% of single and 84.1% and none of multiple organ dysfunction patients, respectively.

In *P. vivax* malaria patients with multiple organ dysfunction 22.7% needed hemodialysis and it was needed only in 1.7% with single organ dysfunction patients. In multiple organ failure patients 15.9% needed ventilator support. Of 11 patients needing hemodialysis, 18.2% expired and 81.8% survived. Of *P. vivax* malaria patients all 7 patients needing ventilator support had expired.

DISCUSSION

Out of 460 vivax mono infection, 102 admissions of severe vivax malaria fulfilling WHO criteria of severe malaria were included in our study. Incidence of severe vivax malaria found to be lower (22.2%) as compared to falciparum (30.9%) and mixed infection (35.3%). Limaye *et al.*[3] in their study noticed similar that incidence of severe malaria in vivax, falciparum and mixed infection were 14.8%, 31.1%, and 35.3% respectively.

In our study, the incidence of *P. vivax* malaria is more in younger age group and maximum, i.e., 23.5% in age group of 21-30 years which is comparable to 23.15%, 37.5%, and 25.9% of studies conducted by Nadkar *et al.*,[1] O'brien *et al.*,[4] and Bansal *et al.*,[5] respectively. The factors responsible for age pattern include outdoor work for young adult males and outdoor sleeping habits which are more prone to get mosquito bites.

In our study, the percentage of males is 62.37% and females is 37.3% which is comparable to males - 71.9% and females - 28.1% in a study conducted by Nadkar *et al.*[1] and males - 57% and females - 43% in a study conducted by Apte *et al.*[6] and males 52.5% and females - 47.5% in a study conducted by Bansal *et al.*[5]

In our study incidence of fever with chills and rigors is 98% which is comparable to 99% in a study done by Apte *et al.*[6] and Echeverri *et al.*[7] and to 100% in a study done by O'brien *et al.*[4] In our study 66.7% patients have acute illness of fever up to 7 days, 25.5% have fever of 8-14 days duration and 5.9% more than 14 days which is comparable to 78 up to 7-8 days, 18% between 8 and 14 days and 4% more than 14 days in study conducted by Sarkar *et al.*[8] Apte *et al.*[6] found that 94% had fever up to 8 days while 6% had more than 8 days.

We observed 84.3% patients with splenomegaly and 62% with hepatomegaly, while Apte *et al.*[6] in their study shows splenomegaly in 54% and hepatomegaly in 43%. We observed that all the studies from Indian subcontinent show high percentage of splenomegaly as compared to other international studies, this might be due to most of the subjects in this region are from malaria endemic area.

Incidence of multiorgan dysfunction in our study is 43.1% of patients. This is in concordance with the studies done by Nadkar *et al.*,[1] Sarkar *et al.*,[8] Kochar *et al.*[2] and Bansal *et al.*[5] which were 42.8%, 46%, 47.5% and 39.9% respectively.

In present study in hematological investigations, we found thrombocytopenia as commonest finding in 89.2% either mild or severe which is comparable to 86.4% in a study conducted by Singh *et al.*[9] and to 89.7% in a study conducted by Bansal *et al.*,[5] to 89.3% in a study conducted by Nadkar *et al.*[1] Bleeding tendency is seen in 5.9% in severe thrombocytopenia which also had deranged PT >16. All these patients required platelet transfusion. But we had no fatality due to bleeding complication.

Anemia was present in 39.1% while severe anemia according to WHO definition (Hb <5 g%) found in only 2.9% which required whole blood or PCV transfusion. It is comparable to studies conducted by Apte *et al.*[6] and SP Singh *et al.*[9] who found severe anemia in 4% and 7.9% respectively. Limaye *et al.*[3] observed that severe anemia (Hb <5 g/dL) was significantly less common in vivax infection (2.96%). the need for packed red cell transfusion was less in vivax malaria (2.37%).

Anaemia in vivax malaria is due to hemolysis and bone marrow dyserythropoiesis. The cause of hemolysis is increased fragility of both parasitized as well as non-parasitized red blood cells.

In our study most patients 67.6% have CBC in normal range (5000-10000), while leucopenia was observed in 20.6% and increased CBC in 11.8%. In a study conducted by Echeverri *et al.*[7] the white cell count was abnormal in 34% of the patients: 29% leucopenia and 5% leukocytosis. 21% patients in a study conducted by Apte *et al.*[6] had leucopenia, (11%) had leukocytosis and (68%) had normal count.

Table 1 shows comparison of CBC profile in vivax malaria with other studies.

In present study 41.2%, 27.5%, 20.6%, and 10.8% severe vivax malaria patients have 1+, 2+, 3+, and 4+ grade of parasitemia respectively. This is in concordance with a study conducted by Apte *et al.*,[6] they found out of 140 patients 39% had +1 parasitemia, 26% had +2 parasitemia, 22% had +3 parasitemia, and 13% had +4 parasitemia. While

Table 1: Comparison of CBC profile in vivax malaria with other studies

Parameter	Present study (%)	Apte *et al.*[6] (%)	Singh *et al.*[9] (%)	Limaye *et al.*[3] (%)	Echevverri *et al.*[7] (%)	Nadkar *et al.*[1] (%)	Bansal *et al.*[5] (%)
Thrombocytopenia (%)	89.2		86.4			89.7	89.3
Severe anemia (Hb<5 g)	2.9	4	7.9	2.96			
Normal CBC	67.6	68			66		
Leucopenia	20.6	21			29		
Leukocytosis	11.8	11			5		

CBC: Complete blood count, Hb: Hemoglobin

Arthi *et al.*[10] found 84.7% having 1+ parasitemia 11.5% having 2+ parasitemia and 3.8% having 3+ parasotemia but no patients having 4+ parasitemia. In our study, all patients with multiorgan dysfunction had 2+ or more than 2+ grade of parasitemia.

This is similar to a study conducted by Arthi *et al.*[10] who observed that parasitic index can be correlated well with severity and course of malarial disease.

In present study of 102 severe vivax malaria patients organ dysfunction observed were hematologic, renal, hepatic, CNS and respiratory. Hematologic dysfunction, including thrombocytopenia and severe anemia was the most common organ dysfunction, found in 89.2% patients which is in concordance to 89.1% and 89.7% in a studies conducted by Nadkar *et al.*[1] and Bansal *et al.*[5] respectively.

In present study next common organ dysfunction observed was renal present in 34.3%, followed by hepatic dysfunction, present in 21.6%. Nadkar *et al.*[1] also mentioned renal dysfunction as 2nd most common complication presented in 31.9% followed by hepatic dysfunction presented in 19.5%. Apte *et al.*[6] in their study, found hepatic dysfunction 2nd common dysfunction in 40% next to thrombocytopenia (68%). Singh *et al.*[9] observed renal dysfunction only in 6.4%.

In our study, CNS dysfunction was observed in 7.8% which was in concordance with 6.4%, 8.1% and 3.5% in a studies conducted by Bansal *et al.*,[5] Nadkar *et al.*,[1] and Limaye *et al.*,[3] respectively.

In present study ARDS as respiratory dysfunction found in only 2 cases (2%). This is in concordance with 1.4%, 1.6%, 3%, and 2.1% in studies conducted by Bansal *et al.*,[5] Nadkar *et al.*,[1] Limaye *et al.*,[3] and Singh *et al.*,[9] respectively. Apte *et al.*[6] found slightly more incidence of ARDS, i.e., in 12%.

Table 2 shows comparison of incidence of multiorgan dysfunction in severe malaria with different studies.

Incidence of multiorgan dysfunction in our study is 43.1% of patients while that in studies done by Nadkar *et al.,*[1] Sarkar *et al.*,[8] Kochar *et al.*,[2] and Bansal *et al.*[5] which were 42.8%, 46%, 47.5%, and 39.9%, respectively.

In present study 33.3% had presented with 2 organ dysfunction while 3 organ and 4 organ dysfunction were presented in 7.8% and 2% patients. This is in concordance with studies done by Nadkar *et al.*[1] and Bansal *et al.*[5] Nadkar *et al.*[1] observed 2, 3, 4 organ dysfunction in 33.8%, 8.8%, 0.2%, respectively while Bansal *et al.*[5] observed that in 29.1% and 10.7%. They didn't find four organ involvements.

In our study, in 2 organ dysfunction hematological along with renal was commonest presentation, seen in 18.6% followed by hematological with hepatic dysfunction present in 10.8%. Hematologic dysfunction and cerebral vivax malaria in combination was seen in 3.9%. This is similar to a study conducted by Nadkar *et al.*[1] in which the commonest organ combination observed was thrombocytopenia with renal involvement. While Sarkar *et al.*[8] mentioned renal failure with jaundice (12/44, 27%) was the most common combination in their study.

In our study hematological dysfunction along with hepatic and renal dysfunction was commonest three organ dysfunction seen in 3.9%. This finding is consistent with previous studies. Sarkar *et al.*[8] in their study mentioned that out of 92 multiorgan complication patients 39.1% had three organ dysfunction in which jaundice, renal failure and anemia was commonest combination followed by cerebral malaria, jaundice and anemia. Kochar *et al.*[2] in their study observed three organ dysfunctions in 9 patients (22.5%) in which, renal failure, jaundice and thrombocytopenia was commonest combination.

We observed four organ dysfunction in only two patients, one had hematological, renal, CNS and hepatic dysfunction and other had hematologic, renal, respiratory and hepatic dysfunction. This is comparable with previous studies. Kochar *et al.*[2] in their study of 40 severe vivax infections, only 2 had 4 organ involvement. That were with cerebral malaria, renal failure, severe anemia, thrombocytopenia and ARDS, jaundice, renal failure and severe anemia. Nadkar *et al.*[1] in his study observed 4 organ complications were seen in 1 (0.20%) patient.

Table 2: Comparison of incidence of multiorgan dysfunction in severe malaria with different studies

Organ disfunction	Present study (%)	Nadkar *et al.*[1] (%)	Bansal *et al.*[5] (%)	Limaye *et al.*[3] (%)	Singh *et al.*[9] (%)	Apte *et al.*[6] (%)
Hematological	89.2	89.1	89.7	68	86.4	68
Renal	34.3	31.9	11.6	3.5	6.4	17
Hepatic	21.6	19.4	19.8	5.3		40
CNS	7.8	8.1	6.4	3.5	19.3	10
Respiratory	2	1.6	1.4	3	2.1	12

CNS: Central nervous system

In present study, it is found that Incidence of multiorgan involvement increases with increasing age. Maximum multiorgan dysfunction patients (34.1%) were in age group >60 years. While in younger age group majority patients had single organ involvement. Dondorp *et al.* in a large multicenter treatment trial conducted in Asia concluded that presenting syndromes in severe malaria depend on age.[11]

In present study, we found that mortality associated with severe vivax malaria was 6.9% which is concordance with 9%, 6.9% in studies conducted by Nadkar *et al.*,[1] and Bansal *et al.*[5] respectively. This is discordance with studies conducted by Limaye *et al.*[3] who found lower mortality 1.7% and by Sarkar *et al.*[8] who found 20% motality.

In our study statistically significant difference ($P < 0.05$) was observed of outcome in patients more than 60 years compared to younger patients. Maximum mortality of 18.8% was found in patients more than 60 years. This is comparable with studies conducted by Nadkar *et al.*,[1] and Bansal *et al.*,[5] they found 17.5% and 29.4% mortality in patients more than 60 years, respectively.

None of the patients with single organ dysfunction expired. However, mortality in multiorgan dysfunction was 15.9%. Nadkar *et al.*[1] observed similar in their study that mortality in single organ dysfunction was 6.9% but it rose to 27% in multiorgan dysfunction.

In our study, all 7 patients expired had 4 plus parasitemia grade and in total 11 of 4+ parasitemia grade 63.6% severe *P. vivax* patients expired. Thus, we observed statistically significant difference of outcome of patients according to severity of parasitemia. Aarthi *et al.*[10] in their study also noticed only one patients having heavy parasitemia expired while 25 severe vivax patients having low parasitemia recovered.

Hematologic Dysfunction

In hematologic dysfunction thrombocytopenia was most common finding present in 89.2%. Platelet count was below 40000 in 5.9% patients. All these patients suffered from abnormal bleeding in the form of petechiae, ecchymoses, malena, mild hematemesis, hematuria, all necessitating platelet transfusion. Bleeding due to thrombocytopenia was not fatal.

46.1% patients had thrombocytopenia as only single organ patients. None of the patients among them expired. But mortality found to be increasing when increasing associated organ involvements This is comparable to findings of a studies conducted by Nadkar *et al.*[1] and Bansal *et al.*[5]

Renal Dysfunction

In present study renal dysfunction, as acute renal failure (ARF) according to WHO criteria found in 34.3% in severe vivax malaria. Majority patients were treated conservatively with fluids and diuretic. 31.4% (11/35) required renal replacement therapy in the form of hemodialysis. Maximum creatinine observed was 9.5%. This is in concordance with studies conducted by Nadkar *et al.*[1] and Bansal *et al.*[5]

There were no death observed when patients presented with renal dysfunction as a single organ dysfunction but mortality rose to 5.3% when associated with thrombocytopenia. Mortality increased when there was increased in associated organ involvements.

Hepatic Dysfunction

In present study, Incidence of hepatic involvement was found in 21.6% which is in concordance with 19.5% in a study conducted by Nadkar *et al.*[1] Maximum bilirubin seen was 7.6 mg%. None of the patients had signs of hepatic encephalopathy or DIC.

No mortality was found when presented as single organ dysfunction or associated with thrombocytopenia but mortality increased when associated with 3 or 4 organ dysfunctions along with renal or respiratory dysfunction.

ARDS

We found two patients with respiratory distress syndrome both were associated with other organ dysfunction and developed ARDS after admission. Both of these patients required ventilator support. Both patients died because of ARDS. Nadkar *et al.*[1] found 62.5% mortality in ARDS patients.

Cerebral Malaria

In our study incidence of cerebral malaria was 7.8%. All patients with CNS involvement were having associated organ involvement. In other words in single organ involvement no patient had cerebral malaria. All 7.8% patients having cerebral malaria was having altered sensorium with Glasgow coma scale <13 at the time of presentation. All patients of cerebral malaria along with hepatic or hematologic dysfunction survived. Mortality was 100% in patients with renal dysfunction along with hematologic and hepatic dysfunction.

Table 3 shows comparison of outcome associated with different organ involvement which is 100% if associated with ARDS and lowest with thrombocytopenia.

Table 4 shows none of the patients with single organ dysfunction expired. But mortality in multiorgan dysfunction was 15.9%. Nadkar *et al.*[1] observed similar in their study that mortality in single organ dysfunction was 6.9% but it rose to 27% in multiorgan dysfunction.

Table 5 shows in present study we reported different organ dysfunctions (thrombocytopenia-89.2%, ARF-34.3%,

Table 3: Outcome according to organ dysfunction

Organ dysfunction	Present study (%)	Nadkar *et al.*[1] (%)	Bhansal *et al.*[5] (%)	Singh *et al.*[9] (%)	Aarthi *et al.*[10] (%)
Hematologic	7.7				
Renal	20				50
Hepatic	18.2				
CNS	25	5		18.51	
Respiratory	100	62.5	60	66.7	

CNS: Central nervous system

Table 4: Number of organ dysfunction and mortality

Author	One organ (%)	Two organ (%)	Three organ (%)	Four organ (%)
Present study	0	2.9	50	100
Nadkar *et al.*[1]	6.9	13.9	6.9	100
Bansal *et al.*[5]	8.3	33.3	58.3	

Table 5: Comparison between severe vivax and severe falciparum infection

Parameter	Nadkar *et al.*[1] (%)	Bansal *et al.*[5] (%)	Limaye *et al.*[3] (%)	Aarthi *et al*[10] (%)	Singh *et al.*[9] (%)	Present study (%)
Thrombocytopenia						
Vivax	89.1	89.8	68		86.4	89.2
Falciparum	79.8	82.3	73			
Severe anemia						
Vivax			2.9		7.9	2.9
Falciparum			12.6			
ARF						
Vivax	31.9	11.6	3.5	7.4	6.4	34.3
Falciparum	55.1	49.7	19.4	31.2		
Jaundice						
Vivax	19.5	19.8	5.3	3.7	12.1	21.6
Falciparum	36.3	35.7	22.3	25		
Cerebral malaria						
Vivax	8.2	6.4	3.5	-	19.3	7.8
Falciparum	14.4	31.8	13.2	31.2		
ARDS						
Vivax	1.6	1.4	3	3.7	2.1	2
Falciparum	2.2	2.5	7.7	25		
Mortality						
Vivax	9	6.9	1.8	3.7	6.4	6.9
Falciparum	16.1	15.3	9.7	25		
Age group having max. mortality						
Vivax	>60 years	>60 years			>70 years	>60 years
Falciparum	41-50 years	31-50 years				

ARDS: Acute respiratory distress syndrome, ARF: Acute renal failure

jaundice-21.6%, and cerebral malaria-7.8% ARDS-2%) and associated mortality 6.9% in severe vivax infection which is comparable with those observed in previous studies as mentioned in above studies. In present study incidence of different organ dysfunctions and mortality is found to be less in severe vivax infection compare to severe falciparum malaria as observed in above mentioned studies.

CONCLUSION

In our study single organ dysfunction is present in 55.9% of severe vivax infection which is more common than multiorgan dysfunction in severe vivax malaria present in 43.1%.

In our study common age group of patients with severe vivax malaria is 21-30 years age group, but maximum incidence of multiorgan dysfunction is in >60 years age group. Increased mortality is seen in patients with age >60 years. Males (62.75%) are more common affected than females (37.25%).

In our study fever with chills along with headache is common presentation and majority of multiorgan dysfunction patients have duration of fever >14 days.

Thrombocytopenia (89.2%) is most common single organ dysfunction followed by ARF (34.3%). Jaundice is seen in 22.5% followed by cerebral malaria (7.8%) and ARDS 2%.

Two organ dysfunction are seen in (33.3%) and thrombocytopenia with ARF is most common 2 organ dysfunction, while ARF Jaundice and thrombocytopenia is most common three organ dysfunction. Three organ dysfunction are seen in 7.8%. Four organ dysfunction are less common seen in only 2 patients.

Outcome is better in single organ dysfunction but it rises to 15.9% in patients with multiorgan dysfunction ($P < 0.01$).

In our study, we noted that ARF if present as single organ dysfunction doesn't have any mortality, but mortality increases if associated with other complications. 80% patients with ARF survived and 11 required hemodialysis out of which 2 died. ARF in severe vivax infection has favorable outcome if treated promptly. In our study it is found that ARDS is associated with poor outcome. Ventilator requirement is more in multiorgan dysfunction and outcome is poor in patients with ventilator requirement.

In present study, similar to severe falciparum malaria as mentioned in past studies multiorgan dysfunction and associated mortality though less common and less severe is seen in severe vivax malaria.

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Original Article

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Clinical Spectrum and Outcome of Acute Post-infectious Glomerulonephritis in Children: A Hospital Based Study

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Abstract

Background: Post-infectious glomerulonephritis (PIGN) has a wide spectrum of clinical presentation and may mimic a wide variety of glomerular diseases.

Aim: To evaluate, the clinical presentation, complications, and outcome of acute PIGN in children.

Materials and Methods: A retrospective observational study of all children in the age group of 1-13 years who were diagnosed to have acute PIGN based on the clinical features, urine analysis, and C_3 levels admitted in Sri Manakula Vinayagar Medical College and hospital between January 2012 and December 2014 are included in this study. Case sheets were analyzed to obtain data on the clinical characteristics, laboratory parameters, complications, and outcome of these children. Descriptive analysis of the collected data was performed.

Results: Out of 52 cases of PIGN, 88.4% the etiology was post-streptococcal. Pneumonia (11.5%) was another important cause identified. There was no difference in the occurrence between males and females, and the majority of cases (52%) are in the age group of 5-10 years. Among clinical features, hypertension was observed in 100% of the cases. Hematuria, oliguria, and edema were seen in 58%, 94%, and 90% of the children, respectively. Laboratory parameters include the presence of hematuria (100%) in all cases. Though mild proteinuria was seen in the majority of cases, nephrotic range proteinuria was observed in 11.5% of cases. The complications include acute kidney injury in 27%, congestive cardiac failure in 15%, hypertensive emergency in 23%, and encephalopathy in 7% of cases. No mortality was observed.

Conclusion: Post-streptococcal glomerulonephritis is an important cause of acute PIGN. Children in the age group of 5-10 years are most affected. Acute kidney injury, congestive cardiac failure, and hypertensive encephalopathy are potential serious complications of this disease which requires intensive care monitoring to yield a positive outcome.

Key words: Acute kidney injury, Child, Glomerulonephritis, Hematuria, Streptococcal infections

INTRODUCTION

Post-infections glomerulonephritis (PIGN) occur due to immunologically mediated injury to the glomerulus by various infectious agents such as viral, bacterial, or protozoa organisms. Among the infectious causes post-streptococcal glomerulonephritis (PSGN) is the most common and it is a non-suppurative sequel to Group A β-hemolytic streptococci.[1] The nephrogenic strains include those associated with cutaneous infections and pharyngitis with strains M4, M12, M25, and M49 being the most common.[2,3] In tropical areas, there is tendency to have pyoderma associated PSGN[4] where in temperate climate there is predominance of pharyngitis associated PSGN.[5,6] The incidence of PSGN has decreased in the

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developed world but in developing nation like India it is still an important public health problem.[7] PIGN is one of the leading cause requiring hospital admissions in children,[8] and it is also an important cause of acute renal failure in developing countries.[9] Though deaths due to this disease are rare it can cause serious complications such as hypertensive emergency, congestive cardiac failure, renal failure, encephalopathy, and retinopathy.[10] Recent data on clinical profile and complications of PIGN are very few in India hence the present study was under taken.

MATERIALS AND METHODS

This retrospective observational study was carried out at Sri Manakula Vinayagar Medical College and Hospital after due permission from the hospital authorities. All case records of children with the diagnosis of acute PIGN admitted from January 2012 to December 2014 were taken from the medical records department and the case sheets were analyzed. Children in the age groups of 1-13 years. Presenting with acute nephritic syndrome is included in the study. Acute nephritic syndrome was defined as acute onset of hematuria, hypertension and oliguria, and edema.[11] Acute PSGN was diagnosed in the presence of (a) features of acute nephritic syndrome, (b) evidence of recent streptococcal infection, and (c) lower serum complement C3 levels. PIGN was defined as features of acute nephritic syndrome combined with the evidence of an infectious etiology, e.g., PSGN, Pneumonia, Varicella, etc. Hematuria was defined as presence of 5 red blood cells per high power field on a centrifuged urinary specimen.[12] Hypertension was defined as systolic and or diastolic blood pressure values exceeding the 95th centile for age sex and height.[13]

The patients are reviewed with respect to the age, sex, skin or throat infection, blood pressure at admission, general, and systemic examination findings. The laboratory parameters included in the study were hemoglobin (Hb) at admission, urine analysis, blood urea, serum creatinine, serum albumin, serum cholesterol, urine spot protein creatinine ratio, antistreptolysin O (ASO titer), and serum complement C3 levels at admission. ASO titer >200 units/ml was considered as evidence of recent streptococcal infection.[14,15] Nephrotic range proteinuria was defined as urinary protein: Urinary creatinine ratio >2. Acute kidney injury was defined as an abrupt reduction in renal function leading to increase in serum creatinine >0.3 mg/dl, or a percentage increase in serum creatinine of more than or equal to 1.5 fold from the baseline.[16] Details of the treatment given including the usage of one or more antihypertensives and the complications observed during the hospital stay, whether the child recorded fully or partially were all entered in the structured proforma. Full recovery at discharge was defined as absence of edema, hypertension, and normal renal function.[12]

The data were entered and analyzed using Epi info version 3.5.4. The clinical features, laboratory parameters, and outcome of the children were taken for analysis.

RESULTS

Of the 52 children diagnosed to have PIGN between January 2012 and December 2014, 46 (88.4%) was post-streptococcal in etiology. Upper respiratory tract infections, pyoderma and chicken pox preceded APGN in 17%, 6.5%, and 5.5% of the cases, respectively. Pneumonia (11.5%) was found to be an important cause of PIGN other than PSGN. The male to female ratio was 1.08:1. Age of patients ranged from 2.6 years to 13 years with large proportion of cases, 27(52%) in the age group of 5-10 years. Table 1 deficits the distribution of cases in different age groups.

Clinically, hypertension was noted in all cases (100%) at admission. Gross hematuria, oliguria, and edema were noted in 58%, 94%, and 90% of children, respectively. The other clinical features of these children include abdominal pain (23%), dysuria 11.5%, and fever (28.5%). Some presented with central nervous system manifestations (7%) such as seizures, headache, and/or altered sensorium, while few others (8%) presented with congestive cardiac failure. Table 2 elaborates the pattern of clinical presentation in PIGN.

Laboratory parameters of these children included the presence of hematuria in all cases by urine microscopy.

Table 1: Distribution of acute PIGN cases in different age groups

Age group	Number (*n*)	Percentage
1-5 years	21	40.3
5-10 years	27	52
>10 years	4	7.7

PIGN: Post-infectious glomerulonephritis

Table 2: Clinical presentation of acute PIGN

Signs and symptoms	Number (*n*)	Percentage
Hypertension	52	100
Stage I hypertension	36	69.3
Stage II hypertension	16	30.5
Oliguria	49	94
Generalized body swelling	47	90
Abdominal pain	12	23
Dysuria	6	11.5
Fever	15	28.5
Central nervous system manifestations	4	7
Cardiovascular system manifestations	8	15

PIGN: Post-infectious glomerulonephritis

Mild proteinuria was seen in many children, but nephrotic range proteinuria (Spot polymerase chain reaction >2) was seen in 6 (11.5%) of cases. ASO was positive in 24 (46%) of the children, and the C3 value was low in all (100%) of cases. Renal biopsy was not done any case. Tables 3 and 4 illustrate the various laboratory parameters observed in the present study.

The complications observed include acute kidney injury in 14 (27%) of the cases of which all improved by conservative management and none required dialysis. Other complications include hypertensive emergency 12 (23%), congestive cardiac failure in 8 (15%), and encephalopathy in 4 (7%) of cases. No case had hypertensive retinopathy in our study. Table 5 shows the various complications observed due to PIGN.

While most of them (72%) were managed with the use of only diuretics and calcium channel blockers, few required the need of other antihypertensives. Complete recovery was note in 76.9% of cases while few were discharged on oral medications for the control of hypertension.

Table 3: Laboratory parameters of the patients with PIGN

Laboratory characteristics	PIGN cases (*n*=52)	Percentage
Low Hb level at admission	25	48
Urine spot PCR		
0.2	14	27
0.2-2	32	61
>2	6	11
Raised renal function test	7	13.4
ASO positivity (>200 units/ml)	24	46
Low C3 value	52	100
Low serum albumin	13	25

ASO: Antistreptolysin O, PIGN: Post-infectious glomerulonephritis, PCR: Protein creatinine ratio, Hb: Hemoglobin

Table 4: Laboratory values in cases of PIGN

Laboratory parameters	Values*
Hb levels	9.3 (5.8-12)
Urea	40.75 (5-148)
Creatinine	0.644 (0.3-1.2)
C3 levels	0.37 (0.12-0.87)
S. albumin	3.67 (2.4-4.7)

*Values depicted as median (interquartile range), PIGN: Post-infectious glomerulonephritis

Table 5: Complications noticed in subjects due to acute PIGN

Complications	Number	Percentage
Acute kidney injury		
Stage I	8	15
Stage II	5	9.5
Stage III	1	1.9
Hypertensive emergency	12	23
Hypertensive encephalopathy	4	7
Congestive cardiac failure	8	15

PIGN: Post-infectious glomerulonephritis

DISCUSSION

Fifty-two children who had features of acute nephritic syndrome following an infectious cause were included in the study period of which 88.4% the etiology was found to be post-streptococcal. Similar observations were made by other studies.[8,10,17]

There is no difference in male to female ratio, but the previous studies[10,12,17] indicate a male preponderance. The lowest age of presentation was seen in a 2 years 6 months old child but many falls in the age group of 5-10 years, which was in accordance with previous studies.[1,10,11]

Hypertension was noted in all patients. Cerebral complications of hypertension was seen in 7% of cases which is similar to the observations made by other studies,[10,18] but few studies[17] showed higher occurrences of central nervous system manifestations.

The percentage of children presenting with congestive cardiac failure (15%) was high which was similar to a previous studies[10,18] However, in a study done by Lagunju *et al*.,[19] children presenting with cardiac failure was very low.

On analyzing the laboratory parameters all of them had hematuria by urine analysis. Proteinuria in the nephrotic range was seen in 6 (11.5%) of cases which was less compared to other studies[6,10,20] were a higher percentage was noted. The Hb value was low (<10 g/dl) in 48% of cases. The serum albumin values in majority of them (64%) was between 2.6 g and 3.5 g per deciliter which is similar to observations made by Malla *et al.,*[17] but in 25% of the children the serum albumin was very low (<2.5 g/dl). The low hemoglobin and serum albumin was probably due to the high prevalence of malnutrition among these children.

ASO titer was positive in 48% of children which was similar to other studies[6,17,21] but in some studies[10] the positivity was very low. Serum C3 value was low in all patients.

In the present study, acute kidney injury as per acute kidney injury network classification was seen in 27% of cases which is slightly higher compared to study done by Gunasekaran *et al*.[10] where he reported an occurrence of 20.8%. The mean duration of hospital stay was 9.2 days. There was no mortality observed in the study period.

The present study is important as recent studies based on the clinical features of PIGN are very few and secondly

it highlights the potential serious complications of this disease in detail so that timely interventions of these problems may bring down the morbidity and mortality of this illness.

The present study has a few limitations as it was a retrospective study, and the long-term outcome of these children could not be done as many were lost on follow-up in our nephrology clinic.

CONCLUSION

PSGN is the commonest cause of Acute PIGN. Acute kidney injury, congestive cardiac failure, and hypertensive encephalopathy are the dangerous complications of this disease which necessitates the need for monitoring these patients in pediatric intensive care set up. Though the incidence of this disease is strongly influenced by social, environmental and better economic conditions, the availability of a vaccine against Group A streptococcus in near future may curtain its occurrence.

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Original Article

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Anterior Wall Myocardial Infarction with Special Reference to Carotid Intima Media Thickness, Ankle Brachial Pressure Index, and Echocardiographic Evaluation

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Abstract

Introduction: Acute coronary syndromes, comprising unstable angina, non-ST-segment elevation myocardial infarction (MI) and ST-segment elevation MI, are the most common causes of mortality in patients with coronary artery disease (CAD), which is the leading cause of mortality and morbidity in the world.

Aims and Objectives: To study the correlation between carotid intima media thickness (CIMT), ankle brachial pressure index (ABI), echocardiography (ECHO), and anterior wall MI (AMI).

Results: CIMT was abnormal in 54.4% patients, ABI was found to be abnormal in 13.3% patients, 2D ECHO was abnormal in 91.1% patients. Hypertension, diabetes and that with family history of MI were statistically significant ($P < 0.01$), while dyslipidemia, smoking status, obesity and previous history of MI were not statistically significant ($P > 0.05$) in abnormal and normal CIMT groups. Furthermore, hypertension, smoking status, and family history of MI were statistically significant ($P < 0.05$), while diabetes, dyslipidemia, obesity, previous history of MI were not statistically significant ($P > 0.05$) in abnormal and normal ABI groups. There was statistically significant ($P < 0.05$) difference of abnormal ABI according to CIMT abnormality and also a significant difference of abnormal CIMT according to ABI abnormality. The presence of regional wall motion abnormalities and depressed left ventricular ejection fraction (LVEF) were statistically significant in abnormal and normal CIMT groups.

Conclusion: CIMT, a measure of carotid atherosclerosis, denotes generalized atherosclerosis due its correlation to MI, asymptomatic peripheral artery disease and should be used as a screening test for detecting adults at risk of CAD; while ABI does not correlate with MI and can be used in combination with CIMT for effective high-risk screening.

Key words: Ankle brachial pressure index, Carotid intima media, Myocardial infarction

INTRODUCTION

Acute coronary syndromes (ACS), comprising unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI), and STEMI, are the most common causes of mortality in patients with coronary artery disease (CAD), which is the leading cause of mortality and morbidity in the world.[1]

Extracranial carotid artery disease has been associated with increased prevalence of significant coronary atherosclerosis and acute coronary events.[2-5]

Carotid intima media thickness (CIMT) measurement is a surrogate marker for atherosclerosis.[6]

CIMT is closely associated with many traditional cardiovascular risk factors (such as cholesterol, diabetes, blood pressure [BP], and smoking), some new risk

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factors (such as lipoprotein, platelet aggregability, and hyperhomocysteinaemia), and target organ damages (such as left ventricular hypertrophy, microalbuminuria, and decreased ankle-brachial index [ABI]).[7]

CIMT is strongly associated with the risk of MI and stroke in asymptomatic older adults.[8]

ABI is a reliable indicator of high coronary risk[9] and is significantly related to the presence of CAD.[10]

An ABI cut-off point of 0.9 or less has been used in clinical practice and epidemiologic studies as the indicator of PAD. ABI at this level is statistically significantly associated with higher prevalence of clinical CHD, stroke, and preclinical atherosclerosis and may be indicative of generalized atherosclerosis in middle aged men.[11]

In 1993, Newman, *et al.*,[12] found that participants with an AAI <0.8 were more than twice as likely as those with an AAI of 1.0-1.5 to have history of MI, angina, congestive heart failure, stroke, or transient ischemic attack (all $P < 0.01$).[12]

Various studies have documented an inverse correlation between ABI and IMT.[11,13-16]

Echocardiography (ECHO) is commonly used to evaluate CAD.[17] It is increasingly used as a practical and reliable means of assessing both global ventricular function and regional wall motion abnormalities (RWMA) in MI.[18]

In this study, an attempt is made to study patients having anterior wall MI (AMI) and establish the correlation of CIMT, ABI, and ECHO with AMI.

Aims and Objectives

To study, the correlation between CIMT, ABI, ECHO, and AMI.

MATERIALS AND METHODS

Study Population

A total of 90 patients with AMI were recruited on admission to the intensive care unit at Jawahar Medical Foundation's Annasaheb Chudaman Patil Memorial Medical College and hospital, from October 2012 to September 2014. In this study, we included 62 males and 28 females. Patients with confirmed diagnosis of ST-elevation (71.1%) and non-ST elevation (28.9%) AMI and satisfying the inclusion and exclusion criteria were included in the study group.

Inclusion Criteria

1. Patients more than 18 years of age
2. Patients with ST-segment elevation AMI
3. Patients with non-ST-segment elevation AMI on the basis of history, examination, cardiac enzymes, electrocardiogram changes, and 2D ECHO
4. Patients willing to give informed consent.

Exclusion Criteria

1. Patients <18 years of age
2. Patients with documented prior peripheral artery disease
3. Patients not willing to give informed consent.

Clinical Data

A detailed history with clinical examination, routine blood investigations, lipid profile, and special investigation of carotid Doppler, ABI and ECHO was performed.

Carotid Doppler Examination

Color duplex ultrasound scanning was performed by a single trained sonographer using a Toshiba Nemio XG machine with 7 MHz linear-array transducer. Subjects were examined in the supine position with the subject's neck extended and the head turned 45' to the left or right.

Ultrasound scans of the right and left last distal centimeter of the common carotid artery and the bifurcation, i.e. carotid bulb, and of the first proximal centimeter of the internal carotid arteries were performed and CIMT was measured on the far (posterior) wall using computer program based calipers.

Intima media thickness is defined as the distance from the leading edge of the lumen-intima interface of the for the present study CIMT values >0.9 mm were considered abnormal.

Carotid Plaque

Any focal thickening in the carotid lumen or CIMT >1.5 mm.

Carotid Stenosis

Lumen narrowing by >50%.

ABI

BP readings were calculated in both upper limbs and lower limbs in supine position, by raising the pressure of sphygmomanometer cuff 10-20 mmHg above systolic and cuff deflated at the rate of 2 mmHg/s; pressure at which appearance of blood flow detected by 8 Mhz probe of Toshiba Nemio XG was recorded as systolic pressure. ABI was calculated as the mean of ankle systolic pressure divided by the mean of brachial systolic pressure.

For the present study CIMT values <0.9 were considered abnormal.

ECHO

2D Transthoracic ECHO was performed on Envisor-C machine using 3.5MHz probe. RWMA were identified as akinesia, hypokinesia, and dyskinesia, left ventricular ejection fraction (LVEF) was calculated by Tecoliz's method.

Statistical Analysis

Data were analyzed using SPSS 16. The categorical data were presented in frequency and percent distribution. Patients were analyzed for characteristics with reference to normal and abnormal categories of CIMT (<0.9 mm normal, >0.9 mm abnormal) and ABI (>0.9 normal, <0.9 abnormal). In between parameters, association was tested using nonparametric Pearson Chi-square test or Mann–Whitney U test. Mean values of parameters in normal and abnormal CIMT was compared using the unpaired *t*-test. The level of significance was selected at $P < 0.05$, for accepting the difference in between the parameters as significant.

RESULTS

Baseline characteristics of the study population are given in Table 1.

CIMT was abnormal in 54.4% patients with AMI, a carotid plaque was present in 32.2%, ABI was found to be abnormal in 13.3% patients, 2D ECHO was abnormal in 91.1% patients.

Hypertension, diabetes and those with family history of MI were statistically significant ($P < 0.01$) while, dyslipidemia, smoking status, obesity, and previous history of MI were not statistically significant ($P > 0.05$) in abnormal and normal CIMT groups.

Furthermore, hypertension, smoking status, and family history of MI were statistically significant ($P < 0.05$), while diabetes, dyslipidemia, obesity, previous history of MI were not statistically significant ($P > 0.05$) in abnormal and normal ABI groups.

In our study, there was statistically significant ($P < 0.05$) difference of abnormal ABI according to CIMT abnormality and also significant difference of abnormal CIMT according to ABI abnormality.

CIMT was abnormal in 100% patients and carotid plaque present in 91.7% patients with abnormal ABI. There was statistically very highly significant ($P \leq 0.001$) difference of carotid plaque presence in abnormal ABI of AMI patients.

RWMA were more in abnormal then normal CIMT of AMI patients (statistically significant, $P < 0.05$)

About 98% abnormal CIMT patients had ejection fraction within 30-44% and abnormal echo findings which were statistically significant ($P < 0.05$) difference of in normal and abnormal CIMT of AMI patients.

Regional wall motion abnormality, percentage ejection fraction and abnormal 2D ECHO findings were not statistically significant ($P > 0.05$) in abnormal and normal ABI groups (Table 2).

All 12, i.e., 100% patients with abnormal ABI and 7.7% having normal ABI had carotid stenosis of more than 50%. There was statistically very highly significant ($P < 0.001$) difference of carotid stenosis within normal and abnormal ABI in AMI patients.

Table 1: Baseline characteristics of study population

Parameter	Mean±SD (range)
Age (years)	60.9±10.2 (42-76)
BMI (kg/m^2)	28±2.53
WHR	0.86±0.09
Mean CIMT (mm)	1.06±0.37
Mean ABI	1.00±0.11
LVEF (%)	42.4±5.9
Total cholesterol (mg/dl)	218.48±26.74
LDL (mg/dl)	138.3±29.8
HDL (mg/dl)	45.26±9.54
Triglycerides (mg/dl)	182.04±79.29
Hypertension (%)	62.2
DM (%)	44.4
Dyslipidemia (%)	65.6
Smoking (%)	41.1
Obesity (%)	20.0
Family history of MI (%)	23.3

MI: Myocardial infarction, ABI: Ankle brachial pressure index, CIMT: Carotid intima media thickness, DM: Diabetes mellitus, HDL: High density lipoprotein, LDL: Low density lipoprotein, LVEF: Left ventricular ejection fraction, BMI: Body mass index, WHR: Waist to hip ratio, SD: Standard deviation

Table 2: Abnormalities of CIMT, ABI, and ECHO in study group

Parameter	Percent
CIMT	
Abnormal	54.4
Normal	45.6
Carotid plaque	
Present	32.2
Absent	67.8
ABI	
Abnormal	13.3
Normal	86.7
2D ECHO	
Abnormal	91.1
Normal	8.9

ABI: Ankle brachial pressure index, CIMT: Carotid intima media thickness, ECHO: Echocardiography

Mean CIMT showed a linear increase with increasing number of risk factors. While such a relation could not be seen with decreasing mean ABI.

There was a highly statistically significant ($P < 0.001$) difference in mean CIMT values in diabetics (0.95 ± 0.31 mm) as compared to non-diabetics (0.74 ± 0.14 mm).

All 6 patients that died were having all 3 abnormalities, i.e., CIMT, ABI and ECHO abnormal in them. While of those 12 patients having AMI with these 3 abnormalities 50% survived and 50% had died (Table 3).

DISCUSSION

As a screening test, imaging must be safe, sensitive, and affordable. Measurement of CIMT by B-mode ultrasound is non-invasive, sensitive, and reproducible technique for identifying and quantifying atherosclerotic burden and cardiovascular disease (CVD) risk.[19]

Nine published prospective studies that included at least 1000 asymptomatic participants have examined CIMT and CVD risk. Each study demonstrated that CIMT was significantly associated with risk for MI, stroke, death from coronary heart disease, or a combination of these events. In most of these studies, the ability of CIMT to predict future CVD events was independent of traditional risk factors.[19]

The ABI may help to identify asymptomatic individuals in the general population who are at increased risk of subsequent cardiovascular events. It has shown the most promise as a potential tool in clinical practice and has been most wide investigated.[20]

Su *et al.*, 2005,[21] found cardiovascular events in 50% of patients with ABI <0.9 as compared to only 7% in group with ABI ≥0.9, which was statistically very significant ($P < 0.01$).[21]

They also observed that ABI <0.9 and three-vessel CAD were significant predictors of cardiovascular events.[21]

Table 3: Number of risk factors present with their mean CIMT and ABI of patients with AMI

Number of risk factors	Frequency	Percent	Mean CIMT	Mean ABI
0	7	7.8	0.721	1.078
1	13	14.4	0.751	1.006
2	26	28.6	1.003	1.022
3	16	17.8	1.215	0.966
4	23	25.6	1.197	1.025
5	5	5.6	1.563	0.900
Total	90	100.0		

AMI: Anterior wall myocardial infarction, ABI: Ankle brachial pressure index, CIMT: Carotid intima media thickness

In our study, mean age was 60.9 ± 10.2 years (range 42-76 years). This was comparable with Kablak-Ziembicka *et al.*[22] (59.3 years), Shetty *et al.*[23] (58.72 years), Keo, *et al.*, 2011[24] (65.5 ± 9.4 years), Aljabri, *et al.*[25] (62 ± 14.3 years).

While it was not comparable with Jadhav and Kadam[26] (52.8 ± 8.7 years), and Hansa *et al.*,[5] (49.7 ± 10.5 years).

We did not find any statistically significant difference of age groups according to abnormal (>0.9 mm) and normal (≤0.9 mm) CIMT. Also, there was no significant difference of mean age in between abnormal and normal CIMT.

We did not find any statistically significant difference of age groups according to abnormal (<0.9 mm) and normal (≥0.9 mm) ABI. Furthermore, there was no significant difference of mean age in between abnormal and normal ABI.

This is not comparable to Su, *et al.*[21] and Brasileiro, *et al.*[16] who demonstrated that elderly population has a lower ABI. This is because only 34% of patients above 70 years. Were smokers in our study and as smoking is significantly related to abnormal ABI, our observations lack the association.

In our study, we did not observe any statistically significant difference of gender according to abnormal (>0.9 mm) and normal (≤0.9 mm) CIMT. Furthermore, there was no statistically significant difference in the mean values of CIMT according to gender. This is not concordant with Linhart, *et al.*,[27] who observed CIMT to be significantly increased to a greater extent in young men than young women, as their patients were <45 years males and <50 years females.

We did not observe any statistically significant difference of gender according to abnormal (<0.9 mm) and normal (≥0.9 mm) ABI. This is concordant with observations of Newman, *et al.*,[12] and Brasileiro, *et al.*, 2013.[16]

In our study, family history of CAD was present in 23.3% of patients. There was a statistically significant difference of presence of family history of CAD in patients with abnormal CIMT (81%) and abnormal ABI (28.6%).

Linhart, *et al.*, 2012,[27] found statistically significant difference of presence of history of cardiovascular events in first-degree relatives in men and women as compared with controls.

In our study, 71.1% were overweight and 20% were obese, comparable with Kablak-Ziembicka *et al.*[22] (20.3% obese), and Keo *et al.*[24] (45.3% overweight, 21.1% obese).

In our study, there was no significant difference of BMI groups according to abnormal and normal CIMT.

In our study, there was no significant difference of BMI groups according to abnormal and normal ABI, comparable to Newman *et al.*;[12] Su *et al.*;[21] Aljabri *et al.*[25] and Brasileiro *et al.*[16]

In our study, current smoking was found in 41.1% of AMI patients. It was higher than that observed by Jadhav and Kadam[26] (31.3%), Gupta Hansa, *et al.*,[5] (21%), Keo *et al.*,[24] (11.7%).

While it was lower as compared to that observed by Kablak-Ziembicka *et al.*[22] (64.4%), Shetty, *et al.*[23] (51.4%).

In our study, there was statistically significant difference of smoking in AMI patients as regards abnormal and normal ABI, comparable with Newman *et al.*;[12] Su *et al.*[21]

Papamichael *et al.*[28] found smoking ($P = 0.025$) was significantly related to ABI in the multiple regression analysis.

However, Aljabri *et al.*[25] and Brasileiro *et al.*[16] found no significant difference of ABI in between smokers and nonsmokers.

We observed 62.2% of AMI patients to be hypertensives. It was comparable with Kablak-Ziembicka AK, *et al.*[22] (62 %), Gupta Hansa, *et al.*[5] (54.5%), Shetty *et al.*[23] (52.96%) Keo, *et al.*[24] found 83.5% of CAD patients to be hypertensives.

In our study, hypertension was statistically highly significant in patients with abnormal CMIT as compared to those with normal CIMT. This is comparable to Jadhav and Kadam[26] who observed that abnormal IMT had the strongest correlation for CAD in subjects with hypertension (with an incidence of 22.2%) as against those without CAD (only 3.6%).

Linhart *et al.*[27] found hypertension 15.3% and 30% of young male and female MI survivors respectively. The lower prevalence as compared to other studies is attributed to the younger cohort in their study.

In our study, hypertension was statistically highly significant in patients with abnormal ABI as compared to those with normal ABI. However, it is not comparable with below studies.

Aljabri *et al.*[25] found hypertension in 55% of CAD patients, which was not significant as regards abnormal and normal ABI.

Brasileiro *et al.*[16] found statistically no significant difference of ABI in between patients with and without hypertension.

We found diabetes in 44.4% of AMI patients. This was comparable with Jadhav and Kadam[26] (51.5%). However, it was higher as compared to with Gupta Hansa, *et al.*, 2003[5] (31%), Keo *et al.*[24] (31.2%) and Shetty *et al.*[23] (20%).

In our study, there was a highly statistically significant difference in mean CIMT in diabetics as compared to non-diabetics. We also found statistically highly significant difference ($P < 0.001$), with higher percentage of patients (75%) having abnormal CIMT in diabetics compared to normal CIMT (25%) amongst the AMI patients.

It is comparable to the Chennai Urban Population Study[29] where mean IMT values in Diabetic subjects were significantly raised (0.95 ± 0.31 mm) compared to non-diabetic subjects (0.74 ± 0.14 mm; $P < 0.001$).

We found statistically no significant difference of diabetes in patients having abnormal ABI comparable with Aljabri *et al.*[25] and Brasileiro *et al.*[16]

While Papamichael *et al.*[28] found diabetes ($P = 0.01$) was significantly related to ABI in the multiple regression analysis.

In our study, there was no statistically significant difference of presence of dyslipidemia or individual lipid abnormalities in between abnormal and normal CIMT.

In our study, there was no statistically significant difference of presence of dyslipidemia or individual lipid abnormalities in between abnormal and normal ABI. These observations are comparable with Su *et al.*;[21] Aljabri *et al.*;[25] and Brasileiro *et al.*[16]

In our study, mean CIMT increased with the increasing number of risk factors with mean IMT being highest in patients with 5 risk factors. This finding is concordant with Atherosclerosis Risk in Communities study,[30] and Gupta Hansa, *et al.*[5]

CIMT: In our study, CIMT was abnormal in 54.4% of AMI patients. This was comparable to Jadhav and Kadam[26] (59.2%) and not comparable to Brasileiro, *et al.*[16] (69.5%) and Liu *et al.*[7] (77.78%).

In our study, mean CIMT was 1.06 ± 0.37 mm which was comparable with Simons *et al.*[31] (0.94 ± 0.33 mm), Shetty, *et al.*[23] (0.923 ± 0.123 mm) and not comparable to Gupta Hansa, *et al.*[5] (0.82 mm) Visonà *et al.*[32] (1.45 ± 0.95 mm).

We found, CIMT was increased in both ST elevation and non ST elevation MI, but the difference was not statistically significant.

We found carotid plaque in 32.2 %, which is comparable to study by Salonen and Salonen,[6] who found small plaques in 30% subjects. It is not comparable to Sirimarco *et al.*[33] (44%).

We observed very highly statistically significant relation of patients with carotid plaque with abnormal ABI. Similarly, presence of carotid stenosis was very highly statistically significant in patients with abnormal ABI. This is comparable to Newman *et al.*[12] Ogren *et al.*[34]

ABI

In our study, ABI was abnormal in 13.3% of patients, which is comparable with Newman *et al.*[12] who found abnormal ABI in 13.8% males and 11.4% females.

In our study, mean ABI was 1.00 ± 0.11 in patients with anterior wall myocardial infarction. Mean ABI of those with ABI <0.9 was 0.81 ± 0.03. This was comparable to Su *et al.*[21]

ABI and CIMT

In our study, there was statistically significant difference of abnormal ABI according to CIMT abnormality and also significant difference of abnormal CIMT according to ABI abnormality. This is concordant with Zheng *et al.*;[11] Allan *et al.*;[13] Simons *et al.*;[14] Sodhi *et al.*;[15] Papamichael *et al.*;[28] and Brasileiro *et al.*[16]

In our study, 2D ECHO was abnormal in 91.1% of patients. There was statistically significant difference of ECHO abnormalities of RWMA, and LVEF, being more in abnormal CIMT group. As ECHO is a proven definitive test for detecting MI, our above finding suggests CIMT is correlated to AMI patients.

Horowitz *et al.*[18] observed 94% patients with clinical AMI had RWMA on the initial 2D ECHO.

In our study, RWMA were seen in patients as akinesia (31.1%), dyskinesia (31.1%), and hypokinesia (28.9%).

Chizynski *et al.*[35] observed diffuse hypokinesis in 38%, regional akinesis in 29%, and regional dyskinesis in 33% with impaired dilated left ventricular systolic and diastolic function in patients with ST elevation MI. While in Non ST elevation MI, diffuse hypokinesis in 42%, regional anterior wall hypokinesis with the normal function of other walls in 10%, and regional anterior wall akinesis with the diffuse hypokinesis of other walls in 48% was observed.

In 2004, Kablak-Ziembicka *et al.*[22] found highly statistically significant ($p<0.001$) 70.4% of CAD patients with RWMA, as compared to non-CAD.

In our study, LVEF was <45% in 91.1%, and mean LVEF was 42.4 ± 5.9%. This is comparable to McClements *et al.*[36] who in their study observed the mean LVEF significantly lower in anterior than in inferior MI (44.8% ± 11.5% vs. 53% ± 8.6%; $P = 0.001$).[36]

While, it was not comparable to, Chizynski *et al.*[35] observed LVEF range between 10 and 36% (mean: 24%) in patients with ST elevation MI, and 19-47% (mean 32%), in patients with non ST elevation MI.

In our study, we observed that 6.7% patients with AMI met with fatal outcome within the hospital stay. Of those who died, all 6 (6.7%) patients had abnormal CIMT, ABI, and ECHO findings. This is comparable to Sirimarco *et al.*[33] who observed 8.2% mortality in persons with carotid atherosclerosis, which was highly statistically significant ($P < 0.0001$) as compared to that without.[33]

Heald *et al.*[20] observed a low ABI (<0.9) was associated with an increased risk of subsequent all-cause mortality and cardiovascular mortality after adjustment for age, sex, conventional cardiovascular risk factors and prevalent CVD.[20]

CONCLUSION

In our study, mean CIMT correlates with number of risk factors. While, mean ABI does not correlate with number of risk factors. CIMT correlates with abnormalities seen on ECHO. As ECHO is proven diagnostic test of MI, we conclude that CIMT correlates with AMI. CIMT and ABI correlate with the in-hospital mortality of MI. CIMT correlates with ABI in AMI patients. ABI does not correlate with ECHO abnormalities. As ECHO is proven diagnostic test of MI, we conclude that ABI does not correlate with AMI. CIMT, a measure of carotid atherosclerosis, denotes generalized atherosclerosis due its correlation to MI, asymptomatic peripheral artery disease and should be used as a screening test for detecting adults at risk of CAD; while ABI does not correlate with MI and can be used in combination with CIMT for effective high-risk screening.

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Original Article

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Clinical Presentation and Outcome Laryngotracheal Stenosis: A Retrospective Analysis

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Abstract

Introduction: Laryngotracheal stenosis (LTS) is a complex condition that results in a compromised airway, involving trachea and/or larynx. LTS is recalcitrant, the management of which poses a significant surgical challenge.

Objective: To analyze the outcomes following surgical management of LTS.

Patients and Methods: Retrospective chart review of 53 patients diagnosed with LTS, managed by various surgical approaches over a period of 8 years from 2006 to 2014 were included. The following data, on etiology, site of the stenosis, the surgical outcomes and complications between various procedures performed in management of LTS were collected and analyzed.

Results: Among the 53 cases of LTS, majority (56%) were managed by Montgomery T-tube stenting (temporary and permanent), 20% underwent tracheal resection and anastomosis, and 6% cricotracheal resection and anastomosis. About 86% of the all the patients were managed successfully and decannulated, 6% failed and are on T-tube and 6% are on a tracheostomy tube, and 2% are awaiting decannulation. The others procedures, complications, and management are discussed.

Conclusion: Laryngotracheal resection and anastomosis should be the preferred procedure for managing LTS with a successful outcome of 90% in our case series. Surgical management has to be catered to the needs of the individual case and keeping in mind, the feasibility of the procedure.

Key words: Decannulation, Laryngotracheal stenosis, Resection anastomosis, T-tube, Tracheostomy

INTRODUCTION

Laryngotracheal stenosis (LTS) is a complex condition that results in a compromised airway, involving trachea and/or larynx. The etiology of LTS has changed over the years, the common cause now being iatrogenic; post-intubation and post-tracheostomy. The reported incidence of LTS following laryngotracheal intubation and tracheostomy ranges from 6% to 21% and 0.6% to 21%, respectively.[1,2] In the study by Herrak and Ahid, the incidence was as high as 55.17% post-intubation and 44.82% post-tracheostomy.[3] In another recent multicentric study, the incidence of post-intubation subglottic stenosis is reported to be as high as 11.38% in children.[4] Because the subglottis is the narrowest part of the laryngotracheal lumen in infants and children, it is more prone to injury.[4] This problem is compounded by the formation of a scab, granulation, or post-intubation edema, which leads to respiratory distress that requires emergent intervention. The other causes for LTS are tracheostomy, external trauma, an autoimmune process, and tumors.

In endotracheal intubation, LTS is caused either by the mechanical trauma of placement of an endotracheal tube or its contact pressure. Mucosal hyperemia and edema will result in mucosal necrosis secondary to compression of capillaries in the tracheal mucosa causing ischemia; which is observed within hours of intubation and can result in exposure of the perichondrium of the cricoid cartilage. The resulting perichondritis secondary to infection will lead to healing with scar formation. If it heals with fibrous tissue formation - this tissue contains fibrocytes that

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possess directional memory. Due to this memory, merely incising and separating scar tissue will only lead to tissue trying to replace itself in its previous and original scarred state. Myer *et al.*[5] devised a classification scheme from I to IV for grading circumferential subglottic stenosis. This grading system applies mainly to circumferential stenosis and does not apply to other types of subglottic stenosis Grade I: <50% luminal obstruction and Grade II: 50-70% luminal obstruction. Grade III: 71-99% luminal obstruction and Grade IV: Decannulation on the basis of the anatomic location of the stenosis. 90% Grades I and II, 70% of Grade III and 40% of Grade IV patients are successfully decannulated.

There is no "standard" recommended procedure that gives consistent results. Hence, various techniques and surgical procedures are described to manage LTS; this in itself bears evidence to the complexity of the problem. The goal of laryngotracheal surgery is to restore its function namely, airway patency, phonation, and glottic competence to prevent a cough and aspiration. The surgery can be performed by either endoscopic or external approach. The first described by Gerwat and Bryce in 1974 and later by Pearson and Andrews in 1975, resection and anastomosis was subsequently refined and popularized by Grillo *et al.*[2] Resection of the stenosis and end to end anastomosis as a single staged procedure is advocated by some as the initial procedure of choice though this procedure may not be possible in various scenarios.[6] It is performed for management of acquired inflammatory (mainly post-intubation and post-tracheotomy) tracheal or cricotracheal stenosis, idiopathic subglottic stenosis, and primary subglottic and/or tracheal tumors, as well as to cancers infiltrating the airway from adjacent sites. Endoscopic treatment includes laryngeal microsurgery, laser assisted excision, traditional dilation, and endoscopic stent insertion.[7] In order to maintain laryngotracheal patency, a Montgomery T-tube can be used following primary surgery or as a principle mode of treatment for patients in whom resection and anastomosis is not feasible.[2] The purpose of this study is to analyze the clinical presentation and outcomes, following surgical management of LTS in our center.

Objective of this Study

To analyze, the clinical presentation and outcomes, following surgical management of LTS and review of the current literature.

PATIENTS AND METHODS

A retrospective analysis and chart review of 53 patients, who were diagnosed as LTS and surgically managed by us over a period of 8 years from 2006 to 2014 were included in our study. Bearing in mind the possible etiology, any suspected case of LTS was evaluated initially by a rigid or flexible laryngeal endoscopy and the site of stenosis, degree of luminal narrowing, the length and type of stenosis and the involvement of glottis, supraglottis, or subglottis noted. In a tracheostomized patient, the stomal and supra or infrastomal were evaluated. Radiological data of computed tomography neck with a 3D reconstruction were obtained where necessary. Data relating to the type of intervention, complications, and outcome were documented and statistically analyzed. The quality of life outcome was assessed using a self-assessment questionnaire at the time of last follow-up.

RESULTS

The etiology of LTS in our case series was predominantly secondary to endotracheal intubation in 38 patients (71.69%), 11 patients (20.75%) were post-tracheostomy sequel, one patient had tracheal infiltration due to thyroid malignancy and had developed stenosis, was stented with Montgomery T-tube for palliative management and 2 patients (3.77%) developed stenosis following polytrauma (RTA). Of the 38 patients who underwent endotracheal intubation, 22 were elective and 16 were emergency intubations. Table 1a shows the site of the stenosis. The predominant site of stenosis in endotracheal intubated patients is the upper trachea (49.05%) and in post-tracheostomy stenosis is the suprastomal region (100%) (subglottis and upper trachea) (Tables 1b and c).

Of the 53 patients with LTS, 31 patients (58.5%) underwent T-tube stenting with Montgomery T-tube (temporary and permanent). Two of the temporarily stented patients had to be stented permanently secondary to the development of complications. One patient developed tracheomalacia

Table 1a: Site of stenosis in all patients

Site of stenosis	Supraglottis	Glottis	Subglottis and upper tracheal	Tracheal	Total
Total number of patients	0	4	23	26	53

Table 1b: Site of stenosis in endotracheal intubated patients

Site of stenosis	Supraglottis	Glottis	Subglottis and upper tracheal	Tracheal	Total
In intubated patients	0	4	8	26	38

and the second patient developed stenosis at either ends of the T-tube or both required reinsertion of the T-tube. Nine patients (16.9%) underwent tracheal resection and anastomosis, 3 (5.7%) underwent cricotracheal resection and anastomosis. Two patients had posterior glottic and subglottic stenosis and underwent excision of the scar tissue followed by Hoods laryngeal stenting. The other procedures performed were keel stenting, Bougie dilatation, Laser assisted scar excision, and anterior cricoid split with hyoid interposition as denoted in Table 2 and in Figure 1. One patient had posterior glottic stenosis and was treated with laserization of the cicatricial scar without stenting. Two patients had collapse of the anterior wall of the trachea in the suprastomal area and were managed with tracheoplasty.

Of the 30 patients who underwent T-tube stenting, the stent was successfully removed in 83% and are stable in 1-year follow-up period, 3% of them are awaiting decannulation and 14% failed decannulation secondary to tracheomalacia, development of stenosis at upper and lower end of tube after decannulation, one of them is on a permanent tracheostomy and one has granulation with Grade IV subglottic stenosis and refused further treatment (Figure 2).

Following resection and anastomosis, 90% had successful outcomes. One patient had wound dehiscence on post-operative days 5 and was put on Montgomery T-tube. The patients who underwent cricotracheal resection and anastomosis had a 100% successful outcome. Considering all the surgical procedures, 87% of the patients with LTS were managed successfully with a good outcome, 6% failed on tracheostomy, 6% failed on T-tube, and 2% awaiting decannulation. The overall success is more with resection and anastomosis procedures (Figure 3).

Table 1c: Site of stenosis in tracheostomized patients

Site of stenosis	Suprastomal (subglottis+ upper trachea)	Stomal	Infrastomal	Total
Post-tracheostomy	11	0	0	11

Table 2: Types of surgery

Procedure	Number of patients	Percentage
T-tube	31	58.5
Tracheal resection and anastomosis	9	16.9
Cricotracheal resection and anastomosis	3	5.7
Hoods laryngeal stent	2	3.7
Keel stent	2	3.7
Bougie dilatation	2	3.7
Tracheoplasty	2	3.7
LASER assisted	1	1.88
Anterior cricoid split with hyoid interposition	1	1.88

Quality of Life (QOL) Indicator

We used a subjective assessment of a 3-point scoring system devised to assess the airway, voice, and aspiration (cough). Figure 4 shows the QOL in post-surgery patients. The airway, voice, and laryngeal protective mechanisms were well preserved in above 85% of the patients with a satisfactory result.

DISCUSSION

Management of LTS is a challenge. LTS is one of the most frequent complications associated with prolonged naso/orotracheal intubation and tracheostomy, such as in intensive care units.[7] Post-intubation tracheal stenosis was identified in 1880, after study by MacEwen.[8] Among intubated and tracheostomized patients, the reported

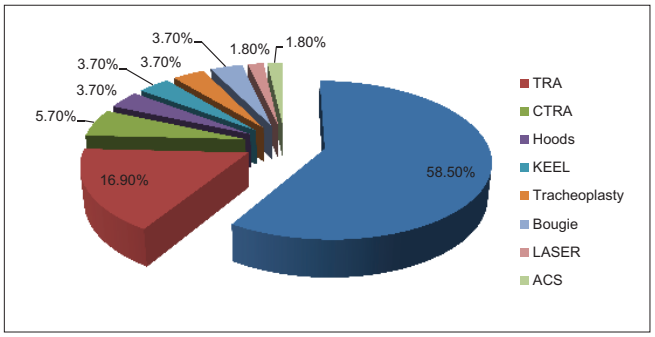

Figure 1: Types of surgery

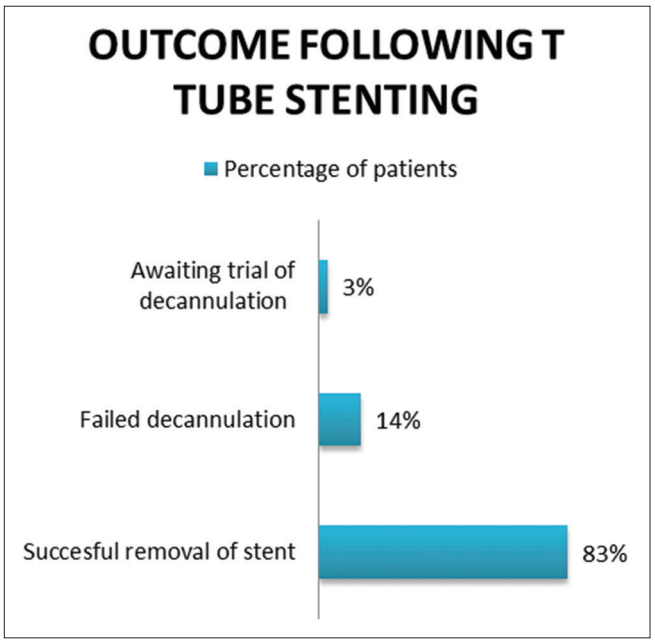

Figure 2: Outcomes following T- tube surgery

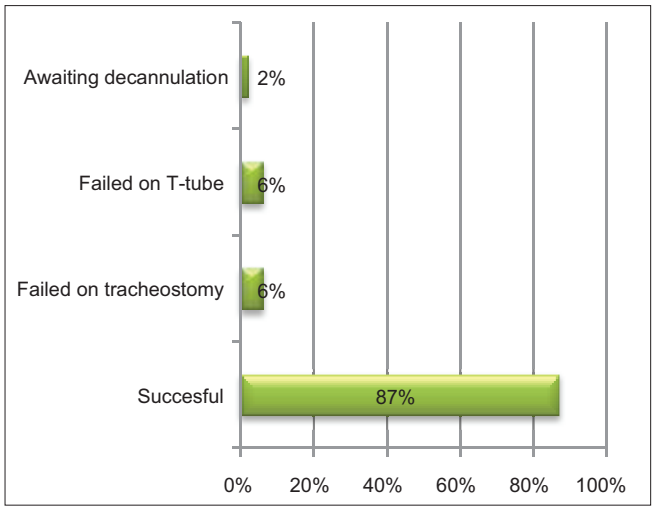

Figure 3: Outcomes following all surgery

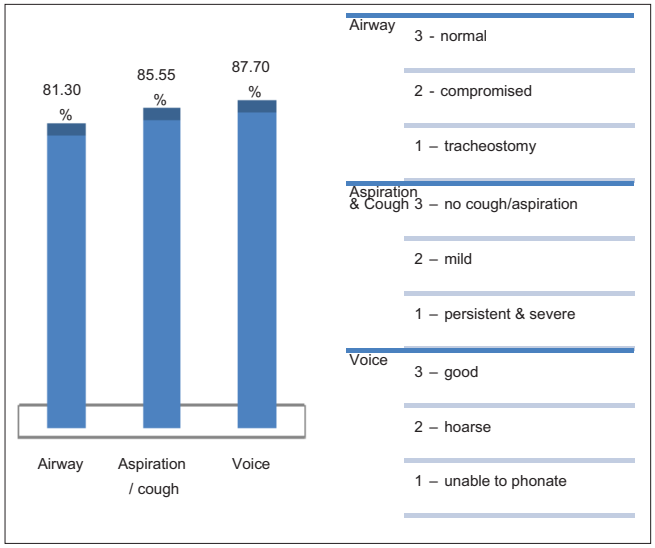

Figure 4: Quality of life outcome

incidence of stenosis varies from 10% to 22%,[8-10] but only 1-2% is symptomatic with severe stenosis.[11,12]

The site of the stenosis varies according to the etiology. Post-intubation stenosis tends to develop web-like fibrous stenosis at the cuff site while tracheostomy patients develop stenosis due to granulation tissue around the stoma site.[11] Furthermore, patients in the elective tracheostomy group would be intubated for longer periods, thus exposing them to more traumas at the tracheal stoma site, and risk of infection.[11] The cuffed endotracheal tube will cause mucosal erosion, pressure necrosis, and if *in situ* for a long time may cause perichondritis. Once withdrawn, the mucosa heals completely within a month and is replaced by metaplastic squamous epithelium and underlying fibrosis. In very severe ulceration involving prolonged intubation and superadded secondary bacterial infection, the risk of LTS is very high. With the advent of high-volume low-pressure cuff, tracheal stenosis at cuff site has reduced.

In this study, 38 patients developed LTS secondary to prolonged intubation in the subglottis, upper trachea and also in the glottis. 11 patients developed LTS secondary to tracheostomy and the stenosis involving the suprastomal region (subglottis and upper trachea) in 100% of the patients. Two patients had developed LTS secondary to injury to the neck, one of them sustained a blunt injury to the neck following attempted suicide by hanging and the other had polytrauma with a fracture of the cricoid cartilage. LTS following blunt injuries and automobile accidents are very meager in our series, due to the secondary to road safety measures.

The most common used classification in evaluating the severity of LTS is Myer–Cotton grading system. The patients with Myer–Cotton Grades I and II were managed conservatively did not undergo any surgical intervention and were therefore not included in our study.

Most authors mention two basic modalities for treatment of LTS - endoscopic and external approach.[13] The procedure of choice is tracheal resection and anastomosis for tracheal stenosis.[6] However, when the glottis and/or the subglottis is involved this surgical approach may not be applicable; moreover it may not be feasible due to the extent of stenosis, underlying disease and general health of the patient.[14] Most of the patients in our series were from the intensive care set up with a poor general health condition and multiple comorbidities where extensive/ major surgeries such as resection and anastomosis could not be performed. The second, some patients had already undergone multiple surgeries before they presented to us, and some patient had economic constrains. These patients were managed by either a temporary or permanent stenting with Montgomery T-tube.

The tracheal T-tube was introduced in 1965 by Montgomery,[15] which acts as stent maintaining airway patency and a tracheostomy tube, made of silicone. It does not harden at body temperature.[13] It is easy to introduce and maintain and cheaper compared to other stents.[16] The ideal duration of T-tube stenting according to Cooper *et al.*[17] is 6-12 months whereas Martinez-Ballarin *et al.*[18] has recommended usage up to 18 months. In our practice, we inspect the tube every 6 months and change it every 12 months. However, there are some complications with T-tube. We experienced surgical emphysema, severe crusting of the tube in another, where we replaced the tube and formation of granulation at either ends of the tube or sometimes resulting in restenosis. We had to reintroduced the T-tube for one patient in view of granulation at the ends of the tube. One of our patients

who had multiple comorbid conditions with T-tube *in situ* for 1-year developed tracheomalacia which was noted during tube change. We did not experience any mortality directly related to T-tube stenting. We were able to successfully decannulate 83% of our patients who were using T-tube. Two patients required flap reconstruction of the tracheal stoma. Nine patients (16.9%) underwent tracheal resection and anastomosis. On 5th post-operative day, one patient developed wound dehiscence. He was put on a temporary T-tube, and the wound explored and reconstructed. 90% of patients were managed successfully.

In our case series, we were able to successfully manage and decannulate 87% of the patients. Results obtained are similar to those published in the literature.[19] The patients with Myer-Cotton[5] Grade IV had difficult decannulation. Low grade stenosis and stenosis inferior to 50% of total tracheal extension seem to be decisive for a better prognosis.[13,20] The majority of the patients have a good quality of life following the surgical procedures assessed by the 3-point scoring system.

CONCLUSION

The outcome following procedures for LTS was successful in 87% of patients in our cases series. We have also shared our experience and complications encountered. Resection and anastomosis are the preferred procedure of choice. A cafeteria of choice is available for surgical options, but the surgical procedures need to be catered to the needs of an individual patient.

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Original Article

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Cerebral Venous Thrombosis in Women: A Study from Teaching Hospital in North Karnataka

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Abstract

Background: Cerebral venous thrombosis (CVT) is a relatively rare subtype of stroke. In young to middle aged adults, it is much more common in women than in men. Because of its diverse presentation and unpredictable clinical outcome, it remains a diagnostic challenge for treating clinicians. CVT is more common in underdeveloped countries and is one of the most common causes of stroke in young in India. Though several studies were done in India and elsewhere on CVT, it has not been extensively studied of late.

Objective: The objective of the study is to study the clinical profile of CVT in women.

Materials and Methods: A total of 50 consecutive patients admitted in medicine and obstetrics and gynecology ward between April 2012 and March 2014 with radiologically confirmed diagnosis of CVT were included in the study. Detailed history, clinical examination, and laboratory investigations were carried out in all the cases.

Results: Out of 50 patients of CVT studied, the age of patients varied from 18 to 50 years. Maximum incidence was seen in 21-30 age group comprising 54% of the cases, with mean age being 29.52 years. Two-third of the patients belongs to the low socio-economic class. The majority of them had subacute presentation with the headache in 74%, followed by altered sensorium (54%) and convulsions (46%) being the most common presenting symptoms. Radiologically the most common finding noted was hemorrhagic infarction (56%), followed by non-hemorrhagic infarction (44%). The most common risk factors identified were postpartum followed by dehydration and infections. Mortality was 4% in the present study.

Conclusion: Cerebral venous sinus thrombosis is a challenging condition because of its variability of clinical symptoms and signs. A high index of clinical suspicion is needed to diagnose CVT. Pregnancy and puerperium are most prevalent prothrombotic states leading to CVT.

Key words: Cerebral venous thrombosis, Puerperium, Young

INTRODUCTION

Thrombosis of the cerebral veins and sinuses is a distinct cerebrovascular disorder that unlike an arterial stroke, most often affects young adults and children.[1] Cerebral venous thrombosis (CVT) is an underdiagnosed condition and less frequent than arterial thrombosis.[2,3] In young to middle aged adults, CVT is much more common in women than men with a ratio of approximately of 3:1.[3] Cerebral venous sinus thrombosis (CVST) is an uncommon condition, which over the past 10 years has been diagnosed the more frequent due to greater awareness and the availability of better non-invasive diagnostic techniques. Because of the generally good prognosis and variable clinical signs, many cases remain clinically undetected but some patients suffer complications and die.[4,5] Little is known about the differences between men and women regarding clinical manifestations and outcome of CVT.[3] The purpose of the present study is to describe the clinical features, etiologies, treatment and prognosis of CVT in women.

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MATERIALS AND METHODS

Total 50 consecutive patients admitted in medicine and obstetrics and gynecology ward between April 2012 and

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March 2014 with radiologically confirmed diagnosis of CVT were included into the study. Detailed history, clinical examination, and laboratory investigations mentioned below were carried out in all the cases and followed until discharge from the hospital or death. The results were analyzed, and descriptive statistics were used.

Exclusion Criteria

1. Computed tomogram (CT) scan inconclusive of CVT
2. Hypertensive hemorrhage
3. Arterial stroke
4. Metabolic encephalopathies
5. Space occupying lesions.

Data were collected by using proforma meeting the objectives of the study. The purpose of the study was carefully explained to the patients and informed consent was taken.

Investigations

Complete hemogram, blood urea, serum creatinine, serum electrolytes such as sodium, potassium and chloride, urine routine, electrocardiography, chest X-ray, ocular fundoscopy, cerebrospinal fluid analysis and computed tomography scan/magnetic resonance imaging + magnetic resonance venogram were done. In relevant cases specifically indicated coagulation prolife, serum homocysteine levels, anti-nuclear antibody, rheumatoid factor, and antiphospholipid, antibodies were done.

Statistical Methods

The results were analyzed by calculating percentages, and the mean values.

Statistical Software

The statistical software namely SPSS 15.0, STATA 8.0, MEDCALC 9.0.1, and SYSTAT 11.0 were used for the analysis of the data and Microsoft word and excel have been used to generate the tables.

RESULTS

Demographics and baseline characteristics of the patients are depicted in Table 1. Out of 50 patients of CVT studied, the age of patients varied from 18 to 50 years. Maximum incidence was seen in 21-30 age group comprising 54% of the cases, with the mean age being 29.52 years. The majority of the patients were illiterates (64%) and the most of them are from the low socio-economic state (64%).

Mode of onset in the present study was classified into acute onset - those presented within 24 h, subacute onset - those presented after 48 h but <30 days and chronic onset - onset more than 30 days (Bousser *et al.*, 1985). The majority of the patients had subacute presentation (68%) with the headache in 74% followed by altered sensorium (54%) and convulsions (46%) being the most common presenting symptoms. All the cases in the present study showed varying degree of consciousness. Among them, 46% were found conscious at the time of admission. 26% were found drowsy followed by stuporous (20%) and comatose (8%).

Table 1: Baseline characteristics of the patients

Characteristics	Number of patients (%)
Demographics	
Mean age	29.52
Literacy status	
Literate	18 (36)
Illiterate	32 (64)
Socio-economic status	32 (64)
Low	
Middle	13 (26)
High	5 (10)
Clinical manifestations	
Mode of onset	
Acute	14 (28)
Subacute	34 (68)
Chronic	2 (4)
Symptoms	
Headache	37 (74)
Seizures	23 (46)
Altered sensorium	27 (54)
Vomiting	18 (36)
Focal deficits	16 (32)
Fever	14 (28)
Papilloedema	12 (24)
Level of conscious	23 (46)
Fully conscious	
Drowsy	13 (26)
Stuporous	10 (20)
Comatose	4 (8)
Neuroimaging findings	
Hemorrhagic infract	28 (56)
Non-hemorrhagic infract	22 (44)

The most common neuroimaging finding noted was hemorrhagic infraction (56%), followed by non-hemorrhagic infraction (44%). Superior sagittal sinus was the most common sinus to be involved in the present study accounting for 76%, followed by transverse sinus (38%) and sigmoid sinus (34%).

Out of the 50 patients, puerperal CVT was the most common (Table 2), seen in 32 patients (54%). The second most common was dehydration (7 patients, 14%), followed by infective CVT (4 patients (08%) - sinusitis (1), Chronic suppurative otitis media + myringitis (2), meningitis (1), Oral contraceptive pills induced (2 patients, 4%), hyperhomocysteinemia (1 patients, 2%) and no cause was found in 4 patients (08%).

Nearly 96% patients received heparin in a therapeutic dose and all of them had complete recovery.

Table 2: Etiology, treatment and outcome of the patients

Causes	Number of patients (%)
Etiology	
Puerperal	32 (64)
Dehydration	7 (14)
Infection	4 (8)
Oral contraceptive pills	2 (4)
Hyperhomocysteinemia	1 (2)
No risk factors identified	4 (8)
Treatment	
Heparin - unfractioned	21 (42)
Low molecular weight heparin	27 (56)
Decompression	2 (4)
Outcome	
Complete recovery	48 (96)
Death	2 (4)

DISCUSSION

CVT is an underdiagnosed condition for acute or slowly progressive neurological deficit. CVT has a wide spectrum of signs and symptoms, which may evolve suddenly or over the weeks.[6] Over the past 5-10 years, it has been diagnosed more frequently due to greater awareness and the availability of better non-invasive diagnostic techniques. Because of the generally good prognosis and variable clinical signs, many cases remain clinically undetected.[4] CVT is slightly more common in women, particularly in the age group 20-35, due to pregnancy, puerperium, and oral contraceptive use.[5] Though several studies were done in India and elsewhere on CVT, it has not been extensively studied of late. 50 consecutive cases with a radiologically confirmed diagnosis of CVT were included into the study. The observations are compared with the studies done by others on the same subject.

In our study of 50 patients, maximum numbers of cases (54%) were seen in the age group of 21-40 years. This correlates well with a similar study by Ameri and Bousser[7] (61%). Mean age of onset in the present study was 29.5 years which is comparable with Daif *et al.*[8] study (27.8 years).

Majority of the patients in the present study were illiterates (64%). This may be due to unhygienic health practices like home delivery, local traditional practice of water restriction in the peripartum period, etc. more common among illiterates. Aaron *et al.*[9] in their study suggested possible role of fluid restriction practice in the causation of CVT and also they noticed that although, this traditional practice is followed even in the hot summer months, there was no increase in the incidence of CVT in the summer months.

Majority of the patients in the present study were in low socio-economic group. This is because the hospital where the study was conducted provides services to the socio-economic deprived persons. Prakash and Bansal[10] in their study mention that reasons for its frequent occurrence in socio-economically backward persons especially of Indian origin need to be researched.

Headache (74%) was the most common symptom noted. Apart from headache, altered sensorium (54%) followed by convulsions (46%). This is comparable to a similar study done by Kumar *et al.*[11] (headache - 66%, seizures - 67%).

In the present study, CVT was commonly seen in peripartum period (64%). The experience of other authors from India had been similar like Neki[12] had found 62% of cases of CVT in postpartum period but Nagaraja *et al.*[13] had found that 200 out of 230 cases (86%) of CVT, seen over eight years, were puerperal in nature.

The most common neuroimaging finding was hemorrhagic infraction (56%), followed by non-hemorrhagic infraction (44%). Nagaraja *et al.*[13] noted hemorrhagic infraction in 40.9% and non-hemorrhagic infraction in 51.6%. Dixit *et al*. study reported hemorrhagic infraction in 48.4% and non-hemorrhagic infraction in 32.3%.

CONCLUSION

CVST can affect all age groups, particularly women of childbearing age. Overall prognosis for survival and functional independence is better than it was believed. Patients with CVT related to pregnancy and puerperium generally do better than patients with other causes.

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Review Article

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Lasers in the Management of Oral Pre-Malignant Lesions

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Abstract

Oral premalignant lesions of the oral cavity such as leukoplakia and erythroplakia remain a diagnostic and treatment challenge. They have a potential for malignant transformation. Management of such lesions includes observation, excision, ablation, or topical medical therapies. The gold standard for management of the clinically evident high-grade premalignant disease is excision or laser ablation. Laser treatment has been a well-established modality for management of premalignant lesions and has potential advantages over surgical excision. With the availability of portable and more cost-effective lasers, this technology is now feasible even for outpatient management of such cases. The angiolytic lasers can be used to target the vasculature of oral lesions, leaving intact mucosa, thereby resulting in less discomfort for the patient. Various studies have shown the application of various lasers such as carbon dioxide, thulium, 532 and 940 nm diode, and 532 nm pulsed potassium-titanyl phosphate laser, in the appropriate management of oral premalignant lesions.

Key words: Carbon dioxide laser, Leukoplakia, Premalignant lesion, Potassium-titanyl phosphate laser

INTRODUCTION

More than 500,000 new cases of head and neck squamous cell cancer arise annually worldwide, making it the sixth most common cancer.[1] Of these oral cavity, malignancies account for 14% and lead to upward of 7000 deaths per year.[2] From a genetic perspective, the progression of oral squamous cell carcinoma (SCC) comprises of a distinct pattern and timing of genetic alterations along a continuum of malignant transformation.[3]

Visible oral lesions such as leukoplakia, erythroplakia, oral lichen planus (OLP), and its mixed forms can alert health care providers to a premalignant disease process.[4] Such lesions may harbor histological changes such as squamous hyperplasia, mild dysplasia, moderate dysplasia, severe dysplasia, and carcinoma *in-situ*. Patients with this condition experience a 50-60-fold greater risk of developing oral cancer than the remainder of the population.[5] According to World Health Organization 2005, oral leukoplakia can be defined as "a white plaque of questionable risk having excluded (other) known diseases or disorders that carry no increased risk for cancer."[6] It is the most common premalignant lesion of the oral cavity and is clearly associated with tobacco abuse with alcohol acting as an additive factor. The term erythroplakia (erythroplasia) is used analogously to leukoplakia to designate lesions of the oral mucosa that present as bright red velvety plaques which cannot be characterized clinically or pathologically as due to any other condition. It is associated with a higher risk of malignant transformation. It is found in association with leukoplakia but has less cellularity and keratinization and thus appears redder in color. OLP is yet another white lesion with characteristic reticular appearance. The reported transformation rate of OLP is between 0.5% and 5%.[7] The management of these lesions has always been controversial.

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DISCUSSION

Evaluation/Workup

A thorough case history should be taken to identify risk factors for SCC such as tobacco, alcohol, betel nut chewing,

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and HIV status. Since some drugs cause lichenoid changes (for example, non-steroidal anti-inflammatory drugs, sulfonylureas, beta-blockers, angiotensin-converting-enzyme inhibitors, and anti-malarials), gingival hypertrophy (e.g. calcium channel blockers and phenytoin), or mucosal ulceration (e.g. sulfonamides and thiol-containing drugs).

A detailed head and neck examination should be performed to exclude the presence of other lesions. The lesion should be comprehensively examined giving special attention to the homogeneity and nodularity. Ulceroproliferative growth, induration, and irregular borders should raise the possibility of malignancy. Potential local causes such as loose dentures or sharp teeth edges should be evaluated and corrected if present. The patient should be strictly instructed to quit the causative habit such as tobacco abuse, alcoholism, etc. and reevaluated clinically in 4 weeks for a potential biopsy if the lesion does not resolve. If on the first visit no etiologic factor is identifiable, a biopsy should be carried out to stage the lesion and exclude frank invasive SCC. Definitive diagnosis relies on biopsy and histopathological assessment of the specimen.[8]

MANAGEMENT OF ORAL PREMALIGNANT LESIONS

Various treatment modalities have been described for OPLs. They can broadly be divided into surgical and non-surgical treatments. The non-surgical treatments include photodynamic therapy and topical or systemic medical treatment using carotenoids, retinoids, bleomycin, etc.

The gold standard for management of the clinically evident high-grade premalignant disease is excision or laser ablation. However, moderate and low-grade pre-malignancy may be treated with observation as well as ablation.[9]

A wide variety of surgical treatments exist for oral premalignant lesions (OPL). Complete excision and primary closure are performed for smaller lesions. Scalpel excision of larger lesions may negatively impact mechanism of deglutition, speech, and swallowing. High vascularity and unfriendly anatomical locations such as oropharynx, tonsil, a floor of the mouth, tongue, gingiva, buccal mucosa, retromolar area, etc. makes scalpel excision extremely difficult. Also, the resulting open wound may necessitate split thickness skin grafting or dressing using collagen, buccal fat pad, etc. Demetri arnaoutakis and others have opined surgical excision of OPLs is better in preventing their malignant transformation, compared to observation and other non-invasive therapies. Laser excision or ablation of OPLs offers unique advantages over scalpel excision like faster and precise removal of diseased tissue and excellent hemostasis. It has good patient acceptance, low morbidity, and favorable healing.[10]

LASER TREATMENT OF OPLS

The practice of oral and maxillofacial surgery has included the use of lasers since the mid-1960s. Goldman applied laser energy to teeth and soft tissue in 1965. Strong *et al.* used the carbon dioxide (CO_2) laser in the early 1970s for a variety of surgical procedures including the excision of malignant and premalignant lesions. Hemophilic patients benefited significantly from Ackermann's use of the neodymium:Yttrium-aluminium-garnet (Nd-YAG) laser for a variety of oral surgical conditions.[11]

The laser of different wavelengths are applied in oral and maxillofacial surgery (OMFS). Depending on the laser's characteristics, one can select the type of laser most applicable under the given circumstances. With the availability of portable and more cost-effective lasers, outpatient office-based laser treatment is evolving as the therapy of choice for OPLs. The lasers commonly used are classified into visible and non-visible (infrared) wavelengths.[12]

Water Avid Infrared Lasers

The CO_2 laser produces coherent laser energy at the 10,600 nm wavelength in the infrared spectrum and does not have a particular preferred chromophore of absorption. It shows good absorption by water – both intracellular and extracellular. It creates rapid heating of target tissues, causing cells to explode, creating a zone of tissue vaporization, and a surrounding zone of thermal damage, which theoretically seals lymphatics and blood vessels. When used in the focused mode it acts as an excisional instrument ensuring precise surgical margin with minimal char. This also helps in the accurate assessment of surgical margins. Furthermore, it can be used for surface ablation in defocused mode. The CO_2 laser has historically been the workhorse in OMFS laser surgeries. In the past years, the use of the laser has been limited owing to its high cost, bulk, and difficulty in using in poorly accessible areas. However, technological advancements have up to an extent successfully overcome these limitations. The introduction of scanning CO_2 laser may offer potential benefits due to the ability to control precisely the depth of vaporization thereby extending its use to the treatment of large area OPLs.[13]

The RevolixJr (Lisa Laser USA, Pleasanton, CA) is a 15-W thulium-based diode pumped solid-state laser. It produces continuous energy in the infrared spectrum at the 2013 nm wavelength. It has comparable tissue characteristics to the CO_2 laser, due to water being the common chromophore. It has a fiber delivery system which makes it superior and

also allows easier access to restricted areas. It has better hemostatic properties compared to the CO_2 laser, probably due to a larger thermal damage zone, which helps with sealing of vessels. While these characteristics are limiting factors in surgeries on delicate tissues like glottis, the instrument is excellent for use in highly vascular tissues such as the tongue. The thulium laser has mainly been used as an excisional instrument, and its small size allows for easy transportation between the office and the operating room.[14]

Other lasers in this range include Nd:YAG, Holmium:YAG, and Erbium:YAG, which are based on yttrium aluminum garnet crystals doped with either neodymium, holmium or erbium. The Nd:YAG was developed in 1973 and emits light of 1064 nm wavelength. Its penetration power is much deeper than the other lasers described and has a thermal damage area well beyond the depth of normal epithelium. These lasers are not routinely used for treating OPLs.[15]

Hemoglobin Avid Lasers

A more recent development in OMFS has been the introduction of hemoglobin avid lasers. The chromophore for these lasers is hemoglobin, and thus they exert effect specifically upon the vasculature.[16]

The oxygenated and deoxygenated hemoglobin have a relative optical absorption peak between 520 and 550 nm and lower absorption peaks at 750 nm and 940 nm.

The Aura XP and the Varilite are examples for lasers of this type. They are both potassium-titanyl phosphate (KTP) lasers, yielding visible green light at 532 nm. It is produced by passing a Nd: YAG laser beam (1064 nm) through a KTP crystal, thus halving its wavelength to 532 nm.[17] Its usefulness in OPLs lies in its ability to ablate the underlying vasculature feeding the lesion while preserving a biological dressing of overlying mucosa.[18] At higher energy levels, these lasers can also be used in an ablation setting although the KTP causes more charring when compared with water absorbed lasers, and superficial char may need to be removed manually. Both have fiber based energy delivery system, allowing easy access to all areas of the oral cavity.[19]

VARIOUS METHODS OF MANAGEMENT OF OPLS USING LASER

Surgical Resection without Reconstruction

Surgical resection is performed in the office or the operating room depending on the size of the lesion and access.[20] *En bloc* excisions facilitates complete pathologic evaluation and accurate assessment of margins to exclude invasive disease. However, surgical resection without reconstruction of large defects, especially in the floor of the mouth may cause functional impairment.[21] There is significant pain associated with a large deep healing wound. Furthermore, leukoplakia has a tendency to recur even after excision, either within the surgical field or at the edges of resection.[22] Thus, excision may be too radical in many cases of OPLs. Many techniques are present for surgical excision including various lasers. The CO_2 laser causes minimal charring providing clean surgical margins for accurate assessment. However, its hemostatic ability is poorer than hemoglobin avid lasers; hence, electrocautery is routinely employed as an adjunct.[23]

Vaporization

Vaporization of OPLs involves surface application of laser energy for ablation. This technique is found to be suitable for larger, shallower OPLs and is also especially useful in difficult to access areas. It allows treatment of the lesion while ablating superficially. Prior to vaporization representative biopsies have to be taken as there is no surgical specimen to examine for evidence of deep invasion. Also, the surgical bed created after vaporization will have to heal by secondary intention. Both laser excision and vaporization are better known tools than electrocautery treatment in terms of post-operative pain and wound contracture. However, it has potential demerits such as scarring, tethering, and secondary bleeding as it leaves an exposed wound. Areas where resection is not possible such as gingival leukoplakia and other more extensive lesions benefit from laser vaporization. The CO_2 laser is the management option due to its properties like minimal thermal damage to underlying tissue, least char, and thus allowing the most accurate assessment of depth.[23]

CONCLUSION

White and red lesions of the oral cavity remain a diagnostic and management challenge. Use of the laser for management of oral premalignant lesions has got many advantages over other treatment modalities. Through various studies, it can be inferred that surgical management is the gold standard for oral premalignant lesions and laser can be used successfully even for office-based surgical management. Surgical management with in-office lasers has been varied in its techniques and use of both water-avid (CO_2 laser and thulium laser) and hemoglobin-avid (green light 532 nm and 940 nm) lasers. Depending on the location and nature of the lesion, vaporization, vascular ablation, or surgical resection may be an appropriate treatment.

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Review Article

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Surgical Treatment of Chronic Pancreatitis: A Literature Review

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Abstract

Chronic pancreatitis (CP) is a continued inflammatory disorder leading to the irreversible destruction of the pancreas which results in disabling chronic pain and permanent exocrine and endocrine dysfunction. The management of CP is a challenging task for surgeons. New methods are needed for the early diagnosis of CP, and new therapies are needed to determine whether the interventions will delay or prevent the progression of the irreversible damage characterizing end-stage CP. The increasing knowledge about the pathophysiology of CP, introduction of sophisticated diagnostic methods in clinical practice and vast gains in surgical skills have immensely improved the outcome of CP patients. The introduction of new surgical techniques has led to better control of pain and other clinical presentations of CP.

Key words: Pancreatitis, Pathophysiology, and Techniques

INTRODUCTION

The utilization of several advances in molecular and genomic technologies along with the progress in pancreatic imaging techniques has provided remarkable insight into genetic, environmental, immunologic, and pathobiological factors leading to chronic pancreatitis (CP). The heterogeneity of the patient population and symptoms, as well as the poor understanding of the pathophysiology in patients with CP, is the obstacles in the effectiveness of patient treatment. The symptom triad of CP includes exocrine and endocrine pancreatic insufficiency and recurrent episodes of pain, which brings patients to their physicians and causes addiction to analgesics. Profound and intractable pain is the main clinical feature in approximately 90% of patients and has the worst impact on quality of life.[1] Although the conservative management may be successful in some patients, the remission of pancreatic pain is uncommon and not consistently observed.[2] Usually, the initial step of managing CP is non-specific conservative medical therapy. After the optimization of symptoms with analgesics and enzyme supplementation, patients with persistent symptoms are candidates for invasive treatments. The vast progress in surgical and interventional techniques has significantly minimized the morbidities and mortality rates.

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SURGICAL TREATMENT

Treatment of patients suffering from the complications of CP remains a major challenge. Surgical treatment of CP has seen its ups and downs in recent decades. The risks of pancreatic surgery initially were high in the past. The pathophysiology of the disease was, and partially still is poorly understood. An appropriate surgical procedure has therefore proven difficult to devise. The choice of surgical procedure is rarely straightforward, and other factors like disease location, prior treatment, and suspicion of cancer have an impact on surgeon's decision.

The operative procedures to relieve the pain are decompressive, or resectional surgery. These two approaches differ on the basis of pathophysiological theories of the etiology of the pain. Proponents of drainage procedures such as the lateral pancreaticojejunostomy (LPJ), which

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is also known as the modified Puestow procedure or Partington procedure, insists that decompressing the affected ductal system suffices, whereas proponents of resectional procedures such as pancreaticoduodenectomy argue that removing the portion of pancreas with affected neural tissue, especially the pancreatic head, is mandatory because the pancreatic head is a pacemaker in CP.[3] The surgery most often used in the treatment of CP since 1950 was pancreatoduodenectomy, which has proved to be beneficial in controlling the pain, and complications of CP.[4,5] Actually this procedure was used for resection of periampullary malignancies, but it has also been introduced for the surgical management of patients with CP. Even though, the Whipple procedure, is successful in achieving the goal of pain relief and managing the complications, but it is associated with poor long-term results regarding the quality of life,[6,7] while the morbidity rates range between 30% and 50%.[8] Also, the sacrifice of otherwise healthy organs, i.e., the distal stomach, duodenum, and common bile duct, is the major disadvantage of this procedure. Even with the modification of Longmire and Traverso,[9] which contributed significantly to the reduction in morbidity and mortality of pancreatoduodenectomy, glandular function deterioration remained a problem that developed in 50% of the patients.[10,11] In their study, Müller *et al.*[12] described the three major problems faced by patients who underwent pylorus-preserving pancreatoduodenectomy (PPPD) for CP: They found the increased incidence of post-operative transient delayed gastric emptying (30-50% of patients), which often led to slower weight gain; the risk of cholangitis; and resulted in long-term irreversible loss of exocrine and endocrine pancreatic function in more than 45% of patients. Sawyer and Frey[13] emphasized that distal pancreatectomy (DP) as a surgical option in CP should be utilized in patients with diseases restricted to the pancreatic body, tail, or both with pancreatic duct diameter <5 mm. With a mean follow-up of 4 years, they found that adequate pain relief was achieved in 90% of patients with distal disease. On the other hand, good pain relief was recorded, by Rattner *et al.*[14] in only 31% of patients in whom DP was done for distal CP. In two recent studies, spleen preserving DP achieved the pain control in 72-82% of patients with CP.[15,16] As ductal ectasia is observed in 40-60% of patients with painful CP, decompression of the pancreatic ductal system has become one of the main therapeutic principles. This is based on the assumption that ductal ectasia suggests the intraductal hypertension.[17,18]

Coffey[19] and Link[20] first described the concept of opening the main pancreatic duct with bypass of the obstruction. Duval[21] and Zollinger *et al.*[22] were the first to apply this principle in clinical applications, independently. The decompression of the main pancreatic duct was achieved by the resection of the pancreatic tail, and retrograde drainage of the pancreatic duct via end to end, or end to LPJ. However, this procedure was effective in patients with a single dominant obstruction between the pancreatic tail and the ampulla of Vater. However, single dominant strictures, or obstruction is rarely found in patients with alcohol abuse, which is the major cause of CP in the most of the patients in the western hemisphere. But relapses of severe pain are frequently observed, even with patent drainage of the duct system. In 1956, Puestow and Gillesby[23] presented another drainage procedure: In which the decompression of the main pancreatic duct was achieved by a longitudinal side to side pancreaticojejunostomy after resection of the pancreatic tail and splenectomy. In 1960, Partington and Rochelle[24] proposed a modification in which the jejunum is directly anastomosised to the anterior surface of the pancreas. This simplification not only allows the preservation of the spleen but also reduces the amount of pancreatic mobilization that is required, thereby decreasing the operation time and blood loss. They also suggested that the whole length of the ductal from the tail of the pancreas to the pancreatic head should be laid open for anastomosis with jejunum; this extended decompression benefits as the removal of pancreatic duct calculi is greatly facilitated. A review of numerous series with this procedure reports that LPJ relieves the chronic abdominal pain in 65-93% of patients[25-27] Morbidity and mortality rates are low, averaging 20% and 2%, respectively.[25-29] Nealon and Matin30 reported the largest series, in which they reviewed the surgical treatment of 124 patients with CP who had undergone a modified LPJ. They found that 106 of 124 patients, at a mean follow-up of 6.5 years, had completed the resolution of pain as defined by an absence of narcotic use. Successful operation seems to be related to both technique and patient selection. Bradley[25] has emphasized that the ductal decompression of <6 cm is associated with inadequate relief of pain compared with >6 cm of decompression. Furthermore, duct size >7 mm also correlated with success. With advances in minimal access the technical feasibility of laparoscopic LPJ has been finally described by Tantia *et al.*[31] and Kurian and Gagner.[32] Even with these encouraging outcome, long-term follow-up of patients after LPJ reveals 10-35% patients fail to obtain any pain resolution and symptoms recurrent develop in up to 50% of patients.[29,33] The reasons for the greater usage of drainage procedures in CP in comparison to resectional procedures, i.e., partial pancreatoduodenectomy (classical Whipple procedure) or more recently PPPD (Longmire–Traverso procedure) is significantly decreased morbidity and mortality as postulated and at least actually recorded in older series. Pain relief is obtained in 60-80% of cases who have dilated duct, i.e., ductal diameter >7 mm, by doing a traditional drainage procedure, i.e., Partington–Rochelle's longitudinal pancreaticojejunostomy.[34,35] Lower mortality and morbidity rates and the preservation of

pancreatic function are the main advantages of these drainage procedures. However, 20-40% of patients will not be helped from these drainage operation.[18,34,35] In order to improve the long-term outcome in patients with CP and to limit the resection of pancreatic tissue to a minimum, the duodenum-preserving pancreatic head resection (DPPHR) was introduced by Beger *et al.*[36] in the 1970. This procedure is indicated in intractable abdominal pain, small duct CP, and head dominant disease. While it is contraindicated in conditions where pancreatic cancer cannot be excluded.[37] Surgical technique involves subtotal head resection with ventral transection of the pancreatic neck. The reconstruction is with Roux-en-Y loop of jejunum anastomosed to the distal pancreatic remnant, and the rim of pancreatic tissue along the inner surface of the duodenum.[38] The main concern of this technique is to deal with the enlarged pancreatic head, where the disease is usually present, and to spare the duodenum, which has a great role in the regulation of digestion and glucose metabolism. Beger *et al.*[37] presented their 26 years experience with this procedure in 504 patients with CP and pancreatic head inflammatory mass. With a median follow-up of 5.7 years, they concluded that 91.3% of patients got relief from pain following the Beger's procedure, and that the hospital mortality was 0.8%, and the late death rate was 8.9-12.6%, compared to 20.8-35% for the patients without surgery.

In a randomized trial, 20 patients underwent Beger's technique and Whipple's procedure each. It was observed that the patients undergoing Beger's technique had significantly better results with less pain, increased post-operative weight gain, and better glucose tolerance at a 6 months follow-up.[39] In 1987,[40] a modified Beger's technique was innovated by Frey. In this procedure, LPJ was done after subtotal DPPHR. This modified approach avoids more technically difficult aspects which are the division of the pancreatic neck, and the need for two separate pancreatic anastomoses in Beger's technique.[41] The coring in the head of the pancreas allows the debulking of head tissue with opening of the main pancreatic duct as it courses posteriorly toward the duodenum and thus provides more effective drainage.[41] So it is indicated in patients who have "head-predominant" disease with the belief that the pancreatic head, with fibrotic and obstructed ducts, is not properly taken care of with simply decompression of the main pancreatic duct with the Puestow procedure.[41] It is also has advantage for small duct CP, and for patients with mild dilation and stricture of the proximal pancreatic duct.[40,41] The suspicion of malignancy in head of pancreas is a contraindication to Frey's surgery.[41] This modified technique innovated by Frey combines a longitudinal pancreaticojejunostomy as described by Partington and Rochelle with a local excision of the pancreatic head and duodenum preserving excision. In this "extended drainage" procedure (Freys) pancreatic transaction above the portal vein is avoided. A longitudinal pancreaticojejunostomy is attached to the excised cavity of the head, body, and tail of the pancreas, draining almost whole of main duct. This alternative procedure with varying extent of resection, leads to substantial pain relief in 80-90% of patients.[42,43] As reported in the literature and various recent prospective randomized trials, the results of the "extended drainage" operation (Frey) in terms of pain resolution and tackling of pancreatitis - associated complications of adjacent organs match those of the resection procedures, such as the partial pancreatoduodenectomy according to Whipple, the PPPD according to Longmire and Traverso and Beger. The intermediate and long-term achievements in terms of preservation of pancreatic function, and social and occupational rehabilitation were also reported to be comparable after Frey and Beger.[42,43] However, Frey's procedure is technically easier, has significantly lower morbidity. The argument of an increased mortality associated with the resectional procedures such as Whipple[9,44] Longmire, and Traverso[45,46] or Beger[45,46] cannot be used any further in favor of drainage operations, as the mortality of has come down to nearly nil in experienced centers. However, the extended draining procedures are still favored for significantly lower peri- and post-operative morbidity associated with them. Moreover, with the "extended drainage" technique and Beger procedure,[45,46] there is a definitive advantage in terms of development of endocrine and exocrine pancreatic dysfunction as compared to Whipple[9,44] or Longmire-Traverso.[45,46]

CONCLUSIONS

It has been observed that the surgical treatment provides better long-term resolution of pain, a good post-operative quality of life with the preservation of endocrine and exocrine pancreatic function. Surgical procedures are associated with low early and late mortality and morbidity when curtailed as per patient requirement. It is obvious that new studies are needed to judge which procedure is the most beneficial for the management of the particular patients with CP.

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Case Report

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Bilateral Carotid Body Paraganglioma: A Rare Case Report

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Abstract

According to the World Health Organization classification of tumors 2004, paragangliomas are a type of neuroendocrine tumors derived from the embryonic neural crest. The adrenal gland and the extra-adrenal paraganglia of the autonomic nervous system are the most common places for its occurrence. When found in the adrenal gland they are called pheochromocytoma, but in the extra-adrenal paraganglia they are described as paraganglioma. The carotid body paraganglioma is relatively common and has a benign course, but bilateral existence is rare. We present here a case of bilateral carotid body paraganglioma in a 32 years male. Ultrasound of the neck was done, which detected the bilateral mass in carotid bifurcation region. Adrenaline and noradrenaline levels were within normal limits. In two sittings, tumors on both sides of the neck were excised, and histopathological study diagnosed them to be bilateral paraganglioma. Surgical excision is the treatment of choice. One of the possible causes of hypertension in young adults is paraganglioma.

Key words: Bilateral, Carotid body paraganglioma, Neuroendocrine, Surgery

INTRODUCTION

Paraganglioma is the generic term applied to tumors arising along the sympathetic and parasympathetic paraganglia regardless of its location, except arising from adrenal medulla. These are of neuroendocrine origin derived from the embryonic neural crest.[1,2] They are a category of chromaffin cell tumors, secreting catecholamines in 50-60% of cases. The extra-adrenal location accounts for 10-30% of cases.[3]

Carotid body paragangliomas are the important group of extra-adrenal paraganglioma. The first carotid body paraganglioma was reported by Marchand in 1891. They are located at the bifurcation of common carotid artery.[4] They are more frequently seen in people living at high altitude. Men are affected more frequently than women and in the third and fourth decade. Most of them follow a benign clinical course, about 10% of carotid body paragangliomas turn malignant. However, evidence of metastasis is the only definitive criterion to label the tumor as malignant. Metastasis can occur to regional lymph nodes and lungs.[4] Paragangliomas are characterized grossly by the brown color of the cut surface and microscopically by the presence of well-defined nests of uniform cuboidal cells (Zellballen) separated by highly vascularized fibrous septae.[1-4] Individual cells have an abundant granular basophilic cytoplasm. Bizzare nuclei and vascular invasion are sometimes found, but these should not be taken as evidence of malignancy. There are no reliable morphologic criteria to separate benign from malignant, but high mitotic activity and decreased reactivity for neuropeptides suggest malignancy.[4] Characteristic symptoms are headaches, hypertension, palpitations, diaphoresis, and sweating.

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CASE REPORT

A 32-year-old male came with complaints of swelling in both sides of the neck for 3 years. The swellings were rounded, soft to firm, freely mobile, non-tender. He was non-hypertensive. General and systemic examinations were within normal limits.

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Ultrasonography (USG) neck showed masses in bilateral carotid spaces. Magnetic image resonance (MRI) neck revealed bilateral homogenous masses in carotid spaces at the carotid bifurcation, right 4 cm × 3 cm and left sided 2.5 cm × 2 cm. Magnetic resonance angiography showed splaying of internal and external carotid arteries at bifurcation on both sides. Plasma epinephrine and norepinephrine were within normal limits. His X-ray chest, two-dimensional echocardiogram, hemogram, electrolytes, liver and kidney function tests were within normal limits, and he was medically fit for surgery.

Under general anesthesia, bilateral tumor masses were excised completely in two sittings along with surrounding lymph nodes. The excised masses were sent for histopathology which revealed it to be bilateral paraganglioma and bilateral lymph nodes showed reactive hyperplasia and were free from metastasis.

Post-operative USG, MRI neck and color Doppler did not reveal residual tumor.

Morphology

Received two specimen in a space of 15 days. On gross, right-sided mass was single rounded 4 cm × 2 cm × 1 cm grayish firm mass, cut surface brownish firm. Also received a single 1 cm × 1 cm grayish soft tissue, cut surface grayish. Also received another specimen after 15 days with two oval 2 cm × 1.5 cm × 1 cm grayish firm mass, cut surface brownish firm. Also received a single 1 cm × 1 cm grayish soft tissue, cut surface grayish. No necrosis or haemorrhages seen (Figure 1).

Microscopic Features

Sections from larger masses of both specimens showed tumor tissue arranged in small clusters and cords separated by fibrovascular septae (Zellballen pattern) consisting of the round to oval cells with rounded nuclei with granular cytoplasm. Infrequent mitoses were observed. No necrosis or hemorrhages were seen. The capsule was not infiltrated by tumor cells (Figure 2).

Sections from smaller nodules in both specimens revealed lymph node tissue showed hyperplastic lymphoid follicles with sinuses filled with histiocytes. No metastasis was seen.

So, the diagnosis of carotid body paraganglioma was offered.

The blocks were sent for an opinion from higher center with immunohistochemistry (IHC). The IHC results were: Chromogranin - Strongly positive in tumor cells, S-100 proteins - Positive in sustentacular cells, KI 67 3-5% positive and pan cytokeratin - Negative. Synaptophysin - strongly positive in tumor cells. That confirmed our diagnosis of paraganglioma (Figure 3).

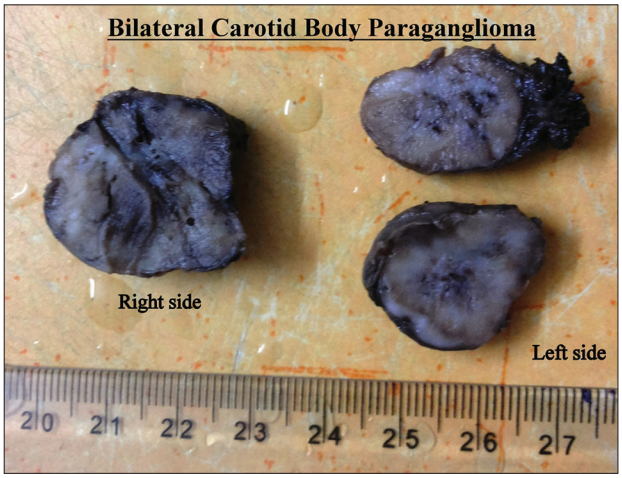

Figure 1: Gross appearance of bilateral carotid body masses

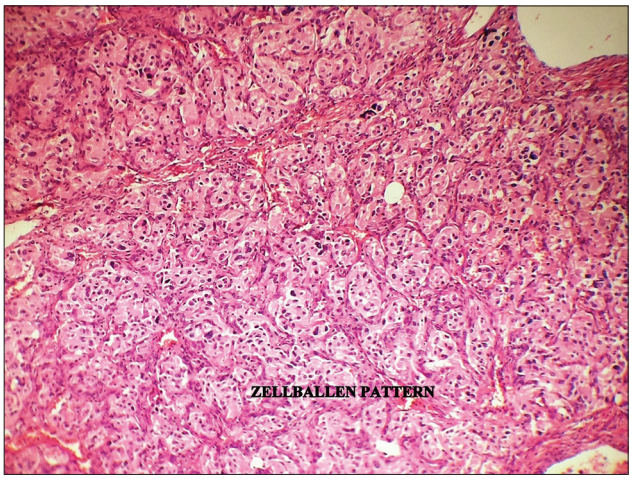

Figure 2: Typical "Zellballen pattern" of tumor cells arranged in groups separated by fibrous septae (H and E, ×40, ×10)

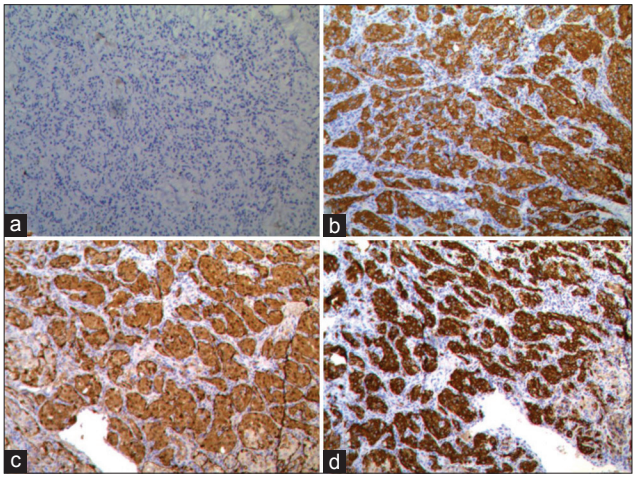

Figure 3: Immunohistochemical stains used: (a) Ki 67 positivity, (b) synaptophysin positivity in tumor cells, (c) S-100 proteins positive in sustentacular cells, (d) chromogranin positivity in tumor cells

DISCUSSION

Carotid body paragangliomas often manifest as slow-growing, non-tender masses in the neck, located anterior to the sternocleidomastoid muscle at the level of the hyoid bone. They are movable in the horizontal plane, but their mobility is limited in the vertical plane (Fontaine sign). Occasionally, a carotid pulse, bruit or thrill may be associated with the mass.[1,4] Symptoms such as fluctuating hypertension, blushing, and palpitations suggest the tumor may be producing catecholamines. Bilateral involvement is uncommon but occurs more frequent in familial cases. Paragangliomas arising from parasympathetic paraganglions are non-secretant. Histology and IHC remain the gold standard for making the definitive diagnosis. Approximately 10% of them are malignant, nevertheless, this cannot be determined on a biochemical or histological basis. It is the presence of local invasion on microscopic examination and presence of metastasis confirms malignancy.[4] Plasma free epinephrine and norepinephrine or urine epinephrine are the first tests to make the diagnosis of the disease.[1,2] Imaging studies such as computed tomography-scan and MRI are essentials before surgery for localization, size and evidence of metastasis. The treatment for paraganglioma is total resection when possible.

CONCLUSION

Carotid body paragangliomas are uncommon lesions mostly in the head and neck region; Bilateral lesions are rarely found or diagnosed. Hence, one should be well versed in its clinical aspects in order for early diagnosis and treatment.

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Case Report

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Incidental Finding of Cysticercosis of Breast: A Rare Presentation

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Abstract

Cysticercosis in human is an infection caused by the larvae of *Taenia solium*. They can affect any part of the body, the most common sites being the brain, cerebrospinal fluid muscle, and the subcutaneous tissues or eye. In this report, we are presenting a case of 32-year-old woman who came with complaints of a painless, mobile lump in the right breast. A clinical diagnosis was a fibroadenoma, and she was advised for ultrasonography, which revealed the presence of cysticercosis larva. Fine-needle aspiration cytology was done, which was reported as foreign body giant cell reaction. Enzyme-linked immunosorbent assay for the antibody was also done, which was positive. Although the diagnosis of cysticercosis in the breast is atypical and rare, and it depends mainly on the histopathological examination. The patient was advised albendazole and glucocorticoid for 28 days followed by excision, to see the effect of the drug. Cysticercosis of the breast it is rare, in spite of this it should be considered as a differential diagnosis for a lump in the breast especially in the areas of a greater prevalence.

Key words: Breast, Cysticercosis, Fibroadenoma, *Taenia solium*

INTRODUCTION

Human cysticercosis, a parasitic infection caused by cysticercus cellulosae, the larval form of *Taenia solium*. It is present world-wide but is the most prevalent in Mexico, Africa, South-East Asia, Eastern Europe, and South America.[1] Cysticercosis in human is a parasitic infestation, which is caused by the larvae *T. solium*,[2] a pork tapeworm. In the developing countries, it is a major public health problem, where open-air defecation and food contamination are unchecked. The common sites of occurrence of cysticercosis are the brain, cerebrospinal fluid, skeletal muscle, the subcutaneous tissues, and the eye; in the decreasing order of frequency. The breast is an uncommon site for cysticercosis, with only a few cases having been reported in the literature.[3] The patients with cysticercosis is commonly present with a lump in the breast.

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CASE REPORT

A 32-year-old married female presented to Gynecological Oncology outpatient department with a painless lump in the right breast, which was present from a period of 6 to 7 month. On examination, a freely mobile lump which measured 2 cm × 3 cm was found in the right lower outer quadrant of the breast, which was non-tender and firm in consistency having a smooth surface. Her ultrasonography (USG) revealed oval cystic lesion of size 30 mm × 13 mm with central calcified nidus. Enzyme-linked immunosorbent assay (ELISA) for the antibody of cysticercosis was positive. Fine-needle aspiration cytology (FNAC) was reported as cells showing mixed inflammatory cell infiltrate and foreign body giant cell reaction. She was advised albendazol 400 mg and wysolone 5 mg daily for 28 days with tapering dose, following which lesion was observed after 6 weeks and USG shown in Figures 1 and 2 was repeated, after which the size was unnoticeable. The excision of the lump was now done, and sample sent for histopathological examination.

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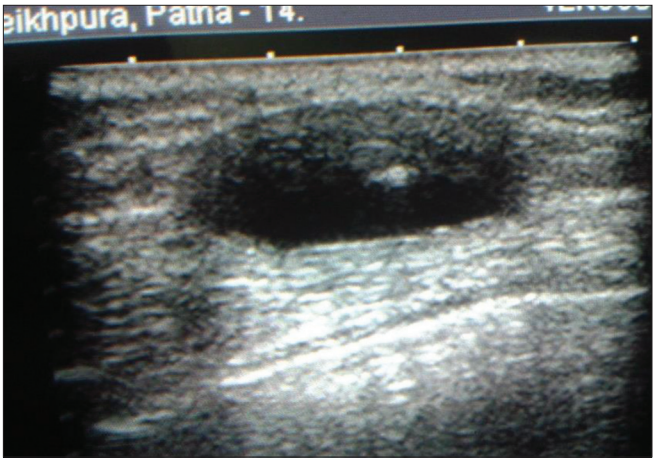

Figure 1: Thin-walled cystic lesion with posterior acoustic enhancement and central hyperechoic foci noted within it (Before treatment)

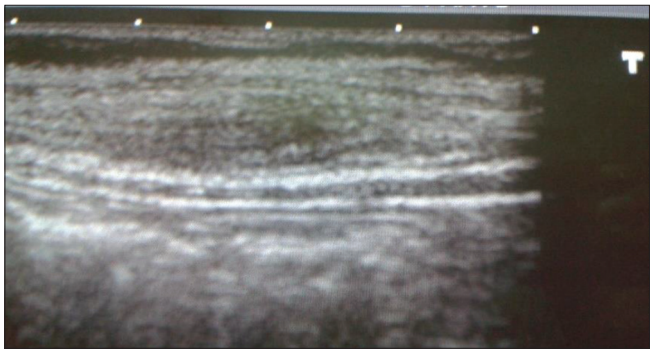

Figure 2: Thin-walled cystic lesion with central hyperechoic foci noted in previous image disappears after treatment

Pathological Finding

On gross appearance, the lump consisted of a gray-white, cystic, and nodule of size 2.5 cm × 2.5 cm. The external surface was smooth and glistening. The cut section of lump showed a cyst with clear serous fluid, and a white mural nodule seen in the cyst wall. The nodule measured 2 mm × 1 mm.

Microscopic sections showed a cyst which was composed of three layers, the outer cuticular layer, the middle cellular layer, and the inner fibrillary layer forming a racemose pattern. After the histological diagnosis of cysticercosis, an extensive search was made, to exclude the infestation at the other sites in the body. The physical and the radiological examinations of the whole body were normal. The stool examination did not show any eggs or proglottids.

DISCUSSION

Cysticercosis is caused by the larval stage of tapeworm i.e., *T. solium*. It continues to be a major public health problem in the developing countries, where open-air defecation and a lack of hygiene are uncontrolled. Human cysticercosis, a potentially deadly infestation, is the consequence of the ingestion of the eggs of *T. solium*, which is present in contaminated food, water, unwashed hands, and by means of autoinoculation which results from reverse peristalsis. The common sites of cysticercosis are skeletal muscle, subcutaneous tissue, breast, brain, and eye in the decreasing order of frequency.[4] The breast is an unusual site for the cysticercosis to form and only a few such cases have been reported in the literature.[5] Amatya and Kimula from Nepal reported out of 23,402 biopsy, 62 cases of histologically diagnosed cysticercosis, five of which were found in the breast substance.[6] In this case, an initial diagnosis of fibroadenoma of the breast was made, due to its typical feature of a painless, firm and freely mobile mass.[5,6] Hence, it is clear that at the unusual sites may be difficult to diagnose it clinically. It can be diagnosed by various investigations such as USG, X-ray, computed tomography scan, and ELISA test, but confirmation is done only by the histological demonstration of the parasite in surgically removed tissues. Feature supportive of its diagnosis on imaging: By USG movement of larva, calcific nidus can be seen, by X-ray and computerized tomography visualization of the calcifying cysticerci.[7] FNAC also plays an important role in diagnosing cysticercosis, but it is limited due to the varying cytomorphological features of cysticercosis. The host tissue response is extremely variable, and it ranges from an insignificant response to the markedly cellular response, which consists of epithelioid cell granulomas and histiocytes. In India, a review study of 8364 breast aspirates over 15 years (1978-1992) in All India Institute of Medical Sciences, New Delhi, demonstrated only eight cases of cysticercosis in a study done by Sahai *et al.*[8] The presence of palisading histiocytes and eosinophils was found consistently in the patients with a cysticercosis breast. The hooklets and the scolex were occasionally seen. In the present case, on FNAC we found foreign body giant cell reaction which is informative. Serological tests such as the indirect hemagglutination test, indirect fluorescent antibody test, and ELISA can be used to diagnose cysticercosis in the suspected cases, but these are limited due to low sensitivity and specificity of the test. This case report emphasizes the fact that cysticercosis of the breast should be considered as a differential diagnosis for a mass in the breast, especially in the areas of greater prevalence and it may mimic benign, as well as malignant presentation of breast. In all inflammatory/cystic/inflammatory cystic lesions, the possibility of cysticercosis should be kept in mind.

CONCLUSION

Cysticercosis of breast emphasizes it should be considered as a differential diagnosis of lump of the breast, especially

in the area of great prevalence of this parasitic disease; although the fact that the breast is the unusual site for cysticercosis.

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Case Report

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Minimally Invasive Percutaneous Plate Osteosynthesis Technique for Simple Anterior Acetabular Fractures

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Abstract

High energy trauma has become so common, so are pelvi-acetabular fractures. Acetabular fractures are at time difficult fractures to treat because of their complex surgical approaches and the technically demanding fixation techniques to achieve the good anatomical reduction. To treat such challenging injuries they have long learning curve. However, all acetabular fractures are not that much complex, a few can be managed with a reasonably simple procedure without contemplating complex surgical exposures and fixation methods. This article we present "minimally invasive percutaneous plate osteosynthesis surgical technique," which is simple yet safe and require to be of use in simple fractures in a simple way, acts as an addition to the standard surgical care. It reduces the surgical time and also with reduction of intraoperative complications, for the safe management of a specific group of anterior column fractures.

Key words: Fractures, Surgical care, Symphysis

INTRODUCTION

The anatomic reduction and stable fixation remains the rationale for the surgical exposure and fixation of associated acetabular fractures,[1] and is not different for non-commuted displaced acetabular fracture patterns. However, the surgical approaches, the ability to achieve an anatomic reduction and the application of rigid internal fixation, the techniques are more complex. Various approaches have been advocated for different fracture patterns to achieve this goal. Commonly used are ilioinguinal approach for anterior and Kocher–Langenbeck approach for posterior exposures.[2]

Background

The use of an extensive surgical exposure to visualize and reduce these fractures has been routinely recommended. The extensile exposures especially anterior are associated with increased morbidity with respect to operative time, blood loss, infection, nerve injury, muscle weakness, and heterotopic ossification.

To minimize these complications a minimally invasive percutaneous plate osteosynthesis (MIPPO) surgical exposure utilizing indirect reduction techniques are utilized for the treatment of certain anterior acetabular fractures.[3]

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Procedure

The position and preparation are carried out in a standard procedure. The supine position and a bump under the same side buttock are kept. The bony landmarks are marked and the two small 1.5-2 inch incisions are planned along the standard incision line. First, one starting from the symphysis to pubis is given and it is carefully deepened. Identifying the lateral boarder of rectus, palpating the pubis in deeper plane gradually reach the pubis is not damaging any vital structures. Once over the pubis a subperiosteal dissection is carried out with a long curved 1 cm osteotome, abutting to the bone, gradually precede toward laterally and slight posteriorly. Once reach the midway or up to fracture site, the other side exposure is started with a one

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more 1.5-2 inch incision over the standard incision line at the iliac crest. After reaching to the iliac fossa, dissection continues subperiosteally make a tunnel with one more long curved osteotome along with pelvic brim to reach the opposite osteotome in the other side tunnel. Reduction of fracture is carried out by indirect reduction techniques using procedures, such as traction, rotations of hip, compression/distraction of pelvis according to fracture pattern. Once reduction is achieved, checked under image intensifier, a precontoured recon plate is inserted into the subperiosteal tunnel. Fracture is fixed on either side with 2 or 3 screws either side taking standard precautions. Wounds closed as usual (Figures 1-4).

DISCUSSION

Among the commonly used surgical exposures, a posterior approach is a little simple and having less complications whereas anterior approach is more difficult, elaborative, and also time consuming, needs long learning curve.[4] The anterior approach's incision and exposure transversely crosses the important vital structures, making it technically more challenging.[5] Moreover, its voyage in three different windows makes the exposure somewhat limited, leaving behind some area devoid of direct vision. Like exposure the fixation for acetabulum is cumbersome and risky at times.[3] The MIPPO technique described here is suitable for a specific set of fractures where we can get away with proper reduction and fixation without extensive exposure of tissue. The advantage is decreased morbidity with respect to operative exposure and time, decreased blood loss, easy to perform and more importantly it is extensile, and can be converted to standard exposure[6] any time, if it is not contented with reduction or fixation.

CONCLUSION

The MIPPO technique is a useful procedure in a specific set of patients with anterior acetabular fracture. Though it has

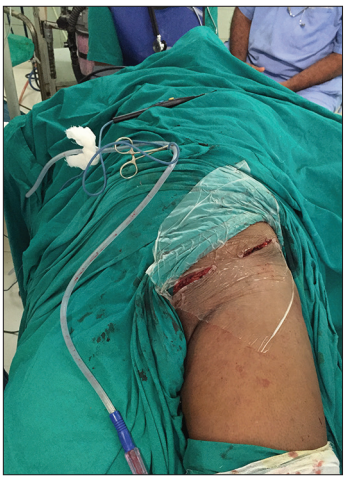

Figure 1: Clinical photo of incisions

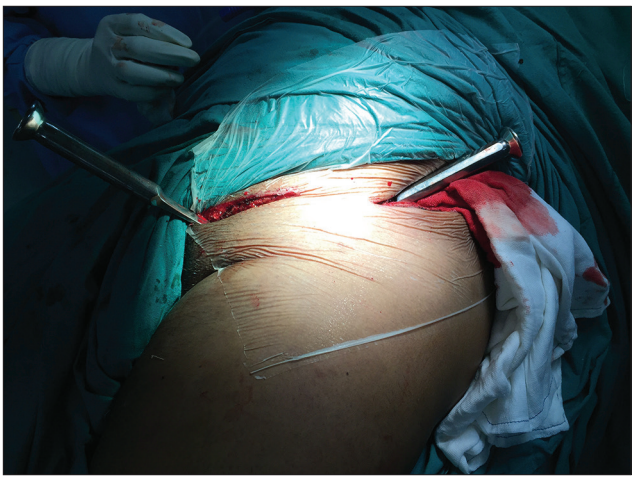

Figure 3: Clinical photo of making subperiosteal tunnel

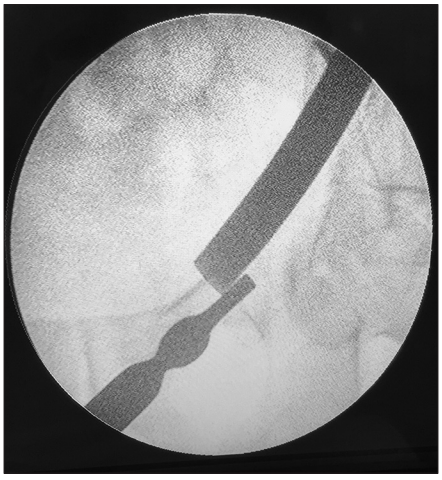

Figure 2: C-arm image of making subperiosteal tunnel

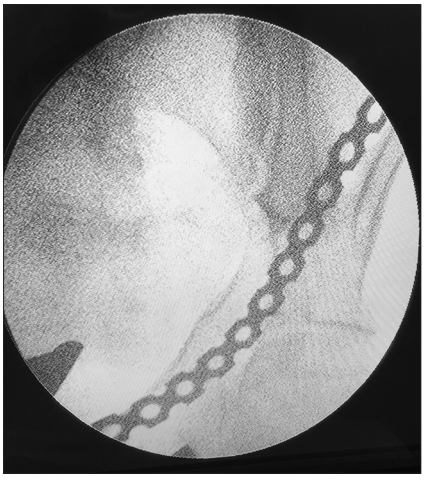

Figure 4: C-arm image of insertion of prebent plate

the disadvantage that it cannot be used in all cases, but has a definite advantage of less complications and extensibility. Careful planning and execution, readiness to convert to a standard approach are the key issues to success.

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Case Report

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Accidental Migration of Epidural Catheter into Subarachnoid Space: A Case Report

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Abstract

Epidural analgesia forms the mainstay of pain relief in abdominal surgeries. Epidural administration of appropriate local anesthetic is helpful in attaining rapid onset of intraoperative surgical anesthesia and post-operative pain relief. We report a case of accidental migration of the epidural catheter into the subarachnoid space. A female aged 42 years with American Society of Anaesthetists Class I was scheduled for total abdominal hysterectomy. The patient was explained about the anesthetic technique and informed high-risk consent was obtained. The patient was taken up in the OT, and baseline pulse and blood pressure were noted as 78/min and 110/80 mmHg respectively. A loading dose of epidural bupivacaine 0.5% + clonidine 50 mcg in 8 ml was given after negative aspiration. After 15 min, bupivacaine 0.5% + clonidine 25 mcg in 4 ml was given after negative aspiration. Five minutes later patient developed convulsions. The patient was aphonic. She went suddenly into respiratory arrest; immediately rapid sequence intubation was done and kept on a mechanical ventilator. She recovered after 1 h.

Key words: Bupivacaine, Epidural analgesia, Epidural catheter migration, Subarachnoid space

INTRODUCTION

Subdural space, a potential space between the arachnoid mater and dura mater, usually remains closed.[1] The incidence of the subdural blockade during neuroaxial block is reported to be approximately of 0.82%. Several recent studies of clinical findings analyzed with radiographic evaluation indicate that the incidence may be much higher than reported, ranging from 1% to 13%.[2,3] The diagnosis of subdural blocks is difficult to make based on the clinical picture because of its varied presentation. Recently, algorithms have been developed which (Lubenow *et al.*'s diagnostic paradigm, Hoffman and Ferrante's four-step algorithm, and an electrical stimulation of the epidural catheter application) provide strong strategies to facilitate diagnosis.[2,4-6]

We often experience the migration of an epidural catheter into an undesirable space. Migration of an epidural catheter into the subarachnoid space is a potentially lethal complication. Although almost all migrations of epidural catheters have been reported to occur at the insertion of the catheter, we experienced a case of catheter migration into the subarachnoid space. The large doses of a local anesthetic agent that is given for epidural injection can block large area of the spinal cord leading to cardio-respiratory arrest. Much needs to be done to support both the systems for a better outcome.

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CASE REPORT

A 42-year-old, 35 kg female diagnosed with abnormal uterine bleeding was posted for total abdominal hysterectomy. On general examination, she was moderately built. She had no history of any chronic illness, seizures, syncopal attacks. She was graded as American Society of Anaesthetists Grade I laboratory results and electrocardiogram were unremarkable except for hemoglobin value of 10 g/dl.

After thoroughly educating the patient regarding the anesthesia associated risks epidural analgesia was planned. Initially patient was loaded with ringer lactate of 5 ml/kg body weight. Under strict aseptic precautions right lateral L_2-L_3, 18 G tuohy, the epidural space was identified by loss-

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of-resistance technique and confirmed with hanging drop method, the epidural catheter was placed up to mark 10. Before giving epidural loading dose her parameters were blood pressure (BP) - 110/80 mmHg and pulse rate (PR) was - 78/min; it was decided to give a total dose of 16 ml bupivacaine along with 75 mcg clonidine. After negative aspiration, 8 ml of the drug was given. After 10 min the findings were BP - 100/70 mmHg; PR - 76/min; the level of sensory loss was - T_8. A further dose of 4 ml of the solution was given; following which patient became aphonic and developed an episode of convulsion. BP felt to 53/21 mmHg and PR - 56/min; SPO_2 - 100%. Injection phenylepherine 40 mcg/IV; injection atropine 0.6 mg/IV was given. She developed apnea and immediately rapid sequence intubation was done and ventilated with 100% oxygen. Epidural catheter aspiration was done and proved positive for cerebrospinal fluid. The patient regained consciousness after 1 h and the parameters were BP - 160/100 mmHg; PR - 80/min; SPO_2 - 100%. The patient regained full consciousness and obeying commands. The patient was extubated and the parameters were BP - 150/100 mmHg, PR - 90/min, SpO_2 - 100% with room air, level - T_4. The patient was shifted to the post-operative ward after removing the epidural catheter.

DISCUSSION

Migration of epidural catheter into subarachnoid space invites serious complications along with the failure of the purpose. Reynolds and Speedy; Abouleish and Goldstein have reported catheter migration into the subarachnoid space.[7,8] Migration to intravascular space was reported by Ravindran *et al*. Subarachnoid injection of large amount of the local anesthetic leads to extensive block, including the cranial nerves and the respiratory muscle. Injection to subarachnoid space should be suspected when there is a negative aspiration but an extensive block occurs in 15-20 min. A cardio-respiratory support is necessary till the effect of local anesthetic wears off.[9]

Migration of catheters was studied in 153 women undergoing analgesia in labor. Inward or outward migration occurred in 36% of patients.[10]

Prevention of migration was done by subcutaneous tunneling of the epidural catheter which showed a success rate of 97% as compared to 79% in the control group;[11] Clark *et al*. studied the efficacy of Lockit Clamp and found that there was no migration in 88% as compared to 28% in standard group.[12]

Song *et al*., reported migration in two cases and concluded that although subdural catheter placement is a relatively rare occurrence, it is imperative for anesthesiologists to recognize the presentation and treat accordingly.[13]

In our case, epidural catheter migration occurred while administering the first dose of the local anesthetic agent.

CONCLUSION

Epidural injection resulted in high subarachnoid block probably because of migration of the epidural catheter into the subarachnoid space, which was confirmed by aspiration of cerebrospinal fluid.

ACKNOWLEDGMENT

We acknowledge all the members of the department, including the technicians who have lent their helping hand in the hour of crisis.

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Case Report

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All that Glitters is not Gold: A Misdiagnosed Case of Retinopathy

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Abstract

Central retinal vein occlusion (CRVO) and diabetic retinopathy are the commonest causes of retinopathies, among several others. The fundus findings alone will sometimes lead to a misdiagnosis. The attending doctor who sees hemorrhages, exudates, venous changes, neovascularization, and edema should not be in a hurry to jump to the diagnosis. All that glitters is not gold. As a clinician - It is very important to take a good history, examine the patient systemically and investigate as necessary, before arriving at a diagnosis, and then managing the patient appropriately. Here, a case is described, where a female in the seventh decade of life, who was visually handicapped at presentation, had undergone cataract extraction with intraocular lenses implanted. She denied having any medical problems in the past. Post-operative fundus evaluation showed features that were diagnosed to be diabetic retinopathy bilaterally. She underwent complete pan retinal photocoagulation in the right eye for neovascularization and macula edema. It was only a few visits later that the attending doctor repeated asking a detailed history and examination and ordered a few investigations and reversed the diagnosis to CRVO secondary to hypercholesterolemia and hypertension.

Key words: Diabetes, Diagnosis, Retinopathy

INTRODUCTION

Retinopathy is a presentation seen in a number of conditions and is more often than not, seen in diabetics. However, retinopathy is fairly common in adults without diabetes.[1-4] The fundus shows dot haemorrhages (DH), blot haemorrhages (BH) and flame hemorrhages, hard exudates (HE), cotton wool spots, neovascularization at the disc or elsewhere, venous tortuosity and dilatation. Fundus examination alone will not be able to diagnose the condition that the patient has, and the treating physician will have to be armed with adequate knowledge and a high index of suspicion in order to arrive at the correct diagnosis and management.

In central retinal vein occlusion (CRVO), thrombosis of the central retinal vein sets a cascade of events which will impede capillary perfusion and cause ischemia. In diabetic retinopathy - The retinal capillaries are affected. In both diabetic retinopathy and CRVO - elevated vitreous levels of vascular endothelial growth factor (VEGF) increases vascular permeability causing macula edema, capillary damage and retinal ischemia. VEGF promotes angiogenesis causing break down in the blood-retinal barrier, which stimulates vascular permeability in the ischemic retina. Several other factors such as insulin-like growth factor, hemodynamic changes, oxidative stress, and activation of the renin-angiotensin-aldosterone system have also been postulated in the pathogenesis of diabetic retinopathy.

Retinal vein occlusion (RVO) and diabetic retinopathy are both major causes of vision loss. Risk factors for retinopathy include systemic conditions like hypertension, arteriosclerosis, diabetes mellitus, hyperlipidemia, vascular cerebral stroke, blood hyperviscosity, and thrombophilia. A strong risk factor for RVO is the metabolic syndrome (hypertension, diabetes mellitus, and hyperlipidemia).[5]

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CASE REPORT

FD, a 76-year-old Malay woman, first presented to the Eye Clinic of Hospital Melaka on 23rd March 2012 with a complain of bilateral progressive blurring of vision since

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the past 2 years. She had been relatively well in the past with no ocular or systemic disorders. Her visual acuities were hand movement bilaterally. There was a brunescent cataract in the right eye and a white mature cataract in the left eye. The intraocular pressures and the rest of the anterior segments were unremarkable. The fundi could not be assessed due to the density of cataracts. B-scan ultrasonography showed flat retinas and clear vitreous cavities bilaterally.

Left phacoemulsification converted to extracapsular cataract extraction (ECCE) with sponge vitrectomy and sulcus posterior chamber intraocular lens (PCIOL) was done on April 9th, 2012. Intraoperatively, the surgery was complicated by zonular dehiscence and vitreous loss. Therefore, the phaco was converted to ECCE. Right ECCE with anterior vitrectomy and implantation of anterior chamber intraocular lens (ACIOL) was done on May 31st, 2012. Intraoperatively, there was a complication of posterior capsule rupture and vitreous loss.

The pupils were dilated, and the fundi were assessed on July 19th, 2012. The pupils were not dilated earlier as one eye had an ACIOL and the other had a PCIOL placed in the sulcus. Both eyes showed extensive DH and BH and HE. The right eye showed neovascularization between the superior and inferior temporal arcades as well as edema of the macula (Figure 1). No neovascularization was seen in the left eye (Figure 2). A diagnosis of right proliferative diabetic retinopathy (PDR) and left moderate non-PDR (NPDR) was made. The patient refused fundus fluorescein angiogram. Complete panretinal photocoagulation (PRP) was given for the right eye.

Almost 6 months later (on December 5th, 2012), the attending ophthalmologist decided to do a systemic review. There was no pallor, skin changes or peripheral neuropathy seen in poorly controlled diabetics. On further questioning, the patient denied ever having had diabetes mellitus. However, the patient admitted to having had high blood pressure 7 years earlier but had defaulted treatment. The blood pressure on that visit was controlled at 120/80 mmHg, but it was 170/110 mmHg on the next visit. The serum cholesterol was elevated (6.59) with an increase in low-density lipoprotein (4.26). The blood sugars were within normal limits each time; it was tested. Carotid Doppler ultrasound was normal bilaterally.

The diagnosis of the patient was reversed to bilateral CRVO secondary to uncontrolled hypertension and hyperlipidemia. The patient was referred to the physician for appropriate management of the medical conditions.

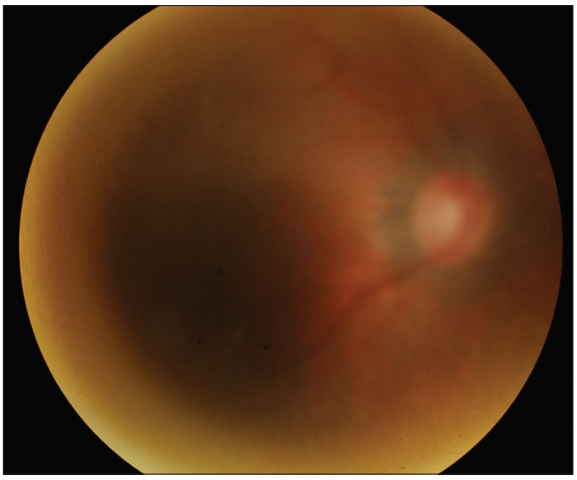

Figure 1: Right fundus

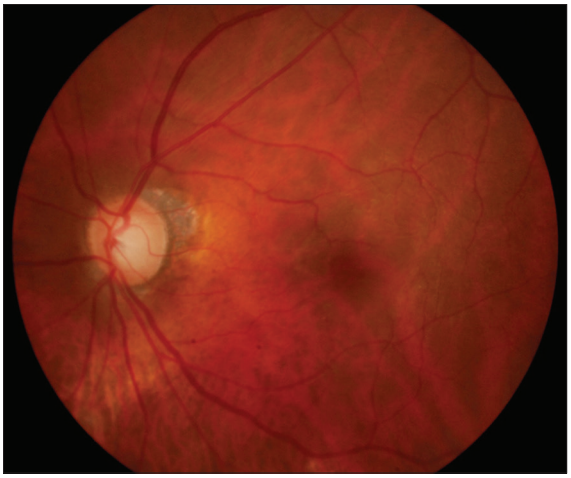

Figure 2: Left fundus photo

DISCUSSION

Fundus examination alone will not be able to diagnose the condition that the patient has, and the treating physician will have to be armed with adequate knowledge and a high index of suspicion in order to arrive at the correct diagnosis and management.

Ophthalmologically, both types of retinopathies are treated in the same manner.

Laser remains the therapy of choice when neovascularization secondary to CRVO is detected. Adjunctive anti-VEGF could be considered in managing neovascularization secondary to RVO in cases of vitreous hemorrhage.[6] PDR is also treated with laser and anti-VEGF. According to the CRVO study Macular grid photocoagulation was effective in reducing angiographic evidence of macular edema, but it did not improve visual acuity in eyes with reduced vision due to macular edema from CRVO. At present, the results of this study do not support a recommendation for macular

grid photocoagulation for macular edema.[7] Some anti-VEGF therapies, including bevacizumab, ranibizumab, and aflibercept have been shown to be effective in short-term studies for the treatment of patients with macular edema and CRVO.[8] CRVO study found that prophylactic PRP did not prevent the development of iris neovascularization and recommended to wait for the development of early iris neovascularization and then apply PRP.[9]

Royle *et al.*[10] recommend a trial of PRP for severe NPDR and early PDR compared with deferring PRP till the high risk-PDR stage. ETDRS Report No. 9 recommends that when retinopathy is more severe, scatter photocoagulation should be considered and usually should not be delayed if the eye has reached the high-risk proliferative stage.[11]

Using these guidelines, had we diagnosed the right eye of the patient to have CRVO and not low risk PDR with macula edema, we would have observed and not done the laser.

However, medically, the systemic disorders are treated based on the etiology of the disease. Hence, the disease must be diagnosed correctly in order to treat the underlying cause and to prevent further complications from occurring.

A diabetic may have symptoms of polyuria and polydypsia which are not seen in other conditions causing retinopathy. A simple dextrostix test done will show whether the patient has diabetes. A more sophisticated test would be to do hemoglobin A1c. Diabetics are treated with either oral hypoglycemic agents or insulin. The aim of treatment apart from arresting the disease would be to prevent complications such as nephropathy, dermatopathy and neuropathy apart from ocular complications such as neovascular glaucoma. Adequate blood sugar control and lifestyle modification including a low sugar diet will achieve this.

A patient who has high cholesterol will usually be asymptomatic. The treating doctor whether a family physician or general practitioner or ophthalmologist - Should do a blood lipid profile when a patient presents with retinopathy. Hypercholesterolemia will need life style modification of low fat diet in addition to statins specific in lowering cholesterol. The aim of treatment is to prevent complications such as cerebrovascular accidents and myocardial infarction apart from neovascular glaucoma.

Hypertension patients can be asymptomatic – As seen in our patient or can present with headaches and dizziness. Again, the treating doctor must be inquisitive enough to find out the cause of hemorrhages in the fundus and use the sphygmomanometer which can be done by the nurse. Again apart from lifestyle modification - The specific treatment to prevent complications is by using anti-hypertensive drugs.

CONCLUSION

All that glitters is not gold. The presence of hemorrhages in the fundus can be due to a wide variety of diseases, apart from diabetic retinopathy. The attending doctor should take a history, do a systemic examination and order relevant blood/radiological investigations to diagnose the condition correctly and treat it to prevent further complications from occurring. Prevention is better than cure.

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We thank the patient for consenting for photography and publication. We thank the photographer for the beautiful fundus photo.

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Case Report

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Jejunal Diverticular Perforation with Intra-abdominal Abscess: A Case Report

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Abstract

Jejunal diverticular perforation is rare and few cases have been reported in the literature. Jejunal diverticula have a prevalence of approximately 1% in the general population. The incidence reported of 0.2-1.3% in from autopsy studies and 0.5-2.3% from contrast studies. Perforation of jejunal diverticulum and abscess formation is very rare. Clinically, this diagnosis is challenging task and confused with other causes of an acute abdomen. It is usually asymptomatic, but may present as diffuse vague pain in the abdomen or acute abdominal pain. However, they may present with non-specific symptoms leading to delay in diagnosis causing catastrophic consequences. Here, we present a rare case of jejunal diverticular perforation with intra-abdominal abscess.

Key words: Abdominal abscess, Acute abdomen, Jejunal diverticulosis, Jejunal perforation

INTRODUCTION

Jejunal diverticular perforation is a rare entity; Jejunal diverticula have a prevalence of approximately 1% in the general population. Incidence reported of 0.2-1.3% in from autopsy studies and 0.5-2.3% from contrast studies.[1-3] Jejunal diverticula are pseudo diverticula which were first described by Somerling in 1794 and by Sir Astley Cooper in 1807. Most of the cases of jejunal diverticulosis remain asymptomatic, only 10-30% of patients complications are reported.[4] Small bowel diverticula occur most frequent in the duodenum, duodenal diverticulum (45%), followed by Meckel's diverticulum (23%).[5] In one retrospective review of 208 patients with symptomatic small bowel diverticulosis, diverticula were located in the duodenum in 79%, in the jejunum or ileum in 18%, and in all three segments in 3%.[6] Jejunal diverticula are the least common type of small bowel diverticula.[7] Jejunal diverticula is slightly more common in men than women, 58% compared to 42% in a reported series.[8] Jejunal diverticula are usually multiple and predominantly localized to the proximal jejunum (75%), followed by the distal jejunum (20%). Jejunal diverticula may be composted of mucosa and submucosa only, or of all layers of jejuna wall. They are frequently associated with disorders of intestinal mobility, such as progressive systemic sclerosis and neuropathies, and myopathies. Familial aggravation have been described in literature and some cases may be heritable.[9,10] Jejunal diverticula may present as chronic abdominal pain, malabsorption, hemorrhage, diverticulitis, obstruction, diverticular perforation, and rarely abscess formation.[11] Jejunal perforation with intra-abdominal abscess formation of jejunal diverticula is a rare complication. Peritonitis caused by perforated jejunal diverticula can be localized and self-limiting, because most of the diverticula are at the mesenteric border of the bowel and readily allow the small bowel mesentery to seal them off. The treatment of choice for perforated jejunal diverticulum with peritonitis is segmental intestinal resection with primary anastomosis including non-inflamed diverticula.[12]

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CASE REPORT

A 40 years male patient presented with a history of pain abdomen since 2 days admitted in our hospital. The clinically patient looks ill and on examination guarding and rigidity of abdomen is present. The patient is afebrile, pulse rate: 96/min, blood pressure: 100/60 mm of Hg and respiratory rate: 32/min. X-ray erect abdomen showed

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multiple air fluid levels. X-ray chest showing air under diaphragm. Ultrasound abdomen shows intra-abdominal abscess in-between jejunum and transverse colon. CT abdomen shows jejunal diverticulitis in association with abdominal abscess (Figure 1).

Initial management consisted of intravenous fluid administration, broad spectrum antibiotics, blood transfusion was done.

Laparotomy revealed that purulent fluid in-between jejunum and transverse colon with jejunal diveriticula in mesenteric boarder, each diveriticula measuring about 90-140 mm, about 30 cm away from duodenal-jejunal flexure and length of involved jejunal bowel segment measuring about 10 cm was excised and end to end anastomosis performed. Peritoneal lavage was done. Histopathology of resected specimen confirmed jejunal divericulitis with perforation mucosa. The patient recovered well and discharged on the tenth post-operative day. The patient is followed for 3 months and patient doing well (Figures 2 and 3).

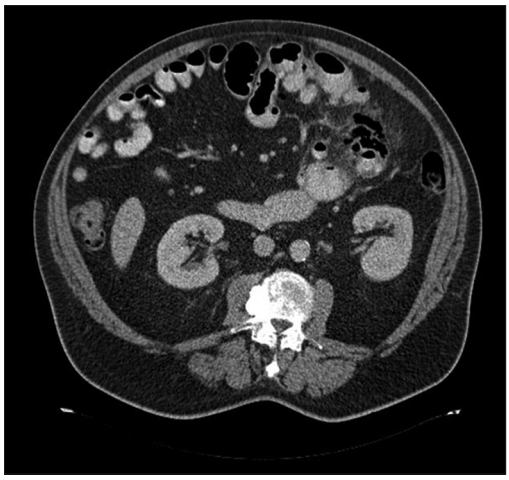

Figure 1: Computed tomography abdomen suggestive of jejunal diverticulosis

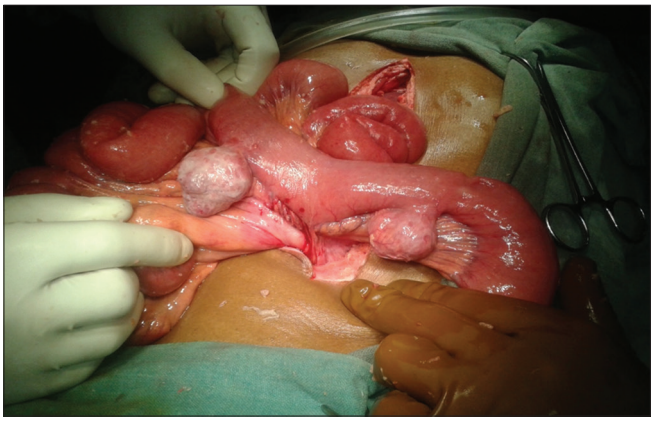

Figure 2: Intra-operative photograph suggestive of jejunal diverticula

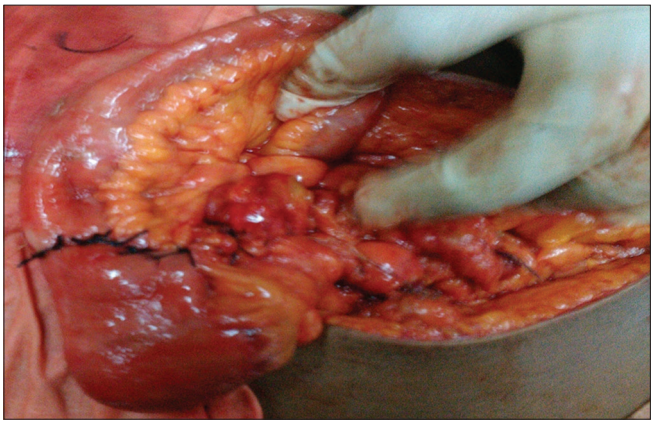

Figure 3: Intra-operative resection and anastomosis photograph

DISCUSSION

Jejunal diverticular disease is such a rare pathology, diagnosis would be challenging task. Diverticula are multiple outpouchings of mucosa and submucosa. All though the exact etiology of jejunal diverticulosis is unknown, believed to develop from a combination of abnormal peristalsis intestinal dyskinesis, and high segmental pressures.[9,10] The majority cases are asymptomatic, few cases associated with non-specific gastrointestinal symptoms. They may be solitary, few cases are multiple. They are always situated on the mesenteric border where mesenteric vessels penetrate and weak. Usually, this condition is clinically silent. Diagnosis of this condition is delayed till it becomes complicated. Acute complications are diverticulitis, hemorrhage, obstruction and rarely perforation of the diverticula leads to abdominal abscess formation. X-ray erect abdomen, ultrasound abdomen and computed tomography abdomen can identify the diverticula and reveals intra-abdominal complications, but no truly reliable diagnostic tests are there to diagnose jejunal diverticulosis prospectively.[13,14] Cessation of symptoms after surgical resection is the only definitive way to say that jejunal diverticulosis is the primary cause of abdominal pain.

Management depends on the severity of symptoms. Decision of surgical procedure depends upon the presentation of the case. Diagnostic laparoscopy very useful in investigating patients presenting with complications, this aids in accurate diagnosis and avoids unnecessary laparotomy. Laparotomy with segmental bowel resection of an end to end anastomosis of entire involved bowel is warranted only in patients presenting with generalized peritonitis. The extent of bowel resection depends upon the length of involved segment and perioperative conditions to avoid complications like short bowel syndrome.[15,16]

If patient present with only local peritonitis and stable, nonoperative measures like guided aspiration with appropriate intravenous antibiotics can be tried.[7]

In our case, we did laparotomy with resection of an entire involved segment of bowel with through peritoneal lavage is done.

CONCLUSION

Jejunal diverticulosis is rare disease and usually asymptomatic. However, these patients may present with acute complications like bleeding per rectum, perforation and abscess formation. Jejunal diverticulosis in an elderly patient may lead to high morbidity and mortality. This condition requires high index of suspicion to diagnose and to take appropriate decision to treat the patient. Rarely, jejunal diverticulosis may present as a perforation and abscess formation, for which surgical resection is the treatment of choice.

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Case Report

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Auto Amputation of Left Ovary: An Incidental Finding during Cesarean Section

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Abstract

A free floating intraperitoneal mass is extremely rare condition and mostly originates from the ovary. Usually, the torsion of ovary or adnexa presents as a surgical emergency with acute pain abdomen. The asymptomatic autoamputation of ovarian is an extremely rare phenomena that may be due to etiology of torsion/inflammation. This atypical presentation may result in clinical dilemma. We report an interesting case where the intraperitoneal free floating autoamputated ovary was an incidental finding at the time of cesarean section. The calcified, necrotic mass was found free in the abdomen and histopathology showed necrotic tissue debris with calcifications.

Key words: Auto amputation, Cesarean section, Ovarian cyst

INTRODUCTION

An autoamputation of the ovary is a very rare case of intra-abdominal mass. The primary pathological event of an autoamputation of ovary is torsion of a normal ovary or an ovarian cyst and the adnexa, followed by infarction and necrosis.[1-5] While most of the cases of ovarian torsion may present as acute abdomen, very rarely it may be asymptomatic and may be diagnosed incidentally during a surgery or during an ultrasound or while investigating a unrelated disease. This clinical entity is termed as the autoamputation of ovary and is the extremely rare phenomena.[6-8]

CASE REPORT

A 22-year-old, booked primigravida with full term pregnancy presented to outpatient department with labor pains since 12 h and leaking per vagina since 4 h and decreased fetal movements since 1 day. When history of present pregnancy was elicited, she revealed that in the present pregnancy she had on and off pain abdomen for which she had taken analgesics and the pain was relieved. The ultrasound report in 1st and 2nd trimesters showed a left sided ovarian cyst of 4 cm^2 × 4 cm^2, which was managed conservatively. The cyst reduced in size subsequently in the third trimester.

On Examination

The patient was well built and nourished. The cardiovascular, respiratory examination was normal and vitals were stable. On per abdomen examination uterus was term size with mild contractions, cephalic presentation, spine to left, head mobile, FHS 144/min, regular, LOP position. On per speculum examination, thin meconium stained liquor was seen. On per vaginal examination the cervix admitted 1 finger, 30-40% effaced, mid position, vertex high, membrane absent, pelvis average. The diagnosis of primigravida with full term pregnancy with cephalic presentation with unengaged head in early labor with acute fetal distress was made.

Management

Emergency ultrasound was done which showed single live intrauterine gestation, cephalic presentation with 38-39 weeks gestation, placenta Grade 3, AFI-6, BPP, no adnexal/pelvic mass was revealed. The patient was put on left lateral position, oxygen and intravenous fluids were given. The cardiotocogram (CTG) was reactive.

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The patient was advised augmentation of labor with oxytocin infusion. After 4 h of trial of labor the CTG showed persistent late deceleration, hence emergency lower segment caesarean section was done for fetal distress.

Intraoperative Findings

The abdomen was opened by pfannensteil incision. When the parietal peritoneum was opened, greenish flakes similar to meconium were seen in the left lower abdomen. A soft globular, pearly white structure with greenish yellow flakes adherent to its surface, was seen lying freely in the left lower abdomen adjacent to uterus with no ligamentous or direct connection to pelvic organs. The medial 2/3 of the left fallopian tube was seen, while the lateral 1/3 of the fallopian tube including the fimbria was absent. The left sided ovary was not visualized. The right sided fallopian tube and the ovary were in situ and normal. The free lying mass was sent for histopathology. The histopathology reported ovarian tissue with inflammatory and hemorrhagic changes with areas of necrosis. The diagnosis of the autoamputation of left ovary due to torsion or inflammation was made (Figure 1).

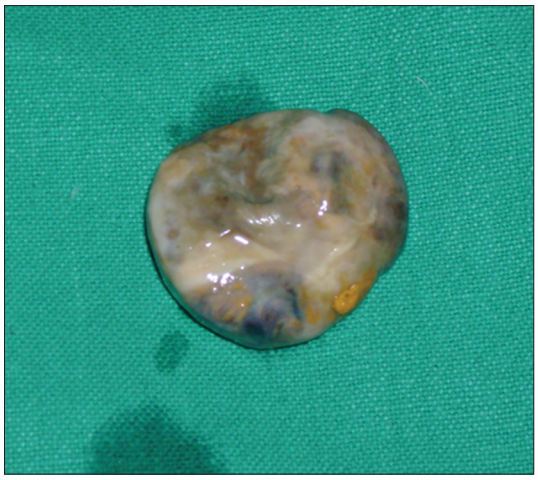

Figure 1: Specimen of Left Ovary

DISCUSSION

An auto amputated ovary is a very rare cause of an intra-abdominal mass.[1,2]

The primary pathological event of an auto amputated ovary is torsion of a normal ovary or an ovarian cyst and adnexa followed by infarction and necrosis. An auto amputate ovary is usually found incidentally during an antenatal ultrasound or at surgery.[1-3]

A free floating intra-peritoneal mass is extremely rare, and almost all originate from an ovary. To date, only two cases in the literature originate from other organs.[9,10] One such mass in a geriatric woman was from gallbladder, due to torsion, and caused acute abdomen, while the other was from appendix, due to torsion. There have been 36 cases of intraperitoneal free floating auto amputated ovary in children ranging from 1 day to 12 years of age.[1] Computed tomography and magnetic resonance imaging may be performed if the mass is complex.[4,5] While ultrasound is a safe and sufficient for diagnosing most ovarian cyst and autoamputation.[1,5,9]

Pathologically necrosis was seen in all cases and calcification was seen in many cases. Small amount of ovarian tissue were seen in several specimens.[1,6]

The review of literature suggests that an auto amputated ovary may re-implant, develop into omentum or peritoneum, and possibly undergo malignant transformation.[1,3,6] Therefore, we suggest that all auto amputated ovary should be excised instead of wait and watch approach.[1,5] The clinicians should make sure about the presence of two ovaries on ultrasound in patients with acute abdomen.[10]

CONCLUSION

An auto amputated ovary is a very rare condition that can result due to torsion. Most of the cases are diagnosed incidentally and can be a challenge to the clinicians. All autoamputation of ovary should be excised instead of wait and watch approach. The ultrasound is a safe and sufficient for diagnosing most ovarian cyst and autoamputation.

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