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Original Article

Frequency of Middle Mesial Canals in Mandibular First Molar in Malabar (North Kerala) Population without Advanced Aids – An *In Vivo* Study

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ABSTRACT

Introduction: This study was undertaken in department of conservative and endodontics, KMCT dental college, Kozhikode, within the span of 2 years ranging from June 2017 to June 2019. Total of 227 teeth were evaluated from 220 patients. All the teeth evaluated were mature mandibular permanent first molars referred for endodontic therapy to the department.

Purpose: The presence of middle mesial (MM) canals is quite high in North Kerala population. Missing these canal space would potentially lead to failure of root canal treatment.

Methods: All the mature mandibular first molars treated between June 2017 and June 2019 were considered for the study. Mesial developmental groove was inspected and explored in every case to detect accessory canal. If cases were that having MM canal was found, it was cleaned, shaped, and recorded. Results were analyzed using Chi-square test.

Results: A total of 227 first molars from 220 patients were treated during the specified period, of which 78 teeth (34.36%) had negotiable MM canals. Statistical analysis revealed no significant relationship between different age groups with incidence of MM canals but gender had slight influence, wherein female patients had more.

Conclusion: The presence of MM canals is quite high in North Kerala population.

Key words: Accessory canal, Mandibular molar, Middle mesial canal, Root canals

INTRODUCTION

A successful endodontic treatment depends on complete debridement of pulp space and creating a fluid tight seal. Favorable environment for healing should be created, which is free of microbes and necrotic tissue. However, this is not always possible in teeth with unusual canal morphologies. They are probably more prone to treatment failures due to insufficient knowledge of canal anatomy and aberrations associated with it.

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Mandibular first molars normally have two roots and three to four canals (two mesial and one-two distal).[1] The incidence of variation is quite high, including seven to eight canals, C-shaped canals, isthmus, and an additional third canal in the mesial root.[2,3]

The middle mesial (MM) canal used to be an occasional entity, which lies in the developmental groove between the mesiobuccal (MB) and mesiolingual (ML) canals. Since its first reporting by Vertucci and Williams as well as Barker *et al.* in 1974, the MM canal has been extensively studied. Its incidence has been reported to be 0–46%.[4]

Pomeranz *et al.* classified MM canals into three categories – (1) Fin: The file passes freely between the main mesial canal (ML or MB) and the MM canal (transverse anastomosis), (2) confluent: The MM canal merges with the main mesial canals in the apical third, and (3) independent: The MM

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canal originates as a separate orifice and ends with a separate apical foramen.[5]

Radiographic examination using conventional intraoral periapical views is important for the evaluation of the canal configuration. However, it has its inherent limitation to assess the root canal system completely. Advanced technology like cone beam computed tomography (CBCT) and magnification with the aid of ultrasonic troughing would be of great help in finding extra canals. Dentists worldwide often do not have access to these tools like CBCT[6] and unfortunately majority of practitioners in North Kerala would not be an exception. Hence, our aim was to estimate the incidence of MM canals in conventional practice without advanced tools and also to show the importance of knowledge about extra canals and tactile sense in locating orifices.

Ours is the first *in vivo* study from North Kerala that was aimed primarily to record the incidence of MM canals in patients who underwent endodontic treatment at a Dental School in North Kerala. The secondary aim was to evaluate the relationship of age, gender, location of orifice, and type of canal with the detection rate of MM canals in mandibular first molars.

MATERIALS AND METHODS

This study was undertaken in department of conservative and endodontics, KMCT dental college, Kozhikode, within the span of 2 years ranging from June 2017 to June 2019. Total of 227 teeth were evaluated from 220 patients. All the teeth evaluated were mature mandibular permanent first molars referred for endodontic therapy to the department. Mean age of the patients was 28 years. Proposal of the study was submitted to ethical committee and approval was obtained. A written consent was taken from patients before starting the treatment.

After administering anesthesia teeth were isolated with rubber dam and access cavities were prepared. Access cavities inspected and explored using endodontic probe. Mesial and distal canals were located. Initial glide path was created using stainless K file #10 (mani, inc, Japan). Canals were prepared using rotary nickel-titanium instruments (Edge Endo, Albuquerque, New Mexico). In retreatment cases, previous root canal filling were removed using protaper retreatment files (Dentsply Maillefer, Ballaigues, Switzerland) and Endosolv E (Septodont, Delaware, USA).

The pulp chamber floor was then carefully examined, during visual inspection looked for additional bleeding points between orifices, difference in color, and pulp tissue strangled at isthmus. DG 16 endodontic explorer was carefully moved over these suspected areas to see for a catch, [Figure 1] exploration, and negotiation of that point was done with #10 K files. Working length was established with woodpex gold III – electronic apex locator (Guillin Woodpecker medical instrument co ltd. China)

Root canals were prepared in crown down fashion. Irrigants used were saline, 5.25% sodium hypochlorite/2% chlorhexidine (retreatment cases) throughout the procedure. Canals were dried using paper points and master cone periapical radiograph was taken using distal angulation. Obturation was done using gutta-percha and zical sealer using cold lateral comapaction. Final radiographs were taken after access cavities were restored.

The incidence of MM canals, their course, and location with respect to main mesial canals was recorded and categorized using the Pomeranz classification. [Figure 2] The distributions of MM canals with respect to age and gender were also noted. The data were analyzed using Chi-square test. Statistical analysis was performed using SPSS (Version 20; IBM Corp., Armonk, NY) and $P < 0.05$ was considered as statistically significant.

RESULTS

Out of 227 molars treated, 78 (34.36%) had negotiable MM canals. Mean age of the treated patients, male – 28.97 with standard deviation 12.27 and female – 28.45 with standard

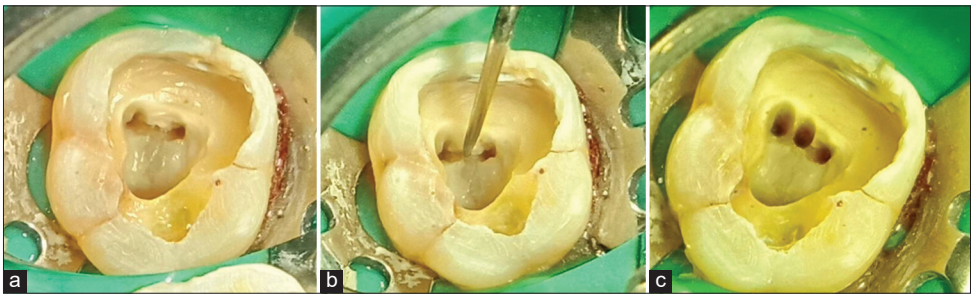

Figure 1: (a-c) Exploring mesial groove in search of middle mesial canal

deviation 11.75. There was no significant difference in the incidence of MM canals with an increase in age.

The distribution of MM canals based on gender was found to be statistically non-significant ($P > 0.05$). However, MM canals slightly more common among female patients (41% male and out of 78 MM canals).

Most common type of MM canals found was type II 64.1% (50/78), where canals were confluent with either of the mesial canals [Figure 2b] following Type I, where it was a fin rather than actual canal 32% (25/78) [Figure 2a] and the least found type was Type III a separate canal with a separate portal of exit 3.8% (3/78) [Figure 2c].

Most common location of MM canal orifice was in the center between the main mesial canals 60.2% (47/78) of the cases [Figure 3a], following toward the MB canal in 25.6% (20/78) of the cases [Figure 3b] and least was closer to or in close proximity to ML canal in 14.1% (11/78) of the cases [Figure 3c].

Association between location of orifice and canal type was found to be statistically significant (< 0.001%).

Type I canals had orifice location most commonly in proximity to MB orifice (60%) following in center (28%) and least toward ML canal(12%).

Type II canals had orifice location most commonly in the center (80%) following in proximity to MB orifice (16%) and least toward ML orifice (4%).

About Type III canals, it was interesting to find that orifice location was 100% only in the center between MB and ML canal orifice.

DISCUSSION

A successful endodontic treatment can be attributed to removal of bacterial biofilms in root canal ramifications such as fins, deltas, loops, accessory canals, and isthmuses[7]

The isthmuses of mandibular first molars are classified into five types
Type I is two separate canals,
Type II is two separate canals connected by an isthmus,
Type III is three canals connected by an isthmus,
Type IV is two elongated canals that join in the center, and
Type V is a single, very broad, and elongated canal.[8]

The MM canal or accessory mesial canal lies in the subpulpal groove or the isthmus connecting the main mesial canals. Since its first mention in the literature in 1974, the incidence of MM canal has been reported by various authors in both *in vivo* and *in vitro* studies.[9,10,11] These studies can be further classified into those done with and without magnification.

Detection of accessory canals can be increased evidently using advanced tools like microscope/loupes and ultrasonics. A recent *in vivo* study reported the highest ever occurrence of MM canals (46.2%).[9] In our study, advanced tools were not used as stated that aim of the study was to check incidence rate in conventional treatment without

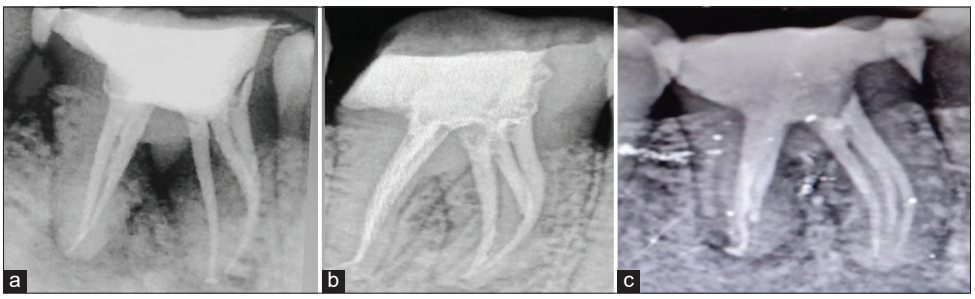

Figure 2: Types, a) Type 1, b) Type 2, and c) Type 3

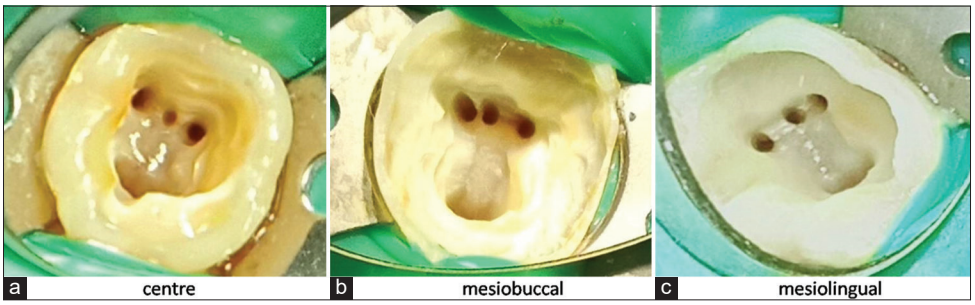

Figure 3: (a-c) Recording location middle mesial orifice in relation to mesial canal orifice

advanced aids. We aimed at dental practice which is done in majority of the place. Dentists worldwide often do not have access to these tools like CBCT.[6]

Few authors argue that third mesial canal is not an accessory canal but sequelae of instrumenting isthumus between MB and ML canals. However, these accessory canals when negotiated and cleaned will definitely increase the chance of cleaning the otherwise inaccessible istumus. There by increase the success rate of non-surgical root canal therapy.[10]

Troughing the mesial pulpal groove in a mesioapical direction away from the furcation is a significant factor in detection and negotiation of MM canals. Troughing the groove up to 2 mm has resulted in increased detection rates and subsequent negotiation of MM canals. A recent *in vivo* study has demonstrated that 39.6% more MM canals were detected and explored after controlled troughing to within 2 mm depth using a 1 mm diameter round bur head as a depth guide. However, it requires clear visibility, specialized instruments, and care to avoid perforation and its potential complications.[9]

One of the clinically significant factors in detecting orifice was age of the patient in previous studies.[5,9,12,13] The incidence rate decreased with an increase in age. However, in contrast, our study did not find any significant influence with age of the patient in finding the orifice. However, definitely younger patients had larger MM canals which were easier to negotiate.

We also noted the location of orifice in relation MB and ML canal orifice. It MM canal orifice was most commonly located in the middle of the MB and ML orifices (60.2%) followed by orifice located closer to the MB canal (25.6), while remaining 14.1% had orifices toward ML canals. These findings are not in consistent with those of previous studies which reported that the MM canal was located closer to the ML canal in majority of the cases followed by the MM orifice located in the middle of MB and ML canals, while the least number of cases showed the orifice closer to the MB canal[9] Our results are partly in agreement with another study, they found that MM orifice is most commonly located in the middle followed by closer to ML canal and least near MB canal.[13,14]

Most common type of canal configuration found in our study was confluent type (TYPE 2) – 64.1% followed by Fin (TYPE 1) – 32% and rarely found – only 3 cases were separate canal (TYPE 3) – 3.8%. These findings are in consistent with those of previous studies.[9,13,14]

CONCLUSION

Within limitations of study, we found that the presence of MM canals is quite high in North Kerala population. Missing these canal space would potentially lead to failure of root canal treatment.

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Original Article

Sirenomelia: A Fetal Autopsy Study

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ABSTRACT

Introduction: Sirenomelia is a very rare congenital, evolutionary malformation in the caudal region with varying degrees of lower limb adhesion. Fetus looks like of Mermaid of Greek mythology, and hence, the synonym of Mermaid syndrome is also given to the defect.

Materials and Methods: The study was done in the Department of Anatomy in Government Medical College, Chandigarh, on fetuses sent for autopsy from Gynecology and Obstetrics department. The obstetric histories of all the mothers were taken thoroughly. The medical histories, drug history, qualification, and socioeconomic status of the parents were also noted. Fetuses were examined externally. Photograph and radiograph of each case were taken. Autopsy of all the fetuses was done for internal examination by following directions in Cunningham's manual.

Results and Conclusion: In our study, we came across fetuses with sirenomelia out of 1900 cases, which accounts for about 0.002%. In three cases, one femur falling in between simpus apus and simpus unipus. Case number one, with some variation in looked like simpus unipus, because it has two femur and two tibia and one foot. The etiology is unknown in all cases but hypothyroidism and anemia may have been a factor in the two reported cases.

Key words: Sirenomelia, Mermaid syndrome, Congenital malformations

INTRODUCTION

Sirenomelia is a very rare congenital, evolutionary anomaly, in which baby is born with defect in the caudal region of the body with varying degrees of lower limb adhesion. The defect may lead to complete absence of the lower limb to joining or adhesion of part of lower limb. It is also associated varying degree of defect in perianal region.[1] Fetus looks like of Mermaid of Greek mythology, and hence, the synonym of Mermaid syndrome is also given to the defect.[2] The prevalence of this anomaly is 1 in 100,000 births.[1] The anomaly is lethal in severe cases. Incidence of stillbirth is 50 %. Defect is much more common in identical twins.[3] In live born babies, head and trunk are such as humans and tail looks like fish.[2] Most live born cases die shortly after birth.[1] A spectrum of anomalies affects primarily the musculoskeletal, genitourinary, and gastrointestinal systems.[4]

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Kallen suggested that diabetes may be a cofactor that modifies the action of one or more unknown teratogens.[5]

Raabe *et al.* reported sonographic antenatal diagnosis of sirenomelia at 18 week' gestation as evidenced by (i) oligohydramnios, (ii) bilateral renal agenesis (non-visualization of the kidneys and bladder on serial prenatal examinations), and (iii) fusion of the lower extremities.[6]

Sirenomelia is closely associated with Potter's syndrome. It consists of (i) Potter's facies (large, low-set ears, prominent epicanthal folds, hypertelorism, flat nose, and receding chin), (ii) oligohydramnios, and (iii) pulmonary hypoplasia. This syndrome is almost invariably present with bilateral renal agenesis. Although a strong association between caudal regression syndrome and maternal diabetes has been described, no such relationship exists between Potter's syndrome and diabetes.[7]

MATERIALS, METHODS, AND OBSERVATIONS

The study was done in the Department of Anatomy in Government Medical College, Chandigarh, on fetuses sent for autopsy from gynecology and obstetrics department.

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The obstetric histories of all the mothers were taken thoroughly. The medical histories, drug history, qualification, and socioeconomic status of the parents were also noted [Table 1].

Fetuses were examined externally [Table 2]. Photograph and radiograph were taken. Autopsy of all the fetuses was done for observing internal examination [Table 3] by following directions in Cunningham's manual. Associated

Table 1: Case histories

	CASE I	CASE II	CASE III	CASE IV
Maternal history	24 years G_2A_1	30 years $G_3P_1L_1A_1$	26 years $G_3P_1L_1A_1$	24years, $G_3L_2A_1$
Gestational age and sex	20 weeks Un differentiated	18^{+4} weeks Un differentiated	19 weeks Appears to be Male	14^{+2} weeks Not determined
History of previous pregnancy	Spontaneous expulsion 1 year back	1 live female child 2^{nd} pregnancy history not available	Not available	Normal, 2 live female child
Past history	Hypothyroidism	Not suggestive	Not suggestive	Anaemia in mother
Family history	Not suggestive	Not suggestive	Not suggestive	Not suggestive
Antenatal history of present pregnancy	Regular intake iron, folic acid and vaccination	Not available	Medicines for hypothyroidism up to 2 weeks present gestation	T.T injection given to mother
Investigations	Multiple anomalies	Cystic hygroma	Multiple anomalies	USG not done
Termination of pregnancy	Spontaneous Expulsion	Spontaneous Expulsion	MTP	MTP

Observations: Four cases of sirenomelia were found in 1900 cases of fetal autopsies attempted

Table 2: Showing the findings on External examination

FEATURES	CASE I	CASE II	CASE III	CASE IV
Head, curvature of spine	Antero posteriorly lengthening of skull, different shape of pinna on both sides	Low set ears, prominent epicanthal fold	Broad nasal bridge, asymmetrical ear.	Normal
Limbs	Both lower limb joined till thigh. Below knee fused limb has appendage on the right side, left leg terminated in foot which has polydactyly	Fused lower limb, feet without toes	Only one limb in midline seen, foot degenerated	Only one limb present , deviated towards left by the extruded abdominal contents
Thorax	Normal	Normal	Normal	Broad and short thorax
Abdomen	Absence of anal and urinary opening	imperforate anus	Absence of anal, and urinary opening small male genitalia	Abdominal contents protruding out
Number of umbilical vessels	Two umbilical Vessels	Two umbilical Vessels	Two umbilical Vessels	Umbilicus could not be seen

Table 3: Showing the findings on internal examination

FEATURES	CASE I	CASE II	CASE III	CASE IV
Skeletal system	2 femur, 2 tibia foot bones not visible	1 femur, 1 tibia, foot bones not visible	1 femur, 1 tibia, foot bones not visible,	X-Ray could not be taken
CNS	Normal	Normal	Normal	Normal
CVS	Normal	Normal	Normal	Thorax has only great vessels Heart shifted to abdomen , Present in midline between abdominal lungs
GIT	Blind gut end, Imperforate anus	Blind descending colon, megacolon, imperforate anus	Blind sigmoid colon, No anal opening seen	All the gut, liver extruded from abdominal cavity. Contents covered by only a membrane. Gut opens in cloaca along with both the ureters
Respiratory System	Fluid seen in thoracic cavity	Normal	Horizontal fissure not seen in right lung	Both the lung lying in abdomen embracing heart. Left lung partially lying in thoracic cavity. Big gap in diaphragm
Urinary system	Bilateral renal agenesis along with urinary tract and bladder, No opening of urinary tract seen	Kidneys present (Left kidney ascended)	Both kidneys present with normal ureters No urinary opening.	Bilateral small kidneys, ureter opening in cloaca . no external urinary opening
Genital System	No genetalia visible as limbs are joined	No external genetalia seen	Small male genetalia seen	Undifferentiated internal gonads

congenital malformations were also observed and noted. Pictures of each fetus's external examination as well internal examination are given below (Figures 1-4).

DISCUSSION

Sirenomelia is a congenital structural anomaly involving abnormal development of the whole of the caudal region of the body. The fusion of the lower limbs varies from fusion of thigh only, thighs, and legs to whole lower limbs.[3]

The defect was first reported in 1542 by Rocheus *et al* and later by Palfyn *et al* in 1543.[8,9]

The incidence of male-to-female is 3 to 1.[10]

The anomaly may vary clinically from mild and severe varieties. In mild form, the baby has two limbs fused into one, only up to the extent of the skin. All the three main bones of the leg are fully and correctly formed. The feet are also formed and may be only attached at the ankles. A small surgical correction in these cases is required to correct the deformity. In severe variety, both limbs are completely joined and appear ill-formed. There is absence of foot structures and out of the three long bones; two bones may be present in the entire limb.[3]

Another classification of Sirenomelia has been divided into three types, simpus apus (no feet, one tibia, and one femur), simpus unipus (one foot, two femur, two tibia, and two fibula), and simpus dipus (two feet and two fused legs (flipper like) – this is called a mermaid).[3]

In 1961, Duhamel classified the mermaid syndrome as type 5 caudal regression syndrome (CRS) for the similarity with CRS anomalies.[11]

Nowadays, mermaid syndrome is considered a separate syndrome, and the diagnostic features are the presence of single umbilical artery and renal agenesis, while in the Caudal Regression Syndrome, there is dysfunctional kidneys rather than renal agenesis.[12]

In 1987, Stocker and Heifetz noted and reported that all patients with Sirenomelia had a large umbilical artery, separated from the upper abdominal artery aorta slightly below the celiac artery, and the branches of other aorta had not evolved. This suggested that due to the lack of blood supply and inadequate nutrition, the growth of the lower part of the body was stopped and led to sacral agenesis, lower limb fusion, imperforated anus, rectal agenesis, internal and external absence of genitalia, and renal agenesis.[4]

Although the main factor for mermaid syndrome is unknown. The other important hypotheses about mermaid syndrome are vitelline artery steal hypothesis and defective blastogenesis hypothesis.

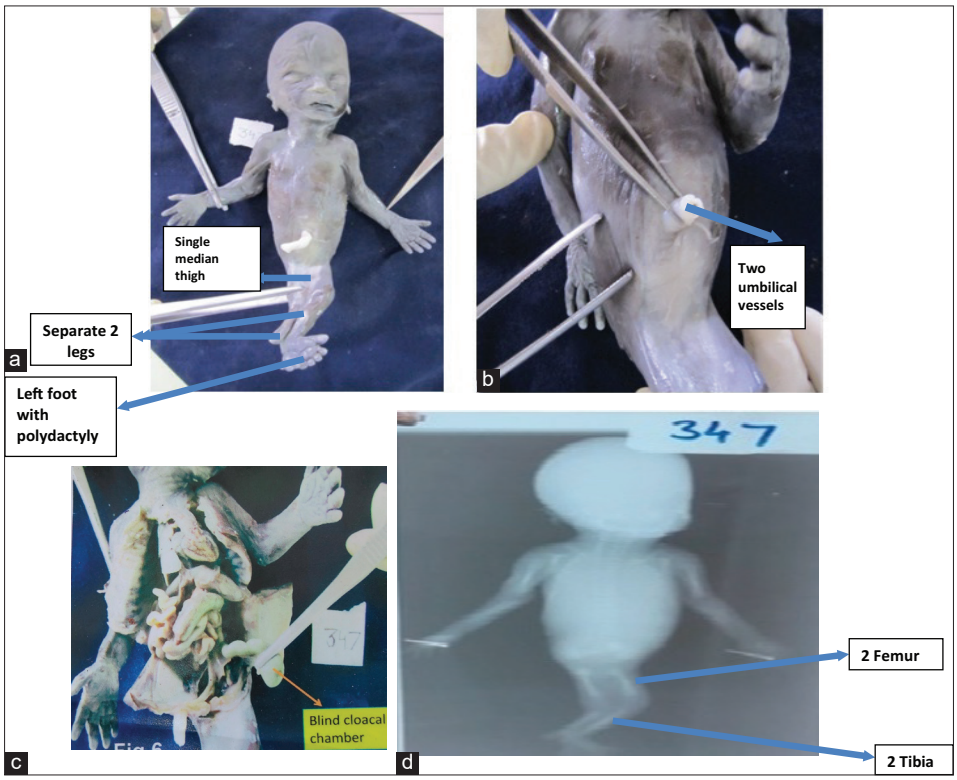

Figure 1: Case I - (a) Anterior aspect of fetus. (b) Representing single. (c) Internal examination of fetus. (d) Radiological examination of fused limb

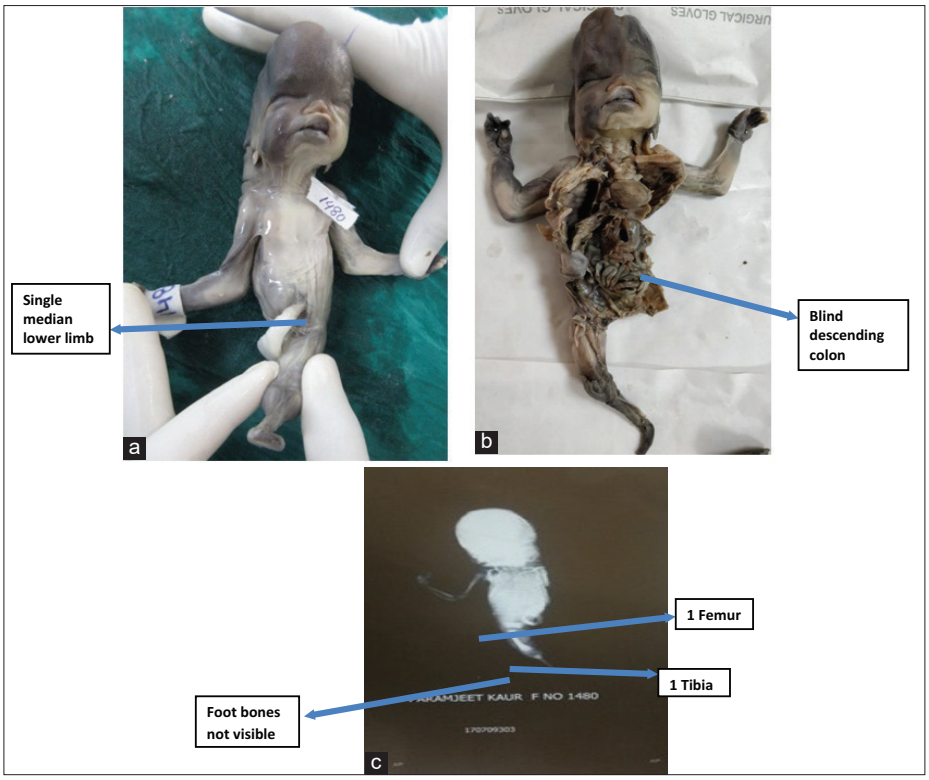

Figure 2: Case II - (a and b) External as well as internal examination of fused limbs. (c) showing X-Ray of fused limbs

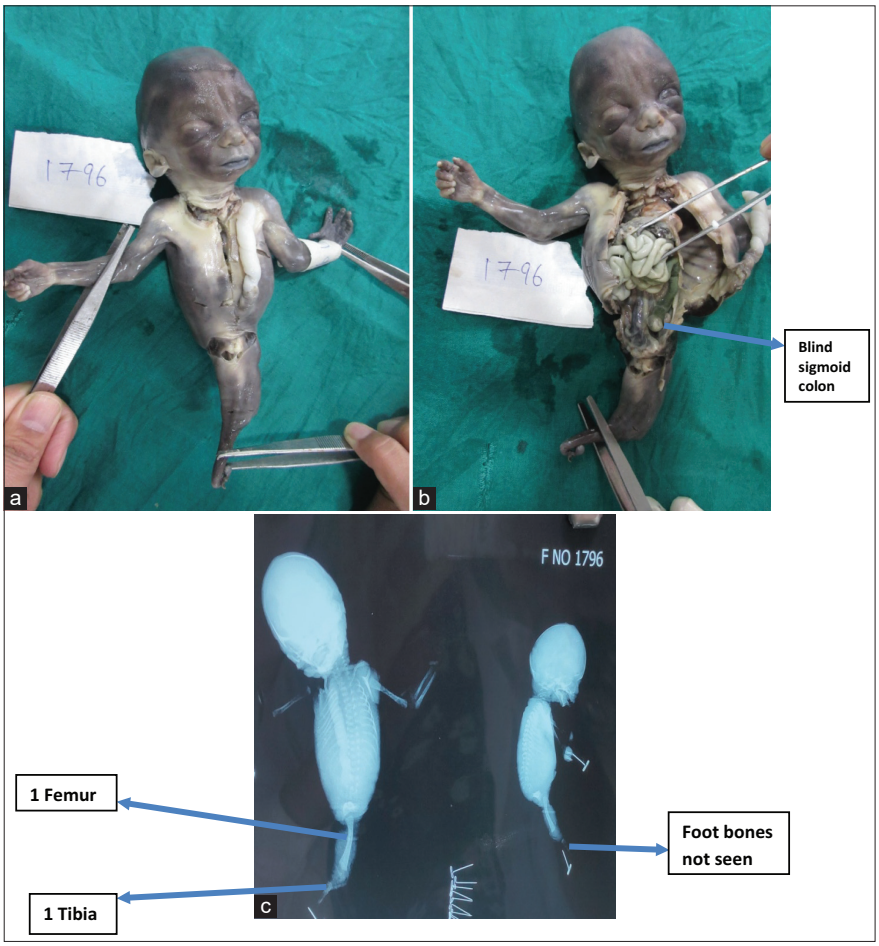

Figure 3: Case III - (a and b) Anterior aspect and internal features of fused lower limb, respectively. (c) Radiographic examination

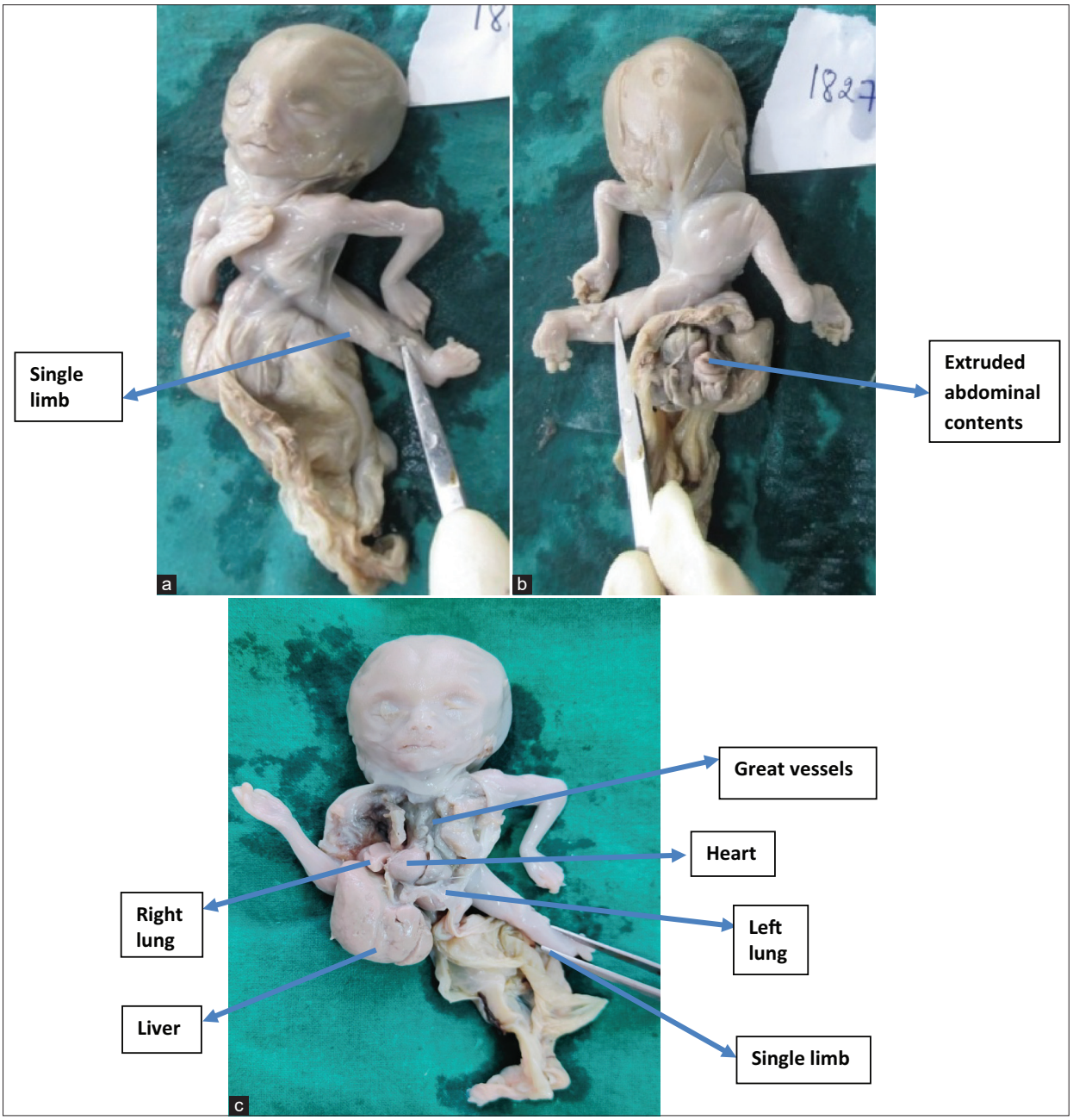

Figure 4: Case IV - (a and b) Anterior and posterior aspects of fetus. (c) Internal examination

According to the theory of vitelline artery steal hypothesis, the ventral branches of abdominal aorta other then coeliac are either absent or hypoplastic. This reduces the blood flow that feeds the caudal portion of the embryo by diverting blood flow from the embryo to the placenta. This occurs in the 3rd and 4th weeks of intra uterine life.[13]

Based on the theory of defective blastogenesis, an impaired blastogenesis, in which the lower body organs have inappropriate angiogenesis, leads to insufficient growth and incomplete development of the caudal region.[14]

Anomalies that are commonly seen with the mermaid syndrome include cleft palate, pulmonary hypoplasia, cardiac defects, omphalocele, pentalogy of Cantrell, and meningomyelocele.[15,16]

Neonates born with mermaid syndrome often have normal karyotype.[17]

The abnormalities of embryologic development, leading to the sirenomelia sequence, occur around 4th week of gestation and involve the medioposterior mesodermic axis and the caudal blastema.[18]

Most of the cases were observed in maternal age ranging from 20 to 30 years and all of them are multiparous. Fetuses were ranging from 14 to 20 weeks gestational age.

At this gestational age, the cloaca is formed; the kidneys are located in the pelvis, while the gonads are intra-abdominal. It seems logical that any damage to the caudal extremity of the embryo would affect the development of the external and internal genital organs (except the gonads, which are intra-abdominal), the terminal bowel, the bladder, the kidneys, and the pelvic bones.

CONCLUSION

In our study, we came across four fetuses with sirenomelia out of 1900 cases, which accounts for about 0.002%. In three cases one femur, one tibia was present along with foot like appendage. No foot bone was visible in X-ray. This case fall in between Simpus apus and simpus unipus. Though there are some variations in case number 1, which looked like simpus unipus because it has two femur and two tibia and one foot. This makes case fall in simpus unipus category. Associated anomalies observed were epicanthic folds, low set ears, absent external genitalia, blind sigmoid colon, and imperforate anus. The etiology is unknown in all cases, but hypothyroidism and anemia may have been a factor in the two reported cases. However, the emphasis should be both on prenatal diagnosis and genetic abnormalities to ensure an optimal management.

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Original Article

Effect of Transforaminal Steroid Injection on Inflammatory Process in Lumbar Disc Herniation – Functional and Laboratory Assessment

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Abstract

Background: Lumbar disc herniation is major cause of low back pain with lower limb radiculopathy. Lumbar radiculopathy is the result of compression or inflammation or both, of the nerve roots exiting the spinal column. Epidural and transforaminal steroid injection is widely used for treatment of low back pain and lower extremity pain associated with lumbar disc herniation for pain relief. Steroid is administered through the injections and is thought to be integral in decreasing inflammation around the affected nerve tissue [4], hence leading to a reduction in pain. The purpose of this study was to evaluate the effect of transforaminal steroid injection over inflammatory markers such as ESR and CRP, which may demonstrate its effect over inflammation in lumbar disc herniation and also assess functional outcome measured by the Roland–Morris Disability Questionnaire and Oswestry Disability Index.

Materials and Methods: This prospective study enrolled 30 patients (male and female) who were selected with set inclusion and exclusion criteria. Serum ESR and serum CRP were assessed as markers of inflammation, functional activity was assessed by Rolland–Morris and Oswestry Disability Index scoring system. Comparison of initial (pre-procedure) and serial ESR and CRP level was done, and pre-procedure and post-procedure day 1, 2nd month, 6th week, 12 week, and then 6 months, which was done. Unpaired t- test was used for collected data.

Results: Sample size was of thirty patients. Mean age of our sample is 45 (maximum being 78 and minimum 26 years). Mean serum ESR of sample was 24.8 (maximum being 42 and minimum 12). On Follow up measurement post TFESI, Mean values were 23.4 on ppd (post-procedure day) 1, 21.5 on ppd 2 weeks, 19.9 on ppd 6 weeks and 12 weeks, and 21.2 after 6 months. On paired t-test, p value at each fallow-up was not statistically significant. Mean serum CRP of sample was 2.54 at start of study (maximum being 4.6 and minimum being 0.6). Post-TFESI mean value was 2.21 at post-operative day 1, 2.14 at post-operative 2 weeks, 2.14 at 6 weeks, 1.94 at 12 weeks, and 2.02 after 6 months. On applying paired *t* test, change in each level compare to pre-operative was not statistically significant. Functional assessment was also studied and documented.

Conclusion: This study did not reveal significant fall in serum ESR and CRP level following transforaminal steroid injection (TFSI), but showed statistically significant clinical improvement assessed by ODI and RMDQ. This study shows significant improvement in OSI and RMDQ, post-transforaminal steroid injection. As per this study, TFSI is effective tool for non-surgical management of disc radiculopathy.

Key words: Lumbar disc herniation, Transforaminal steroid injection, ESR, CRP

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INTRODUCTION

Lumbar disc herniation is major cause of low back pain with lower limb radiculopathy. Lumbar radiculopathy is the result of compression or inflammation or both of the nerve roots exiting the spinal column.[1] The causes and pathophysiology of back pain and acute radiculopathy

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remain unclear. The most common causes being compression of the nerve root by protruded disc, also several studies have identified inflammatory mediators (phospholipase A2, prostaglandin E2, leukotrienes, nitric oxide, immunoglobulins, and pro-inflammatory cytokines such as interleukin [IL]-1alpha, IL-1beta, IL-6, and tumor necrosis factor alpha [TNF-alpha]) and autoimmune reaction (macrophages expressing IL-1beta and intercellular adhesion molecules) as a cause**.** An appealing hypothesis is that the leakage of these agents may produce an excitation and irritation of the nociceptors, a direct neural injury, a nerve inflammation, or an enhancement of sensitization to other pain-producing substances (such as bradykinin), leading to the nerve root pain so inflammation plays a major role in radiculopathy.[2,3] Once inflammation has been established, the nerves become exquisitely sensitive to pressure, producing prolonged, and pain-generating discharge with either gentle manipulation or pressure.[4] Such local inflammation is caused by inflammatory mediators such as interleukin-6 produced by macrophages and monocytes at the inflammatory site. High concentrations of inflammatory mediators may cause a systemic inflammatory reaction.[2,5,6] Therefore, it is believed that the levels of high-sensitivity C-reactive protein (hsCRP) are increased by low back pain. Laboratory measurement of acute phase protein is a valuable indicator of the presence and extent of inflammation and its response to treatment. Among acute phase proteins, C-reactive protein is the first to appear. It is a sensitive systemic marker of inflammation and tissue damage[5] and it also appears 6–8 h after infection. Another marker of inflammation is the erythrocyte sedimentation rate (ESR), a common hematology test that tracks the rate of red blood cell precipitation for 1 h. There are several reports in the literature regarding hsCRP and ESR levels in patients with acute and chronic lumbar radiculopathy pain.[7,8]

Epidural and transforaminal steroid injection is widely used for treatment of low back pain and lower extremity pain associated with Lumbar disc herniation for pain relief. Steroid is administered through the injections and is thought to be integral in decreasing inflammation around the affected nerve tissue,[4] hence leading to a reduction in pain.

The purpose of this study was to evaluate the effect of transforaminal steroid injection over inflammatory markers such as ESR and CRP, which may demonstrate its effect over inflammation in lumbar disc herniation. This study also aims to assess the efficacy of transforaminal epidural steroid injection in patients using pain scales. Pain is major symptom of inflammation. Hence, its variation with treatment may hint at effect over inflammation in disc herniation.

MATERIALS AND METHODS

This was a prospective and single-center study. The study was reviewed and approved by the Institutional Ethical Committee. Information about the study was given comprehensively, both orally and in written form, to the patients. Accordingly, all patients gave their written informed consent before their inclusion into the study.

The study was conducted at a tertiary well-equipped hospital (C-ARM, MRI (Magnetic Resonance Imaging) and Laboratory Facility). The study enrolled 30 patients who met the inclusion criteria.

The inclusion criteria were as follows – all patients above age of 20 years with MRI proven lumbar disc herniation with history of back pain with radiculopathy without sensory motor deficit.

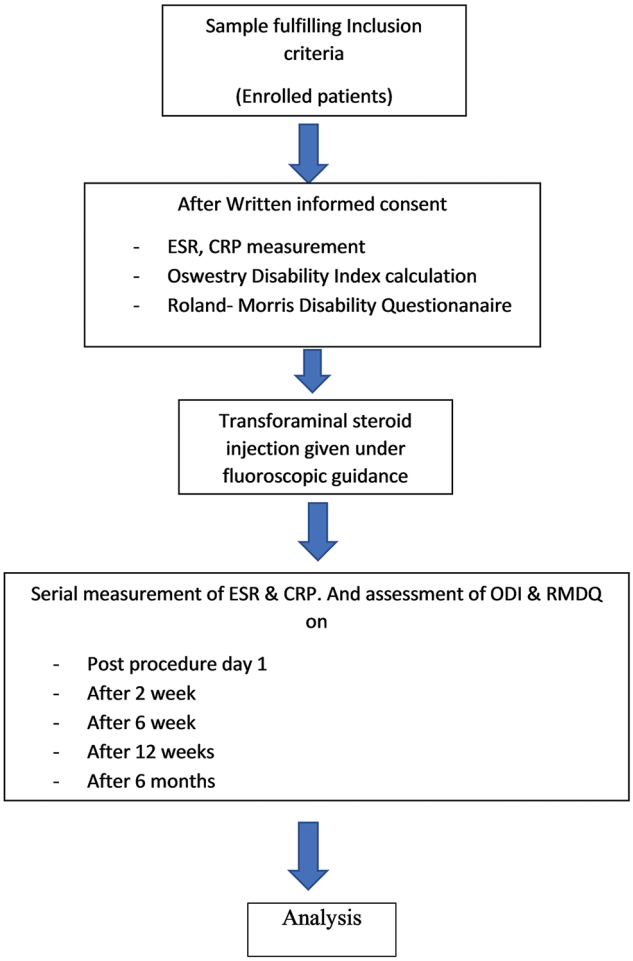
The exclusion criteria were as follows acute symptoms due to infection, compression fracture, malignancy, inflammatory diseases including rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, Reiter disease, etc., use of steroids. Body temperature > 36.5°C. Pregnancy and bleeding disorder.

All consenting individuals were enrolled into the study. The pre-determined protocol was used to either include or exclude consented patients from the study. MRI was conducted of all patients. To rule out other systemic inflammation USG abdomen pelvis, urine analysis and chest radiographs were done. Functional assessment of patients was done by Rolland–Morris Disability Questionnaire (RMDQ) and Oswestry Disability Index (ODI) scales provided to patients in vernacular languages. Serum ESR (Erythrocyte Sedimentation Rate) and CRP (C-Reactive Protein) level were the inflammatory markers which were done in the hospital, which was measured 1 day before procedure.

Enrolled patients were then given transforaminal steroid injection under fluoroscopic guidance, a single transforaminal epidural 40 mg triamcinolone acetonide injection along with 1% of lidocaine was given. The patient was monitored for an hour post-procedure.

Follow-up of such patients was done at next day, 2nd week, 6th week, 12 week, and then 6 months. On every visit, ESR and CRP counts were done and documented. Similarly, patients were asked to fill up both questionaries. At the end of 6 months comparison of initial (pre procedure) and serial ESR, CRP level was done, and functional activity was assessed by Rolland–Morris and Oswestry Disability Index scoring system.

Study Method



RESULTS

In this prospective study, 30 patients with back pain with radiculopathy were included in the study. Serial ESR and CRP measurements done. Minor reduction in its values occurred in patients, but no statistically significant difference was found among pre-operative levels and post-operative level.

Unpaired *t*-test was used for collected data.

Sample size was of 30 patients. 63% Female And 37% Male. Mean age of our sample was 45, (maximum being 78 and minimum 26 years) [Table 1 and Figures 1 and 2]. All patients underwent procedure of single TFESI (transforaminal epidural steroid injection) under fluoroscopic guidance, 40 mg triamcinolone acetonide along with 1% of lidocaine was used.

Mean serum ESR of sample was 24.8.(maximum being 42 and minimum 12). On Follow up measurement post

Table 1: Age in years

Age in years	
Mean	45.2
Standard error of mean	1.02
Standard deviation	10.106
Minimum	26
Maximum	78

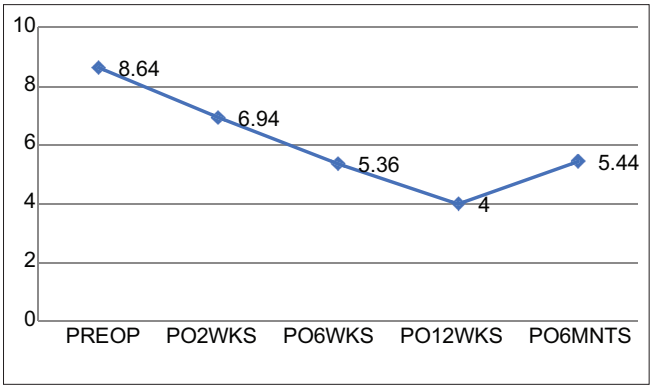


Figure 1: Gender distribution of study sample

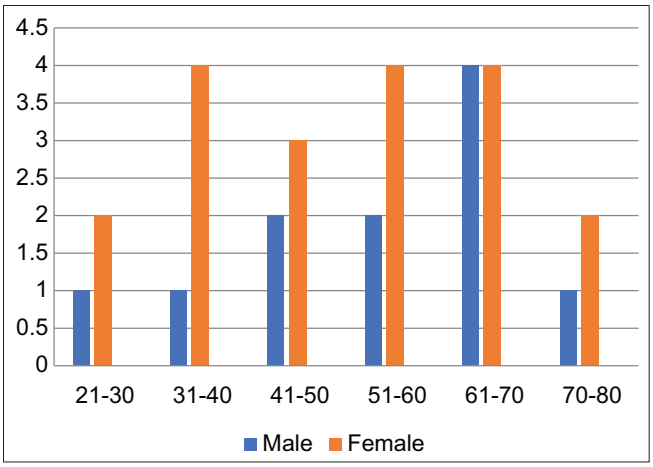


Figure 2: Age distribution of study sample

TFESI, Mean values were 23.4 on PPD (post-procedure day) 1, 21.5 on PPD 2weeks, 19.9 on PPD 6 weeks and 12 weeks, and 21.2 after 6 months. On paired *t* test, *P* value at each fallow-up was not statistically significant (Figures 3 and 5 and Table 2].

Mean serum CRP of sample was 2.54 at start of study (maximum being 4.6 and minimum being 0.6). Post-TFESI mean value was 2.21 at PPD 1, 2.14 at PPD 2 weeks, 2.14 at 6 weeks, 1.94 at 12 weeks, and 2.02 after 6 months. On applying paired t-test ,change in each level compare to pre-operative was not statistically significant [Figures 4 and 6 and Table 3].

Our study had comparable results with some studies in the literature which also suggests that there is no statistically

significant change in serum ESR, CRP level in response to transforaminal epidural steroid injection.

Significant improvement occurs in ODI and RMDQ over 3 months (Figures 7 and 8 and Tables 4 and 5).

Statistically significant difference found, hence concluding pain and general disability decreased after transforaminal steroid injection.

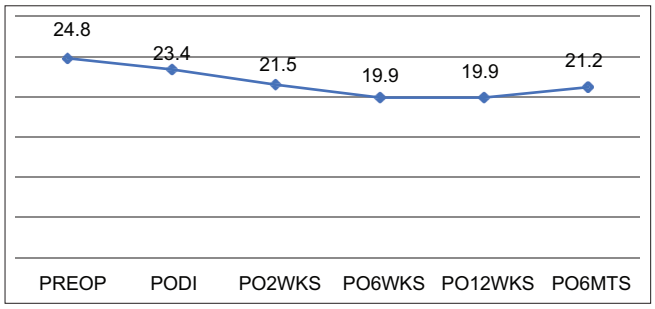


Figure 3: Analysis of serum ESR

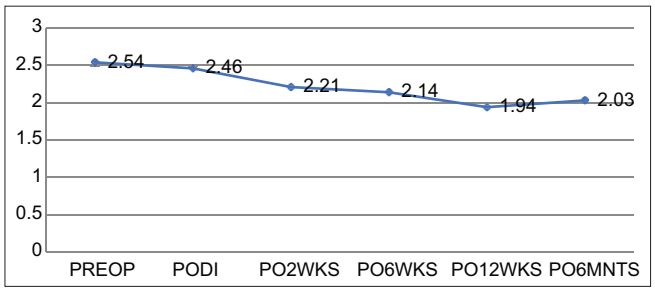


Figure 4: Analysis of Serum CRP (mg/l)

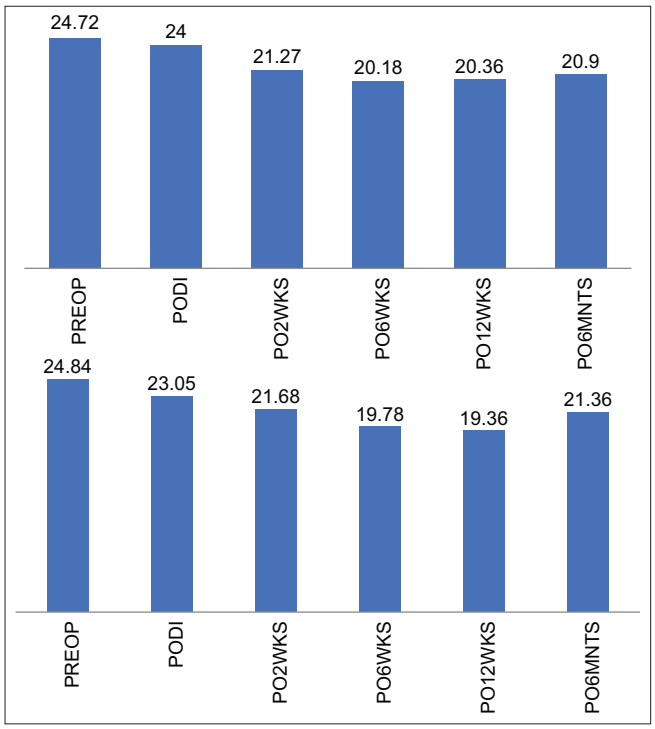


Figure 5: Assessment of ESR (male and female)

DISCUSSION

Low back pain with radiculopathy due to disc herniation has now become a real rehabilitation and management challenge in our society. Herniated lumber disc is the most common cause of radicular pain.

The pathophysiology of disc protrusion associated with low back pain with radiculopathy is incompletely understood.[9]

Table 2: Assessment of ESR

Comparison test	Mean difference	*P* value	Significant
Pre-injection versus post-operative day 1	1.4	0.030505	No
Pre-injection versus post-operative 2 weeks	3.26	0.105154	No
Pre-injection versus post-operative 6 weeks	4.83	0.019438	No
Pre-injection versus post-operative 12 weeks	5.06	0.01223	No
Pre-injection versus post-operative 6 months	3.6	0.08143	No

PPD: Post-procedure day

Table 3: Assessment of CRP

Comparison test	Mean difference	*P* value	Significant
Pre-injection versus post-operative day 1	0.08	0.7349	No
Pre-injection versus post-operative 2 weeks	0.33	0.1514	No
Pre-injection versus post-operative 6 weeks	0.41	0.0685	No
Pre-injection versus post-operative 12 weeks	0.62	0.0051	No
Pre-injection versus post-operative 6 months	0.51	0.0184	No

Table 4: Analysis of ODI

Comparison test	Mean difference	*P* value	Significant
Pre-injection versus post-operative 2 weeks	3.6	0.2227	No
Pre-injection versus post-operative 6 weeks	7.73	0.001	Yes
Pre-injection versus post-operative 12 weeks	11.46	0.0016	Yes
Pre-injection versus post-operative 6 months	4.9	0.0928	No

Table 5: Analysis of RMDQ

Comparison test	Mean difference	*P* value	Significant
Pre-injection versus post-operative 2 weeks	1.7	0.1104	No
Pre-injection versus post-operative 6 weeks	3.2	0.001	Yes
Pre-injection versus post-operative 12 weeks	4.6	1.1805	No
Pre-injection versus post-operative 6 months	3.1	0.001	Yes

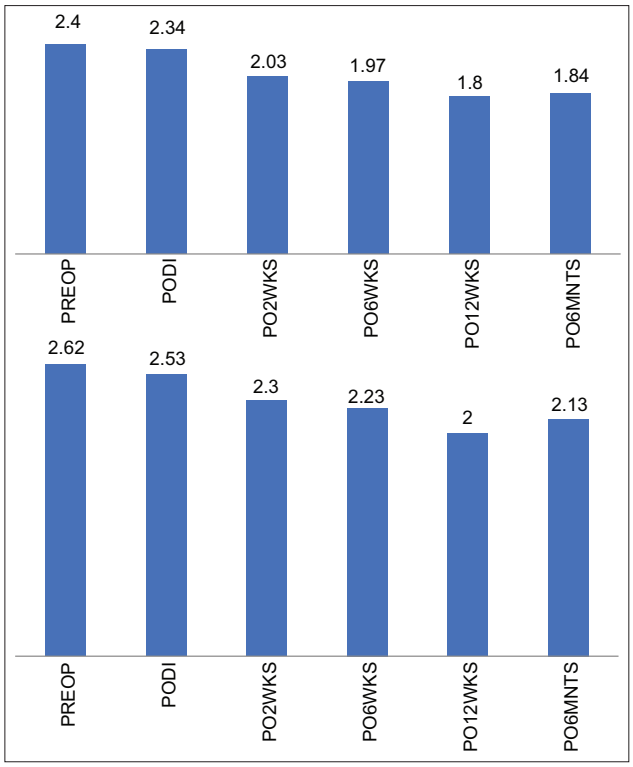


Figure 6: Assessment of CRP (male and female)

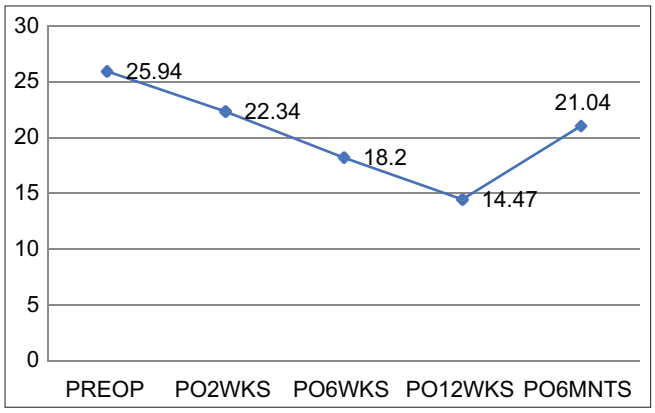


Figure 7: Assessment of ODI

The changes which occur as a disc degenerates are well documented, but are unhelpful in determining whether a degenerate disc will cause pain.[10]

It is known that disc tissue from patients undergoing discectomy for sciatica synthesizes pro-inflammatory mediators and cytokines.[11-20] Sequestrated and extruded discs produces higher levels of these mediators than specimens, in which the annulus is intact.[13,18,20,21]

In recent years, attention has begun to focus on the cellular and molecular activity of intervertebral disc tissue in the search for an understanding of the pathophysiology of sciatica and discogenic low back pain.[11-20] It is clear

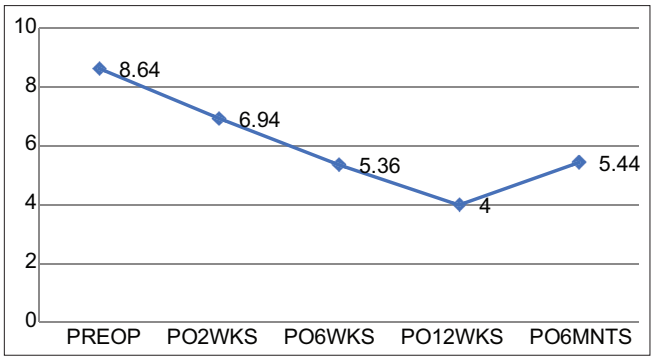


Figure 8: Assessment of RMDQ

from imaging studies that radicular pain is not simply a mechanical phenomenon.[22,23]

However, multiple studies have shown conflicting results in role of inflammation in disc pain. Transforaminal steroid injection provides relief in disc radiculopathy. In this regard, we took up our study to assess effect of transforaminal epidural steroid injection over inflammatory markers.

In this study, we measured ESR and CRP level pre- and post-TFESI, along with pain score assessment to assess effect of steroid on radiculopathy-related disability using Oswestry Disability Index calculation and Roland–Morris Disability Questionnaires.

As per the results in our study and on comparison to previous studies, most of previous studies have reached to the similar conclusions.

Benny *et al.*[24] showed that in patients with radicular pain that there is insufficient and conflicting evidence that either supports or refutes prognostic accuracy of hs-CRP in determining epidural steroid outcomes (two Class III studies). Chan Hong Park *et al.*[25] came to conclusion that there was no correlation between pre-treatment hsCRP and post-treatment VAS. Choi *et al.*[26] concluded there were no significant differences of inflammation markers (ESR and CRP) between responders and non-responders after CIES. Chan Hong *et al.*[27] found normal ESR levels in chronic back ache patients indicated that inflammatory processes were not occurring in low back pain patients.

However, post-TFESI, the patient showed improvement in pain relief. Pain assessment was done with the Roland–Morris Disability Questionnaire and Oswestry Disability Index at start of study mean ODI that was 25.94 and among Male 23.45 and 27.36 In Female. After TFESI, it was 22.34 at 2 weeks, 18.2 at 6 weeks, 14.4 at 12 weeks, and 21.01 at 6 months. On applying paired *t* test, improvement in score compare to pre-injection score is statistically significant at 6 weeks and 12 weeks.

Similarly, mean RMDQ score at start of study was 8.64. among men 8.81 and female 8.52. After TFESI, it was 6.94 at 2 weeks, 5.36 at 6 weeks 4 at 12 weeks, and 5.44 at end of study. On applying paired *t* test, difference with pre-injection is statistically significant at 6 weeks and 6 months.

Ghahreman *et al.*[28] reported favorable results from a prospective randomized controlled trial assessing the efficacy of transforaminal injection of steroid to local anesthetic, local anesthetic alone, normal saline alone, intramuscular injection of steroid, or normal saline on radicular pain secondary to lumbar disc herniation. Outcomes were assessed at 1 month and 12 months using Numeric Rating Scale, Roland–Morris, SF-36, and proportion of patients who underwent each treatment who obtained complete relief or at least 50% relief of pain for at least 1 month after treatment This outcome was statistically significant compared to the transforaminal normal saline, transforaminal local anesthetic, intramuscular normal saline, and intramuscular steroid groups. Robert *et al.* showed that there is fair evidence supporting TFESIs as superior to placebo for treating radicular symptoms.[29]

Mondal *et al.* concluded that transforaminal epidural steroid injection is an effective adjunct to usual conservative treatment protocol. It causes improvement not only in numerical rating scale of pain intensity measurements and Modified Oswestry Disability Index scores significantly but also improved walking pattern by changing pelvic angulations significantly.[30]

Some other studies have also demonstrated the efficacy of epidural steroid injections for the treatment of radiating pain in patients with lumbosacral disk herniation, leading to improvement in various rating scales.[29,32,33]

In our study, it was observed that there was no effect of TFESI over laboratory markers of inflammation ESR and CRP in disc radiculopathy patients, but TFESI found to be effective therapy for pain management in disc radiculopathy.

Our study had some limitations. Although ESR and CRP are markers of inflammation, these are relatively non-specific. Perhaps evaluation of more markers involved in disc inflammation such as IL-1, IL-6, and TNF-alpha may present more actual picture of effect of TFESI over disc inflammation and its response to steroid injection.

This study did not reveal significant fall in serum ESR and CRP level following transforaminal injection, but showed statistically significant clinical improvement assessed by ODI and RMDQ. This study shows significant improvement in OSI and RMDQ, post-transforaminal steroid injection. As per this study, TFSI is effective tool for non-surgical management of disc radiculopathy.

CONCLUSION

In this prospective study, conducted in Tertiary Hospital, with sample size of 30, all. All patients were having MRI diagnosed disc hernia with symptoms of radiculopathy. According to several studies cause of pain in disc herniation is local inflammation of nerves and compression of the nerves. This local inflammation leads to rise in certain markers of systemic inflammation. More easily measurable being serum ESR and CRP levels.

The study aimed at assessing effect of transforaminal steroid injection over improvement in symptoms of radiculopathy. Following conclusions were drawn from study – No effect of TFESI over ESR and CRP levels in Lumbar disc herniation and radiculopathy, However there was Improvement in functional outcome following TFESI as measured by the Roland–Morris disability questionnaire and Oswestry Disability Index.

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Original Article

Knowledge, Attitude, and Practices Regarding Coronavirus Disease 2019 Protocols among Doctor's Nurses, Technicians at District Hospital Vidisha – A Pre- and Post-Intervention Analysis

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ABSTRACT

Aim: The aim of the study was to conduct a pre- and post-intervention analysis of knowledge, attitude, and practices regarding coronavirus disease 2019 (COVID-19) protocols among doctor's nurses, technicians.

Materials and Methods: Study was carried on the doctors, staff nurse, technicians, and working in hospital. A scientifically designed questionnaire was distributed to the doctors, nurses, and technicians, they were explained about the questions and responses were marked.

Results: The results of questionnaire analysis before intervention session show that doctors, nurses, and technicians had least knowledge about the various COVID-19 protocols, that is, 10%, 7.5%, and 5%, respectively. In addition, knowledge about practices regarding COVID-19 protocols at institute level was 32.5%, 27.5%, and 30% in doctors, nurses, and technicians, respectively. Knowledge about fundamentals of COVID-19 was found good in doctors (64%), nurses (41%), and technicians (46%). The results of questionnaire analysis after intervention session show that doctors, nurses, and technicians scores improved significantly in all aspects of knowledge.

Conclusion: Knowledge regarding COVID-19 protocols plays a key role in prevention and spread of the disease. Proper intervention through training programs at regular time interval has great influence on various aspect of prevention and spread of the disease. Training programs not only increase knowledge and awareness among health-care professionals but also develops sense of responsibility, which reflects in their attitude and practices.

Key words: Analysis, Coronavirus disease 2019 protocols, Intervention, Knowledge, attitude, and practices

INTRODUCTION

India braces for the coronavirus disease 2019 (COVID-19) pandemic; healthcare workers (HCWs) on the frontlines are particularly vulnerable to this infection. With this mode of transmission, HCWs are among the highest risk of being infected. The highly contagious severe acute respiratory syndrome coronavirus 2 virus is an additional hazard for the healthcare system apart from the burden of extended work hours, physical and psychological stress, burnout, and fatigue.

HCWs of all levels and groups are involved in caring for patients with this highly transmittable pathogen. COVID-19 has posed serious occupational health risks to HCWs due to their frequent exposure to infected individuals. The literature suggests that lack of knowledge and misunderstandings among HCWs lead to delayed diagnosis, spread of disease, and poor infection control practice. Preventing intra-hospital transmission of this communicable disease is, therefore, a priority. Amidst the current pandemic, the WHO has issued several guidelines,

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and started online courses and training sessions to raise awareness and preparedness regarding prevention and control of COVID-19 among HCWs.

The objective of this study was to assess the awareness of COVID-19disease and its related infection control practices among health-care professionals in the Indian health-care scenario. This was a questionnaire-based survey adapted from current interim guidelines and information for health-care personnel provided by the US Centers for Disease Control and Prevention and WHO. Therefore, this study was undertaking, as knowledge, attitude, and practice survey is a suitable way to evaluate existing programs and to identify effective strategies for behavioral change in society.

MATERIALS AND METHODS

The study was carried on the doctors, staff nurses, technicians, and working in a 750 bedded hospital. A scientifically designed questionnaire was distributed to the doctors, nurses, and technicians in OT and Intensive Care Unit was explained about the questions and responses were marked. Cross-sectional surveys through the questionnaire and discussion were done to assess the knowledge and attitude; the team to assess the practices conducted observational surveys. After noting the responses to the questionnaire, the intervention was made by conducting interactive sessions with audio-visual aids to provide basic knowledge about COVID-19 protocols. After this intervention, a self-assessment test (SAT) was given followed by the session and finally SAT was reviewed.

The questionnaire consisted of questions assessing demographics; information source; knowledge, attitude, and practice toward COVID-19; and perceived barriers to infection control (see online supplementary material). Demographic characteristics included were gender, age, profession and experience, and one item regarding source of information about COVID-19.

The knowledge section had 14 items and each question was answered "yes," "no" or "I don't know." Correct answers scored 1 and incorrect answers scored 0. The attitude section had seven items, and responses were recorded on a five-point Likert scale (1, strongly agree; 2, agree; 3, undecided; 4, disagree; and 5, strongly disagree). The practice section had six items and each item was answered "yes" (1 point), "no" (0 points), or "sometimes" (0 points).

Seven items assessed the perception of HCWs regarding barriers to infection control. Responses were recorded on a five-point Likert scale (strongly agree, agree undecided, disagree, and strongly disagree). Responses are presented as frequencies and percentages.

Observation Chart

The two-tailed *P* value is less than 0.0001.

By conventional criteria, this difference is considered to be extremely statistically significant.

RESULTS

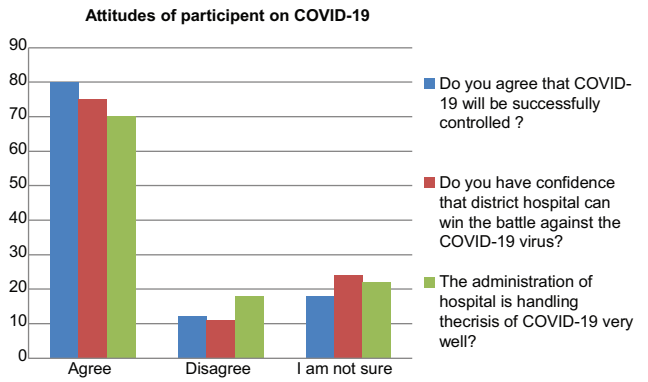
Study conducted with a total of 110 people including 34 doctors, 50 nurses and 26 technicians. The demographic characters in relation to age, gender, and education are shown in Tables 1 and 2. The results of questionnaire analysis before intervention session show that doctors, nurses and technicians had least knowledge about COVID-19 protocols, that is, 10%, 7.5%, and 5%, respectively, as shown in Table 3.

Furthermore, knowledge about practices regarding COVID-19 at institute level was 32.5%, 27.5%, and 30% in doctors, nurses, and technicians, respectively, knowledge about fundamentals of COVID-19 was found good in doctors (64%), nurses (41%), and technicians (46%). The results of questionnaire analysis after intervention session show that doctors, nurses and technicians scores improved significantly in all aspects of knowledge.

The questionnaire analysis of attitude before intervention shows that all the three groups of doctors, nurses, and technicians were in consensus that COVID-19 is new

Table 1: Distribution of groups

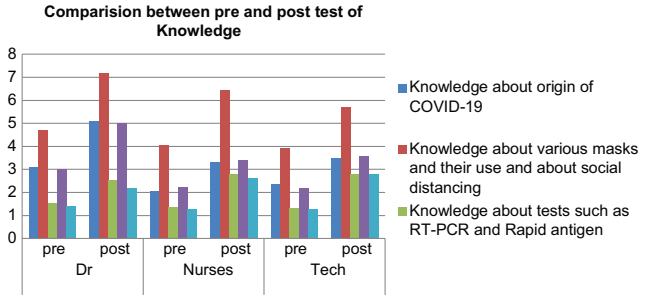
Category	College			Hospital		
	M	F	Total	M	F	Total
Doctors	14	8	22	9	3	12
Nurses	4	28	32	7	11	18
Technicians	17	3	20	5	1	6
Total	35	39	74	21	15	36



to them and they all irrespective of their educational background, need training. There was misconception in all three groups that COVID-19 is responsibility of institute mainly, and subjects of all three groups after training felt that they could create awareness and can deal with the disease better after they are briefed and trained. Majority in three groups, that is, doctors (25), nurses (37), and technicians (17) would like to get some more training on Bio Medical Waste COVID-19. Post-intervention analysis shows that the majority of subjects in all three groups agreed that COVID-19 is an important issue that should be dealt collectively by both individual and institute.

Table 2: Demographic characteristics

Variable	Doctors (34)	Nurses (50)	Technicians (26)
Age			
<25.	8	24	13
25–34	16	14	10
34–44	6	8	3
>45	4	4	-
Gender			
Male	23	11	22
Female	11	39	4
Education			
Primary	-	-	-
Secondary	-	-	-
Graduation	9	42	25
Postgraduation	25	8	1



The assessments of practices were mainly done by observing different tasks at defined locations. Observation was made for wearing masks, social distancing, wearing personal protective equipment (PPE) Kit properly, and proper doffing and donning.

Observation reports of practices before intervention session showed that nurses had best score rating of 80 in following COVID-19 protocols, whereas technicians and doctors scored 60 and 30, respectively, on a scale of 0–100. Scores for knowledge about various tests such as real-time polymerase chain reaction and rapid antigen were 20, 60, and 30 in doctor's nurses and technicians, respectively. Scoring about doffing and donning was 20, 50, and 50 in doctors nurses and technicians, respectively. Doctors performed poorly in the practice of donning and disposal of used PPE kit. After the intervention session observation of practice is done at 29 locations with total duration of 72.5 h. There was improvement in all three categories, that is, doctors nurses and technicians in relation to COVID-19 protocols. Doctors showed maximum improvement after the intervention session.

Statistical Analysis

Descriptive and inferential statistics were applied using SPSS Version 21 (IBM Corp.). Chi-squared test, independent sample *t*-test, and one-way analysis of variance were used to compare differences in knowledge, attitude, and practice of HCWs by demographic characteristics. Pearson's rank correlation test was used to identify any correlation between knowledge, attitude, and practice. A binary logistic regression analysis was applied to identify possible determinants of good knowledge and practice, with results expressed as odds ratio and 95% CI. $P < 0.05$ was considered to indicate significance in all tests. Reliability was calculated using SPSS Version 20 (IBM Corp., Armonk, NY, USA), and Cronbach's alpha was 0.77.

Table 3: Comparison between various pre-test and post-test values

Variables studied	Doctor (*n*=34)			Nurses (*n*=50)`			Technicians (*n*=26)		
Knowledge	**Pre-test mean**	**Post-test mean**	***P* value**	**Pre-test mean**	**Post-test mean**	***P* value**	**Pre-test mean**	**Post-test mean**	***P* value**
Knowledge about origin of coronavirus disease 2019	3.12	5.09	0.0001	2.04	3.32	0.0001	2.38	3.50	0.0001
Knowledge about various masks and their use and about social distancing	4.71	7.18	0.0001	4.06	6.46	0.0001	3.92	5.73	0.0001
Knowledge about tests such as real-time polymerase chain reaction and rapid antigen	1.53	2.56	0.0001	1.36	2.78	0.0001	1.31	2.81	0.0001
Knowledge about personal protective equipment Kit. How to do doffing and donning	3.01	5.02	0.0001	2.26	3.40	0.0001	2.2	3.6	0.0001
Knowledge about rules and regulation	1.4	2.2	0.0001	1.28	2.64	0.0001	1.28	2.78	0.0001

P value and statistical significance

DISCUSSION

A cross-sectional survey from Pakistan was done by Saqlain *et al.* regarding knowledge, attitude, practice, and perceived barriers among health-care professionals regarding COVID-19. It was a multi-centric cross-sectional survey-based study, which was conducted in March 2020 during a period of strict lockdown to implement social distancing to avoid the spread of COVID-19. A questionnaire was designed on Google forms, and a link was shared to WhatsApp groups of HCWs.[1]

Similar survey on COVID-19 awareness among health-care students and professionals in Mumbai metropolitan region was done by Modi *et al.* It was a questionnaire-based survey. This is the first Indian study that evaluates the awareness of COVID-19 among health-care students and professionals. In the midst of this crisis, the Indian health ministry has proposed to provisionally permit medical undergraduates of senior grades to treat COVID-19 patients. This move could help plug the shortage of health-care professionals and potentially provide care to a large number of people. Hence, students from various health-care professions were included in our study. This study showed that there is a strong need to implement periodic educational interventions and training programs on infection control practices for COVID-19 across all health-care professions. Conducting periodic webinars for educational intervention for all health-care students and professionals including non-clinical and administrative staff, paramedical, and nursing sub-groups could be a useful and safe tool to create more awareness.[2]

Zhou *et al*. did a cross-sectional survey regarding knowledge, attitude, and practice among HCWs in Henan, China. Huynh *et al.* did similar studies. Both the studies analyzed HCWs knowledge, practices, and attitudes regarding COVID-19. In addition to knowledge level, some risk factors including work experience and job category influenced HCWs' attitudes and practice concerning COVID-19. Measures must be taken to protect HCWs from risks linked to job category, work experience, working hours, educational attainment, and frontline HCWs.[3,4]

Roy *et al.* did study of knowledge, attitude, anxiety, and perceived mental health-care need in Indian population during COVID-19 pandemic. Novel COVID-19 originating from China has rapidly crossed borders, infecting people throughout the whole world. This phenomenon has led to a massive public reaction; the media has been reporting continuously across borders to keep all informed about the pandemic situation. All these things are creating a lot of concern for people leading to heightened levels of anxiety. Pandemics can lead to heightened levels of stress; anxiety is a common response to any stressful situation.[5]

There is moderate awareness related to transmission and symptoms of COVID-19 among educated population in India. There is adequate awareness among public regarding preventive measures for COVID-19 infection. There is a positive attitude of public toward social-distancing, avoiding party and travel and maintaining hygiene. People report anxiety, worries, and paranoia about acquiring infection and sleep disturbances during this pandemic. More the 80% people perceive mental healthcare need to deal with their issues during this COVID-19 pandemic.[6]

In various other studies, assessment of knowledge, attitudes, and perception of HCWs regarding COVID-19 was done and it was found that inadequate knowledge and incorrect attitudes among HCWs can directly influence practices and lead to delayed diagnosis, poor infection control practice, and spread of disease. A positive correlation between knowledge and attitude scores was detected. Unavailability of PPE, fear of transmitting the disease to their families, and social stigma were the most frequently reported reasons for increased risk perception. The overall knowledge level of HCWs was generally good especially among physicians. A positive attitude was detected among allied health professionals more than physicians. Risk perception was high among HCWs.[7,8]

Elhadi *et al.* did assessment of HCWs levels of preparedness and awareness regarding COVID-19 infection in low-resource settings. This was also similar to our study. A significant number of HCWs expressed low levels of awareness and preparedness regarding COVID-19. This raises a concern regarding the ability of the Libyan health-care system and its HCWs to combat COVID-19 infection. Despite these concerns, along with the poor local health-care infrastructure in Libya, HCWs continue to work during COVID-19, risking their lives to save their patients. Meanwhile, no official courses or training programs are available, and HCWs have to purchase PPE themselves, as they are not provide by the hospitals in adequate amounts.[9,10]

This study attempted to assess the knowledge, attitude, anxiety experience, and perceived mental healthcare need among adult Indian population during the COVID-19 pandemic. An online survey was conduct using a semi-structured questionnaire using a non-probability snowball sampling technique. The responders had a moderate level of knowledge about the COVID-19 infection and adequate knowledge about its preventive aspects. The attitude toward COVID-19 showed peoples' willingness to follow government guidelines on quarantine and social distancing. The anxiety levels identified in the study were high. There is a need to intensify the awareness and address the mental health issues of people during this COVID-19 pandemic.

Our study provides considerable insights into the necessity of immediate and determined efforts focused on training programs and providing an adequate supply of PPE to alleviate these challenges during the COVID-19 pandemic.

CONCLUSION

Our study has illuminated the current level of knowledge and awareness of COVID-19 among doctors, technicians, and nurses, with special consideration for those working in departments responsible for caring for COVID-19 patients. We focused on HCWs who come into direct contact with COVID-19 patients, and are thus expected to have adequate knowledge and preparedness. By contrast, other studies have focused on more general populations of HCWs. This study provides an overview of HCWs preparedness regarding the current pandemic. The respondents had a lower level of preparedness, which highlights the importance of education and training programs for HCWs, to control and prevent infection from COVID-19. However, the absence of an organized and effective governmental plan, along with a poor health-care infrastructure, renders developing countries like India vulnerable. Moreover, educational initiatives, along with more tangible forms of support, such as the provision of PPE, should be carried out to help developing countries improve their abilities to control and prevent COVID-19 infection.

What this Study Add to Existing Knowledge

The situation demanded urgent development of strategies to prevent infection among high-risk populations including pre-exposure and post-exposure prophylaxis. This study showed that there is a strong need to implement periodic educational interventions and training programs on infection control practices for COVID-19 across all health-care professions. Conducting periodic webinars for educational intervention for all health-care students and professionals including non-clinical and administrative staff, paramedical, and nursing sub-groups could be a useful and safe tool to create more awareness.

Limitation

Sampling for the study was conducted through a convenience, sample through the networks of the researchers and disseminated through different social media platforms (WhatsApp, Facebook, Twitter, etc.). As a result, there is a possibility of *bias* as underprivileged populations may not have been able to participate in the study. In addition, when compared to current population statistics in hospital, the sample of the study was over-representative of women, people below the age of 50, and those employed in the public sector. Therefore, there are limitations to the representativeness of the findings. A more systematic, inclusive sampling method was warranted to improve representativeness and generalizability of the findings. A further limitation of the present study is the possibility of participants giving socially desirable responses. As this study used self-reported data, it is possible that participants will have answered attitude and practice questions positively based on what they perceive to be expected of them.

CONTRIBUTION BY DIFFERENT AUTHORS

- First, author corresponding author concept and motivator to data collection.
- Second author: Data assessment and treatment.
- Third author: Data collection, compilation, and statistical analysis.

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Original Article

A Prospective Study on Hearing Assessment of High-risk Neonates in South Tamil Nadu Population

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Abstract

Background: Hearing loss is one of the major abnormalities present at birth. Delayed recognition of hearing impairment has a significant impact on speech development. Universal hearing screening is the ideal strategy. However, in resource-poor country like ours, there should be screening of high-risk neonates at least.

Methods: This is a prospective study done in neonates with risk factors for hearing impairment (*n* = 100). Initial screening was done by otoacoustic emissions (OAE). Hearing impairment was confirmed with automated auditory brainstem response (AABR). If OAE could not be done, neonates were directly subjected to AABR.

Results: One hundred babies were enrolled in the study and 99 neonates were subjected to OAE testing and one baby was directly subjected to AABR; 2 babies who failed in the initial screening by OAE were also subjected to AABR. All the three babies had abnormal AABR.

Conclusion: The incidence of hearing impairment among high-risk neonates in our study is 3.06%. Hearing impairment is not identified in very low birth weight, meningitis, hyperbilirubinemia, and ventilated babies in our study.

Key words: Automated auditory brainstem response, Hearing loss, High-risk neonates, Newborn screening, Otoacoustic emissions

INTRODUCTION

Hearing loss is one of the major abnormalities present at birth. About one in every thousand children is born profoundly deaf and 4 times as many are born with moderate or severe bilateral hearing loss.[1] Infants in neonatal intensive care units (NICUs) are 10–20 times more likely to have significant hearing loss than the healthy population. In India, the incidence of hearing loss is 1 to 6/1000 live births, with an average of 4/1000 live births.[2] The first 3 years of life are most important for language and speech development. Consequently, for many infants and young children, much of the crucial period for language and speech development may be lost if hearing impairment is not diagnosed in infancy.[3]

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In 1993, a consensus statement from the national institute of health recommended universal newborn hearing screening by the age of 3 months and also stated that otoacoustic emissions (OAE) might be the technology used for screening.[4] OAE was first described by Kemp in 1978. The sensitivity of OAE is 80–98% and that of AABR is 84–90%. Both have specificity of >90%.

The early hearing detection and intervention program of the center for disease control recommend the "1-3-6" plan. This means all children should be screened by 1 month, those children who do not pass the screening test must receive diagnostic audiological testing by 3 months, and children with confirmed hearing loss should be enrolled in an appropriate intervention program by 6 months. This screening will lead to early identification of hearing loss and aid in initiating treatment by the age of 6 months.[5]

METHODS

This is a prospective study on hearing assessment of high-risk newborns, conducted in the NICU of the institute

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of child health and research center, Government Rajaji Hospital, Madurai, over a period of 12 months from October 2018 to September 2019. One hundred neonates with risk factors for hearing loss were recruited for this study. Informed consent from parents was recorded, and approval from the Institutional Ethical Committee was obtained. Neonates with the following risk factors were enrolled for the study [Table 1].[3,6,7]

1. Birth weight <1500 g.
2. Apgar scores of 0–3 at 1 min.
3. Hyperbilirubinemia requiring exchange transfusion.
4. Ototoxic medications – Aminoglycosides and loop diuretics used for >5 days.
5. Mechanical ventilation lasting 5 days or longer.
6. Bacterial meningitis.
7. In utero infections by TORCH group of organisms.
8. Craniofacial anomalies, including those with morphological abnormalities of the pinna and ear canal.
9. Family history of permanent childhood sensorineural hearing loss.

Neonates with the above risk factors were subjected to hearing assessment by OAE after 72 h or at the time of discharge. If the neonate passes the first screening, then the hearing is presumed to be normal. If the neonate fails in the first screening, then the second screening by OAE will be done after 1 month. If the second screening is normal, then the hearing is presumed to be normal, and the baby is advised follow-up every 6 months up to 3 years. If the second screening is abnormal, then the baby is subjected to automated auditory brainstem response (AABR). If OAE could not be done due to anatomical defects of the ear, neonates would be subjected directly to AABR. Based on the results of AABR, early intervention is done.

Table 1: Risk factors

Risk factor	Male	Female	Percentage
Severe birth asphyxia	28	24	52
VLBW	10	10	20
Meningitis	06	04	10
Hyperbilirubinemia	04	04	08
Ototoxic drugs	03	01	04
Ventilated babies	02	01	03
Craniofacial anomaly	02	00	02
TORCH infection	00	01	01

VLBW: Very low birth weight

OBSERVATION, ANALYSIS, AND RESULTS

One hundred babies were enrolled in the study, and 99 neonates were subjected to OAE testing. Sixteen (16.2%) babies failed after the first screening. They include seven babies with birth asphyxia, four babies with very low birth weight, three babies who were treated for meningitis, and two babies for whom exchange transfusion was done for hyperbilirubinemia. One baby with severe birth asphyxia and one baby with hyperbilirubinemia dropped out after the first screening. Twelve out of 14 (85.7%) babies passed the second screening by OAE. Two out of 14 babies (14.3%) failed after the second screening by OAE and were subjected to AABR. One baby was directly subjected to AABR as OAE could not be done due to bilateral atresia of the external auditory canal. Totally three babies were subjected to AABR and all three babies had abnormal AABR [Table 2].

Three (3.06%) babies were diagnosed to have hearing impairment out of 98 high-risk babies (mean = 0.03, S.D = 0.17). To compare the mean of this study with the standard incidence rate, *t*-test has been used. The confidence interval (90%) for the mean is 0.00098–0.05902. The incidence rate is higher in this study as compared to the standard incidence rate but not significant statistically ($P = 0.13$).

Of the 52 babies with birth asphyxia, 45 babies passed the first screening. Two babies had impairment in one ear and five babies had impairment in both ears. One baby with impairment in both ears dropped out. The other six babies were subjected to second screening by OAE after 1 month. Of these six babies, four babies passed the second

Table 2: Results of screening

Risk factor	First screening by OAE		Dropouts	Second Screening by OAE		AABR Done	Abnormal AABR
	Pass	fail		Pass	Fail		
Severe birth asphyxia (52)	45	7	1	4	2	2	2
VLBW (20)	16	4	0	4	0	0	0
Meningitis (10)	7	3	0	3	0	0	0
Hyperbilirubinemia (8)	6	2	1	1	0	0	0
Ototoxic drugs (4)	4	0	0	0	0	0	0
Ventilated babies (3)	3	0	0	0	0	0	0
Craniofacial anomaly (2)	1	0	0	0	0	1	1
TORCH infection (1)	1	0	0	0	0	0	0
Total	83	16	2	12	2	3	3

OAE: Otoacoustic emissions, AABR: Automated auditory brainstem response, VLBW: Very low birth weight

screening and two babies failed the second screening test. These two babies were subjected to AABR.

Of the 20 babies with very low birth weight, 16 babies passed the first screening. Three babies had impairment in one ear and one baby had impairment in both ears. All these four babies were subjected to second screening by OAE after 1 month. All the four babies who failed in the first screening passed when subjected to a second screening by OAE after 1 month and had normal hearing.

Of the ten babies with meningitis, seven babies passed the first screening. Two babies had impairment in one ear, and one baby had impairment in both ears. All these three babies were subjected to second screening by OAE after 1 month. All the three babies who failed in the first screening passed when subjected to second screening by OAE after 1 month.

Of the eight babies for whom exchange transfusion was done for hyperbilirubinemia, six babies passed the first screening. One baby had impairment in one ear and one baby had impairment in both ears. Baby which failed in one ear dropped out. Another baby was subjected to second screening by OAE after 1 month and the baby passed the second screening.

Four babies who received ototoxic drugs were screened and all four babies passed the first screening.

Of the three babies who were ventilated for 5 days, all three babies passed the first screening by OAE.

Two babies had craniofacial malformation. One baby was directly subjected to AABR because OAE could not be done due to bilateral atresia of the auditory canal. The another baby passed the first screening by OAE.

One baby diagnosed with congenital cytomegalovirus (CMV) infection was screened and the baby passed the first screening by OAE.

Two babies who failed in both the screening tests were subjected to AABR and one baby was directly subjected to AABR as OAE could not be done in that baby. AABR was abnormal in all three babies. Of these three babies, two neonates had severe birth asphyxia and one baby had craniofacial malformation. Both the babies have been referred to otorhinolaryngology department for further management [Table 3].

Table 3: AABR for failed second screening test

AABR (*n*=3)	Results
Normal hearing	0
Hearing loss in one ear	1
Hearing loss in both ears	2
Total babies with hearing loss	3

AABR: Automated auditory brainstem response

Table 4: Final outcome of babies with risk factors

Risk factor	Total cases	Normal hearing (%)	Hearing impairment (%)
Severe birth asphyxia	51	49 (96.1)	2 (3.9)
VLBW	20	20 (100)	0
Meningitis	10	10 (100)	0
Hyperbilirubinemia	07	07 (100)	0
Ototoxic drugs	04	04 (100)	0
Ventilated babies	03	03 (100)	0
Craniofacial anomaly	02	01 (50)	1 (50)
Stigmata of TORCH	01	01 (100)	0
Total	98	95 (96.94)	3 (3.06)

VLBW: Very low birth weight

Table 5: Final outcome of screened infants

Outcome	Number of cases (%)
Normal hearing	95 (96.94)
Hearing impairment	03 (3.06)

DISCUSSION

Ideally, all newborns should be screened for hearing impairment before discharge from the birth hospital [Table 4]. However, in developing country like ours, with limited resources, this is not always feasible. Hence, newborns with risk factors for hearing loss should at least be screened. OAE is the technology to be used for screening and AABR for confirmation of hearing impairment.

Fifty-two babies with severe birth asphyxia were screened by OAE, and two babies with birth asphyxia had hearing impairment at the end of the second screening which was confirmed with AABR. A study by Nagapoornima *et al.*[6] who screened 51 babies with severe birth asphyxia and identified hearing impairment in 1 baby. Ohl *et al.*[8] screened 12 babies with severe birth asphyxia and identified four babies with hearing impairment which is much higher than our study.

Twenty neonates who were very low birth weight were by screened by OAE. All the babies passed the hearing screening by OAE. A study by Ohl *et al.*[8] also showed that very low birth weight is not a risk factor for hearing impairment as in our study, in which babies with very low birth weight (VLBW) had normal hearing. A study by Finckh-Kramer *et al.*[9] and Hess *et al.*[10] also concluded that VLBW was not a predictor of hearing impairment as in our study.

Ten babies who were treated for meningitis were by screened by OAE. All the babies passed the hearing screening by OAE. Nagapoornima *et al.*[6] screened

14 babies with meningitis, but none had hearing impairment as in our study [Table 5].

Eight babies who underwent exchange transfusion for hyperbilirubinemia were by screened by OAE. Two babies failed the first screening by OAE. One baby dropped out after the first screening. The another baby had impairment in the left ear and passed when subjected to second screening by OAE. Nagapoornima *et al.*[6] screened 38 babies with severe hyperbilirubinemia requiring exchange transfusion, but none had hearing impairment as in our study.

Four babies who received ototoxic drugs for septicemia were screened by OAE and all four babies passed the screening test. Finckh-Kramer *et al.*[9] concluded that aminoglycosides are not an important risk factor. Similar results were obtained by Hess *et al.*[10] and our study also showed aminoglycosides are not a risk factor for hearing impairment.

Three babies who were ventilated for birth asphyxia and sepsis were screened, and all three passed the first screening by OAE. MohdKhairi *et al.*[11] conducted two-stage hearing assessment in 401 at-risk neonates and concluded that mechanical ventilation of more than 5 days was not an independent risk factor for hearing impairment.

Two babies with craniofacial malformation were included in our study. One baby passed the first screening by OAE. Another baby was directly subjected to AABR as the baby had bilateral atresia of the external auditory canal and the baby had abnormal AABR. Nagapoornima *et al.*[6] screened 24 babies with craniofacial malformation, but none had hearing impairment in contrast to our study, in which 1 of the 2 babies with craniofacial malformation had hearing impairment.

One baby was diagnosed with congenital CMV infection and passed the screening by OAE. Nagapoornima *et al.*[6] screened six babies with TORCH infection, but none had hearing impairment as in our study.

Out of 16 babies who failed after the first screening, two dropped out. Of the remaining 14 babies, 12 babies passed when subjected to second screening. Finally, two babies failed after second screening. These two babies along with the baby who had craniofacial malformation were subjected to AABR and all three babies had abnormal AABR.

Hence, in our study of high-risk screening, three babies had hearing impairment (3.06%) out of 98 and it is higher than the incidence of study by Nagapoornima *et al.* who identified 3 out of 279 high-risk babies (1.07%). Ohl *et al.*[8] screened 1461at risk babies among whom 4.55% were diagnosed as deaf which is higher than our study. The incidence is higher in our study probably due to smaller sample size.

CONCLUSION

Overall incidence of hearing impairment among high-risk neonates is 3.06%. About 3.9% of babies with birth asphyxia were diagnosed to have hearing impairment which is quite high and 1 out of 2 (50%) of babies with craniofacial malformation had hearing impairment. Hearing impairment is not identified in VLBW, meningitis, hyperbilirubinemia, and ventilated babies in our study.

Limitations

Risk factors could not be compared as the number in each group showed variation.

All high-risk babies require hearing assessment every 6 months up to 3 years which could not be done in our study.

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Original Article

Vertical Fracture Resistance of Endodontically Retreated Teeth Using Two Instrumentation Systems

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Abstract

Introduction: Vertical root fractures are the most challenging complication associated with endodontically treated teeth. Different nickel-titanium (NiTi) instrument designs are associated with different levels of stress and resistance of roots to fractures.

Purpose: This study was designed to evaluate the fracture resistance of retreated roots using two different rotary retreatment systems.

Materials and Methods: Sixty freshly extracted human mandibular premolar with single, straight roots were randomly divided into four groups of fifteen specimens each. Samples of negative control were left untreated. Samples of positive control were cleaned and shaped with ProTaper files up to F_3. Obturation was done using gutta-percha and AH Plus sealer (Dentsply Detrey, Konstanz, Germany). For the samples of experimental groups three and four, removal of gutta-percha was performed using ProTaper Universal (Dentsply Maillefer, Ballaigues, Switzerland) and Mtwo (Sweden and Martina, Padova, Italy) rotary retreatment systems. The specimens were then embedded in a self-curing polymethyl methacrylate resin, and the force required to cause vertical root fracture was measured using a universal testing device. The force of fracture of the roots was recorded, and the results in the various groups were compared. Statistical analysis was accomplished by one-way analysis of variance and a *post hoc* Turkeys tests.

Results: There were statistically significant differences between the control groups and experimental groups ($P < 0.05$). However, there were no significant differences among the experimental group.

Conclusion: Type of rotary files used for retreatment does not significantly alter the fracture resistance of the tooth.

Key words: Endodontically retreated tooth, Fracture resistance, Retreatment files

INTRODUCTION

Residual necrotic tissue or bacteria existing in an obturated canal can be responsible for recurrent periapical inflammation and pain.[1] Thus, the main objective of nonsurgical retreatment is to regain access to the apical foramen and eliminate persistent organisms.[2] Efficient removal of the existing root canal filling material is essential for optimal non-surgical retreatment. The techniques applied to remove gutta-percha are varied and include the use of hand or rotary instruments, with or without heat, solvents, and/or ultrasound.[3] However, manual removal of gutta-percha using is time-consuming, especially in well-condensed canals. Thus, the use of contemporary rotary nickel-titanium (NiTi) instruments is more efficient and less fatiguing to the patient and operator.

Vertical root fractures (VRF) are the most challenging complication associated with endodontically treated teeth.[4] True vertical root fracture is defined as a longitudinal fracture confined to the root that usually initiates on the internal canal wall and extends outward

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onto the root surface.[5] Bender and Freedland have suggested that the highest incidence of vertical root fracture occurs in endodontically treated teeth.[6] Aggressive instrumentation of the root canal leads to loss of dentin, which may structurally weaken the tooth. Retreatment procedures might cause more damage to the root canal wall and weaken the root canal with further biomechanical preparation.[7] Furthermore, the alterations in the mechanical features of dentin, such as low plasticity due to dehydration, decreased strength, and toughness due to microbe-induced degradation or modification of collagen, predisposes endodontically treated teeth to fracture.[8]

The literature contains numerous studies about the effect of various nickel-titanium rotary files on root dentin and fracture formation. Different NiTi instrument designs are associated with different levels of stress and resistance of roots to fractures. However, studies on Mtwo retreatment systems and their effect on the fracture resistance of roots are few. Thus, the main aim of this *in vitro* study was to compare the fracture resistance of endodontically retreated teeth instrumented using two different rotary retreatment file systems, namely, ProTaper R and Mtwo R.

MATERIALS AND METHODS

A total of 60 extracted mandibular premolars with fully formed apices were used in this study. The teeth were decoronated using a diamond disk at the cementoenamel junction to obtain standard root lengths of 14 mm. They were then divided into four groups with 15 specimens each.

Group 1 (negative control) – Intact teeth.

Group 2 (positive control) – Teeth that underwent endodontic treatment. The working length of the canal was obtained by subtracting 1 mm of a #10 K-file inserted until the tip was visible at the apical foramen. Canal shaping was done using ProTaper Universal NiTi rotary files following the manufacturer's instructions in the sequence of S_x, S_1, S_2, F_1, F_2, and F_3 to obtain a final apical size of 0.30 mm. The canals were irrigated with 2 ml of 2.5% sodium hypochlorite during instrumentation. Seventeen percent ethylenediaminetetraacetic acid irrigant was used for 1 min after completion of instrumentation to remove the smear layer. A final rinse was done with 10 ml 2.5% sodium hypochlorite followed with saline. Canals were dried with paper points. A #30; 6% master cone was selected and canals were then obturated using single cone technique and AH plus sealer (Dentsply DeTrey; Germany). Excess gutta-percha was removed to 1 mm below the canal orifice and condensed. The canal orifice was then sealed using, Cavit and the teeth stored at 37°C in 100% humidity for 2 weeks. Specimens for the experimental groups were retreated 48 h after endodontic treatment to ensure complete sealer setting.

Group 3 – Retreatment was done using ProTaper Universal NiTi rotary retreatment instruments (Dentsply Maillefer, Ballaigues, Switzerland) at 300 rpm and 3 N/cm torque. The retreatment files were used in the recommended sequence; D1 file (tip size 30, 0.09 taper) for removal of root filling in the coronal third, followed by D2 file (size 25, 0.08 taper) for the middle-third, and finally, D3 file (size 20, 0.07 taper) for gutta-percha removal to working length. Root canal refinement was then accomplished using the F_2, F_3, and F_4 ProTaper Universal rotary.

Instruments. The instruments were used in a gentle brushing action at a speed of 300 rpm with sodium hypochlorite irrigation during instrumentation.

Group 4 – Retreatment was done using Mtwo retreatment files. The root canal obturating material was gradually removed first using Mtwo R_2 (5% taper, tip size 25) and Mtwo R_1 (5% taper, tip size 15) files, respectively, until slight resistance was encountered. These two instruments were used with circumferential filing movements and without downward pressure. After the working length was reached, conventional Mtwo rotary instruments were used in a circumferential filing motion in the sequence of Mtwo 6% taper #20; Mtwo 6% taper #25, and Mtwo 5% taper # 30 with copious irrigation with sodium hypochlorite.

All specimens in Group 3 and Group 4 received a final rinse similar to the positive control and dried. A #30 6% master cone was placed to the appropriate working length and confirmed with a radiograph. Obturation was completed using the gutta-percha master cone and AH plus sealer. The excess gutta-percha was seared off and condensed with a plugger 1mm below the orifice and the orifice sealed with Cavit. The teeth were stored at 37°C in 100% humidity for 2 weeks.

Mounting of Specimens for Mechanical Testing

The roots were coated with 0.3 mm layer of polyvinylsiloxane to simulate the periodontal ligament. Each teeth were mounted individually on a custom made acrylic blocks such that the apical root ends were embedded to a depth of 3 mm and was allowed to polymerize for 1 h. This was in accordance with the model proposed by Apicella *et al.*[8] Each acrylic block was mounted on the universal testing machine with the roots aligned vertically. A circular stainless steel rod

of 3 mm diameter and 45° bevel tip was fixed to the upper stage of the Instron universal testing machine. The rod was centered over the access opening. Vertical compressive force was applied at a crosshead speed of 0.5 mm/min. In this study, "fracture" was defined as the point at which a sharp and instantaneous drop was observed. For most specimens, an audible crack was also heard. The test was terminated at this point and the force applied was recorded and measured in Newtons as the force needed to fracture the tooth. [Figure 1]. The mode of application of the vertical loading force required to fracture the root specimens was similar to the technique proposed by Sedgley and Messer to test the brittleness of endodontically treated teeth.[9]

Statistical Analysis

Mean (±standard deviation) was calculated for each group. The inter groups comparison was done using one-way analysis of variance, and a multiple comparison test was performed using Turkey *post hoc* test (SPSS software version 20, SPSS (Inc., Chicago, IL).

RESULTS

The mean fracture load required for Group 1 (negative control) was 303.46 ± 80.25 N, Group 2 (positive control) 278.58 ± 66.08 N, Group 3 (ProTaper R) 143.55 ± 70.78, and Group 4 (MTwo R) was 151.25 ± 63.4.9 [Table 1].

Table 1: Means and standard deviations (SD) of fracture resistance of the groups

Groups (*n*=15)	Mean (N)	SD
Group 1 – Unprepared tooth [negative control]	303.64	80.25
Group 2 – Root canal treated with Protaper Universal NiTi rotary files	278.58	66.08
Group 3 – Retreated with ProTaper Universal NiTi rotary retreatment\files	143.55	70.78
Group 4 – Retreated with Mtwo rotary retreatment files	151.25	63.45

Figure 1: Fracture resistance test of specimens using universal testing machine

All the specimens exhibited fracture. However, it was observed that the fracture resistance was significantly reduced after primary endodontic treatment in comparison with the negative control. Fracture resistance was further reduced after retreatment.

There was no statistically significant difference in the fracture resistance between MTwo and ProTaper-retreatment files [Figure 2].

DISCUSSION

Endodontic success is related to the appropriate execution of the different treatment phases. During root canal instrumentation, the removal of dentin is necessary to promote cleaning and disinfection, as well as to prepare the root canal system to receive the obturating material. It is generally accepted that this unavoidable loss of dentin may weaken the root and create an increased risk of fracture.

The result of this study showed a significant reduction in the fracture resistance after primary endodontic treatment. Vertical root fracture is a sequel of gradual propagation of microcracks in the tooth. Kim *et al.*[10] reported that there is a relationship between the design of the Ni-Ti instruments and the incidence of VRF. ProTaper Universal rotary files (PTU; Dentsply Maillefer, Ballaigues, Switzerland) facilitate active cutting motion and remove relatively more dentin coronally compared with other systems. After canal shaping, a 30% reduction in vertical fracture resistance can occur.[11] During canal instrumentation with NiTi rotary files, momentary stresses are concentrated in dentin due to contact and friction between the instrument and canal walls. This causes cracks, which have been observed and reported at various levels.

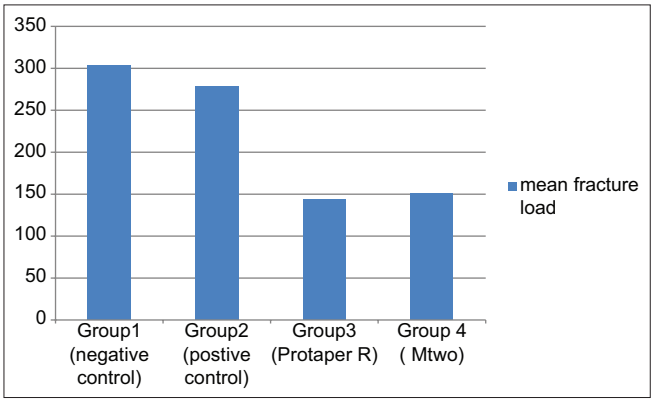

Figure 2: Bar graph showing the mean fracture load in four groups

The persistence of bacterial colonies within the complexity of the root canal system leads to apical pathology in endodontically treated teeth. Such circumstances advocate non-surgical retreatment by employing techniques for removal of obturating material followed by sufficient cleaning and reshaping procedures to provide adequate disinfection.

The results of our study, which shows that the fracture resistance in all retreatment groups was lesser than un retreated groups. This result is supported by Shemesh *et al*.[12] who found that the retreatment groups had more defects than the unretreated groups. Using finite-element analysis, Ricks-Williamson *et al.* found the magnitude of generated radicular stresses to be directly correlated with the simulated canal diameters. During retreatment or after long-term functional stresses such as chewing, craze lines occur in 4–16% and these may develop into fractures.[13] Wilcox *et al.* found that root surface craze lines formed on roots in areas of greater percentages of dentin removal. Hence, during the re-treatment procedures, care should be exercised to prevent excessive loss of dentin that may occur from aggressive re- instrumentation of root, which substantially weakens the structural integrity of the tooth making it more susceptible to fracture.[14]

ProTaper, universal retreatment file, not only cut gutta-percha but also the superficial layer of dentin during root filling removal. The instrument is designed to drive the debris coronally while in rotary motion.[11] The Mtwo R files have an S-shaped cross-section, an increasing pitch length in the apical-coronal direction and characterized by a positive rake angle with two cutting edges, which are claimed to improve cutting efficiency. It has a cutting tip to allow the instrument to progress easily into the filling material. Unlike other NiTi instruments, the Mtwo rotary instruments do not require a crown-down instrumentation sequence. Mtwo retreatment files are R2 (5% tip size 25) R1 (5% tip size 15) with uniform taper.

There was no statistically significant difference among the retreated groups in this study. Zandbiglari *et al*.[15] demonstrated that fracture resistance of instrumented roots is significantly lower when canals are prepared with instruments with an increasing taper. However, Sathorn *et al.* showed that the dentin thickness was not the only determining factor. Curvature of the external proximal root surface, canal size, and shape all interact to influence susceptibility and the pattern of fracture as well.[16] Pitts *et al.* demonstrated that no significant correlation exists between fracture load and size of the root, width of the canal walls after instrumentation, and taper of the root or of the canal.[17] Root canal filling material is removed during re-instrumentation. However, at the same time, an amount of extra dentine is removed from the root structure. This may explain the difference between the experimental and control groups in this study. In addition, during re-instrumentation, the coronal taper increases and the coronal third of root stresses tend to increase for masticatory loading.

CONCLUSION

Properly performed endodontic treatment is the cornerstone of restorative and reconstructive dentistry. After retreatment, the fracture resistance can be significantly reduced. Hence, conservative re-treatment with judicious use of the instrumentation systems and preservation of tooth structure is important.

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Original Article

Urine Protein Creatinine Ratio as a Predictor of Disease Severity in Dengue Fever in a Tertiary Hospital in South Tamil Nadu

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Abstract

Introduction: Dengue mainly affects the pediatric age group and causes high mortality initiating management after the occurrence of shock or hemorrhage results in a higher mortality rate. The need for the hour is a simple and valuable clinical or biochemical tool to predict the severity in dengue patients. This study was undertaken to establish urine spot protein creatinine ratio as an early predictor of disease severity.

Materials and Methods: This is a hospital-based prospective study with a sample size of eighty cases that were categorized based on the severity of the WHO guidelines. Urine spot protein creatinine ratio was done daily since the day of admission and the values were compared with the clinical parameters and blood indices.

Results and Conclusions: Out of 80 dengue cases, 28 (35%) belonged to Category A, 32 (40%) belonged to Category B, and 20 (25%) belonged to Category C. Urinary protein creatinine ratio was significantly raised in severe cases of dengue (Category C). Increased level of peak urine creatinine ratio has a positive correlation with clinical severity, severe thrombocytopenia, rising hematocrit, and low blood pressure levels. Urine spot protein creatinine ratio can be an accurate marker in predicting disease severity, bleeding manifestations, need for inotropes, and adverse outcome in children with dengue fever.

Key words: Dengue fever, Dengue hemorrhagic fever, Dengue shock syndrome, Severe dengue, Urine spot protein creatinine ratio

INTRODUCTION

Dengue is one of the most important emerging viral disease of humans in the world afflicting humanity in terms of morbidity and mortality. At present, the disease is endemic in all continents except Europe.[1] Dengue mainly affects the pediatric age group and mortality due to dengue is due to capillary permeability, abnormalities of hemostasis, and in severe cases, dengue shock syndrome.[2]

Initiating management after the occurrence of shock or hemorrhage results in a higher mortality rate. The risk factors for the development of severe disease are poorly characterized, and consequently, uncomplicated cases are frequently hospitalized for observation during the critical phase for capillary leakage syndrome, thereby increasing the financial cost to patients. Therefore, improvements in early diagnosis and risk prediction for severe disease are urgently needed, particularly with respect to the identification of simple clinical and/or laboratory indicators that are practical and affordable for use in resource-poor countries. This would enable appropriate and early intervention. Ideally, the test should be cheap, fast, easy to perform, highly sensitive, and specific. This study was undertaken to establish urine spot protein creatinine ratio as an early predictor of disease severity.

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Aim

To assess, whether urine protein creatinine ratio could be used as a predictor of disease severity in children diagnosed with dengue.

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MATERIALS AND METHODS

This study was a prospective study done over a period of 1 year between May 2018 and April 2019 in the Institute of Paediatrics, Government Rajaji Hospital, Madurai. An informed oral consent was obtained from the parent/guardian of the child during enrolment into the study. The study was approved by the Institute Ethical Committee.

Patients diagnosed as dengue using nonstructural protein 1 (NS1) antigen or IgM antibody depending on the day of admission were followed up from the day of admission during the acute period and subsequent days. Demographic and epidemiological data were collected at enrolment. Detailed clinical examination, biochemical analysis, and imaging studies were done as per standard treatment protocol.

The patients were categorized into three categories based on the WHO guidelines. Symptoms and signs were recorded each day. Complete blood count and spot urine collection were done every day. Urine protein is detected and quantified by pyrogallol red method and creatinine by modified Jaffes method.

In children with age <2 years, a urine protein creatinine ratio (UPCR) value of <0.5 and in subjects with age more than 2 years a value <0.2 was considered as normal. Values lower than this range were considered insignificant.

Peak value of urine protein creatinine ratio in patient with dengue with no warning signs, dengue with warning signs, and severe dengue was compared.

Statistical Analysis

Data obtained were analyzed using SPSS software – version 19. Outcomes were tested using the Chi-square test. $P < 0.05$ was considered significant.

RESULTS AND ANALYSIS

A total of 80 dengue cases were enrolled in the study and were grouped into three categories based on the WHO guidelines. Of the total 80 cases, 28 cases belonged to Category A, 32 belonged to Category B, and 20 cases belonged to Category C.

Majority of the children were male, but gender distribution has no correlation with dengue severity. Majority of cases are admitted during the 4th or 5th day of illness in all categories [Figure 1].

Of the total 80 participants, 25% (n = 5) of cases with severe dengue (category 3) had very high protein creatinine ratio (PCR) on admission which is found to be statistically significant. ($P < 0.001$) [Table 1].

Majority of cases had peak UPCR on day 5 which is the critical phase [Figure 2].

In all the six cases, for whom the UPCR value was more than 1.5, thrombocytopenia (platelet below 50000/cu.mm) was seen, which was statistically significant [Table 2].

In terms of bleeding manifestations, patients presented with bleeding had high UPCR values, which were statistically significant ($P = 0.006$) [Table 3].

The presence of third space fluid was compared to the peak UPCR, which was found to be statistically not significant [Table 4]. Out of 13 patients who had hypotension during the hospital stay ten cases had peak

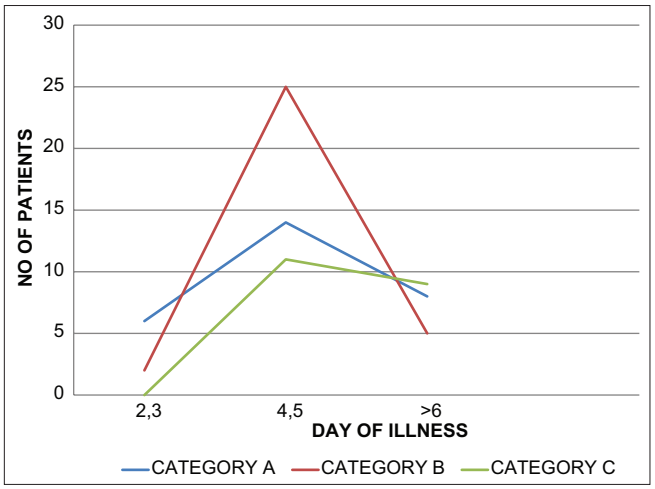

Figure 1: Day of illness on admission versus severity categories

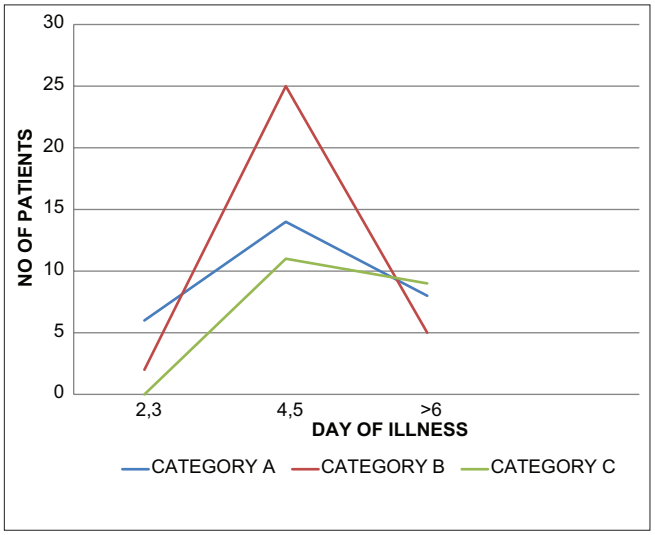

Figure 2: Peak UPCR versus Day of illness

Table 1: Spot PCR on day of admission

Spot PCR on admission	Category A	Category B	Category C	Total
<0.5	16	20	3	39
0.5–1.0	10	10	11	31
1.0–1.5	2	2	1	5
>1.5	0	0	5	5
Total	28	32	20	80
Chi-square		23.298		
p value		<0.001 Significant		

PCR: Protein creatinine ratio

Table 2:Platelet count versus peak urine protein creatinine ratio

PLT on peak spot PCR	Peak value				Total
	<0.5	0.5–1.0	1.0–1.5	>1.5	
<50000	5	6	3	6	20
50000–1 lakh	16	14	1	0	31
>1 lakh	20	5	4	0	29
Total	41	25	8	6	80
Chi-square		28.556			
p value		<0.001 Significant			

PCR: Protein creatinine ratio

Table 3: Bleeding manifestations versus peak urine protein creatinine ratio

Bleeding	Peak value				Total
	<0.5	0.5–1.0	1.0–1.5	>1.5	
Yes	3	5	4	3	15
No	38	20	4	3	65
Total	41	25	8	6	80
Chi square		12.518			
p value		0.006 Significant			

Table 4: Third space fluid versus peak urine protein creatinine ratio

3rd space collection	Peak value				Total
	<0.5	0.5–1.0	1.0–1.5	>1.5	
Yes	5	7	3	3	18
No	36	18	5	3	62
Total	41	25	8	6	80
Chi-square		6.565			
p value		0.087 Not significant			

UPCR more than 1, which was statistically significant ($P = 0.00001$) [Table 5].

Peak urine PCR was compared with the hematocrit levels and it was found that variability in hematocrit is statistically significant with rise in UPCR [Table 6].

Mean urine protein creatinine ratio was calculated, and it was found that mean UPCR was higher in Category C which is statistically significant [Table 7].

Table 5: Blood pressure versus peak urine protein creatinine ratio

BP	Peak value				Total
	<0.5	0.5–1.0	1.0–1.5	>1.5	
Normal	40	24	2	1	67
Hypotension	1	2	6	4	13
Total	41	26	8	5	80
Chi-square		42.3659			
p value		0.00,001 Significant			

Table 6: Hematocrit levels versus peak urine protein creatinine ratio

HCT	Peak value				Total
	<0.5	0.5–1.0	1.0–1.5	>1.5	
<20	1	3	1	2	7
20–30	2	4	3	1	10
30–40	36	15	3	1	55
>40	2	3	1	2	8
Total	41	25	8	6	80
Chi-square		25.281			
p value		<0.05 Significant			

HCT: Hematocrit

Table 7: PCR versus severity categories

Spot PCR	Category A	Category B	Category C
Mean	0.407	0.461	1.427
SD	0.302	0.285	1.413
p value		<0.001 Significant	

PCR: Protein creatinine ratio

DISCUSSION

Dengue hemorrhagic fever and dengue shock syndrome result in significant mortality in children.[1] There are many studies available predicting the severity in adult patients, and only few are available in pediatric children. Hence, this study is undertaken to predict the severity of dengue, thereby improving the outcome. An increase in vascular permeability is the hallmark of dengue infection. This is due to the damage to the endothelial cells. Hypoalbuminemia and proteinuria are well recognized in dengue infection. This is due to altered filtration of the glycocalyx as dengue virus and NS1 are known to attach to heparan sulfate, which is part of the glycocalyx. Hence, we studied to estimate urine protein creatinine ratio from the day of admission.

Eighty children of our study were categorized based on the clinical findings and laboratory parameter into three categories. Out of 80, 28 (35%) belonged to Category A, 32 (40%) belonged to Category B, and 20 (25%) belonged to Category C.

Majority of admissions occurred on the 4th and 5th day of illness. The values of UPCR estimated on the

day of admission were increased in cases belonging to Category C.

We divided the age group of children into two groups as <2 years and more than 2 years based on the normal values of UPCR. Age does not show any correlation between UPCR which is similar to the study done by Datla *et al.*[3]

Thirty percent of Category C had UPCR more than 1.5 which is similar to study by Vasanwala *et al.*[4]

Third space collection was observed in 18 cases, of whom only three cases had UPCR >1.5, which is statistically insignificant ($P = 0.087$), but in a study by Datla *et al.*,[3] 58% cases had third space collection who showed significant elevation of UPCR.

Thirteen (16%) children had hypotension, of whom 4 (30%) cases had UPCR value higher than 1.5. Most of the children had a peak value on days 4 and 5 of illness, which is the critical phase. This was similar to many other studies where elevated UPCR was observed before the shock.[5-8]

When UPCR was compared with hematocrit, the majority of cases had hematocrit between 30 and 40, drastic fall and rise in hematocrit values were associated with an increase in UPCR which was significant and also the predictor of shock.[6]

When platelet count was compared with UPCR, very low platelet count of <50,000 was associated with a significant rise in UPCR. Hence, low platelet and rise in UPCR indicated that the children can develop shock.[7,8]

In our study, we calculated the mean UPCR with Categories A, B, and C. It was found to be significantly high in our study which was also similar to many other studies.[8,9]

We observed that the peak UPCR could distinguish patients likely to develop dengue hemorrhagic fever (DHF) from those who did not and that peak UPCR occurred on day 4–7 of the illness. A significant increase in UPCR was seen on the day which corresponded to 1 day before the development of DHF. Patients with uncomplicated dengue fever had significantly lower UPCR than patients with impending DHF and dengue shock syndrome. Daily follow-up in this prospective study enabled a time-course analysis showing that the discriminatory value of UPCR was not evident in the early febrile period, but it is discriminatory between days 4 and 7, just before defervescence when maximal plasma leakage classically occurs.

Limitations

Our study had less number of patients with severe dengue. Another limitation is that no single diagnostic assay in isolation is adequately sensitive and specific enough to diagnose all acute cases of dengue. We used either reverse transcriptase (RT) PCR or NS1 structural protein to diagnose patients with dengue. RT-PCR is a robust test during the viremic febrile phase but is less sensitive during the time of the defervescence. NS1 rapid diagnostic tests have 49.4–98.9% sensitivity and 90.6–100% specificity in the detection of dengue ranging from 1 to 15 days of illness.

CONCLUSIONS

Increase occurrence of dengue fever and its associated complications necessitates the need for early predictors of disease severity. Such markers have not been well studied in the pediatric population. UPCR assessment is easy to perform and inexpensive. This study found UPCR to be an accurate marker in predicting disease severity, bleeding manifestations, need for inotropes, and adverse outcome in children with dengue fever.

We, therefore, recommend the usage of both UPCR estimation in all children afflicted with dengue fever as a screening device for hospitalization, management, and prognostication.

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Original Article

Analysis of the Profile and Outcome of the Ingested Poisoning Cases in Pediatric Intensive Care Unit of a Tertiary Care Urban Medical College Hospital in South Tamil Nadu

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Abstract

Background: One of the common causes of admissions in the pediatric intensive care unit is ingestion of harmful substances, which is more common in toddler and school age. Recently with the harmful impact of social media and change in family environments, deliberate consumption of poisoning agents is seen in adolescents.

Objectives: The aim of this study is to analyze the profile and outcome of children admitted with a history of ingestion of poisoning in urban medical college hospital.

Materials and Methods: Children admitted with a history of consumption of poisoning agents over 1 year from January 2019 to December 2019.

Results: Out of 220 children admitted majority belongs to the toddler age group which accounts to 54%. Among 220 children, 131 (59.5%) were male and 89 (40.5%) were female. A total of 88 children had consumed kerosene/thinner which is the common agent in our study, contributing 40% of the cases. The major etiology is accidental (91.8%). Moreover, 217 children (98%) recovered completely and mortality percentage is only 1.36%.

Key words: Accidental, Children, Kerosene, Poisoning, Urban Medical College

INTRODUCTION

Poison is any agent of self-injury absorbed into the system through epithelial surfaces. Accidents, poisoning, vehicular trauma, and falls are important causes of childhood morbidity and mortality. Toddlers are especially predisposed as they are mobile and inquisitive and cannot differentiate between harmful and harmless things. These harmful products are usually familiar, visually appealing in glossy containers, and sometimes even tasty in children.[1]

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Poisoning in children is predominantly accidental than adults and accounts for 1–6% of bed occupancy in pediatric hospitals and 3.9% in the pediatric intensive care unit in India.[2-4] Recently among adolescents, poisoning is increasingly self-inflicted.[5] Poisoning is the second most common cause of injury resulting in the hospitalization of children under the age of 5 years.[6]

High incidence of poisoning in toddlers and preschool children is a direct consequence of the development stage of child. As infants start to mobilize easily around 1 year of age, their human instincts lead them into exploring the surroundings and putting the objects into the mouth. By the age of 21/2–3 years, the children's motor development makes themselves vulnerable for exposure to potentially noxious things. Incidence of accidental poisoning decreases after 4 years of age as the child gets more selective in choosing objects for mouthing and ingestions.

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Male children outnumber female due to their greater activity and tendency of exploration of the environment.

The incidence is also higher among children from lower socioeconomic groups due to poor storage facilities of household products and greater accessibility of children to those potentially harmful things.[7] Incidence is also higher in rural population due to the use of pesticides in agriculture purpose and poor storage facility of such pesticides.[7] Incidence of kerosene poisoning is common in rural and slum population because in summer months, there is a frequent power failure and also some households may not have electric connection. Due to curiosity and easy accessibility, children often drink kerosene, mistaking it for water. In a poor socioeconomic setup, it is not possible to store kerosene in a childproof pack. Household products rather than pharmaceuticals are now implicated in the majority of pediatric poisoning.[2,5,8]

These accidents are preventable as the main reason for such incidents is a lack of knowledge, awareness, and adult supervision. The cause of pediatric poisoning varies in different age groups, and hence, preventive strategies should be planned accordingly.

The objective of this study is to analyze the pattern and outcome of childhood poisoning under the age of 12 years in an urban medical college hospital in India to characterize the problem of acute pediatric poisoning.

MATERIALS AND METHODS

This study was conducted in the pediatric intensive care unit of an Urban Medical College Hospital.

Sampling

This was the retrospective study conducted for 1 year duration from January 2019 to December 2019. The data were compiled from the information entered into pediatric intensive care unit as the admission register and nominal register.

All the children with a history of consumption of harmful or unknown substances were included in the study.

All were admitted initially in the pediatric intensive care unit for treatment and continuous monitoring. The parameters analyzed were age, sex, agents consumed, duration of stay, outcome of the act, and treatment.

RESULTS

A total of 7590 children were admitted in the pediatric ward during our study duration of 1 year between January 2019 and December 2019.

Among them 220 children had consumed alleged poisoning agents contributing to 2.89% of the total admission during the study duration [Table 1].

Out of 220 children who had been admitted with the alleged history of consumption of either harmful poisoning agents or unknown substances in the pediatric intensive care unit, increased number was noted in the month of March and May 2019 [Table 2].

On analyzing the age-wise distribution of cases, we found that the majority of the children were toddlers who made 54% of the cases.

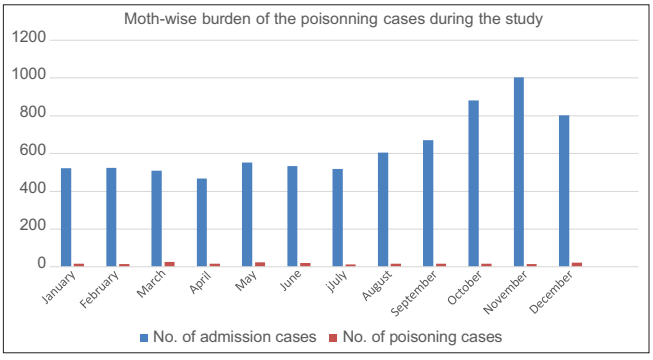
Nearly, 6% were infants, 54% were toddlers, 15% belong to preschool age, and 25% were in school age [Table 3].

Table 1: Burden of poisoning cases among total admissions for 1 year period

Duration	Number of admission cases	Number of poisoning cases (%)
January 2019–December 2019	7590	220 (2.89)

Table 2: Month-wise distribution of poisoning cases during the study

Months	Number of admission cases	Number of poisoning cases (%)
January	523	17 (3.3)
February	524	15 (2.9)
March	509	27 (5.3)
April	467	16 (3.4)
May	552	25 (4.5)
June	533	20 (3.8)
July	519	12 (2.3)
August	605	17 (2.8)
September	670	17 (2.5)
October	881	16 (1.8)
November	1004	15 (1.5)
December	803	23 (2.9)
Total	7590	220 (2.9)



In our study, 131 males and 89 females had consumed harmful substances contributing to 59.54% and 40.45%, respectively [Table 4].

Among the various agents consumed, kerosene and thinner topped the list. A total of 88 children had consumed kerosene/thinner that makes 40% of the poisoning burden and toddlers were the majority victims.

The next common agents consumed were pesticides and rodenticides. Among the pesticides, OPC, carbamates, herbicides, and pyrethroids, contributing 6.8%, 1.8%, 1.8%, and 1.8% of the total poisoning cases, respectively [Tables 5 and 6].

Coming to the etiology behind, the consumption of the listed substances most of them was accidental consumption amounting to 202 (91.81%) of cases, homicidal cases 12 (opc-7, carbamate-4, and rodenticide-1) (5.45%), and suicidal 6 (opc-4 oleander-2) (2.72%) [Table 7].

Totally, 6 children who belong to early adolescents groups had consumed with suicidal intention. Among these 3 girls and 3 boys belong to school-age children. Agents used for suicidal were OPC and oleander seeds. All were saved and discharged.

Among the homicidal cases of 12 children, seven were OPC, four were carbamates, and one was rat killer paste. There were 3 children (1.36%) who unfortunately died due to poisoning. Among these three, two had been given OPC by mother and stayed for 8 and 3 days, respectively. Another one was given rat killer paste by father and stayed for 4 days. Totally 168 children (76%) had been discharged successfully after the treatment and careful observation period of 1 week [Table 8].

Table 3: Age-wise distribution of poisoning cases

Age group	Age range (years)	*n* (%)
Infants	<1	13 (6)
Toddlers	1–3	119 (54)
Preschool	3–6	33 (15)
School	6–12	55 (25)

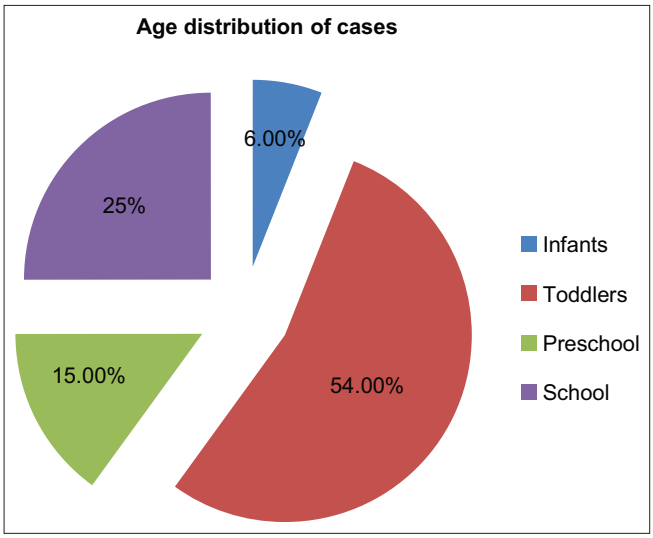


Table 4: Gender-wise distribution of poisoning cases

Total cases	Males (%)	Females (%)
220	131 (59.5)	89 (40.5)

DISCUSSION

In our study, the burden of the poisoning cases among total admission during 1 year period of January 2019 to December 2019 was 2.89%. Mandal *et al.* had reported 89 cases of poisoning during 1 year, constituting 1% of all pediatrics admission.[9,10] In our study, males ($n = 131$, 59.5%) outnumbered females ($n = 89$, 40.5%). Devaranavadaji *et al.* had reported a slight female preponderance that out of 38 cases of poisoning, 16 (42%) are male and 22 (58%) are females.[11] Jadhav *et al.* state that according to her study, the incidence of poisoning was more common in males (72%) at most 3 times those in females (28%). In Mandal *et al.* study, 57 cases were male (64%) and 32 cases were female (38%; $n = 89$).[9]

Analysis according to the age of the children in our study shows that majority are toddlers ($n = 119$, 54%) between 1 and 3 years of age, giving $P < 0.0033$ which is statistically significant. This fact is supported by Mandal *et al.*, who reported that out of 89 cases, 62 (69.66%) were between 1 and 3 years.[9]

In our study, the common agent consumed is kerosene/thinner being consumed by 88 children (40%) followed by pesticides by 27 children (12.3%).

In Jadhav *et al.*[10] study, hydrocarbon poisoning (kerosene) was the most common type of poisoning 32% of total cases followed by insecticides 10% of cases correlating with our study results.

In our study, only 10 had been admitted with consumption of medicine (tablets and syrups) that makes 4.54%. Roy *et al.* reported ingestion of medicine ($n = 34$, 17%).

In our study, 91.81% ($n = 202$) had consumed the harmful substances accidentally. In Mandal *et al.* study, all poisoning cases ($n = 89$) were accidental in nature by substances with-in reach of children. Jadhav *et al.* stated that most of

Table 5: Case distribution according to consumed poison

Agents	Infant	Toddler	Pre-school age	School age	Total
Kerosene/thinner	3	62	13	10	88
Rodenticide	1	6	1	10	18
OPC	0	7	1	7	15
Mosquito repellent/coil	2	6	2	0	10
Acid	0	2	3	4	9
Lice killer	0	1	2	4	7
Camphor	1	3	1	1	6
Oleander	0	1	2	2	5
Ant Killer	0	3	1	1	5
Carbamate	0	3	0	1	4
Herbicide	0	3	0	1	4
Pyrethroid	0	3	0	1	4
Neem oil	1	3	0	0	4
Diazepam	0	0	0	3	3
Alkali	0	0	1	2	3
Oduvanthalai	0	0	0	2	2
Paint	1	1	0	0	2
Diesel	0	0	1	1	2
Lindane	0	0	1	1	2
Matchstick powder	0	2	0	0	2
Cowdung powder	0	2	0	0	2
Fish egg	0	0	2	0	2
Phenol	0	0	1	1	2
Dettol	1	1	0	0	2
Iron tablet	0	1	0	0	1
Paracetamol	1	0	0	0	1
Cough syrup	0	1	0	0	1
GBHC	0	1	0	0	1
Sulfa powder	0	1	0	0	1
Mefenamic	0	1	0	0	1
Sodium fusidate	0	1	0	0	1
Contaminated lizard water	1	0	0	0	1
Turpentine oil	0	0	0	1	1
Ear oil	0	1	0	0	1
Pvc paste	0	1	0	0	1
Vapor absorber	0	0	0	1	1
Bleaching powder	0	1	0	0	1
Povidone iodine	0	0	0	1	1
Kmno4	1	0	0	0	1
H202	0	1	0	0	1
Abrus precatorius	0	0	1	0	1
Total	13	119	33	55	220

the cases (94%) were due to accidental ingestion of the concerned agents.

In our study, out of all poisoning cases, 202 were accidental(91.8%), 12 were homicidal (5.54%), 6 were suicidal (2.72%). Agarwal *et al.*, all poisoning episodes were either suicidal (38, 46.9%) or accidental (43, 53.1%) and none were homicidal.

In our study, the mortality percentage was 1.36% and majority was discharged successfully.[12] Roy *et al.* study revealed that out of 195 cases, 75% (n = 154) of children with poisoning were discharged and 16% of children (n = 37) left the hospital without any intimation. Death occurred in four (2%) cases (n = 4). Mandal *et al.* study reported that number of death was 6 (6.67%) and that of survival was 83 (93.25%).

Table 6: Agents consumed

Groups	Agents	No. of cases (%)
Rodenticides		18(8.2)
Pesticides	OPC	15 (6.8)
	Carbamates	4 (1.8)
	Pyrethroids	4 (1.8)
	Herbicides	4 (1.8)
Plant poisoning	Oleander	5 (2.3)
	Oduvanthalai	2(0.9)
	Abacus	1 (0.45)
Tablets	Diazepam	3 (1.36)
	Paracetamol	1 (0.45)
	Ferrous sulfate	1 (0.45)
	Mefenamic	1 (0.45)
	Sulfa powder	1 (0.45)
	Sodium fusidate	1 (0.45)
	GBHC	1 (0.45)
	Cough syrup	1 (0.45)

(*Contd...*)

Table 6: (*Continued*)

Groups	Agents	No. of cases (%)
Corrosive	Acids	9 (4.09)
	Alkali	3 (1.36)
	Kerosene/thinner	88 (40)
Others	Mosquito repellant	10 (4.5)
	Lice killer	7 (3.18)
	Camphor	6 (2.72)
	Ant killer	5 (2.2)
	Neem oil	4 (1.8)
	Lindane ingestion	2 (0.9)
	Povidone iodine	1 (0.45)
	H_2O_2	1 (0.45)
	$KMnO_4$	1 (0.45)
	Cow dung powder ingestion	2 (0.9)
	Fish egg ingestion	2 (0.9)
	Phenol ingestion	2 (0.9)
	Match stick powder	2 (0.9)
	Dettol	2 (0.9)
	Diesel	2 (0.9)
	Paint ingestion	2 (0.9)
	Lizard contaminated water ingestion	1 (0.45)
	Turpentine ingestion	1 (0.45)
	Ear oil ingestion	1 (0.45)
	PVC paste ingestion	1 (0.45)
	Vapor absorber	1 (0.45)
	Bleaching powder	1 (0.45)

Table 7: Etiology distribution of cases

Mode	Accidental	Homicidal	Suicidal
Percentage	202 (91.81%)	12 (5.45%)	6 (2.72%)

Table 8: Final outcome of poisoning cases

Outcome	*n* (%)
Discharged	217 (98)
Death	3 (1.36)
Total	220

In our study, among three deaths, two were due to OPC poisoning and one was due to aluminum phosphide poisoning. Devaranavadagi *et al.* had documented that out of 38 cases of poisoning, two cases (5.2%) died both due to aluminum phosphide poisoning.

CONCLUSION

Accidental poisoning is common among toddlers and suicidal poisoning is on the rise among early adolescents. Lack of parental care, influence of social media, and peer pressure can be attributed to this emerging rise of suicides among adolescents. Unconditional parental love and proper moral classes by teachers can prevent poisoning. Parents should be educated through newspapers, advertisements, and media about accidental exposures and curious instincts of toddlers and also measures to prevent accidental poisoning among toddlers. Moreover, for medical professionals, it should be remembered that a high index of suspicion is required for the identification of poisoning. History of poison ingestion should be thought and sought whenever any hyperacute onset of symptoms occurs in an apparently healthy child.

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Original Article

Cephalic Index and Facial Index of Adults in Rural South Kerala, India

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Abstract

Introduction: Standardized cephalometric measurements such as cephalic index and facial index are useful in the scientific disciplines, namely anthropology, archeology, anatomy, plastic surgery, forensic medicine, and genetics, to identify individuals' race and sex and for treatment of problems related to craniofacial morphologies. Indian studies on craniofacial measurements are available in the literature from states other than Kerala. The present research work has been planned to find the cephalic index and facial index of the adult population residing in rural South Kerala, India.

Purpose: The objectives of the study were to estimate the cephalic index and facial index of adults of rural South Kerala, India, and to determine the factors related to cephalic and facial indices of the study participants.

Methods: Cross-sectional study among adults aged 18 years and above residing in Perumkadavila block, Thiruvananthapuram district, Kerala, India, was conducted during a period of 6 months from January 2019. Cephalometric measurements were made on the participants sitting on a chair in a relaxed mood with the head in anatomical position. Cranial index and facial index were calculated using appropriate formulae.

Results: Among 1600 adults, 792 (49.5%) were males and 808 (50.5%) females with mean age 52.3 ± 3.2. Mean cephalic index in males was 77.1 ± 1.2 and 78.4 ± 1.3 in females with maximum number of participants having mesocephalic type of head. Mean facial index in males was 80.13 ± 1.3 and mean facial index in female participants 80.53 ± 1.4, the difference being statistically significant.

Conclusion: Understanding the cranial and facial indices of individuals from different geographical areas will be beneficial in anthropometry archeology, forensic medicine, pediatrics, plastic surgery, and genetics.

Key words: Adult population, Cephalic index, Facial index, Participants, Rural

INTRODUCTION

Craniometry[1] is one of the disciplines of anthropology, in which the dimensions of head and face are measured. The craniometry is helpful to study the frequency distribution of human craniofacial morphologies, craniofacial variations in different human races, ethnic groups and sex, as well as for clinical diagnosis and treatment.[2] Comparison of changes in craniometric measurements between parents, children, and siblings may give a clue to genetic transmission of inherited characteristics.[3] Data on standardized cephalometric measures help diagnostic comparisons between patients and the normal population.[4] Craniometric measurements are useful in pediatrics, forensic medicine, plastic surgery, otolaryngology and syndromology, and oral surgery dentistry.[5] Craniofacial measurements are also employed to classify people according to race, criminal temperament, and intelligence.[6] Cephalic index and facial index are the measurements used by anthropologists, anatomists, plastic surgeons, and forensic scientists to identify individual's race and sex and for treatment of craniofacial problems.[7] Comparison between cephalic indices and facial indices with race, age, and sex is valuable for treatment monitoring and prediction of orthodontic treatment and in plastic and reconstructive surgeries concerned with craniofacial deformities.[8] The data on cephalic index and facial index of a population are necessary for the preparation of cranial remodeling band or helmet as durable medical equipment.[9]

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Manual measurements of craniometry are considered more easy and economical even though sophisticated radiologic methods are available now.[10]

Morphology of the face depends on many factors such as sex, ethnicity, race, climate, nutrition, genetic constitution, and socioeconomic status.[11] India is a nation with a complex and varied ethnic composition of its population, indicating multiple lines of ancestry and geographic origins.[12]

Literature shows international research studies on craniofacial measurements.[11,13] Indian studies[7-9] on craniofacial morphologies are available from states other than Kerala. No such research studies have been reported on the cephalic index and facial index of the rural population of Kerala. This research work had been planned to find the cephalic index and facial index of the adult population of Perumkadavila block of Thiruvananthapuram in rural South Kerala, India.

Objectives

The objectives of the study were as follows:

1. To estimate cephalic index and facial index of adults of rural South Kerala.
2. To determine the factors related to cephalic and facial indices of the study participants.

METHODOLOGY

Study design: Cross-sectional study.

Study setting: Perumkadavila block, Thiruvananthapuram district, Kerala, India.

Study duration: Six months from January 2019.

Study population: Adults aged 18 years and above residing in Perumkadavila block, Thiruvananthapuram district, Kerala, India.

Inclusion Criteria

Adults aged 18 years and above belonging to both genders residing in the study setting and willing to participate were included in the study.

Exclusion Criteria

The following criteria were excluded from the study:

- All adults fulfilling the inclusion criteria but not willing to give consent.
- Adults who were absent on the day of data collection.
- Any adults having physical deformity or history of craniofacial trauma.

Sampling technique: Multistage sampling.

Study participants: All adults residing in the wards selected by multistage random sampling satisfying inclusion criteria.

Study tool: Pretested, semi-structured questionnaire containing two sections.

Section A: Sociodemographic details of the study participants.

Section B: Details on general health and anthropometric measurements.

Definitions

The anatomical landmarks were defined as follows.
Glabella: The central point between the eyebrows above the nose.

Inion: The projecting part of the occipital bone at the base of the skull.

Nasion: The point on the root of the nose where the midsagittal plane cuts the nasofrontal sutures.

Gnathion: The lowest point of the mandible where the lower margin of the lower jaw is intersected by the midsagittal plane.

Zygion: The most laterally placed point on the zygomatic arch.

$$\text{Cranial index} = (\text{Maximum head breadth}/\text{Maximum head length}) \times 100.$$

$$\text{Facial index} = (\text{Morphological facial height}/\text{Bizygomatic facial width}) \times 100.$$

Table 1 shows the classification of the head according to cephalic index.[7]

Table 2 shows the classification of face according to facial index.[14]

Data Collection Method

After obtaining ethical committee clearance from the parent institution, data on sociodemographic characteristics

Table 1: Classification of head according to cephalic index[7]

Type of head	Cephalic index
Hyperdolichocephalic	65.5–69.9
Dolichocephalic	70.0–74.9
Mesocephalic	75.0–79.9
Brachycephalic	80.0–84.9
Hyperbrachycephalic	85.0–89.9
Ultabrachycephalic	90.0–>90

and general health were collected by interview method using pre-tested and semi-structured questionnaires. Cephalic index and facial index were calculated using the data on anthropometry collected by making cephalometric measurements.

Cephalometric measurements[15] were made on the participants sitting on a chair in a relaxed mood with the head in anatomical position. Anthropometric points for the cephalic index were measured using spreading calipers. Facial index measurements were taken by measuring tape. The head length was measured from the glabella to the inions to the nearest centimeter (cm), with an accuracy of 0.10. The head breadth was measured as the maximum transverse biparietal diameter between the two fixed points over the parietal bones to the nearest centimeter (cm), with an accuracy of 0.10.

The cephalic index and facial index were calculated for each subject using the following equations.[16]

$$\text{Cranial index} = (\text{Maximum head breadth}/\text{Maximum head length}) \times 100 \text{ and}$$

$$\text{Facial index} = (\text{Morphological facial height}/\text{Bizygomatic facial width}) \times 10.$$

Data Analysis

Data were entered in MS Excel Spreadsheet and analysis was done using SPSS 16.0 trial version.

RESULTS

The cross-sectional study was conducted among 1600 adults from Perumkadavila Block Panchayath to find out the cephalic index and facial index and related factors. Statistical analysis was done from the data collected. Cephalic index and facial index were calculated. Results were expressed in numbers and percentages for both genders [Figure 1].

Mean age of the participants = 52.3 ± 3.2 years.

Most of the participants belonged to the age group 36–49 years [Table 3].

Table 2: Classification of face according to facial index[14]

Type of face	Facial index
Hypereuryprosopic	<79.9
Euryprosopic	80.0–84.9
Mesoprosopic	85.0–89.9
Leptoprosopic	90.0–94.9
Hyperleptoprosopic	95.0–>95

Mean cephalic index in males was 77.1 ± 1.2 and mean cephalic index in female participants 78.4 ± 1.3, with a maximum number of participants having mesocephalic type of head [Table 4].

As per Banister's classification of the facial index, most (49.1%) of the male participants had leptoprosopic type of face with facial index 80.13 ± 1.3. Majority (59.53%) of the females presented with euryprosopic type of face and mean facial index 80.53 ± 1.4. None of the female participants had hyperleptoprosopic type of face [Table 5].

The observed difference in cephalic index and facial index between male and female participants was statistically

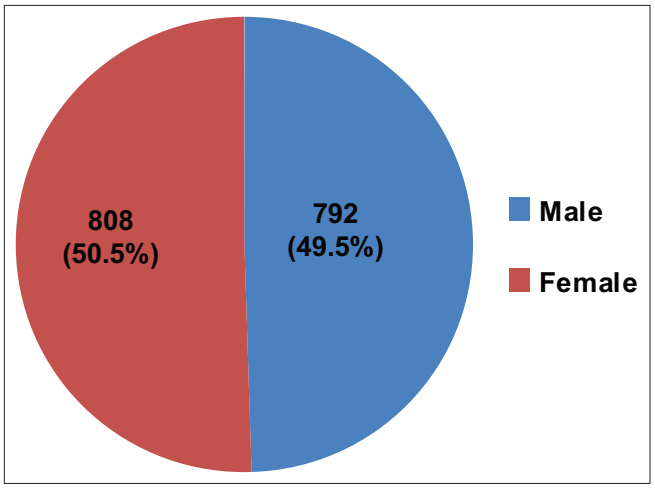

Figure 1: Gender-wise distribution of study participants

Table 3: Age-wise distribution of study participants

Age (range) in years	Study participants Number (percentage)
18–25	166 (10.4)
26–35	212 (13.3)
36–49	702 (43.8)
50–65	404 (25.3)
66–75	98 (6.1)
≥76	18 (1.1)
Total	1600 (100)

Table 4: Distribution of participants according to cephalic index

Type of head	Cephalic index	Study participants	
		Male Number (%)	Female Number (%)
Hyperdolichocephalic	65.5–69.9	39 (4.92)	9 (1.1)
Dolichocephalic	70.0–74.9	76 (9.6)	10 (1.2)
Mesocephalic	75.0–79.9	392 (49.5)	272 (33.7)
Brachycephalic	80.0–84.9	230 (29.04)	471 (58.3)
Hyperbrachycephalic	85.0–89.9	26 (3.28)	22 (2.7)
Ultabrachycephalic	90.0–>90	29 (3.66)	24 (3.0)

significant at 95% confidence interval. However, the differences in socioeconomic status were not statistically significant [Table 6].

DISCUSSION

The present study was conducted among 1600 adults, including 792 males and 808 females participants from Perumkadavila Block Panchayath of rural South Kerala, India.

Among male participants, 4.92% showed hyperdolichocephalic, 9.6% dolichocephalic, 49.5% mesocephalic, 29.04% brachycephalic, 3.28% hyperbrachycephalic, and 3.66% ultrabrachycephalic type of head based on cephalic index. Among females, as per cephalic index, most of them (58.3%) showed brachycephalic type of heads followed by 33.7% mesocephalic, 3.0% ultrabrachycephalic, 2.7% hyperbrachycephalic, 1.2% dolichocephalic, and 1.1% with a hyper dolichocephalic type of head.

Table 5: Categorization of participants according to facial index

Type of face	Facial index	Participants	
		Male Number (%)	Female Number (%)
Hypereuryprosopic	<79.9	26 (3.3)	56 (6.93)
Euryprosopic	80.0–84.9	212 (26.76)	481 (59.53)
Leptoprosopic	85.0–89.9	389 (49.11)	207 (25.62)
Mesoprosopic	90.0–94.9	136 (17.17)	64 (7.92)
Hyperleptoprosopic	95.0–>95	29 (3.66)	-

Table 6: Factors related to cephalic index and facial index

Test variable	Gender	Mean	SD	SE	"Z"	Significance
Cephalic index	Male	77.1	1.2	0.061	21.3	Significant*
	Female	78.4	1.3			
Facial index	Male	80.13	1.3	0.067	5.970	Significant*
	Female	80.53	1.4			

*Significant at 95% CI

Literature includes research studies* conducted in other parts of the country showing varying types of head and face.

Cephalic Index

Table 7 shows the comparison of cephalic index of various populations and present study participants.[17-19]

Facial Index

In the present study, among male participants based on facial index 49.11% possess leptoprosopic type of face, 26.76% euryprosopic, 17.17% mesoprosopic, 3.66% hyper leptoprosopic, and 3.3% with hypereuryprosopic type of face. In females, majority of them (59.53%) showed euryprosopic type of face, 25.62% of females with leptoprosopic, 7.92% mesoprosopic, and 6.93% were with hypereuryprosopic type of face.

Table 8 shows a comparison of facial index of various populations with that of the present study.[20-25]

The close resemblances to Northern Indians in the study conducted by Heidari *et al*.[26] explains a common origin of immigrant Aryans of India and Bauchs and Sistanis of Iran.

Table 7: Comparative studies on cephalic index of various populations

Study setting/population	Authors	Cephalic index Male/Female
Indians (Male/Female)	Yagin *et al*.[17] (2012)	77.92/80.85
Maharashtra (Male/Female)	Sultan *et al*.[18] (2017)	79.12/78.67
Mumbai (Male/Female)	Khair *et al*.[19] (2011)	94.41/75.22
Andhra Pradesh (Male/Female)	Kumari *et al*.[7] (2015)	80.21/79.25
Punjab (Male/Female)	Seema and Verma[9] (2016)	80.52/84.32
Present study – South Kerala (Male/Female)	Ranga and Mallika (2020)	77.1/78.4

Table 8: Comparative studies on facial index of various populations

Study setting/population	Authors	Type of Face Male/Female
Nigeria (Male/Female)	Raji *et al*.[20] (2010)	Hyperleptoprosopic (Very long face)
Iran (Male/Female)	Jahanshahi Metal[21] (2008)	Mesoprosopic to Euryprosopic (Round to broad)
West Bengal (Male/Female)	Ghosh and Malik[22] (2007)	Euryprosopic to Hypereuryprosopic (Broad to very broad)
Andhra Pradesh (Male/Female)	Kumari *et al*.[7] (2015)	Leptoprosopic/Mesoprosopic
North India (Male/Female)	Prasanna *et al*.[23] (2013)	Hyperleptoprosopic/Mesoprosopic to Euryprosopic
Andaman and Nicobar Island (Male/Female)	Pandey[24] (2006)	Hypereuryprosopic (Very broad face)
South India (Male/Female)	Senthil *et al*.[25] (2019)	Leptroprosopic/hyper leptoprosopic
South India (Male/Female)	Soames[14] (2008)	Euryprosopic to Leptoprosopic (Broad to long face)
Present study (Male/Female)	Ranga and Mallika (2020)	Leptroprosopic/Euryprosopic

Factors Related to Cranial and Facial Indices

The observed difference in cephalic index and facial index between male and female genders was found to be statistically significant in the present study.

A similar finding showing a statistically significant difference between the two genders with respect to the facial morphology was observed in other studies also.[25,27]

A study[28] conducted for investigating correlations between the cranial and facial types observed that certain dentomaxillary anomalies' share both in geographical space and in a population group. All the facial parameters and facial indices were found to be statistically highly significant and they showed interregional and gender variations.

CONCLUSION

Cranial index and facial index show variations with respect to race, gender, geography, and ethnicity. Estimating these indices will be beneficial clinically in various disciplines for facial reconstruction surgeries, maxillofacial surgeries, forensic medicine, pediatrics, and genetics as well as for determining the stature and sex of the individual.

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Original Article

Study of Ilioinguinal Neurectomy on Reducing Chronic Pain Following Inguinal Hernia

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Abstract

Introduction: Inguinal hernia is a protrusion of the contents of the abdominal cavity through the inguinal canal and is the most common male diseases that occur worldwide. Chronic neuralgia is a serious and debilitating complication following inguinal hernia repair and ilioinguinal neurectomy (IIN) has shown to reduce the chronic post-operative pain (PCP).

Aim: The aim of this study was to determine the effect of IIN on chronic PCP in patients who underwent open unilateral inguinal hernia repair through the Lichtenstein method.

Materials and Methods: In this randomized control study, patients with unilateral inguinal hernia were randomized into two groups: 40 cases in the nerve-excised group and 40 cases in the nerve preservation group. The method of hernia repair was the classic Lichtenstein method. Pain and numbness were evaluated at day 1, day 3, day 7, 1 month, and 6 months after surgery through visual analog scale system. Data were analyzed using SPSS ver.16.

Results: Out of the 80 study patients, 40 were in Group 1 and 40 were in Group 2. The mean of the patients in Group 1 and Group 2 is 36.44 and 38.21, respectively. One case of hypoesthesia was observed in Group 1 and one case of hyperesthesia was observed in Group 2.

Conclusion: IIN may be considered as a routine method in reducing chronic PCP following herniorrhaphy.

Key words: Hypoesthesia, Ilioinguinal nerve, Inguinal hernia, Lichtenstein method, Neurectomy

INTRODUCTION

Chronic post-operative pain (PCP) is the most frequent complications following inguinal hernia repair and can be disabling in some patients leading to prolonged return to work time. Pain that lasts >3 months is defined as chronic pain and following inguinal hernia repair, the pain can become persistent.[1] The prevalence of post-operative inguinal pain is reported to be 20–30% and these pain syndromes can occur irrespective of the type of repair. Patients may require nonsteroidal anti-inflammatory drugs to physical therapies or even addition surgery to alleviate this pain.[2] Excision of the ilioinguinal nerve to reduce the incidence of chronic pain has been practiced in the recent years but a lot of controversies persist over this procedure. Neurectomy relieves PCP caused by entrapment and inflammation around the nerve and this procedure seems to have some theoretic benefit.[3,4]

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Along with the anteroproximal portion of the base of the penis or labia majora, the ilioinguinal nerve innervates the mons pubis and inguinal crease. In 40.6% of cadavers, the identified innervation patterns were bilaterally symmetric and hernia surgery related neuropathic pain syndromes must be differentiated from other sources.[5] The increasing number of publications in the last decade regarding PCP syndrome following inguinal hernia repair indicates that it is a significant clinical problem and steps must be taken to address this pain. It is also mandatory to differentiate chronic pain from acute pain while early PCP may also present in a similar way. Early post-surgical pain usually resolves in 15–30 days while chronic pain generally begins in the 3rd post-operative month incurring the need for extensive management and hospitalization. In some cases, even a second surgery may be needed.[6]

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PCP also puts the surgeon under risk of litigation and about 5–7% of the surgeons are sued. Neurectomies can eliminate the incidence of chronic groin pain which arise due to neuroma of the ilioinguinal, iliohypogastric, or genitofemoral nerve.[7] Surgical approach to the ilioinguinal nerve has been reliably established in the recent years. This study aims to evaluate the outcome of ilioinguinal neurectomy (IIN) in reducing chronic pain following inguinal hernia repair.

Aim

The aim of this study was to determine the effect of IIN on chronic PCP in patients who underwent open unilateral inguinal hernia repair through the Lichtenstein method.

MATERIALS AND METHODS

This randomized controlled study was conducted on patients with unilateral inguinal hernia who were admitted to the Department of General Surgery at Government Headquarters Hospital, Dindigul, during the time period of February 2019–December 2019. Informed consent was obtained before surgery from hospital-admitted patients. Patients were randomized into two groups: 40 cases in nerve-excised group (Group-1) and 40 cases in nerve-preserved group (Group-2). Pain and numbness were evaluated at day 1, day 3, day 7, 1 month, and 6 months after surgery with visual analog scale (VAS) system. Data were analyzed using SPSS ver.16. Pain and numbness were assessed before the operation and on days 0, 1, 3, 7, 1 month, and 6 months after surgery. The hernia repair was done through Lichtenstein's method in both the groups. Patients with recurrent, bilateral, strangulated, and incarcerated hernias and with a history of diabetes mellitus, hypertension, asthma, previous abdominal surgeries, opium addiction, and cerebrovascular accident were excluded from the study.

All probable complications were clearly explained to all patients. Age, gender, pre-operative and PCP, and post-surgical complications such as surgical site infection, hematoma, testicular ecchymosis, tingling or numbness in the site of surgery, and mean incision length were the parameters studied. The surgical incision length was measured with a ruler on the 1st day after surgery. The study was approved by the Institutional Ethics Committee.

RESULTS

A total of 80 patients were enrolled in the study and divided into two groups: Group 1 – inguinal hernia mesh repair and neurectomy through Lichtenstein's method. Group 2 – hernia mesh repair through Lichtenstein's method with nerve preservation the patients were of the age group 31–40 years. In Figure 1, the mean age of the patients in Group 1 is 36.44 years and in Group 2 is 38.21 years. About 8% of patients had pain during presentation. In nerve-excision group, 56% of patients had right inguinal hernia and 40% had left inguinal hernia. The mean incision length in Group 1 was 7.3 cm and in Group 2 was 4.5 cm. Follow-up was done on days 0, 1, 3, 7, 1 month, and 6 months and pain assessment was made using VAS. In Group 1, hypoesthesia was observed in one case, and in Group 2, hyperesthesia was noted in one case. Figure 2 depicts the pain intensity in both the groups on day 1, 3, 7, 1 month, and 6 months after surgery. The pain intensity in neurectomy group on day 1 is 7.12 and in the nerve preservation group is 8.1 which is higher. The pain intensity in both the groups decreases gradually over a 6-month period, but at any point of time, the pain sensation was lower in the neurectomy group than in the nerve preservation group, Figure 3.

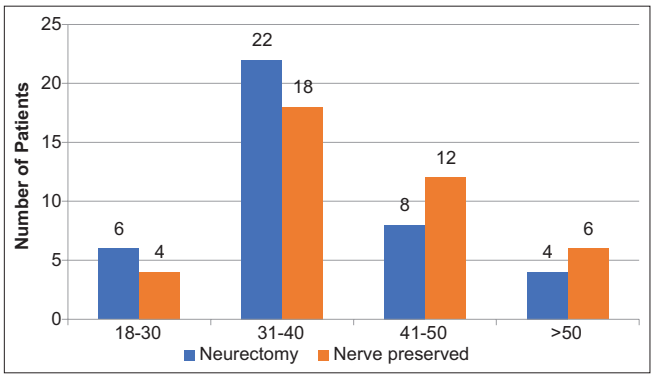

Figure 1: Age group

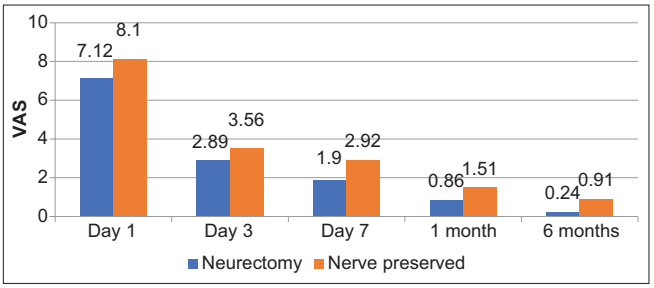

Figure 2: Visual analog score

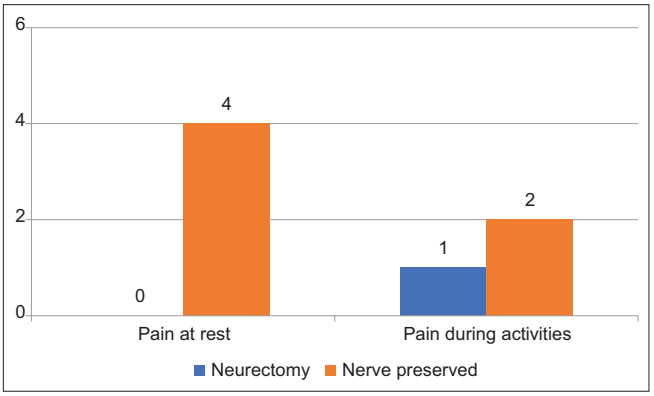

Figure 3: Pain at 6 months

DISCUSSION

In the current study, we compared the different pain scores between ilioinguinal nerve excision group and nerve preservation group following inguinal hernia repair through Lichtenstein method.

The results showed that the routine IIN can reduce chronic PCP rate and pain score at 6 months. Post-operative numbness and sensory disturbance were noticed in one patient in the IIN group and one patient in the nerve preservation group presented with hyperesthesia. The residual pain at the end of 6 months was lower in the IIN group than in the nerve preservation group. Chronic post-operative inguinal pain (CPIP) is a complex of nociceptive and neuropathic pain and the predisposing factors of the pain may vary.[7]

Wright *et al.* agreed in his study that preoperative groin pain is caused by local nerve compression and edema, and the severity of CPIP has a positive correlation with the severity of pre-operative pain.[8] In addition, CPIP is assumed to be caused by neurological factors such as nerve entrapment, direct nerve/suture injury, and neuromas. Ilioinguinal nerve, iliohypogastric nerve, and the genitofemoral nerve are the commonly involved nerves in CPIP and preserving them can lead to severe pain.[9,10] The incidence of CPIP after the 1st post-operative year is approximately 29% according to the Danish Hernia Database Group.[11] In a study by Caliskan and his team members, where the patients underwent Lichtenstein and neurectomy, the incidence of CPIP was significantly lower in the neurectomy group than in the nerve preservation group.[12]

In a pilot study conducted by Ravichandran *et al.*, where preservation or division of the ilioinguinal nerve in an inguinal hernia open mesh repairs was compared, pain was present in 1 out of 20 patients (5%) on the nerve preserved side versus 0 out of 20 patients (0%) on the nerve division side. Moreover, numbness was present in 2 out of 20 patients (10%) on the nerve divided side. The differences between the two study groups were non-significant and elective nerve division can reduce the PCP.[13] Picchio suggested that the reduction in CPIP following neurectomy is due to increased wound anesthesia.[14]

Based on our study, the ilioinguinal nerve excision during Lichtenstein procedure significantly reduced the PCP up to 6 months follow-up. It also reduced the return to work time which shows the superiority of this procedure. Numbness is an unavoidable complication after the nerve excision, but from patient point of view, pain relief seems to be more important. Hence, IIN can be performed as a routine procedure during inguinal hernia repair and this simple intraoperative maneuver can greatly reduce patient morbidity.

CONCLUSION

Routine IIN can reduce the incidence of chronic pain following hernia repair surgery. Hypoesthesia is a complication associated with IIN. Sample size calculations were not carried out in this study which may affect the credibility of the outcome of the study. The pain evaluation method was also not consistent and no perfect data conversion standard was followed. Further studies and evidence are needed to verify the findings.

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Original Article

Prophylactic Single-dose Antibiotics to Prevent Surgical Site Infection

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Abstract

Introduction: Surgical site infections (SSIs) are associated with multiple hospital visits and incur additional costs. The infection can be translocated to a sterile site through the endogenous flora. Seeding of the surgical site from a prosthesis or implant can also occur. The reasons for SSI include virulent bacterial inoculums, host defense, and poor intraoperative/post-operative care. This study was conducted to investigate the prevention of SSI in patients who receive a single dose of prophylactic antibiotic before surgery.

Aim: This study aims to evaluate the effect of prophylactic single-dose antibiotic in surgical wound site to prevent surgical site infection and assess the outcome.

Materials and Methods: Fifty patients posted for elective surgery were selected for the study and informed consent was obtained. Patients with comorbid conditions were excluded from the study. Surgeries were performed following NICE guidelines and the study was conducted after approval from the Institutional Ethics Committee.

Results: The mean age of the patients was 46 years and most of the study patients were of the age group 41–50. Majority of the patients underwent hernioplasty (32%). SSI was noted in 3 patients (6%), and *Staph. aureus* was the predominant bacteria found in the infected site.

Conclusion: A single prophylactic dose of antibiotic is effective in preventing SSI, provided the surgical procedure is uncomplicated.

Key words: Antibiotic prophylaxis, Single-dose antibiotic, Surgical site infection, hernioplasty, Surgical wound infection

INTRODUCTION

Surgical site infection (SSI) is the leading cause of nosocomial infection that occurs at or near the surgical incision within 30 days of the operation.[1] In the United States, approximately 500,000 surgical site infections occur annually as estimated by the Centers for Disease Control and Prevention (CDC).[2] The economic burden of patients with surgical site infections is much higher than that for surgical patients without the infections. SSIs reduce patients' quality of life and also account for prolonged hospital stays and an annual cost of more than $1.6 billion.[3] Furthermore, SSI is also associated with an increased mortality rate and the chances of being readmitted to the hospital are above 60%. Methicillin-resistant *Staphylococcus aureus* (MRSA)-related SSIs have a relatively high mortality rate than those of the other organisms.[4]

The efficacy of single-dose antibiotic prophylaxis in clean surgery has been well established over the past 20 years. Antibiotics augment the natural immune defense mechanisms in the host and kill bacteria that are inoculated into the wound. This is the guiding principle behind antibiotic prophylaxis and it should be ensured that the systemic antibiotic levels are maintained above the minimum inhibitory concentration (MIC) of the pathogen of concern throughout the surgery.[5] Studies report that the incidence of post-operative SSI without an antibiotic prophylaxis is around 30–40%

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and a single-dose (SD) administration is as effective as multiple dose (MD) antibiotic prophylaxis. A recent randomized control study even proved that a SD of the 2nd generation cephalosporin was equally effective as MD antibiotics.[6,7]

The use of the less expensive appropriate antimicrobial agents for the prevention of SSI has also been demonstrated in many published studies. This study was conducted to evaluate the effectiveness of a prophylactic single-dose antibiotic in elective surgery to reduce surgical site infection in clean and contaminated wounds.

Aim

This study aims to evaluate the effect of prophylactic single-dose antibiotic in surgical wound site to prevent surgical site infection and assess the outcome.

MATERIALS AND METHODS

The study was conducted in the surgery Department of General Surgery at Government Headquarters Hospital, Dindigul. Among 50 patients posted for elective surgery during the period February 2019–December were included 2019. All patients above 18 years of age and who had no signs of infections, with a normal renal and coagulation profile and with no comorbid conditions such as HT, diabetes, asthma, and bleeding disorders were included in the study. No patient received any antibiotics 14 days before the surgery and informed consent was taken from all the study participants. Patients under 18 years of age, who had comorbidities, those who were on antiretroviral drugs, steroids, and other immunosuppressants, those with signs of infection, and those not willing to participate in the study were excluded from the study. The study was duly approved by the Institutional Ethics Committee and all pre-operative tests (hemoglobin, RFT, coagulation profile, chest X-ray, ECG, blood sugar, and BP) were performed on all the study patients.

NICE guideline for patients as well as medical professionals was followed. The patients were asked to bath using a non-medicated soap 1 day before the surgery and the specific surgical theaters were washed and dried. The operating team washed the hands (following NICE guideline) before the surgery and sterile gowns and two pairs of operating gloves were used. Antibiotic (?) prophylaxis injection was administered intravenously 30 min before the incision. Intraoperative homeostasis was achieved following NICE guideline and a sterile dressing was given to the surgical incision at the end of the surgery. The surgical site was regularly assessed until suture removal and proper follow-up visit was scheduled. The patients were examined for fever or deep SSI. In the case of fever/signs of pus or infection, CBC was done, and pus sample was collected for culture sensitivity. Regular wound dressing was done and it was allowed to heal with secondary intention. The patients were followed up for a period of 1 month. Broad-spectrum antibiotics were prescribed to patients with surgical site infection and switched to specific antibiotics after pus culture sensitivity reports. The data were properly analyzed based on distribution of age and surgery.

RESULTS

A total of 50 patients (n = 50) posted for elective surgery were included in the study. The duration of the surgery in majority of the patients was <2 h. Out of the 50 study participants, 32 were male and 18 patients were female. Most of the patients belonged to the age group of 41–50 years (52%) and the mean age was 46 years. About 26% of the study patients were >51 years of age, Figure 1.

Appendicectomy was planned in 4% of the patients, cholecystectomy in 16%, hernia mesh repair in 10%, hydrocele in 8%, cystolithotomy in 2%, and other surgical excisions in 28% of the patients. Majority of the patients underwent hernioplasty (32%) [Figure 2].

Three cases, one each in appendicectomy, cholecystectomy, and hernioplasty, had evidence of pus and sample was sent for pus culture and sensitivity. Figure 3 depicts the distribution of SSI in the patients. All the patients were discharged on the 4th–9th post-operative day. Regular follow-up was done in patients who had surgical site infection, wound dressing was done, and oral antibiotics were started. As a consequence of surgical site infection, patients suffered a longer recovery time and incurred additional cost. Patients even needed multiple visits to the hospital. The pus sample was collected and sent to the laboratory for sensitivity testing. *Staphylococcus aureus* was the predominant bacteria in the pus samples responsible for SSI.

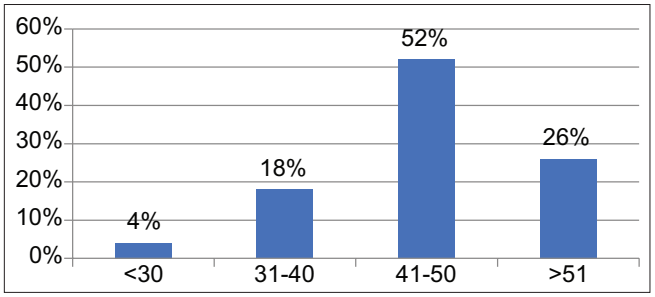

Figure 1: Distribution of age group

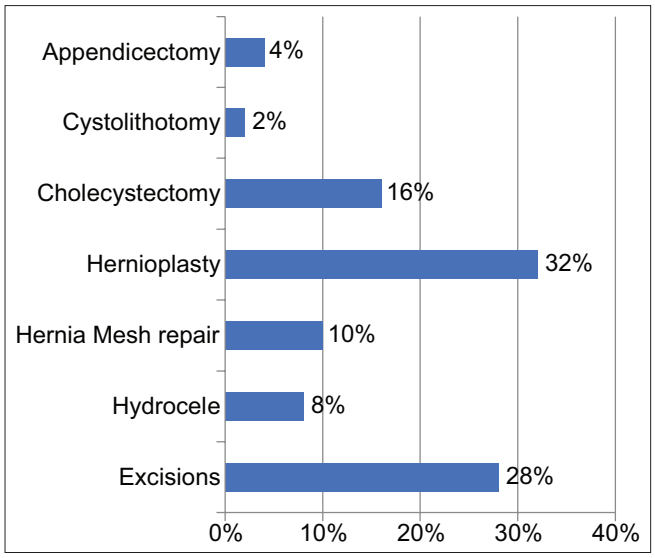

Figure 2: Distribution of surgery

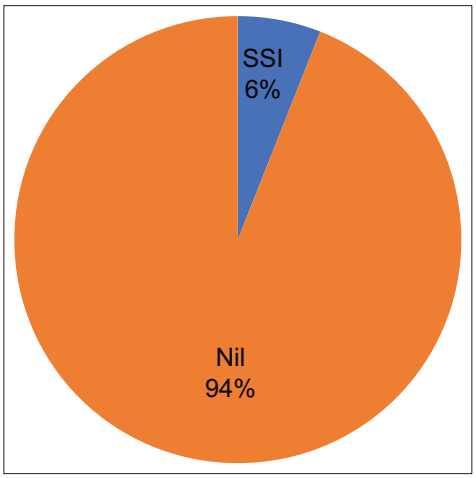

Figure 3: Distribution of SSI

DISCUSSION

Post-operative infections, wound drainage, and sepsis were very common until the mid-19th century until the principles of antisepsis were implemented by Joseph Lister in the late 1860s. This fundamental work changed the infections and deaths associated with an operation to reduced suffering and extended life.[8] The "window" of prophylactic effectiveness was shown by Miles and his colleagues and Bruke, while working with the guinea pig wound infection model. They found that antibiotics administered shortly before or at the time of bacterial inoculation of the guinea pig caused a significant decrease in the size of wound indurations relative to lesions in animals that did not receive any antibiotic prophylaxis.[1]

Prophylactic antibiotics, administered at an optimal time before the surgery, can minimize the risk of SSI. Many studies have been conducted in this regard that prove the effectiveness of a properly administered SD antibiotic in preventing post-operative infections. A double-blind RCT by Thakur and his associates in the year 2010 among 55 patients of inguinal hernia showed that a single dose of cefuroxime sodium had beneficial effects in reducing the incidence of SSI. The percentage of SSI in his study was 10.3% in the prophylactic group in superficial SSI (11.5% in control group) and 0% in deep SSIs (3.8% in control group).[9]

In our study, a low incidence (6%) of post-operative surgical site infection was observed. The infection rates were 2% in appendicectomy, 2% in cholecystectomy, and 2% in hernioplasty. Out of the 32% of the patients who underwent hernioplasty, only 2% incidence of SSI was observed. The association between comorbid conditions and the risk of occurrence of SSI could not be demonstrated in this study. All the surgeries were performed within 2 h and NICE guidelines were followed. Out of the 4% of the appendicectomy patients, 2% had post-operative wound infection which is significant. *Staphylococcus aureus* was the most commonly found organism in the infected sites in our study, and a similar pattern of microflora was demonstrated by Anvikar *et al.* and Olson and Lee in his study.[10,11]

In a trial by Hughes *et al.*, where penicillin was given intravenously in a single prophylactic dose, the post-operative infection rates were significantly reduced when compared to the rate when no prophylactic dose was administered.[12] Age > 46, immunosuppression, poor nutrition, and obesity are all risk factors for SSI. A thorough knowledge in these regards can help the surgeon and the medical staff to effectively prevent SSIs and also reduce the cost burden on the patient. The appropriate time of administration of the prophylactic dose, additional care to contaminated, long and complicated surgical procedures, the half-life of the administered antibiotic, the duration of the surgery, and following proper asepsis measures can play a strong role in reducing post-operative SSI.

CONCLUSION

A single-dose prophylactic antibiotic is very efficient in reducing the risk of post-operative wound infection. Prophylactic antibiotics can be administered within 30 min before incision and have a desired safety from surgical site infection. Complicated, contaminated, or dirty procedures should receive additional post-operative coverage.

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Original Article

The Study of Serum Uric Acid as a Biochemical Indicator for Maternal and Fetal Outcome in Gestational Hypertension

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Abstract

Introduction: Hypertensive pregnancy disorders are among the most common medical disorders during pregnancy and are considered a significant cause of maternal and fetal morbidity and mortality.

Aim: The aim of the study was to study of serum uric acid as a biochemical indicator for maternal and fetal outcome in patients with gestational hypertension (GHT).

Materials and Methods: This prospective study was conducted in the Department of Obstetrics and Gynaecology, Government Theni Medical College and Hospital, Tamil Nadu, from June 2018 to June 2019 in 200 pregnant women with GHT. Informed consent was obtained from the patients. Results were analyzed statistically and discussed below.

Results: Out of 200 pregnant females, the mean age was 24.2 ± 4.5 years. Ninety-four patients were prim gravida, 67 patients were gravida 2, and 30 patients were gravida 3. Ninety-six had GHT with associated abnormalities, 90 were diagnosed with preeclampsia, and 47 had non-severe preeclampsia. In contrast, 43 had severe pre-eclampsia, eight patients had developed eclampsia, while the remaining six subjects were diagnosed with HELLP syndrome. About 66% had serum uric acid level ≤6 mg/dl and 34% had serum uric acid level ≥6 mg/dl. In subjects with normal uric acid level, 31.6% and 11.3% of subjects had non-severe preeclampsia and severe preeclampsia. In a subject with increased uric acid level, 46 patients had severe proteinuria. Preterm delivery was more commonly seen in women with serum uric acid higher than 6 mg/dl.

Conclusion: Our study concludes that the measurement of serum uric acid levels after 20 weeks of gestation is an excellent diagnostic and prognostic tool to assess fetal outcomes. This study shows that the estimation of serum uric acid levels in pregnancies complicated by hypertension and preeclampsia helps assess the severity of the disease.

Key words: Gestational hypertension, Maternal, Fetus, Uric acid

INTRODUCTION

Hypertensive pregnancy disorders (HDP) are among the most common medical disorders during pregnancy and are considered a significant cause of maternal and fetal morbidity and mortality. In developing countries, HDP ranks second only to anemia with approximately 7–10% of all pregnancies complicated by some form of hypertensive disorder and lead to various maternal and fetal complications.[1] In India, the incidence of preeclampsia, as recorded from hospital statistics, varies widely from 5% to 15%, while eclampsia is about 1.5%.[2] Strangely, the exact etiopathogenesis for HDP, including preeclampsia and eclampsia, remains obscured and presents an exciting mystery in obstetric practice.

The diagnosis of preeclampsia is based on the presence of the following clinical features: Blood pressure (BP) 140/90 mmHg after 20 weeks of gestation AND proteinuria 2300 mg/24-h or +1 with the dipstick.[3] There may be other associated abnormalities reported which increase the likelihood of preeclampsia occurrence such as elevated serum creatinine (new-onset), platelet count <100,000/pL, hepatic enzyme abnormalities, persistent headache with or without cerebral or visual disturbances, and epigastric pain. Preeclampsia with the presence of seizures is known as eclampsia.[4]

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The elevated uric acid level in maternal blood, presumably due to decreased renal excretion, is frequently found in women with preeclampsia. Of the several hypothesized factors for elevated uric acid in patients with preeclampsia, the following appear to be most intriguing: Abnormal renal function, increased tissue breakdown, acidosis, and increased activity of the enzyme xanthine oxidase/dehydrogenase.[5]

An association of uric acid elevation in clinically evident pre-eclampsia has been known since 1917.[6] Several studies have correlated the rise in uric acid with the severity of the preeclampsia.[7] Although hyperuricemia does correlate with maternal morbidity, there is an even stronger association of increased uric acid with risk for small or low birth weight infants and with overall fetal mortality.[8-10]

Aim

The aim of the study was to study of serum uric acid as a biochemical indicator for maternal and fetal outcome in patients with gestational hypertension (GHT).

MATERIALS AND METHODS

This prospective study was conducted in the Department of Obstetrics and Gynaecology, Government Theni Medical College and Hospital, Tamil Nadu, from June 2018 to June 2019 in 200 pregnant women with GHT.

Inclusion Criteria

All pregnant women suffering from GHT, preeclampsia, and eclampsia >20 weeks of gestation were included in the study.

Exclusion Criteria

Normotensive pregnant females, patients with hypertension at 20 weeks of gestation (chronic hypertension), patients with chronic renal disease, patients suffering from diabetes mellitus, diagnosed patients of hepatic dysfunction, patients suffering from gout, patients with epilepsy, patients with thyroid dysfunction, patients with cardiac disease, patients with leukemia's, patients with pancreatitis, and patients with hemolysis were excluded from the study.

After obtaining informed written consent from all the study subjects or their attendants (in case of unconscious patients, or patients unable to provide consent due to their condition), relevant data were documented in a pre-defined datasheet. Maintaining all aseptic precautions, blood samples were collected from all subjects to estimate serum uric acid concentration and other parameters.

The data were analyzed using the Statistical Package for the Social Sciences (IBM SPSS Inc.,). Categorical variables were presented as percentages, and continuous variables were presented as mean/median. The association between categorical variables was tested using the Chi-square test. A *P*-value (two-tailed) of <0.05 was considered statistically significant.

RESULTS

In this study, 200 pregnant patients were included in the mean age of 24.2 ± 4.5 years. Ninety-four patients were prim gravida, 67 patients were gravida 2, and 30 patients were gravida 3 [Figure 1]. The mean BMI was 24.1 ± 3.3 kg/m^2.

The earliest presentation of GHT in this study was in 25th week of gestation (24 weeks 5 days) while the latest presentation was in the 40th week of gestation (39 weeks 3 days) [Figure 2].

In 200 patients, 96 had GHT with associated abnormalities. Ninety of the 200 subjects were diagnosed with preeclampsia, 47 had non-severe preeclampsia while 43 had severe preeclampsia. Eight of the 200 subjects developed eclampsia while the remaining six subjects were diagnosed with HELLP syndrome and were considered to be in imminent risk of eclampsia [Figure 3].

Table 1: Distribution of maternal and fetal complications

Complications	UA		*P*-value
	≤6	≥6	
Intra-uterine death	0	10	<0.0001
Intra-uterine growth retardation	13	12	0.128
Intra-cranial hemorrhage	0	0	n/a
Pulmonary edema	0	0	n/a
Abruption	0	2	0.046
Pre-term/low birth weight	66	36	0.701
HELLP syndrome	1	5	0.009
Spontaneous expulsion	0	1	0.167
Maternal death	0	0	n/a

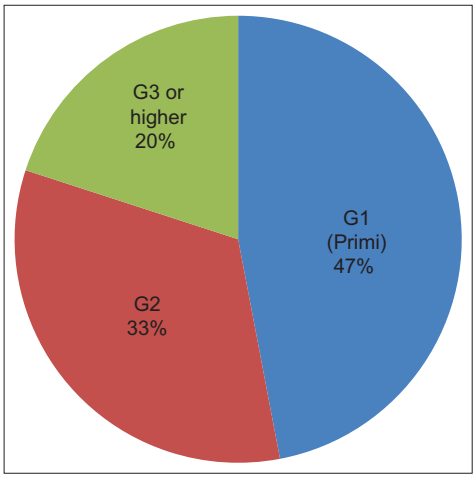

Figure 1: Distribution of obstetrics score

Out of 200 patients, 66% had serum uric acid level ≤6 mg/dl, and 34% had serum uric acid level ≥6 mg/dl [Figure 4].

In comparing gestational age with serum uric acid level 28 patients with gestational age <34, 14 patients between 34 and 36, 91 patients greater than 36 had serum uric acid level ≤6 mg/dl. Twenty-one patients with gestational age <34, 11 patients between 34 and 36, 35 patients greater than 36 had serum uric acid level ≥6 mg/dl [Figure 5].

Out of 200 patients, 46 patients with serum uric acid level greater than 6 mg/dl had severe proteinuria [Figure 6].

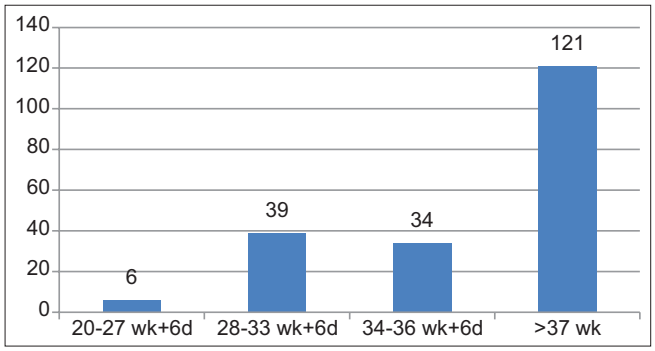

Figure 2: Distribution of gestational age

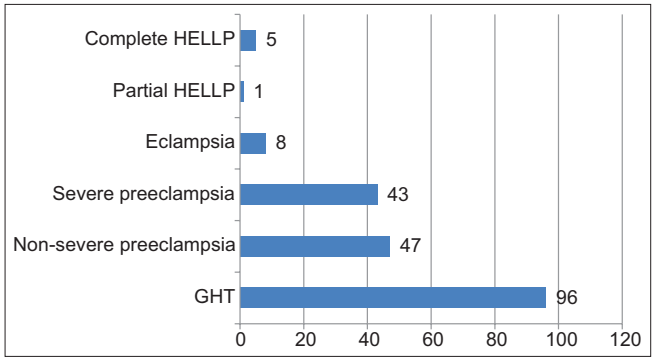

Figure 3: Distribution of diagnosis

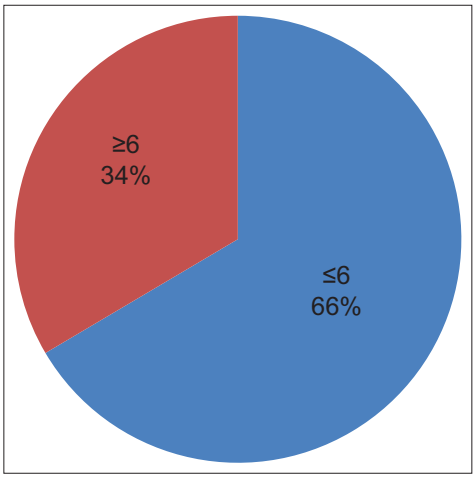

Figure 4: Distribution of serum uric acid levels

In subjects with normal uric acid level, 31.6% and 11.3% of subjects had non-severe preeclampsia and severe preeclampsia ($P < 0.0001$) [Figure 7].

In abnormal uric acid level patients, intrauterine death and HELLP syndrome are observed as statistically significant maternal and fetal complications [Table 1].

DISCUSSION

Uric acid is filtered by the renal glomeruli, absorbed by the first part of the proximal convoluted tubule, with a further secretion and reabsorption phase.[11] Ten percent of the filtered urate is excreted in the urine.[12] During pregnancy, uric acid clearance increases from 6–12 mL/min to 12–20 mL/min, with a 25% decrease in blood concentration.[13-15]

Lim *et al.*[16] recently documented that mean serum uric acid levels were significantly higher in women with transient hypertension, preeclampsia, and superimposed preeclampsia. In Redman's study,[17] the best correlation to predict perinatal mortality was the serum uric acid level at 28–32 weeks' gestation. A serum uric acid level of ~420/l mollL only predicted perinatal mortality of 6–9% in their group with term pregnancies.[17] Plouin *et al.*[18] documented a poor perinatal outcome (including stillbirths and neonatal deaths) in pregnancies

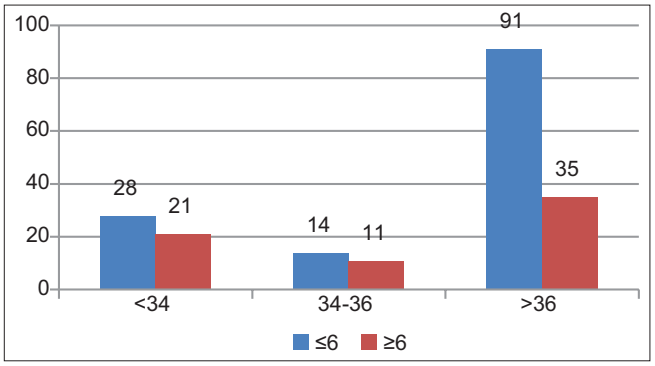

Figure 5: Distribution of gestational age with serum uric acid

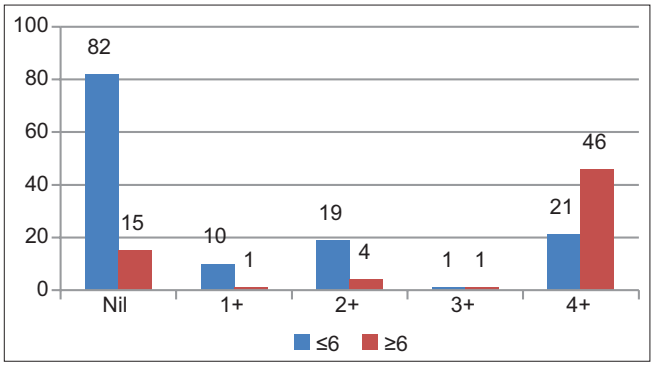

Figure 6: Distribution of proteinuria with serum uric acid

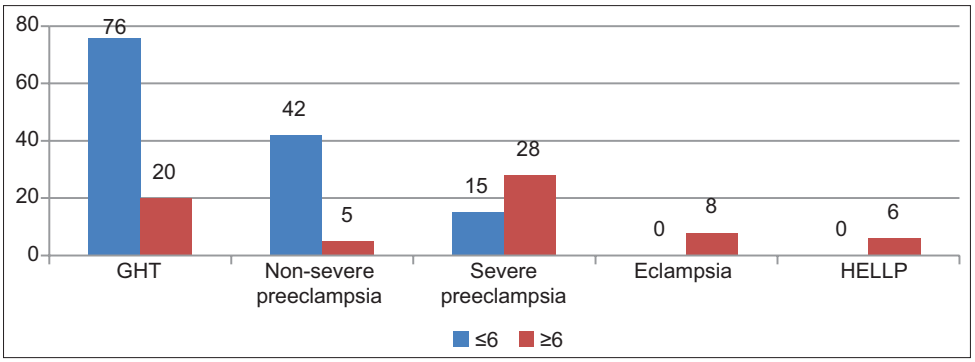

Figure 7: Distribution of gestational hypertension with serum uric acid

complicated by preeclampsia and predicted by serum uric acid levels.

In our study, most hypertensive mothers were in the age group of 20–35 years. Number Indian authors noticed similar age incidence.[19,20]

In his study, Robert *et al.*[21] showed that 6 % of patients had HELLP syndrome, and 16% had eclampsia. In our study, subjects with normal uric acid level, 31.6% and 11.3% of subjects had non-severe preeclampsia and severe preeclampsia, respectively.

Magann *et al.*,[22] there is a positive correlation between increasing/raised SUA level and increased incidence of PNM, stillborn. According to Robert *et al.*,[21] the preterm risk is increased in groups of patients with hypertension proteinuria hyperuricemia. Even in the absence of proteinuria, hyperuricemia is a significant risk factor for preterm birth.

CONCLUSION

Our study concludes that the measurement of serum uric acid levels after 20 weeks of gestation is an excellent diagnostic and prognostic tool to assess fetal outcomes. This study shows that the estimation of serum uric acid levels in pregnancies complicated by hypertension and preeclampsia helps assess the severity of the disease and identify life-threatening maternal and fetal complications as a result of preeclampsia/eclampsia. Since serum uric acid is a very simple analytical tool that can be readily performed at any biochemical laboratory, this is a very cost-effective method to gauge GHT complications and improve maternal and perinatal outcomes.

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Uric acid is as important as proteinuria in identifying fetal risk in women with gestational hypertension. Hypertension 2005;46:1263-9.
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Original Article

A Prospective Observational Study on Risk Factors of Patients with Dilated Cardiomyopathy

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Abstract

Introduction: Dilated cardiomyopathy (DCM) is an important cause of sudden cardiac death and heart failure and is the leading indication for cardiac transplantation in children and adults worldwide. Different etiologies can lead to DCM, including inherited, infectious, and inflammatory diseases.

Aim: The aim of the study was to study the risk factors of patients with DCM.

Materials and Methods: This prospective observational retrospective study was conducted to analyze the risk factors and the etiology of DCM in Headquarters hospital, Dindigul. A total of 75 patients were included in this study. Detailed medical history and physical examination with basic laboratory investigations were made.

Results: Out of 75 patients, 54 were males and 21 were females. The majority were in the age group between 51 and 55 years, followed by 46–50 years. Forty-five patients had ischemic DCM and 30 patients had non-ischemic DCM. Twenty-six patients had diabetes, followed by alcoholic of 26 patients and hypertension of 24 patients. Seven patients of diabetes had moderate left ventricular (LV) dysfunction, and 18 patients of hypertensive had severe LV dysfunction. Overall alcoholic and hypertensive patients had moderate and severe LV dysfunction. Based on the ECG outcome, the majority had LV hypertrophy.

Conclusion: Alcoholism, diabetes, and smoking are the significant risk factors in DCM. The severity of DCM is directly proportional to the number of risk factors present.

Key words: Alcohol, Diabetes, Dilated cardiomyopathy, Hypertension, Risk factors, Smoking

INTRODUCTION

Dilated cardiomyopathy (DCM) is an important cause of sudden cardiac death (SCD) and heart failure (HF) and is the leading indication for cardiac transplantation in children and adults worldwide.[1] DCM is more commonly seen in men than in women. Its prevalence in the general population is estimated at 36 cases/100,000. There are different types of cardiomyopathy caused by a range of factors from coronary artery heart disease to certain drugs. These can all lead to various complications such as atrial fibrillation, cardiac failure, and cardiogenic shock.[2] Ischemic cardiomyopathy caused by coronary artery disease is the most common cause of congestive HF. It is characterized by ventricular chamber enlargement and systolic dysfunction with normal left ventricular (LV) wall thickness. Different etiologies can lead to DCM, including inherited, infectious, and inflammatory diseases. DCM has been associated with mutations in genes for Desmin (cytoskeletal), Lamin C (nuclear membrane), or Myosin (contractile proteins). However, the majority of cases remain unexplained after a thorough review of the secondary cause.[3]

Cardiomyopathy is a progressive disease of the myocardium or heart muscle. In most cases, the cardiac muscle weakens and is unable to pump blood to the rest of the body.[4] In most cases, DCM is progressive, leading to HF and death. Classic symptoms include paroxysmal nocturnal dyspnea, orthopnea, leg swelling, and shortness of breath. Non-specific symptoms of fatigue, malaise, and weakness also can be present. More severe cases can present with thromboembolic complications, conduction disturbances, arrhythmias, or even SCD. Physical examination findings are mostly not specific to other

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causes of cardiomyopathy and consist of typical findings seen with congestive HF.

Findings include crackles in the lung fields, elevated jugular venous pressures, peripheral edema, and an S3 gallop. Classically, the point of maximum impulse or PMI is displaced laterally. Tricuspid or mitral regurgitation murmurs are not uncommon as a result of ventricular enlargement and annular dilation. Neck examination may reveal jugular venous distension, A-wave, large V waves, and positive hepatojugular reflux.

Without a transplant, the survival rates are low. Mortality rate is very high if the cardiomyopathy patient is admitted with serious complications such as cardiac failure and cardiogenic shock.[5] While most patients with DCM have symptoms, few patients may be asymptomatic because of the compensatory mechanisms. The continued enlargement of the ventricles leads to a decline in ventricular function, followed by conduction system abnormalities, ventricular arrhythmias, thromboembolism, and HF. The earlier these patients are identified and treated, the better the prognosis.

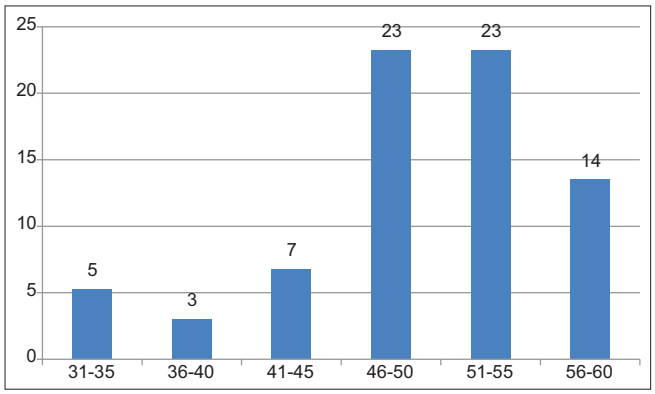

Figure 1: Age distribution

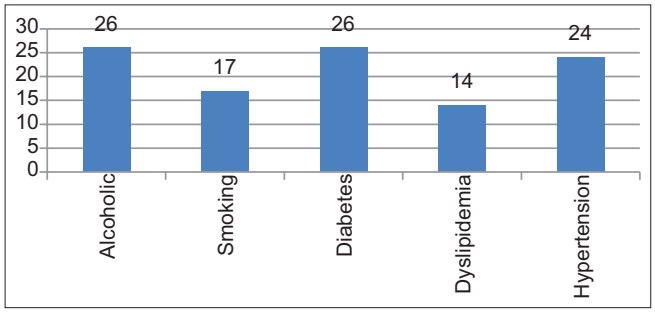

Figure 2: Comorbid of the study patients

Aim

The aim of the study was to study the risk factors of patients with DCM.

MATERIALS AND METHODS

This observational prospective study was conducted in Headquarters hospital, Dindigul. Patients more than 18 years and <60 years with DCM were included in the study. Restrictive cardiomyopathy, hypertrophic cardiomyopathy patients were excluded from the study. Detailed medical history and physical examination with basic laboratory investigations such as complete blood count, blood sugar, renal function tests, liver function test, lipid profile and urine analysis, ECG, X-ray Chest PA view, echocardiogram, and ICTC were done.

RESULTS

Out of 75 patients, 54 males and 21 females are presented in Table 1.

Out of 75 patients, 45 patients had ischemic DCM and 30 patients had non-ischemic DCM [Table 2].

Out of 75 patients, 54 were males and 21 were females. Five patients were in the age group between 31 and 35 years, three patients between 36 and 40 years, seven patients between 41 and 45 years, 23 patients between 46 and 50 years, 23 patients between 51 and 55 years, and 14 patients between 56 and 60 years [Figure 1].

In our study, 26 patients had a habit of alcohol drinking, 17 patients had a habit of smoking, 26 patients had diabetes, 14

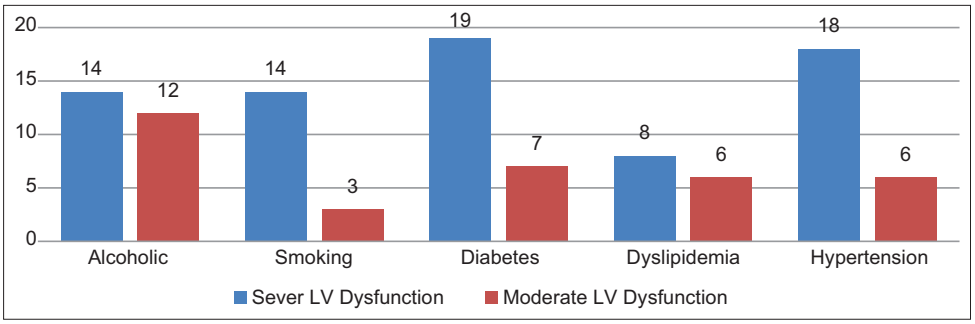

Figure 3: Distribution of severity of dilated cardiomyopathy

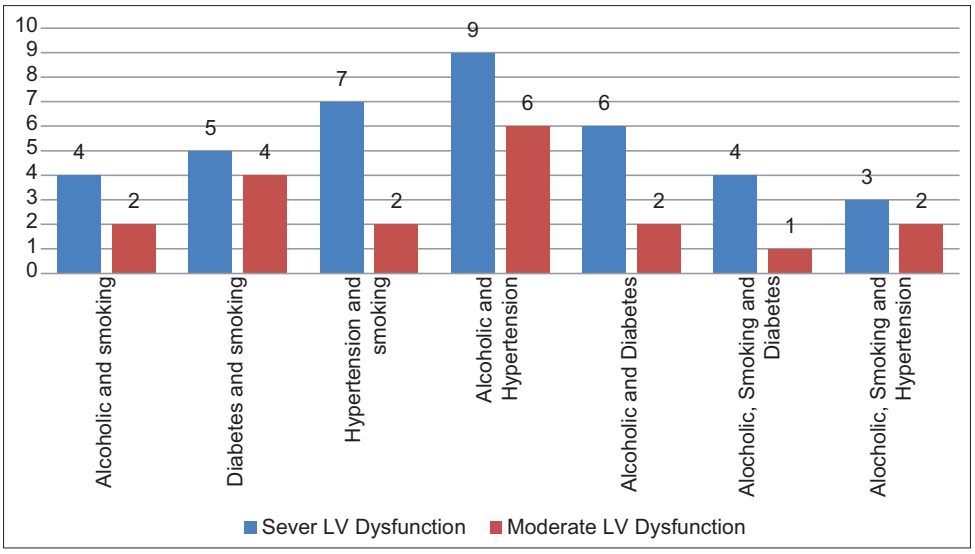

Figure 4: Distribution of severity of dilated cardiomyopathy

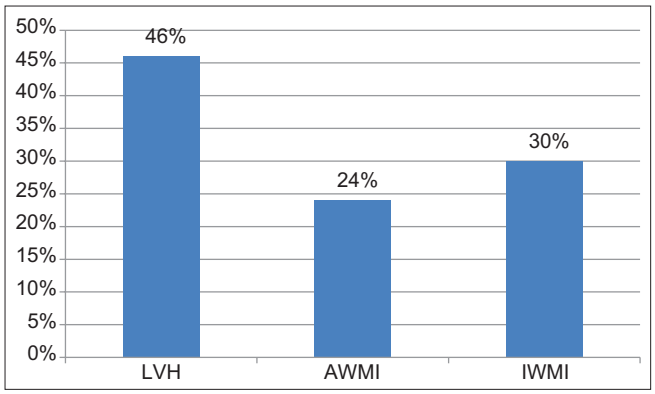

Figure 5: ECG outcome in dilated cardiomyopathy

Table 1: Gender distribution

Gender	Number of Patients
Male	54
Female	21

Table 2: Diseases distribution

Diseases	Number of Patients
Ischemic cardiomyopathy	45
Non-ischemic cardiomyopathy	30

patients had dyslipidemia, and 24 patients had hypertension [Figure 2].

Twelve patients who had a habit of alcohol drinking, three patients who had a habit of smoking, seven patients who had diabetes, six patients with dyslipidemia, and six patients with hypertension had moderate LV dysfunction. Fourteen patients with alcoholic addictions, 14 patients with smoking habits, 19 patients with diabetes, eight patients with dyslipidemia, and 18 patients with hypertension had severe LV dysfunction [Figure 3].

Two patients had a habit of smoking and alcohol drinking, four patients with diabetes and smoking, two patients with smoking and hypertension, six patients with alcohol and hypertension, two patients with alcohol and diabetes, one patient with alcohol, smoking and diabetes, two patients with alcohol, smoking, and hypertension had moderate LV dysfunction. Four patients had a habit of smoking and alcohol drinking, five patients with diabetes and smoking, seven patients with smoking and hypertension, nine patients with alcohol and hypertension, six patients with alcohol and diabetes, four patients with alcohol, smoking, and hypertension, and three patients with alcohol, smoking, and hypertension had moderate LV dysfunction [Figure 4].

Thirty-four patients had LV hypertrophy, 18 patients had anterior wall myocardial infarction, and 23 patients had inferior wall myocardial infarction [Figure 5].

DISCUSSION

In our study, majority were males compared to females who are similar to Deshmukh *et al.*[6] study 2011, where the male:female ratio was 1.5:1. The higher number of patients was in the age group of above 45 years whereas research was done by Deshmukh *et al.*[6] shown that in his study, most of them were in the age group above 60 years.

In our study, the majority of the study, the population had diabetes, followed by alcoholic and diabetes. Therefore, it is said that only alcohol is not enough to cause DCM in most cases; alcoholic cardiomyopathy is more common in those with a genetic predisposition to heart diseases, in contrast

to those without. However, we did not do genetic testing in alcoholic DCM cases due to financial reasons. Once DCM develops in alcoholics or smokers, the prognosis is uniformly poor.[7]

All of the patients who were undertaken for this study either had moderate or severe LV dysfunction. The severity of the LV dysfunction correlated directly with the history of smoking and alcoholism but the study done by Reeves *et al*. on 1978 shown that symptomatic alcoholic patients may have systolic dysfunction of various degrees, known as alcoholic cardiomyopathy. However, data on systolic function in asymptomatic alcoholics are conflicting.[8-11]

In our study, patient with a habit of alcohol and hypertension had LV dysfunction more compared with other comorbidities. Diabetes and smoking also increase the risk of developing DCM. Patients who had a history of alcoholism and who had diabetes showed a greater degree of ventricular dysfunction. Dyslipidemia alone does not seem to cause DCM. When dyslipidemia and diabetes are present, the risk increases tangentially compared to dyslipidemia with systemic hypertension. In Jain *et al*. study ischemic cardiomyopathy comprised 37% of cases followed by idiopathic DCM seen in 30% of patients.[12]

CONCLUSION

The severity of the LV dysfunction correlated directly with the history of smoking and alcoholism. Patients who were both smokers and alcoholics had more significant damage to the heart. Alcoholism, diabetes, and smoking are the significant risk factors in DCM. The severity of DCM is directly proportional to the number of risk factors present.

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Original Article

A Prospective Observational Study on Peripheral Nerve Dysfunction in Chronic Kidney Disease Patients

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Abstract

Introduction: The chronic kidney disease (CKD) is a worldwide public health problem and is a long-term condition caused by kidney damage. The CKD leads to progressive and irreversible destruction of nephron mass, irrespective of cause. Peripheral nerve dysfunction is a recognized complication of CKD.

Aim: The aim of our study was to analyze the peripheral nerve dysfunction in CKDs.

Materials and Methods: This prospective observational study was conducted in headquarters hospital, Dindigul to analyze the peripheral nerve dysfunction in CKDs. Complete neurological examination was done with special emphasis on peripheral nerve examination.

Results: Out of 40 patients, 28 were males and 12 were females. Based on duration of kidney diseases and peripheral nerve dysfunction six patients had duration <1 years. Out of which three had peripheral nerve dysfunction, 11 patients between 1 and 3 years. In that six had peripheral nerve dysfunction, 12 patients between 3 and 5 years. Out of which eight had peripheral nerve dysfunction and eleven patients had duration greater than 5 years. In that nine had peripheral nerve dysfunction. Thirteen patients had sensory motor nerve damage, seven patients had sensory nerve damage, and six patients had motor nerve damage.

Conclusion: From this study, we concluded that if duration of kidney diseases increases then peripheral nerve dysfunction also increases and our study shows that majority were affected with both sensory and motor damage.

Key words: Chronic kidney disease, Peripheral neuropathy, Sensory motor neuropathy

INTRODUCTION

The chronic kidney disease (CKD) is a worldwide public health problem and is a long-term condition caused by kidney damage. The CKD leads to progressive and irreversible destruction of nephron mass, irrespective of cause. It is a well-known fact that patients of CKD are at increased risk of mortality as well as morbidity due to the myriad complications associated with this disease entity. Neurological complications, secondary to the uremic state, contribute largely to the morbidity and mortality in patients with renal failure. CKD is a rapidly growing global health problem, with a prevalence of 15% in developed nations and peripheral neuropathy is most common complication with kidney disease.[1]

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CKD is defined as renal injury of a more prolonged nature, often leads to progressive and irreversible destruction of nephron mass, irrespective of cause, the eventual impact of severe reduction in nephron mass is an alteration in function of virtually every organ system in the body.[2] CKD potentially affects all levels of the nervous system, from the central nervous system through to the peripheral nervous system (PNS).[3] The chronicity and severity of kidney disease appear to be the important cause to the development of neuropathy.

Most of the time, patients who are having features of peripheral nerve dysfunction would not come out with complaints of it unless it is specifically asked or looked for. At present, the medical treatment for kidney disease is

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improving and patient's long-term survival is improving.[4] Peritoneal dialysis, hemodialysis, and transplantation have revolution the prognosis of CKD in recent periods. As patient's lifespan is prolonged due to recent improvement in the treatment of CKD, it is essential to know about the complication that can occur in patient surviving for long period with CKD, of which peripheral nerve dysfunction is one of the recognizable and treatable complication of CKD.[5]

The etiology of CKD is varying in nature, but the clinical symptoms and signs are of the same. There are several etiologies for CKD. It can occur due to either a primary kidney disease or as a complication of a multisystem disorder.[6] DM is the most common cause in developed nations,[6] whereas inflammatory kidney disease, namely, glomerulonephritis and interstitial nephritis remains the most common causes in developing countries.[7] DM along with hypertension – the second most common cause – and glomerulonephritis accounts for about 75% of all adult cases.[8] In young adults a common etiology of CKD is genetic kidney disease.[8]

Aim

The aim of our study was to analyze the peripheral nerve dysfunction in CKDs.

MATERIALS AND METHODS

This prospective observational study was conducted in headquarters hospital, Dindigul to analyze the peripheral nerve dysfunction in CKDs. Informed consent was obtained from the study population. Patients with proved clinical and biochemical parameters in favor of CKD are included in the study. Complete neurological examination was done with special emphasis on peripheral nerve examination. After selecting the patients with reference to inclusion and exclusion criteria, the presence of peripheral nerve dysfunction is assessed in them clinically by means of motor and sensory symptoms and sings.

RESULTS

Out of 40 patients, 28 males and 12 females are presented in Table 1.

Out of 40 patients based on duration of kidney diseases, six patients had duration <1 years, 11 patients had duration between 1 and 3 years, 12 patients had duration between 3 and 5 years, and 11 patients had duration greater than 5 years [Figure 1].

Out of 40 patients based on duration of kidney diseases and peripheral nerve dysfunction, 6 patients had duration <1 years. Out of which three had peripheral nerve dysfunction, 11 patients between 1 and 3 years. In that six had peripheral nerve dysfunction, 12 patients between 3 and 5 years. Out of which eight had peripheral nerve dysfunction and 11 patients had duration greater than 5 years. In that nine had peripheral nerve dysfunction [Figure 2].

Out of 40 patients, 13 patients had sensory motor nerve damage, seven patients had sensory nerve damage, and six patients had motor nerve damage [Figure 3 and Table 2].

Table 1: Gender distribution

Gender	Number of Patients
Male	28
Female	12

DISCUSSION

Peripheral neuropathy is a recognized complication of renal failure. These complications can potentially affect both the central and PNSs. Common neurological complications in CKD include stroke, cognitive dysfunction, encephalopathy, peripheral, and autonomic neuropathies. These conditions have a significant impact not only on patient morbidity but also on mortality risk through a variety of mechanisms. Understanding the pathophysiological mechanisms of these conditions can provide insights into effective management strategies for neurological complications.

In our study, majority had duration of CKDs between 3 and 5 years followed by greater than 5 years. Kumar *et al.* discussed nerve condition study in relation to duration and severity and CKD. They found that reduced suggestive of neuropathy but delayed F-waves and H-reflex are also suggestive of neuropathy.[9] Babu *et al.*[10] conducted a study on this topic and focused on association of CKD and peripheral neuropathy. In that study impact of age was also observed on neuropathy and its severity. Age >65 years is more prove to peripheral neuropathy in CKD.

Rathnakumar *et al.*[11] completed a study in 2018 on peripheral dysfunction and CKD and conclude that distal sensory and motor neuropathy our two common types of peripheral neuropathy associated with CKD. In our study, 64.8% of patients have peripheral neuropathy.

Table 2: Type of peripheral neuropathy

Sensory motor	Sensory	Motor	Total
13	7	6	26

Another study was conducted by Arnold *et al.*[12] reported that CKD is highly associated with neurological complications which may lead to sourobidity and neutrality. May chronic neurological complications such as stroke, dementia, and cognitive impairment were also observed.

In a study by Bolton *et al.*[13] observed similar findings and reported that a number of peripheral neurological disorders

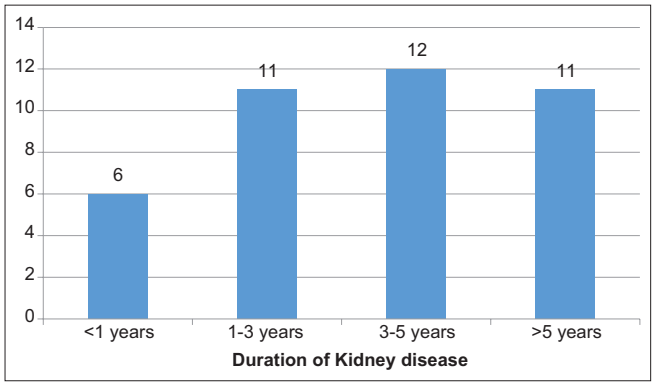

Figure 1: Duration of kidney diseases

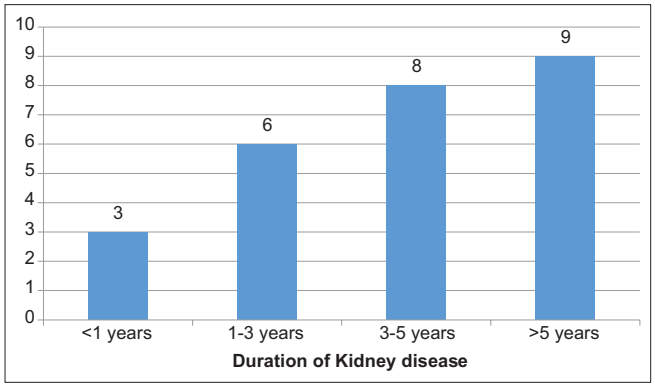

Figure 2: Patients with peripheral nerve dysfunction

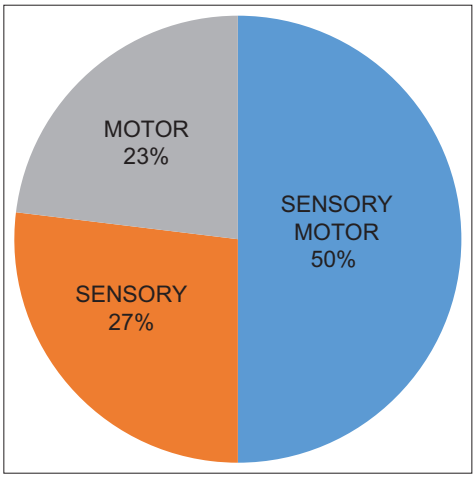

Figure 3: Patients affected with percentage with references to the type of peripheral neuropathy

are associated with CKD. Cause behind this pathology is production of toxins in CKD. Renal transplantation is an option for its recovery.

Another study was conducted by Nielsen *et al.*[14] and concluded that 77% patients with CKD have peripheral neuropathy and remaining have signs of peripheral neuropathy. In our study slowing of nerve conduction was observed in patient with renal derangement since last 2 years.

Aggarwal *et al.*[15] conducted a study on peripheral neuropathy in CKD patients and reported that sensory and motor neuropathies are associated with severity of disease or renal function; he observed symptomatic neuropathy in 51% of predialysis patients. Similar study was conducted by Krishnan *et al.*[16] in 2005 and reported 91% peripheral neuropathy in CKD. This association was reported irreversible that cannot be reversed with early or delayed recovery from renal derangement.

CONCLUSION

From this study, we concluded that if duration of kidney diseases increases then peripheral nerve dysfunction also increases and our study shows that majority were affected with both sensory and motor damage.

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Original Article

Study of Platelet Count and Mean Platelet Volume in Pregnancy-Induced Hypertension – An Observational Study

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Abstract

Introduction: Pregnancy-induced hypertension (PIH) or preeclampsia is a potential life- threatening complication, affecting 3–8% of the pregnancies. The etiology of the disease is unknown and platelet activation markers such as platelet count (PC) and mean platelet volume (MPV) can be used in early disease diagnosis. Platelet indices can be easily measured as a part of routine blood investigation. This study assesses the variations in PC and MPV in preeclamptic women during the 3rd trimester of pregnancy.

Aim: This study aims to analyze the role of PC and MPV in predicting pregnancy-induced hypertension.

Methods: Fifty patients with pregnancy-induced hypertension and proteinuria aged 18–35 years, during their 3rd trimester of pregnancy were included in the study. PC and MPV were measured during early to end of the 3rd trimester.

Results: The mean gestational period at the time of sample collection was 24 weeks. The mean platelet count was 128.27±58.46 lakh/mm^3 and the mean platelet volume was 6.82±2.12 fl.

Conclusion: Platelet count has an association with predicting the increasing grade of PIH. Thrombocytopenia/depleted platelet count is consistently associated with severe PIH and may increase the risk of coagulopathy.

Key words: Platelet count, Mean platelet volume, Preeclampsia, Gestational hypertension, Thrombocytopenia

INTRODUCTION

Hypertensive disorders are responsible for the most common medical complications of pregnancy and are also the reasons for maternal and perinatal mortality and morbidity globally. Pregnancy-induced hypertension (PIH) begins after 20 weeks of pregnancy and is diagnosed with a blood pressure >140/90 mmHg with proteinuria.[1,2] The etiology is unknown but a few studies suggest that PIH may be caused by alterations in coagulation and fibrinolysis. Endothelial dysfunction and platelet activation are one proposed theory for occurrence of PIH.[3] The coagulation pathway gets activated with the release of granule contents on platelet activation and leads to the clinical and biochemical manifestations of PIH. Platelet count (PC), mean platelet volume (MPV), and platelet distribution width (PDW) are the markers of platelet activation and can be easily measured in routine blood investigation. These values are analyzed usually in routine antenatal check-up for any variations. Any change in these values may serve as a marker for the diagnosis thromboembolic diseases.[4]

About 3–10% of the pregnancies present with hypertensive disorders and PIH contributes 14% of maternal deaths. The reasons for morbidity and mortality may be a lack of understanding of the etiology of PIH or the fact that some patients do not present with the usual symptoms of blood pressure (BP) or albuminuria.[5] Early diagnosis of PIH may reduce the maternal mortality by effective care and medication or even timely termination of pregnancy. A change in platelet count or mean platelet volume is more evident before the derangement in prothrombin time

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(PT), thrombin time (TT), or activated partial thrombin time (ApTT).[6] This study was done to find if there is a significant variation in platelet count and mean platelet volume during the 3rd trimester in gestational hypertension.

Aim

This study aims to analyze the role of PC and MPV in predicting pregnancy-induced hypertension.

MATERIALS AND METHODS

This observational study was conducted in the Department of Gynecology, Government Headquarters Hospital, Dindigul. A total of 50 consenting patients with preeclampsia (BP >140/90 mmHg and proteinuria >300 mg/day in patients of >24 weeks gestation) who were of the age group 18–35 years were included in the study. Patients with pre-existing hypertension, renal disorders, diabetes mellitus, and hematological disorders were excluded from the study. Under aseptic conditions, blood sample was collected in ethylenediaminetetraacetic acid vials. The samples were analyzed on which were observed the platelet indices that include platelet count (PC) and mean platelet volume (MPV).

RESULTS

The mean age of the patients was 31.25 ± 3.8 years. Fifty patients with preeclampsia with BP >140/90 mmHg and proteinuria were included in this study. The mean gestational period at the time of sample collection was 24 weeks. The mean platelet count was 128.27 ± 58.46 lakh/mm^3 and the mean platelet volume was 6.82 ± 2.12 fl. The study results show that platelet count was significantly decreased in the third trimester in patients with preeclampsia indicating it as a marker for diagnosis of pregnancy-induced hypertension. The MPV values remained within the normal range (7.5–12.0 fl).

DISCUSSION

Pregnancy-induced hypertension can cause complications such as eclampsia, placental abruption, preterm delivery, and the syndrome of hemolysis, elevated liver enzymes, and low platelets (HELLP) and can even lead to maternal and fetal morbidity and mortality. Gestational hypertension (GH) is the most common cause of hypertension during pregnancy with an incidence of 6–7% in nulliparous and 2–4% in multiparous women. Most cases of GH develop after 20 weeks of gestation. Thrombocytopenia or a decreased platelet count has been observed as an early marker in PIH.[7-9] Many studies reported that the platelet count was normal in the initial stages but decreased with disease progression. In our study too, there was a drop-in platelet count in the 3rd trimester of pregnancy in patients with PIH. The mean platelet count observed in this study was 128.27 ± 58.46/μm^3 (normal range: 150–450).

Earlier studies indicated that platelet activation occurs before the onset of PIH but recent evidence confirms that accumulation of activated maternal platelets within the placenta results in preeclampsia.[10] The genetic inhibition of maternal platelet activation abolished the preeclampsia like phenotype. There is evidence that the platelet indices predated the development of PIH by 2–8 weeks. Annam *et al.* and Freitas *et al.* studied a similar inverse relationship between platelet count and severity of preeclampsia.[11,12] Platelet activation can be measured in terms of reduced platelet count, increased mean platelet volume, elevated β-thromboglobulin, and platelet factor 4.

MPV is easily measured by automated analyzers and is elevated before the onset of PIH in general. Studies by Dadhich *et al.* reported that the MPV values increased with the duration of gestation and also with the disease severity. In our study, the mean platelet values lied within the normal range of 6.82 ± 2.12 fl. These findings are similar to the study findings of Cyehan *et al.* where no significant difference was found in the values of MPV between preeclampsia and normal pregnant women. Kashanian *et al.* also observed a similar finding. He stated that MPV changes did not predict preeclampsia or preterm labor. Altibas *et al.* also reported that MPV is not a significant predictor of severity of preeclampsia.[13-15]

Decreased platelet levels can lead to severe postpartum bleeding that could be life threatening. Our study findings show that decreased platelet count can be an alarming factor in women with PIH and timely treatment should be administered. Although MPV is also increased in certain cases of PIH, our study did not reveal any significant changes in MPV values.

CONCLUSION

PIH is associated with increased maternal and fetal morbidity and mortality. A decreased platelet count can be a strong indicator of disease severity in women with PIH. The mean platelet values did not show a significant change in relation to preeclampsia in our study. Many other diseases can also cause thrombocytopenia and elevated transaminase levels in pregnancy and our study is limited to this extent. Till date, there are no accurate predictors or specific prediction models for PIH at an early stage and further studies in this regard should be encouraged.

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Original Article

Comparison of Oral Iron Therapy with Intravenous Iron Sucrose in Anemic Pregnant Women

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Abstract

Introduction: Anemia is the most common medical problem in pregnancy. Parenteral iron is a new useful agent, used in the treatment of pregnancy/iron deficiency anemia. Oral iron (OI) supplements were associated with more side effects and anaphylactic reactions and IV iron sucrose can overcome the shortcomings of OI therapy.

Aim: The aim of the study was to compare the efficacy and tolerance of intravenous iron sucrose (IVIS) therapy with OI therapy in anemic pregnant women.

Materials and Methods: Fifty pregnant women with mean gestational age 28.26 weeks with Hb <7.0–9.0 g/dL and peripheral smear features suggestive of iron deficiency anemia were included in the study and randomized in two groups of 25 each. Group I received 100 mg ferrous fumarate daily for 4 weeks orally and Group II received IV iron sucrose, dose calculated according to Ganzoni's formula. Target Hb level was 10 mg/dL, hematocrit values were measured at baseline and at day 28, and data were statistically analyzed.

Results: The mean age of the women was 26.85 years and the mean weight was 57.55 kg. The rise in hemoglobin as well as serum ferritin was more in IV iron sucrose group than in OI group at each point of measurement with statistically significant difference ($P < 0.0001$).

Conclusion: IVIS treated iron deficiency anemia of pregnancy more effectively than OI therapy, with no serious adverse drug reactions.

Key words: Intravenous iron sucrose, Iron deficiency anemia, Oral iron therapy, Pregnancy anemia, Serum ferritin

INTRODUCTION

Iron deficiency anemia (IDA) is the most common and widespread problem among all pregnancy related nutritional deficiencies. The World Health Organization (WHO) estimates that 35%–75% of pregnant women in developing countries are anemic.[1] Pregnant women are most vulnerable to anemia and 40–60% of maternal death in non-industrialized countries is caused by pregnancy related anemia.[2] Around 500,000 maternal deaths and 20,000,000 maternal morbidity cases annually are related to iron deficiency anemia according to a WHO data presented at the Federation of International Obstetrics and Gynaecology meeting in 2003 in Chile.[3] About 64.4% of the women who die have a Hb count <8 g/dL and 21.6% had Hb <5 g/dL. The prevalence rate is 57.9% in India.

The fetal consequences of anemia include risk of growth retardation, premature birth, intra-uterine death, infection, and prelabor rupture of membranes. One of the widely practiced treatment methods is the provision of iron supplements to pregnant women that include oral/parenteral iron therapy and blood transfusion.[4] Oral iron (OI) therapy is associated with increased side effects, non-compliance, and delayed treatment response. Blood transfusion is reserved for emergency situations and is also associated with increased risk of cross viral infections. A safe and effective for method for correcting IDA are IV iron sucrose infusion which has reduced risk of infections and anaphylaxis. Many recent studies on IV iron sucrose therapy states that the therapy has a low incidence of side

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effects, anaphylaxis, and tissue toxicity. It is also known to have a high availability for erythropoiesis.[5]

OI therapy requires several weeks to raise the hemoglobin levels and months to replenish the iron stores in the body and many women fail to comply with such prolonged therapy. IV iron sucrose complex has the advantage of replenishing the iron reserves in a short time and also improves the absorption and resistance when compared with OI.[6] This study compares the efficacy of OI therapy and IV iron sucrose therapy in correcting IDA in pregnant women.

Aim

The aim of the styd was to compare the efficacy and tolerance of intravenous iron sucrose (IVIS) therapy with OI therapy in anemic pregnant women.

MATERIALS AND METHODS

This prospective comparative study was conducted at the Department of Gynecology, Government Headquarters Hospital, Dindigul. Fifty pregnant women with gestational age >24 weeks who had established IDA, with confirmed Hb 7.0–9.0 g/dL and peripheral smear features suggestive of iron deficiency anemia were included in the study. Women with any chronic infection, chronic lung, liver, renal, or cardiac diseases were excluded from the study. The study began after obtaining approval from the institutional ethical committee and informed consent was obtained from all the women before the start of the study. Baseline laboratory investigations such as hemoglobin, packed cell volume, mean corpuscular volume, mean corpuscular hemoglobin (MCH), MCH concentration, peripheral smear, serum ferritin, urine routine and culture sensitivity, and stool for ova/cyst were carried out before enrolment. Patients fulfilling the criteria were divided into two groups of 25 each, Group I: OI tablet group (100 mg ferrous fumarate daily for 4 weeks) and Group II: IV iron sucrose group (total iron dose (TID) was calculated according to the Ganzoni's formula: TID (mg) = weight (Kg) × ([ideal Hb - actual Hb] g/dL) × 0.24 + 500 mg (depot iron), rounded up to the nearest multiple of 100 mg. The target hemoglobin was 10 g/dL and treatment was stopped earlier in patients who reached Hb concentration >10.0 g/dL or SF level >300 ng/mL before the administration of the total IV iron. Follow-up evaluation of hematological parameters was done at baseline and at the 28th day. Measurement of serum ferritin was repeated on day 28 after baseline study and clinical improvement in symptoms was assessed. Gastro-intestinal side effects such as nausea, vomiting, constipation and diarrhea, pruritus, fever, myalgia, hypotension, local extravasation, thrombophlebitis, metallic taste, and anaphylactic reactions were noted. Data were analyzed using Independent sample *t*-test and Pearson Chi-square test in SPSS version 21. Value of <0.05 was considered significant and <0.001 was considered highly significant.

RESULTS

Twenty-five cases from each group those who completed the treatment were included in the study. The mean age of the women was 26.85 years and the mean weight was 57.55 kg. Out of the 50 study participants, 28 women had primiparity and 22 women had multiparity. The mean gestational age was 28.26 weeks. No difference in age, weight, gestational age, and parity of the patients between groups was observed. All the pregnant women in IV sucrose iron group completed the full calculated required dose of iron. The two groups were similar in demographic and clinical characteristics. Hb and serum ferritin levels were measured at baseline and at day 28 Figures 1 and 2. The baseline Hb level was 8.64 and 8.28 in the OI group and IVIS group, respectively, and at day 28, the levels were 9.61 and 10.54 in Group I and Group II, respectively. Rise in Hb and serum ferritin was observed in both the groups and the serum ferritin levels at day 28 were 52.64 in the

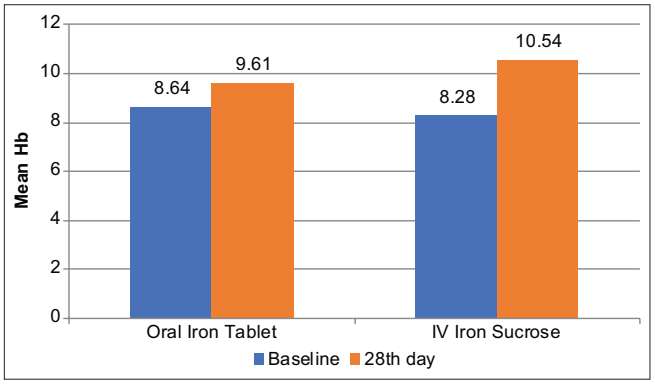

Figure 1: Comparison of mean Hb levels at base line and day 28

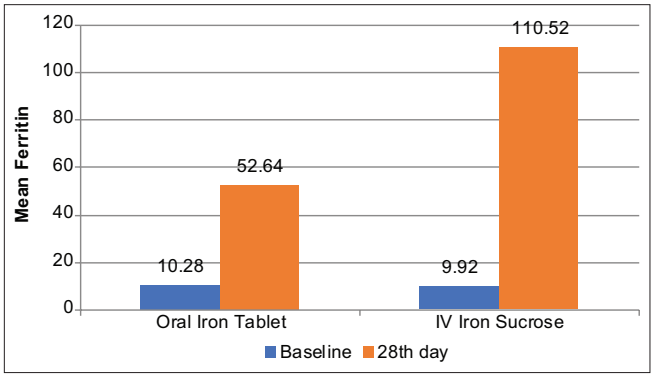

Figure 2: Comparison of mean ferritin levels at baseline and day 22

OI group (baseline – 10.28) and 110.52 in the IVIS group (baseline – 9.92). The rise in hemoglobin as well as serum ferritin was more in IV iron sucrose group than in OI group at each point of measurement with statistically significant difference ($P < 0.05$).

DISCUSSION

OI therapy has been widely used in the treatment of IDA in pregnancy but the patients do not respond adequately. IV iron use was previously underutilized due to the undesirable and sometimes serious side effects. Recent studies have led to the development of the Types II and III iron complexes that offer improved tolerance and efficacy along with a good safety profile.[7] In our study, the efficacy and tolerability of OI were compared with that of IVIS. The study results showed that the mean Hb levels at day 28 were significantly increased ($P < 0.0.12$) in the IVIS group (10.54 g/dL) than in the OI group (9.61 g/dL). There was a significant difference in the mean serum ferritin levels on day 28 between both the groups (52.64 in OI group and 110.52 in IVIS group).

IVIS is safe in pregnancy and corrects anemia at short duration and replenishes iron stores better than OI. Our study findings were similar to the other studies in literature. A case series by Govan and Scott early in 1949 reported the benefits of IV iron.[8] Subsequently, many small observational studies, quasi-experimental studies, and small randomized clinical trials showed improvement in hematological indices with IVIS in pregnant women. Iron sucrose is a type II Fe complex that releases iron to endogenous iron binding protein. It has a half-life of 6 h, and carry a minimum risk of allergic accident or toxic reactions.[9,10] IV administration increases the bioavailability and is directly delivered to the hemopoeitic system.

A randomized open label study by Unlubilgin *et al.* comparing the efficacy of intravenous iron to OI in treatment of anemia in pregnancy concluded that IV iron, treated iron deficiency anemia of pregnancy and restored iron stores faster and more effectively than OI, with no serious adverse reactions.[11] As the rate of increase in hemoglobin is faster, IVIS is suitable for treatment of IDA with lower hemoglobin in the third trimester. Bayoumeu *et al.* observed that a highly significant difference in the ferritin level was observed in the IVIS group than in OI group in his study. Increase in ferritin is because the IVIS complex releases iron rapidly to endogenous iron binding proteins with no deposition in the parenchymal tissue which is an advantage of IVIS over iron dextran or iron gluconate.[12]

Gastrointestinal side effects were reported in 20% in the OI group which included three cases of nausea and vomiting, one case of gastritis, and one case of loose motion. Mild adverse events such as burning sensation and swelling and pain in the injection site were noted one case each in the iron sucrose group. Other studies reported unpleasant taste and fever, which were not observed in our study. The reduced adverse drug reactions and no episodes of anaphylaxis make IVIS safe for anemia in pregnancy. The only disadvantage of IVIS therapy is that it is more expensive than OI and requires admission to hospital. The limitations of the study are that serum ferritin levels were not measured in the post-natal period and also if the hemoglobin levels were maintained in the similar range during the lactation period.

CONCLUSION

OI increases hemoglobin comparably with IVIS, but does not replenish iron stores as much as IVIS. IVIS therapy is better and efficient than OI in improving the Hb levels and serum ferritin levels. The side effects of IVIS are also minimal when compared to that of OI. It is also safe to administer in pregnancy. IVIS is expensive than OI and requires a hospital setting for administration. It can be used as an effective alternative for treating IDA in pregnant women. However, many aspects still require to be studied and many to be re-endorsed before IVIS are used as a routine in management of IDA.

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Original Article

Evaluation of Solitary Nodule of Thyroid using Ultrasonogram and Color Flow Doppler: A Prospective Study

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Abstract

Introduction: Thyroid nodules are common and a frequent reason for referral to secondary care. Clinical assessment and investigation should aim to address the functional status of the thyroid, exclusion of malignancy, and the presence of other symptoms.

Aim: The aim of this study is to correlate the results of sonography, color flow Doppler (CFD), fine-needle aspiration cytology (FNAC), and histopathology of solitary thyroid nodule.

Materials and Methods: This comparative single-institutional study was conducted in the Department of Surgery, Tirunelveli Medical College. A total of 50 patients with solitary thyroid nodule confirmed by ultrasound were included in this study. The patient's demographic data were recorded and written and informed consent was obtained from all the patients. All patients were subjected to a thorough clinical evaluation and went through routine investigations such as FNAC, thyroid profile, X-ray neck-AP, and lateral. The reports were evaluated, statistically analyzed, and discussed.

Results: Out of the 50 patients, 46 were female (92%) and 4 patients were male (8%). The peak age of occurrence of thyroid nodule was in the age group of 41–50 years. On FNAC examination, 32 patients were present with colloidal nodular goiter (64%) followed by simple colloidal goiter in 10 patients (20%), thyroiditis in 3 patients (6%), follicular adenoma in 2 patients (4%), follicular neoplasm in 2 patients (4%), and cystic lesion in 1 patient (2%). Based on echogenicity, 43 patients (86%) showed hypoechogenicity, 6 patients (12%) showed hyperechogenicity, 1 patient (2%) showed isoechogenicity. Perinodular flow was observed in 33 nodules (66%), absent flow present in 8 nodules (16%), and intranodular flow in 9 nodules (18%). Based on histopathology, 25 patients (50%) had a nodular colloidal goiter, 13 patients (26%) had a simple colloidal goiter, 9 patients (18%) had follicular adenoma, and 3 patients (6%) had thyroiditis.

Conclusion: From this study, we concluded that no positive correlation is established between the various sonographic and CFD criteria with malignancy. However, FNAC reports correlated remarkably well with histopathological examination reports. FNAC in combination with ultrasonography and Doppler tests can be remarkable in detecting thyroid malignancies.

Key words: Doppler, Fine-needle aspiration cytology, Histopathology, Solitary thyroid nodule

INTRODUCTION

The solitary thyroid nodule, defined as a palpably discrete swelling within an otherwise normal gland, is usually a benign lesion. Thyroid nodules are common in both hyperthyroid and euthyroid patients; they are present in half of all thyroid glands that are subject to careful pathologic examination. More than 80% of all patients with thyroid nodules are women; palpable thyroid nodules have been detected in 1.5% of men and 6.4% of women between the ages of 30 and 59.2 years. Prevalence of thyroid nodules increases from near zero at age 15 years to 50% by about age 60–65 years.[1]

Thyroid nodule is the most common surgical disease of the thyroid gland inmost centers. About 5–10% of the solitary nodules are malignant. Hence in the past, excision of every solitary nodule was advocated. However, during the past

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decade, with a better understanding of the pathology and with refinements in the investigations and interpretation, only solitary nodules which are at high risk for malignancy are identified and excised.[2,3]

Among the others, only a small number with specific indications for surgery are ablated. A plethora of investigations has evolved over the past 25 years. However, from the diagnostic angle, only ultrasonography (USG)-color Doppler and fine-needle aspiration cytology (FNAC) are commonly required.[4,5] This study aims to correlate the results of sonography, color Doppler flowmetry, and FNAC and evaluate their effectiveness in detecting thyroid malignancies in clinically palpable solitary thyroid nodules.

Aim

The aim of this study is to correlate the results of sonography, CFD, FNAC, and histopathology of solitary thyroid nodule.

MATERIALS AND METHODS

This study was conducted by randomly selecting 50 patients with a clinically palpable solitary nodular goiter who were admitted to the wards under various units in the Department of General Surgery, Tirunelveli Medical College. All patients who had confirmed solitary nodule by ultrasound were included in the study after signing informed consent. Patients with multiple nodules and coexistent neck nodules were excluded from the study.

Data regarding the age and sex of the patients were recorded, the patients were examined, after which FNAC of the nodule was performed using a 25-gauge needle with or without negative pressure. All the patients were subjected to a thorough clinical evaluation and underwent routine investigations such as thyroid profile, X-ray neck-AP, and lateral. Ultrasonogram was performed using a high-resolution sonography by an experienced radiologist. Color flow Doppler (CFD) was performed with a VIVID 3 pro. All the patients who underwent surgery (hemi-thyroidectomy) were followed up in the post-operative period. Their histopathological reports were also reviewed and used to correlate with the FNAC, sonography, and CFD reports. In surgical patients, the post-operative complications were documented. The reports were evaluated, and the results were statistically analyzed and discussed.

RESULTS

Out of the 50 patients, 92% were female (46 patients) and 8% were male (4 patients). Eighteen patients (36%) were in the age group of 31–40 years, 15 patients (30%) between 41 and 50 years, 6 patients (12%) between 21 and 30 years, 5 patients (10%) between 51 and 60 years, 3 patients (6%) <20 years, and 3 patients (6%) greater than 60 years [Table 1].

Based on FNAC examination, 32 patients presented with colloidal nodular goiter (64%) followed by simple colloidal goiter in 10 patients (20%), thyroiditis in 3 patients (6%), follicular adenoma in 2 patients (4%), follicular neoplasm in 2 patients (4%), and cystic lesion in 1 patient (2%) [Table 2].

Based on echogenicity, 43 patients (86%) showed hypoechogenicity, 6 patients (12%) showed hyperechogenicity, and 1 patient (2%) showed isoechogenicity [Table 3].

Based on vascular flow, absent flow was noticed in 8 nodules (16%), perinodular flow in 33 nodules (66%), and intranodular flow in 9 nodules (18%) [Table 4].

Histopathology showed that 25 patients (50%) had a nodular colloidal goiter, 13 patients (26%) had a simple colloidal goiter, 9 patients (18%) had follicular adenoma, and 3 patients (6%) had thyroiditis [Table 5].

DISCUSSION

Thyroid enlargement, whether diffuse or nodular, leads to a battery of investigations, mainly to rule out the

Table 1: Age distribution

Age	Number of patients	Percentage
<20	3	6
21–30	6	12
31–40	18	36
41–50	15	30
51–60	5	10
>60	3	6

Table 2: Fine-needle aspiration cytology (FNAC) distribution

FNAC report	Number of patients	Percentage
Simple colloidal goiter	10	20
Colloidal nodular goiter	32	64
Follicular adenoma	2	4
Follicular neoplasm	2	4
Thyroiditis	3	6
Cystic lesion	1	2

Table 3: Cross-tabulation between echogenicity and number of patients

Echogenicity	Number of patients	Percentage
Hypoechogenicity	43	86
Hyperechogenicity	6	12
Isoechogenicity	1	2

Table 4: Cross-tabulation between vascularity pattern

Vascularity pattern	Number of nodules	Percentage
Absent flow	8	16
Perinodular flow	33	66
Intranodular flow	9	18

Table 5: Histopathology distribution

Histopathology report	Number of patients	Percentage
Simple colloidal goiter	13	26
Nodular colloidal goiter	25	50
Follicular adenoma	9	18
Thyroiditis	3	6

possibility of neoplastic or non-neoplastic lesions. Timely intervention in nodular lesions of thyroid can significantly reduce morbidity and mortality.[6] Solitary thyroid nodules are most commonly seen in adults aged between 21 and 50 years. In our study, the youngest patient was 16 years and the oldest was 65 years. This difference in the age at peak incidence could be due to geographic variation and prevalence of endemic goiter. The highest incidence was in the 3rd and 4th decades and they accounted for 36% of cases. The present study compares favorably with the study reported by Rao and Rao (peak incidence 47% in the 3rd decade) and Sachdeva *et al.* (peak incidence 39% in the 3rd decade).[3]

All the 50 cases in our study underwent FNAC. Of these, there was no "inadequate cytology" report which is quite striking because Van Herle, in his study reported in adequacy rate of 5–12% with at least six aspirations. FNAC reported two cases as malignancy which turned out to be benign on histopathological examination (HPE), which gives a false-positive rate of 4% according to our study. Hence, it can be concluded that FNAC is of definite help in planning the mode of treatment but much reliance cannot be placed on a negative FNAC report.

About 86% of the nodules were hypoechoic and 12% were hyperechoic. In a study by Iannuccilli *et al.*, hypoechogenicity was a common sonographic feature in both benign and malignant nodules and hyperechogenicity was rare in both groups.[5]

Doppler study of the vascular pattern of the nodules showed absent flow in 16% an increased perinodular flow in 66% and an increased intranodular flow in 18%. Iannacuilli's study says that the grade of internal blood flow in color Doppler analysis is not a statistically significant criterion to suggest benign or malignant nature of a lesion. In a study by Frates *et al.*, it has been concluded that solid, hypervascular (grade 4) thyroid nodules had a high likelihood of malignancy.

Another study by Kang *et al.*[7] found that the margin, echo structure and the presence of calcification showed significant differences between benign and malignant nodules. In our study, hypoechogenicity was the predominant feature in benign nodules which does not compare with the results of this study.

Shimamoto *et al.*, in their study with 42 patients, have concluded that color Doppler sonography would not improve the ability to differentiate benign from malignant nodules significantly. As this study was also a small series as in ours, probably, our results are also comparable to this study.[8] The histopathological reports of all cases correlate well with the FNAC report in our study.

No single feature was found to be enough alone, to correlate with malignancy. A combination of features has been described by various studies to correlate with malignancy of these the most consistent feature has been a "solid hypervascular pattern" that has been known to associate well with malignancy.

CONCLUSION

Our study had no malignant nodules as seen by histopathological report after surgery. Hence, no positive correlation could be established between the various sonographic and CFD criteria with malignancy. However, FNAC reports correlated remarkably well with HPE reports. Hence, ultrasonogram and CFD study of thyroid nodules when used in conjunction may be used to screen nodules that are suspicious of malignancy which need to be subjected to scintigraphy and biopsy further to determine the nature of the lesion accurately. FNAC remains the most sensitive method to detect malignant lesions. However, as it cannot distinguish between follicular adenomas and follicular carcinomas, USG and CFD being non-invasive may help to detect malignancy in such cases.

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Original Article

Clinicopathological Study of Solitary Nodule of Thyroid – A Prospective Study

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Abstract

Introduction: Thyroid nodules are a common clinical problem and are noted much more commonly on imaging examinations than are apparent by palpation. Fine-needle aspiration cytology (FNAC), which yields a cytology specimen for analysis, is the standard test to determine whether or not surgical removal of a detected nodule is recommended.

Aim: Our study aims to evaluate the clinicopathological aspects of solitary thyroid nodule.

Materials and Methods: This prospective single-institutional study was conducted in the Department of Surgery, Tirunelveli Medical College. A total of 50 patients with solitary thyroid swelling were included in this study. All the patients underwent thyroid surgery after thorough family history, clinical examination, and FNAC. The histopathological reports were evaluated and correlated with the clinical diagnosis and the results were statistically analyzed and discussed.

Results: Out of the 50 patients, majority were females and only four were male patients. Peak incidence was observed in the age group of 30–40 years. Most patients presented with symptoms of swelling (50%), followed by pain (8%), dysphagia (4%), change of voice (4%), and difficulty in speech (4%). Swelling was located mostly in the right lobe (74%) followed by the left lobe (26%). On FNAC examination, many were present with colloidal nodular goiter (64%), followed by simple colloidal goiter (20%), thyroiditis (6%), follicular adenoma (4%), follicular neoplasm (4%), and cystic lesion (2%).

Conclusion: From this study, we concluded that solitary thyroid nodule is present most commonly in females, most of them are benign with adenoma being common among them seen in the front of the neck. FNAC is a useful tool in the pre-operative diagnosis of the solitary thyroid nodule.

Key words: Fine-needle aspiration cytology, Goiter, Histology, Solitary thyroid nodule

INTRODUCTION

A thyroid nodule is defined as a discrete lesion within the thyroid gland that is radiologically distinct from the surrounding thyroid tissue.[1] Iodine intake, in both insufficient and excessive quantities, confers a higher risk for the development of thyroid nodules.[2] Another important risk factor is exposure to ionizing radiation in childhood.[3,4] Thyroid nodules are common in both hyperthyroid and euthyroid patients and they are present in half of all thyroid glands that are subject to careful pathologic examination. More than 80% of all patients with thyroid nodules are women. Palpable thyroid nodules can be detected in 1.5% of men and 6.4% of women between the ages of 30 and 59.2 years. The prevalence of thyroid nodules increases from near zero at age 15 years to 50% by about 60–65 years of age.[5]

Thyroid nodules more than 1 cm are usually palpable. They are examined for site, size, tenderness, consistency, mobility, fixity to surrounding structures, and lymphadenopathy. A firm to hard, painful, rapidly growing nodule, fixed to surrounding structures and associated with lymphadenopathy and local pressure symptoms are suggestive of malignancy. The most cost-effective initial diagnostic method appears to be fine-needle aspiration; the specificity and sensitivity of this procedure are excellent.[6,7] It can usually determine if the nodule is a macrofollicular lesion (which is benign), a microfollicular or cellular lesion (which may or may not be cancerous), or a papillary malignancy.

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Incidentalomas, that is, nodules <1 cm detected incidentally on imaging of neck are not usually biopsied. The risk of thyroid cancer among patients with incidentally discovered thyroid nodules is similar to patients with palpable nodules. The life expectancy of patients with tumor that is smaller than 1 cm in diameter is the same as that of the general population.[8]

Fine-needle aspiration biopsy (FNAB) is advisable in all patients with palpable solitary nodules more than 1 cm in diameter, in patients of multinodular goiter who have discrete hypofunctioning nodule within the goiter, or a nodule of uncertain functional status that is growing or a cystic nodule after fluid has been removed. The prevalence of carcinoma in these nodules is similar to that in solitary nodules.[9] Biopsy is also indicated in patients of thyrotoxicosis having hypofunctioning nodules. In about 75% of cases, the nodules are benign. Malignancy is detected in about 4% of the cases. Of the remaining cases, roughly half will have indeterminate or suspicious results; the other half will lack a diagnosis because of inadequate tissue sampling. When the result is non-diagnostic, a repeat aspiration should be done. This study was conducted to find out various factors affecting solitary thyroid nodule such as age, sex, and clinical parameters and also to know about the correlation of fine-needle aspiration cytology (FNAC) and histopathology in diagnosing them.

Aim

The aim of our study is to evaluate the clinicopathological aspects of the solitary thyroid nodule.

MATERIALS AND METHODS

This prospective single-institutional study was conducted in the Department of Surgery, Tirunelveli Medical College. A total of 50 patients with solitary thyroid swelling were included in this study. Detailed information about the demographic details, present and past history of the thyroid was obtained. Informed written consent was obtained from the patients. All the general examination, physical examination, clinical examination, thyroid swelling examination, and laboratory investigation such as thyroid profile, FNAC, X-ray of the neck-anteroposterior, and lateral views, chest X-ray, and indirect laryngoscopy were done before going for surgery. Patients with previous thyroid surgery and those who have had an FNAB in the last month and patients with clinically non-palpable nodule discovered at ultrasonography (USG) (incidentalomas) were excluded from this study. All patients underwent surgery, and the final diagnosis was based on the results of the histopathological examination of the removed thyroid gland tissue.

Thyroid nodules that were easily palpable were aspirated by a cytopathologist, and non-palpable thyroid nodules were aspirated under ultrasound guidance by an endocrinologist or radiologist. Most of the solitary nodules were aspirated with 2–6 passes. For multiple nodules dependent on nodule number and size, 2–4 passes were applied to each biopsied nodule. The aspirated contents were expelled onto glass slides. The slides were air-dried and stained with Giemsa stains and cytopathologist immediately checked the samples for adequacy. Samples were defined as sufficient when six or more clusters of follicular cells with each group containing at least 10 follicular cells were present on the slides. The aspiration samples were classified by the cytopathologist as malignant, benign, inadequate, or follicular lesion.

RESULTS

The study comprised 50 patients with a clinically palpable solitary nodule of the thyroid. Patients ranged in the age group of 16–65 years. The youngest was 16 years old, the oldest was 65 years with a peak incidence in the 30–40 years age group [Figure 1]. There were a higher proportion of females with only 4 male cases and 46 female cases. The most characteristic presenting symptom was swelling in the anterior view of the neck in 100% of cases. The following common symptom included pain (8%), dysphagia (2%), change of voice (2%), and dyspnea (2%) [Figure 2]. Toxic symptoms were not seen in any of the cases. There were no symptoms of metastasis. A visible swelling moving up with deglutition was seen in all cases. The location of swelling was in the right lobe (74%), left lobe was involved in 26%, and isthmus in none [Figure 3]. The preferential location of the lesion in the right lobe is probably due to the reason that the right lobe is a little larger than the left lobe in 80% of the cases. All the cases had a smooth surface and were firm in consistency in 45 cases, whereas they were soft inconsistency in 5 cases. All cases had free mobility without evidence of fixity to any surrounding structures. There was no tracheal deviation in any of the cases. None of the patients has clinical lymph node enlargement. This indicates that it is quite difficult to predict malignancy in a solitary nodule of small size on a clinical basis alone. Myxoedema was not present in any of the patients. FNAC revealed that 64% of cases of colloid nodular goiter and 20% was simple colloid goiter [Figure 4]. FNAC reported two cases of malignancy which turned out to be benign on HPE.

DISCUSSION

Thyroid nodules are common, occurring in approximately 4–7% of the population.[10] However, thyroid cancer occurs in fewer than 5% of thyroid nodules.[10]

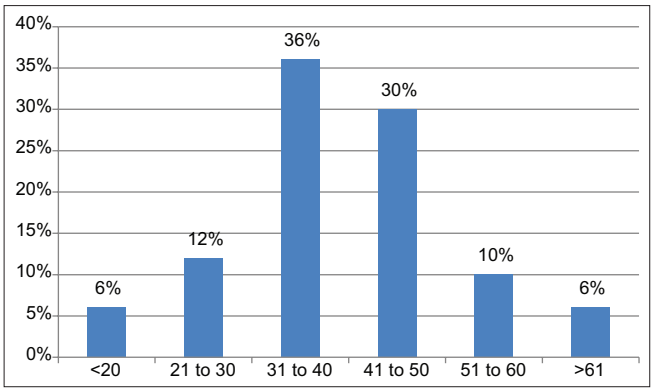

Figure 1: Age distribution

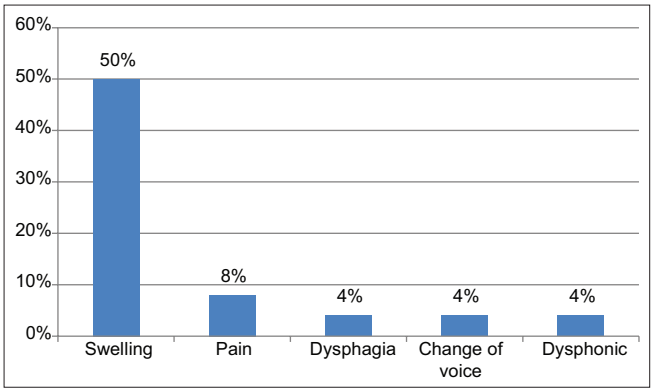

Figure 2: Presenting figures

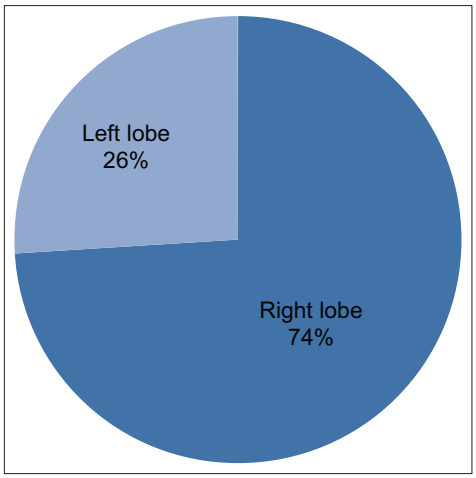

Figure 3: Location of swelling

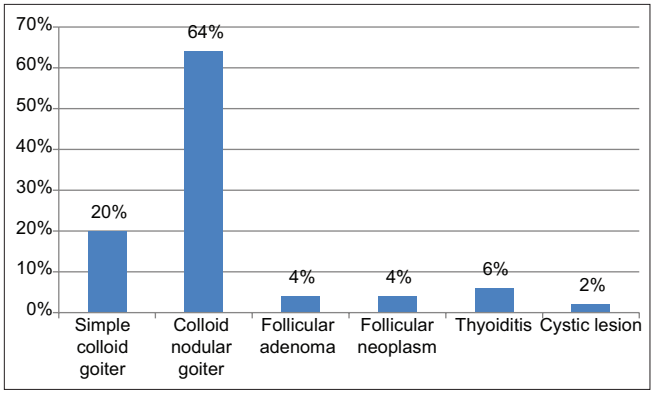

Figure 4: Distribution of fine-needle aspiration cytology

Conventionally, the approach to the solitary thyroid nodule consisted of clinical examination, radionuclide scanning, USG, or response to thyroid suppression therapy to differentiate between benign and malignant lesions. FNAB of thyroid nodules has emerged as a much more accurate diagnostic study for determining benign and malignant nodules. It is safe and accurate and has been shown to be superior to clinical assessment, USG, or thyroid scan in predicting malignancy.[6] In recent studies, FNAB has an incidence of false-positive findings ranging from <1% to 9% and false-negative findings from 0% to 4%.[11] Hashimoto's thyroiditis probably is the most common cause of false-positive FNAC results. The use of FNAB has resulted in a dramatic decrease in the number of patients with solitary nodules requiring operation and an increase in the yield of malignancy in patients undergoing thyroidectomy.[12,13]

In our study, thyroid nodules are more common in females compared to males. The incidence is more in areas of iodine deficiency. Christensen *et al.* conducted a survey of thyroid disease in 477 middle-aged women selected at random in an urban area where goiter was not endemic. The overall occurrence of thyroid disease was estimated to be 16.2%.[14]

In our study, out of the 48 benign cases, 32 were diagnosed to be colloid goiter while in the study by Fai *et al.*, it was 34 cases of colloidal goiter out of 54 benign cases.[15] The most common symptom among all patients in our study was swelling in front of the neck followed by pain. Similar observation was done by Nazmul-Huque *et al.*[16] where he found that thyroid swelling was the most common presentation in all cases (100%). Furthermore, majority of the patients were from the 31 to 40 years' age group (36%) in this study. This result is comparable to the results obtained by Venkatachalapathy *et al.*[17]

Aspiration of a thyroid nodule with a thin needle by an experienced clinician followed by cytological examination by a trained cytologist provides highly useful information in the assessment of solitary thyroid nodules. The procedure is safe, simple to learn, inexpensive, and is the single most cost-effective initial diagnostic tool in the workup of thyroid nodular disease. Best care will be delivered to the patient if a through history and clinical findings are correlated with aspiration cytology reports and other investigative procedures.

CONCLUSION

From this study, we concluded that solitary thyroid nodule is present most commonly in females, most of them are benign with adenoma (colloid nodular goiter) being common among them seen in front of the neck. Thus, FNAC is a most useful tool in the pre-operative diagnosis of solitary thyroid nodule. However, as it cannot distinguish between follicular adenomas and follicular carcinomas, it can be used in conjunction with USG and color flow Doppler to detect malignancy in such cases.

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Original Article

Spectrum of Male Breast Lesions an Institutional Perspective

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Abstract

Background: Diseases of male breast though relatively uncommon compared to diseases of female breast, do occur, but poorly studied. These range from benign lesions to malignant diseases. Benign most commonly affect young males most common is gynecomastia.

Aims and Objectives: The aim of the study was to study the spectrum of male breast diseases (BD) in relation to determine the common types of male BD in the study group and to evaluate the age distribution of different diseases.

Patients and Methods: A prospective interventional study was carried out to observe spectrum of male breast lesions from April 2019 to September 2020 in the Department of General Surgery, Government Medical College, Siddipet, Telangana, India.

Results: Fifty cases of malignant breast diseases were studied. Gynecomastia was the most common 43 cases (86%), and carcinoma 2 cases (4%) is rare. In gynecomastia, swelling of the breast was the most common presenting complaint. 2nd, 3rd, and 4th decades most commonly involved. Idiopathic gynecomastia was most common. Eighteen cases were treated conservatively and rest 25 underwent surgery. Carcinoma presented in old age, in advanced stage.

Conclusion: Benign BD are more common male breast lesions, of them gynecomastia is most common. Carcinoma male breast is rare. Gynecomastia and other benign male BD are common in young age 2nd, 3rd, and 4th decades, carcinoma seen in old age from 5th decade.

Key words: FNAC, Gynecomastia, Male breast lesions

INTRODUCTION

Diseases of the male breast are uncommon, and hence poorly studied. Further, presentation is often late due to embarrassment. Because of toxic masculinity, the stigma and misplaced shame associated with lesions of the breast in male patients can have profound psychological impact, so adequate care must be taken when approaching the insecure patient. Male breast disease is often under recognized due in part to its rarity and also to a lack of awareness. Familiarity with the salient features of the classic benign male breast conditions will allow accurate interpretation and avoid unnecessary treatment.

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Although the overall proportion of male patients is relatively small, the number of men presenting for evaluation seems to be increasing at most centers across the world. Both benign and malignant diseases affect the male breast, with a rising incidence of male breast cancer in recent decades. The most common presentation of male patients with breast pathologies is due to gynecomastia, where cosmetic correction is sought. Approach to breast disease in male patients typically mirrors that employed in female patients. Evaluation of hormonal profile and genetic factors may be further required. Almost all male patients present with a clinical symptom such as breast pain or palpable mass. Other reported benign masses of the male breast include masses arising from the skin and subcutaneous tissues, such as lipomas, epidermal inclusion cysts are also commonly encountered. Pseudogynecomastia, which is due to excess fatty tissue deposition in the breasts, is also common, especially in patients with an elevated body mass index. Others are intraductal papilloma, pseudoangiomatous stromal hyperplasia, granular cell tumors, hemangioma, schwannoma, myofibroblastoma, and fibromatosis.

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Although male breast disease is most often benign, cancer of the vestigial male breast does occur. Male breast cancer is similar to breast cancer in females in its etiology, family history, prognosis, and treatment. Prognostic factors and current treatment regimens have been extrapolated from experiences gathered from female breast cancer.

Over the past two decades, the rate of male breast complaints increased from 0.8% to 2.4%. At present, breast cancer is one of the most infrequent cancer types in men and comprises <1% of all male cancers and 0.65% of all breast cancers. Gynecomastia and male breast cancer have many similarities and 20–40% of cases of male breast cancer have been reported to be associated with gynecomastia. A wide variation in the incidence range is seen in different geographical areas varying from 3.4 cases/100,000 man years to 0.1/100,000. There are about 370 men diagnosed each year in the UK, compared with around 48,400 cases of breast cancer in women that are about one man for every 130 women diagnosed. The female to-male breast cancer ratio is 70–100:1. The mean age at the time of diagnosis in men is 67 years, which is about 5–10 years higher than that of women, and about 50% of men have axillary nodal metastasis at the time of diagnosis.

Diseases of male breast have been underestimated and are often unmentioned in our textbooks. The literature on lesions of the male breast is voluminous, but careful studies of the subject as a whole are scant. In India, much less information is available regarding male breast disorders. Breast carcinoma is thought to be confined to females only, so most of the males do delay in seeking medical attention and have worse prognosis at the time of presentation. Furthermore, male breast malignancies suffer from underdiagnoses leading to delayed treatment. Hence, there is need of more research into this topic.

Hence, this study was conducted to analyze the spectrum of male breast diseases (BD). The purpose of this prospective study was to describe clinical and imaging features of male breast lesions and their correlations to pathologic findings following biopsies or surgery with a view toward helping to evaluate and manage breast masses in males. Here, we describe the normal male breast anatomy and present an evaluation algorithm for the male patient with breast symptoms and signs. Emphasis is placed on male breast cancer, with a discussion of its epidemiology, characteristic clinical, imaging, pathological features, prognosis, and management.

Aims and Objectives

To study the spectrum of male BD in relation to:

1. To determine the common types of male BD in the study group
2. To evaluate the age distribution of different diseases.
3. To study the modes of presentation and clinical features.
4. To evaluate management protocols of male breast disease.
5. To note the response to treatment and complications arising during follow-up.
6. To correlate clinical findings with fine-needle aspiration cytology (FNAC) and Histopathology.

The data obtained would be compared with earlier studies.

METHODOLOGY

Patients and Methods

A prospective interventional study was carried out to observe spectrum of male breast lesions from April 2019 to September 2020 in the Department of General Surgery, Government Medical College, Siddipet, Telangana, India.

The total period of study was 18 months. Cases were selected from the Outpatient Department (OPD) and from inpatients in the wards who presented with disorders of the breast. Pro forma with relevant history, clinical examination and investigations were prepared and patients were assessed.

Sample Number

A total of 50 male patients with BD were included in the study.

Type of Study

This was a prospective study.

Patients satisfying the following inclusion and exclusion criteria were enrolled in the study.

Inclusion Criteria

All male patients with BD between the ages of 14 and 75 years who attended the OPD and those admitted in the Department of General Surgery, Government Medical College, Siddipet, India, and who were willing to undergo investigations and treatment willing for follow-up were included in the study.

Exclusion Criteria

The following criteria were excluded from the study:

- All Female patients with BD.
- All male patients aged 14 years and less and above 75 years.
- History of trauma to the breast.
- Patients who are refusing any sort of treatment.

Study Done As

Screening of cases done by clinical examination in OPD and by investigations such as FNAC and when necessary, mammogram or ultrasonography (USG) was advised.

- Patients were studied and analyzed in detail, with regard to;
  - History
  - Clinical Examination
  - Routine Blood investigations
  - Hormone levels (in certain cases only)
  - FNAC
- Mammogram or USG (in certain cases only) and incisionalor excisional biopsy (in certain cases only).
- Based on the provisional diagnosis, patients were subjected to surgery or conservative management as the case required.
- Cases were again analyzed based on;
  - Operative findings
  - Histopathological findings
- Post-operative course and outcome.
- Patients were followed up for a period ranging from 1 month to 18 months to detect any recurrence.
- Unadjusted, univariate, and raw analysis of data were performed for statistical stratification.

RESULTS

A study was carried out on 50 male patients above 14 years–75 years of age with breast disease at Government Medical College, Siddipet, Telangana, India, over a period of 18 months. The data obtained were tabulated and analyzed. The following observations were made.

Age Incidence [Table 1]

The age distribution of male patients with breast disease in the study group shows that most of the patients, 34% were between 21 and 30 years of age. The study group does not have any patient above 75 years of age, only 10% of patients were above 60 years, and 16% of patients were below 20 years of age. Majority of patients 54% were aged between 21 and 40 years.

The mean age of malignant breast disease (MBD's) was found to be 36 years, median age was 30.5 years. The youngest patient in the study was 20 days old and the oldest being 65 years old. Most of the patients are in the age group of 16–30 years.

Incidence of Benign versus Malignant Diseases [Table 2]

Among 50 patients, 48 (96%) were diagnosed with benign diseases such as gynecomastia, pseudogynecomastia, abscess, lipoma, and two patients (4%) were diagnosed with MBD.

Distribution of Male Breast Lesions [Table 3]

The most common overall and benign male breast lesion in this study was gynecomastia accounting for 86% followed by other less common conditions including pseudogynecomastia 4%, lipoma 2%, sebaceous cyst 2%, and breast abscess 2%. Malignant lesion carcinoma of male breast was 4%.

Mean, Median Age, and Standard Deviation (SD) [Table 4]

The mean age of MBD's was found to be 36 years, median age was 30.5 years. With SD 16.5 showing that 68% of patients are in between 19 and 52 years (36 ± 16.5). Mean age of BBD's was 35 years, and median age was 29.5 years.

The mean age of highest incidence of gynecomastia is (34.86) 35 years, median was 28 years. With SD 16.7 showing that 68% of patients are in between 18 and 52 years (35 ± 16.5).

Table 1: Distribution according to age showing age distribution of the patients with BD

Age in years	No. of patients with BD	% of patients with BD
14–20	8	16
21–30	17	34
31–40	10	20
41–50	4	8
51–60	7	14
61–75	5	10
Total	50	100

BD: Breast diseases

Table 2: The percentage of different types of benign BD in the study group

Type of breast disease	No. of patients with BD	% of patients with BD
Benign	48	96
Malignant	2	4
Total	50	100

Table 3: Distribution of male breast lesions

Sl. no.	Type of lesion		No. of cases	Percentage
1	Gynecomastia	Benign	43	86
2	Pseudogynecomastia		2	4
3	Lipoma		1	2
4	Sebaceous Cyst		1	2
5	Abscess		1	2
6	Carcinoma	Malignant	2	4
Total			50	100

Table 4: Showing mean and median ages and SD of MBD's in years

	Total	Mean age	Median age	Standard deviation (SD)
MBD	50	36	30.5	16.5
Benign BD	48	35	29.5	
Gynecomastia	43	35	28	16.7
MBC	2	58.5	58.5	

Table 5: Presentation and management of other benign breast lesions

No	Etiology	No. of patients	Breast examination	Investigation ns	Management	
					Conservative	Surgical
1	Pseudogyne ecomastia	2	B/L Swelling, Obese	USG, FNA	2	-
2	Lipoma	1	Lump 4,	USG, FNA	-	1
3	Sebaceous cyst	1	Lump with punctum	USG, FNA	-	1
4	Abscess	1	Lump, pain, fever	USG, Aspiration	-	1
T		5			2	3

Table 6: Correlation of fine-needle cytology with histopathological diagnosis

No.	Clinical diagnosis	No. of cases	FNAC			HPE		
			Done in	Diagnosis Consistent	%	Done in	Diagnosis Consistent	%
1	Gynecomastia	43	25	23	92	25	25	100
2	Pseudogynecomastia	2	2	2	100	-	-	-
3	Lipoma	1	1	1	100	1	1	100
4	Sebaceous Cyst	1	1	1	100	1	1	100
5	Abscess	1	-	-	-	-	-	-
6	Carcinoma	2	2	2	100	2	2	100
	Total	50	31	31	-	29	29	-

Table 7: Post-operative complications

	Complication	No. of cases	Percentage
	Subcutaneous mastectomy 25 cases		
1	Wound infection	1	4
2	Seroma	1	4
3	Hematoma	0	0
	MRM 2 cases		
1	Wound Infection	0	0
2	Seroma	1	50
3	Flap Necrosis	0	0
4	Arm edema	0	0

Mean and median age of MBC was 58.5 years.

Mode of Presentation of Male BD

The most common presenting complaint noted was swelling of the breast, in 50 patients of which 26 (52%) patients presented with only swelling, 12 (24%) presented with swelling associated with pain, 6 (12%) with lump, and 2 (4%) with lump, pain.

The next common complaint was lump noted in eight patients of which six (12%) presented with only lump as a complaint, only one patient (2%) presented with ulcer.

And another one patient (2%) presented with fever pain and lump.

Presentation and Management of Other Benign Breast Lesions [Table 5]

Two patients diagnosed as pseudogynecomastia, patients are obese with high BMI, managed conservatively, with weight reduction.

- One patient with lipoma excision done.
- One patient with sebaceous cyst excision done.
- One patient with abscess, incision and drainage done.

Presentation and Management of Carcinoma Male Breast

Two cases were found to be carcinoma of the breast. These patients were aged 45 and 72 years.

One patient had presented with ulcer and lump of the breast. The other patient had presented with eccentric lump. In the latter patient, the primary tumor was traced to the right breast, which had induration and nipple retraction, which the patient had ignored.

Patient with ulcer with edge biopsy showed infiltrating ductal carcinoma, and the other with FNAC showed ductal cell carcinoma. Both showed no nodal involvement and no distant metastasis. Histopathology revealed infiltrative ductal carcinoma in both cases.

Correlation of Fine-Needle Cytology with Histopathological Diagnosis [Table 6]

In 43 patients the clinical diagnosis was gynecomastia, of them idiopathic with no cause identified in 19 patients and few age-related gynecomastias with atypical presentation total 25 were investigated with FNAC, USG. In 23 patients, FNA showed proliferation of fibroglandular tissue impression suggestive of gynecomastia; in two patients it is inconclusive. USG showed subareolar hypoechoic disk-shaped areas. Histopathological examination (HPE) after surgery in all 25 patients report was gynecomastia.

Table 8: The table comparing types of male breast diseases

Sl. no.	Lesions	Present study 2017–2019	Ramji, 2019[1]	Jain *et al.*, 2014[2]	Al-Obaidi 2011[3]
1	Gynecomastia	86%	66.66%	46.67%	82.8%
2	Pseudogynecomastia	4%	-	-	-
3	Lipoma	2%	4.76%	6.67%	4.3%
4	Sebaceous Cyst	2%	4.76%	-	-
5	Abscess	2%	4.76%	6.67%	2.15%
6	Carcinoma	4%	9.52%	16.67%	5.38%

Table 9: The table comparing age incidence of male breast lesions

Sl. No.	Age in years	Present study	Ramji	Al-Obaidi
1	Below 10	-	-	1.08%
2	10–20	16%	14.28%	27.96%
3	21–30	34%	42.85%	23.66%
4	31–40	18%	23.80%	19.35%
5	41–50	8%	9.52%	18.27%
6	51–60	14%	9.52%	8.6%
7	61–70	10%	-	1.08%

In two patients diagnosed as pseudogynecomastia FNAC showed only fibro fatty tissue and no glandular elements.

In lipoma FNAC showed mature adipocytes arranged in clusters findings consistent with HPE.

In sebaceous cyst also features on FNAC consistent with HPE.

In one case of MBC with lump FNAC showed ductal cell carcinoma, HPE infiltrating ductal cell carcinoma. Other MBC presented with ulcer investigated with edge biopsy showed infiltrating ductal carcinoma findings consistent with HPE.

Post-operative Complications [Table 7]

Out of 25 subcutaneous mastectomy surgeries, 1 patient 4% had wound infection, 1 patient 4% had seroma, and no one developed hematoma. Following MRM out of 2 patients 1 developed 50 % seroma, and no flap necrosis.

DISCUSSION

The present study was carried out among the male patients with BD attending the department of surgery at Government Medical College, a total of 50 patients were studied.

Distribution of Variety of Male BD [Table 8]

In present study, among 50 patients, 48 cases (96%) were diagnosed with benign diseases such as gynecomastia, pseudogynecomastia, abscess, lipoma, and 2 cases (4%) were diagnosed with MBD.

The most common overall and benign male breast lesion in this study was gynecomastia accounting for 86% (43 cases) followed by other less common conditions including pseudogynecomastia 4% (2 cases), lipoma 2% (1 case), sebaceous cyst 2% (1 case), and breast abscess 2% (1 case). Malignant lesion carcinoma of male breast was 4% (2 cases).

Gynecomastia (86%) was the most common MBD encountered while MBC constitute 4% of the patients.

- According to Ramji[1], the incidence of gynecomastia is 66.66% and MBC 9.52%. Lipoma is 4.76%, abscess is 4.76%, and saebaceous cyst is 4.76%.
- According to Jain *et al.*,[2] the incidence of gynecomastia is 46.67% and MBC 16.67%. Lipoma is 6.67%, and abscess is 6.67%.

Malignant breast lesions comprised 23.34% of the total. Most common malignant lesion was infiltrating ductal carcinoma (16.67%), followed by malignant epithelial tumor-Eccrine/ Breast origin (6.62) and metastatic breast lesion (3.34).

- Al-Obaidi[3] reported gynecomastia 82.8%, MBC 5.38%. Lipoma is 4.3%, and abscess is 2.15%,

Present study incidence of gynecomastia is consistent with Al-Obaidi[3].

Gill *et al.*[4] One hundred and fifty cases of male BD were diagnosed during study period.

Majority (74%) of the specimens were various benign conditions the most common being gynecomastia (88 cases out of 111).

Other benign conditions included duct ectasia (11 cases), non-specific inflammation (6 cases), fibroadenoma and hemangioma (2 cases each), and a single case of benign blue cell nevus.

Malignant tumors comprised 26% (39 cases) of the total male breast disorders, most common (82%) being infiltrating ductal carcinoma. According to all above-mentioned studies, gynecomastia is the most common.

Age Incidence [Table 9]

The age distribution of male patients with breast disease in the study group shows that most of the patients, 34%

Table 10: Comparison of mean ages and SD

Lesions	Present study 2017–2019		Ramji, 2019[1]		Jain *et al*., 2014[2]
	Mean age	SD	Mean age	SD	Mean age
MBD	36	16.5	31.5	11.6	41.5
BBD	35				28
Gynecomastia	35				42
MBC	58.5				63

Table 11: The table comparing mode of presentation of MBD

Sl. No.	Presenting complaint	Present study	Ramji[1]	Al-Obaidi[3]
1	Swelling of breast	52%	71.42%	-
2	Swelling with pain	24%	-	-
3	Lump	12%	9.52%	48%
4	Painful Lump	4%	-	38%
5	Pain only	4%	9.52%	7%
6	Ulcer	2%	4.76%	-

Table 12: The table comparing side involved in MBD

Sl. No.	Side of lesion	Present study	Ramji	Al-Obaidi
1	Right	30%	33.33%	19.36%
2	Left	44%	28.57%	59.14%
3	Bilateral	26%	38.09%	21.5%

were between 21 and 30 years of age. The study group does not have any patient above 75 years of age, only 10% of patients were above 60 years and 16% of patients were below 20 years of age.

Majority of patients 52% were aged between 21 and 40 years. The mean age was found to be 36 years.

The youngest patient in the study was 15 years old with gynecomastia and the oldest being 72 years old with carcinoma.

Most of the patients are in the age group of 14–40 years.

About 96% of all cases are benign disorders, of these 70% are represented by early and mid-reproductive age group (2nd, 3rd, and 4th decades). Majority (34%) of them belong to age group of 21–30 years with average age being 35 years.

In the present study, majority of the patients are in the age group of 21–30 years (34%) while according to Ramji peak incidence of male breast disorders is between 21 and 30 years 42.85% similar to our study.

Gynecomastia

Youngest patient in this series is 15 year old with gynecomastia, eldest being 72 year old with breast carcinoma. Thirty cases (70%) of gynecomastia occurred between age group of 14 and 40 years. The corresponding literature of Ramji reported 14 cases (66.45%); Al-Obaidi reported 59 cases (63.45%).

The mean age of highest incidence of gynecomastia is 26.25 years, majority (62%) are within the age group of 14–40 years.

In this study, youngest patient of gynecomastia is 15 year old, eldest being of 71 years. Only 12 cases were noted between the age group of 40 and 75 years.

Al-Obaidi age distribution of gynecomastia in our study varied from the highest (25.81% and 21.51%) in the 2nd and 3rd decades, respectively; to the lowest (6.45% and 12.9%) in the 6th and 5th decades, respectively.

Gill *et al*. as well as Anderson *et al*.,[5] the peak incidence of age in gynecomastia occurs during puberty, with peaking around 14 years old. More than half (51.72%) of these patients presented during the 3rd decade of life.[4]

Sazan *et al*.,[6] reported that the peak incidence of gynecomastia in the 2nd decade is 23.4%.

MBC

Among 50 cases studied, two patients were diagnosed as carcinoma, youngest patient is 45 years old, eldest being of 72 years.

MBC accounts for 4% (2 cases) in present study ages are 45 years and 72 years, Ramji found the incidence to be 9.52% (2 cases) 48 years, 55 years, Al-Obaidi reported 5.38% (5 cases) between 40 and 69 years, breast cancer is reported in the 5th decade forward of a total (5.37%) while breast cancer peak distribution is equal in the 5th and 6th decades (2.15%).

Sazan *et al*. reported carcinoma of breast is 9.7% mostly after the age of 50 years old.

Gill *et al*., most (68.4%) of the patients with malignancy presented in 5th, 6th, and 7th decades of life. The age range was 30–78 years.

Other Benign

There were two cases of pseudogynecomastia 29 years and 32 years old, rest of the cases includes 38 year old

lipoma and 52 year sebaceous cyst and 34 years old abscess.

Mean, Median Age, and SD [Table 10]

In this study, mean age of MBD's was found to be 36 years, with SD 16.5 showing that 68% of patients are in between 19 and 52 years (36 ± 16.5).

In Ramji, mean age was 31.5 years with SD 11.6. In Jain *et al.*, mean was 41.5 years.

Median age was 30.5 years in our study, in Jain *et al.* median was 40 years. Mean age of BBD's was 35 years; median age was 29.5 years, in Jain *et al.* mean age was 28 years.

The mean age of highest incidence of gynecomastia is (34.86) 35 years, median was 28 years. With SD 16.7 showing that 68% of patients are in between 18 and 52 years (35 ± 16.5).

In Jain *et al.*, mean age was 42 years.

Mean and median age of MBC was 58.5 years in Jain *et al.* mean age was 63 years. Gill *et al.*, mean age was 52.6 years.

Mode of Presentation [Table 11]

In the present study, the most common presenting complaint noted was swelling of the breast, in 50 patients of which 26 (52%) patients presented with only swelling, 12 (24%) presented with swelling associated with pain, 6 (12%) with lump, painful lump in 2 (4%), 1 (2%) with lump, pain and fever, and 1 (2%) ulcer.

The findings of the present study correlate with the findings of the study mentioned above.

The most common type of presentation of MBD was swelling of the breast constituting 52% in this study and swelling with pain 24%.

- According to Ramji states that the most common presenting symptom was swelling of the breast 15 (71.42%), followed by lump in 2 (9.52%), pain in 2 (9.52%), and ulcer in 1 (4.76%).
- According to Al-Obaidi, most common presenting symptom was painless mass 48 (51.61%), followed by painful mass in 38 (40.86%), pain in 7 (7.53%),

There were 1 case (2%) of pain, fever, lump in this study being abscess, and 1 case (2%) of ulcer being carcinoma

Gynecomastia most commonly present with painless swelling of breast, whereas the symptoms in carcinoma are painless lump and ulcer.

In this study, one patient with primary hypogonadism presented with bilateral gynecomastia, small rt testis, undescended lt testis, absent secondary sexual characteristics, tall slender personality, diagnosed as Klinefelter syndrome, and treated conservatively.

On local examination of breast, swelling is concentric and retroareolar in most cases, few four patients with age-related gynecomastia presented with eccentric lump, investigated further with USG, FNAC, managed with SCM.

Duration of Symptoms

In the present study, 82% of patients with benign presented within 12 months, and 14% of patient, presented after 1 year. About 50% of gynecomastia patients presented between 1 and 6 months, abscess patient presented within 1 month. Both of 2 carcinoma patients presented after 1year of duration.

Side Distribution [Table 12]

Most common side involved, with all the male breast disorders taken into consideration was left, which is in accordance with the study mentioned above.

Al-Obaidi study also shows that left breast (59.14%) was more commonly involved as compared to the right.

In the present study, most common side involved in gynecomastia was left 20 (40%), followed by right 12 (24%).

In carcinoma, both sides were equally involved.

In Ramji, bilateral involvement 38.09% was more common, followed by right side 33.33% and left only 28.57%.

Sazan *et al.* reported that bilateralism in 8.9% all was with gynecomastia, while different disorders involve left breast in (53.2%) and right side in (37.9%).

Gill *et al.* patients with gynecomastia revealed a slight predominance (40%) of right breast involvement; however, both breasts were affected in about 25% of the cases.

Size of Lesion

Majority of lumps (52%) in the present study averaged more than 5 cm in size. About 44% were 2–5 cm, and 4% were size <2 cm.

Benign breast lumps, especially gynecomastia is of size more than 2 cm.

In Al-Obaidi study ingestion of drugs for any cause play an important past relevant history in precipitating

gynecomastia in 42 patients (45.16%), smoking of cigarettes in 11 patients (11.83%), alcohol abuse in eight patients (8.6%); on the other hand, no important relevant history recorded in 16 patients (17.2%) involved in this study.

In our study, no important relevant history recorded in 16 patients (32%), whereas ingestion of drugs for any cause precipitating gynecomastia in 6 patients (12%), smoking of cigarettes in 6 patients (12%), and alcohol abuse in 5 patients (10%), hypogonadism secondary to Klinefelter syndrome presented with bilateral gynecomastia and undescended testis in 1 patient (2%), no tumors recorded as relevant history.

In Glass *et al*.,[7] Plourde *et al*.,[8] and Ewertz *et al*.[9] showing that persistent pubertal gynecomastia occur in 25%, drugs in 10–25%, no detectable abnormality in 25%, cirrhosis or malnutrition in 8%, primary hypogonadism in 8%, testicular tumors in 3%, secondary hypogonadism in 2%, hyperthyroidism in 1.5%, and chronic renal insufficiency in 1%.

In Al-Obaidi study 42 patients (45.16%) gave history of ingestion of different types of drugs. Hyperoestrogenization in men can be caused either by estrogen agonist drugs as digoxin, spironolactone, or estrogen hormone therapy; this group represents 11 patients (11.83%) of patients; or by testosterone target cell inhibitors which are taken by 17 patients (18.28%) of total patients; or the third group; drugs that causing hyperprolactinemia (methyldopa and phenothiazines) reported in 14 patients (15.05%); on the other hand, 51 patients (54.88%) with no history of drug association.

In our study, six patients (13.9%) gave history of ingestion of different types of drugs. Drugs are spironolactone in two patients, digoxin in one patient, amiodarone in one patient, dutasteride in one patient, and isoniazid in one patient. Persistent pubertal gynecomastia occurs in five patients 11.6%, aging related in eight patients 18.6%, no detectable abnormality in 19 patients 44.2%, cirrhosis in four patients 9.4%, and primary hypogonadism in one patient 2.3%.

Hormone Levels in patients with Gynecomastia

In this study, puberty related gynecomastia testosterone levels are normal (N) near lower limit (LL) with normal hCG, and LH. There is relative increase in E/T Ratio (Estrogen/testosterone).

In aging related gynecomastia testosterone levels are decreased, estrogen levels elevated with elevated LH and normal hCG.

In liver failure related gynecomastia estrogen levels elevated with deranged liver enzymes.

In primary hypogonadism testosterone levels are decreased, estrogen levels elevated with elevated LH and normal hCG.

In idiopathic gynecomastia, all hormone levels are in normal range.

All patients who present with gynecomastia should have serum testosterone, estradiol, LH, and hCG measured (using an assay that detects all forms of hCG). Further testing should be tailored according to the history, physical examination, and the results of these initial tests.

An elevated beta-HCG or a markedly elevated serum estradiol suggests neoplasm and a testicular ultrasound is warranted to identify a testicular tumor, keeping in mind; however, other non-testicular tumors can also secrete hCG.

A low testosterone level, with an elevated LH and normal to high estrogen level indicates primary hypogonadism.

If the history suggests Klinefelter syndrome, then a karyotype should be performed for definitive diagnosis.

Low testosterone, low LH, and normal estradiol levels indicate secondary hypogonadism, and hypothalamic or pituitary causes should be sought.

If testosterone, LH and estradiol levels are all elevated, then the diagnosis of androgen resistance should be considered.

Liver, kidney, and thyroid function should be assessed if the physical examination suggests liver failure, kidney failure, or hyperthyroidism, respectively. A chest X-ray should be done if a lung or mediastinal lesion is suspected.

Furthermore, if examination of breast tissue suggests malignancy, a biopsy should be performed.

This is of particular importance in patients with Klinefelter syndrome, who have an increased risk of breast cancer. On the other hand, if the examination finding is compatible with breast abscess, then fine-needle aspiration for microscopy, acid-fast bacilli, and culture are warranted.

Presentation of Carcinoma Breast in Males

Van Geel *et al*.[10] and Heller *et al*.[11] described that nipple involvement is a fairly early event, with retraction in 9%, discharge in 6%, and ulceration in 6%, although ulceration was separate from the nipple in half the cases, with a mean age of 60 years.

Gupta *et al*.[12] described that fixed painless hard mass with retraction ulceration, nipple discharge, and enlarged axillary lymph node are likely to be signs of malignancy.

Clinical breast examination is the key in evaluation of palpable mass in men, and it is found to be important in assessing grade of gynecomastia and further evaluation may or may not be necessary, using Hoffman Kohn scale adapted by McKinny and Simon,[5,12] because there is no convincing evidence to link gynecomastia with male breast cancer.

Ramji two cases, the diagnosis was found to be carcinoma of the breast. One patient had presented with ulcer of the breast. The other patient had presented to the hospital with pain in the back, which on evaluation revealed vertebral metastasis.

In the latter patient, the primary tumor was traced to the right breast, which had induration and nipple retraction, which the patient had ignored. These patients were aged 48 and 55 years, whereas in literature, the average age of presentation is 68 years. Both had ignored their symptoms for prolonged periods. Histopathology revealed infiltrative ductal carcinoma in both cases, with ER PR positivity and Her2 negative.

In our study, two cases were found to be carcinoma of the breast. One patient had presented with ulcer and lump of the breast. The other patient had presented with eccentric lump. In the latter patient, the primary tumor was traced to the right breast, which had induration and nipple retraction, which the patient had ignored. These patients were aged 45 and 72 years, whereas in the literature, the average age of presentation is 68 years. Both patients evaluated patient with ulcer with edge biopsy showed infiltrating ductal carcinoma, and the other with FNAC showed ductal cell carcinoma. Both showed no nodal involvement and no distant metastasis. Histopathology revealed infiltrative ductal carcinoma in both cases.

Management of Male Breast Lesions

Anderson *et al.*[5] pubertal gynecomastia often regresses spontaneously within 6 months, 75% within 2 years of onset, and 90% resolved within 3 years of onset.

USG

In our study, USG indicated in 19 idiopathic gynecomastia with no cause identified patients and few age-related gynecomastia with atypical presentation total 25 patients, similar to FNAC and in other benign lesions and in MBC.

Most of gynecomastia showed presented as generalized prominent proliferation of fibro-glandular tissue unilaterally or bilaterally, in few multiple ill-defined masses as well as retroareolar ill-defined mass.

Breast cancer, on the other hand, presented ultrasonographically with retroareolar and with eccentric ill-defined mass.

Documented that USG alone is not a reliable technique to distinguish male breast carcinoma from other etiologies, where false positive result may be seen in abscess, gynecomastia, and fat necrosis.

The main stay in diagnosis of different male breast disorders is fine-needle aspiration and/or excisional biopsy which should be the integral part of the primary assessment of breast lumps in male.

Management

In our study of 50 patients 20 patients were managed conservatively, 30 were operated.

In 43 gynecomastia patients, five patients diagnosed as pubertal gynecomastia and observed with follow-up for every 3 months, symptoms regressed spontaneously within 1 year in two patients, within 2 years in one patient, whereas two patients underwent surgery after 1 year follow-up for cosmetic purposes.

Eight patients diagnosed as gynecomastia related to aging, four managed conservatively, remaining four operated in view of suspicious lump.

Six patients diagnosed as drug related and the offending agents stopped and on follow-up all showed spontaneous regression in 1–3 months.

One patient with primary hypogonadism due to Klinefelter syndrome managed conservatively.

Four patients with alcohol abuse and liver failure features managed conservatively. In 19 patients no cause identified managed with surgery.

Surgery done in all gynecomastia patients is subcutaneous mastectomy.

Two patients diagnosed as pseudogynecomastia, patients are obese with high BMI, managed conservatively, with weight reduction.

- One patient with lipoma excision done.
- One patient with sebaceous cyst excision done.
- One patient with abscess, incision and drainage done, pus for culture and sensitivity and stain for acid-fast bacilli sent, organism was *Staphylococcus epidermidis*.
- Two patients diagnosed as carcinoma, modified radical mastectomy was done.

Comparison between clinical diagnosis, FNAC report, and HPE report of patients with MBD

Sazan *et al*. in 2008 reported gynecomastia being diagnosed by FNAC in (13.6%) and 2001 (9%) who reported that apocrine metaplasia and epithelial atypia are common finding in gynecomastia; adding that the attention should be directed toward the pattern of the cells.

All the cases of breast cancer diagnosed by HPE which reveal neoplasia and pleomorphism implicated for infiltrative ductal carcinoma 100% (5 of 5 cases).

Although there are many other subtypes for carcinoma of breast the predominant histological type of disease in all literatures is invasive ductal, which forms more than 90% of all male breast tumors.

In this study, most common MBD is gynecomastia (43 cases) according to clinical diagnosis.

The FNAC report shows that the most common MBD is gynecomastia (23 out of 25 cases).

As per HPE report gynecomastia (25 cases) is the most common MBD, followed by lipoma (1 case) and sebaceous cyst (1 case), and infiltrating ductal carcinoma (2 cases). FNAC and HPE were not done in 18 cases of gynecomastia as no indication.

In 43 patients, the clinical diagnosis was gynecomastia, of them 19 idiopathic with no cause identified patients and few age-related gynecomastias with atypical presentation total 25 patients are investigated with FNAC. In 23 patients, FNA showed proliferation of fibroglandular tissue impression suggestive of gynecomastia.

In two patients, it is inconclusive. HPE after surgery in all 25 patients report was gynecomastia.

In two patients diagnosed as pseudogynecomastia FNAC showed only fibro fatty tissue and no glandular elements.

In lipoma FNAC showed mature adipocytes arranged in clusters findings consistent with HPE.

In sebaceous cyst also features on FNAC consistent with HPE.

In one case of MBC with lump FNAC showed ductal cell carcinoma, HPE infiltrating ductal cell carcinoma. Other MBC presented with ulcer investigated with edge biopsy showed infiltrating ductal carcinoma findings consistent with HPE.

FNAC is a very useful tool in diagnosing male BD and in differentiating benign diseases from malignancy, it is a more accurate diagnostic tool as compared to clinical findings and can avoid unnecessary surgery.

However, compared to biopsy and HPE FNAC is less accurate.

Hence, recently true cut biopsy is being preferred over FNAC as more tissue is obtained for examination with diagnostic accuracy similar to HPE.

Post-operative Complications

Out of 25 subcutaneous mastectomy surgeries, 1 patient 4% had wound infection, 1 patient 4% had seroma, and no one developed hematoma.

Following MRM out of two patients one developed 50 % seroma, and no flap necrosis

CONCLUSION

A prospective interventional study was carried out to observe spectrum of male breast lesions from April 2019 to September 2020 in the Department of General Surgery, Government Medical College, Siddipet, India. The total period of study was 18 months. A total of 50 male patients with BD were included in the study.

1. Benign BD are more common male breast lesions, of them gynecomastia is most common. Carcinoma male breast is rare.
2. Gynecomastia and other benign male BD are common in young age 2nd, 3rd, and 4th decades, carcinoma seen in old age from 5th decade.
3. Common mode of presentation of gynecomastia is painless swelling of breast, carcinoma is lump with advanced features such as ulcer.
4. Gynecomastia diagnosed on basis of history, clinical features, careful systemic examination, and baseline hormonal investigations and if required cytological and imaging investigations. Managed based on etiology. Carcinoma investigated, staged, and treated similar to female breast cancer.
5. Subcutaneous mastectomy most commonly performed surgery in gynecomastia. MRM in carcinoma. Seroma most common complication.
6. FNAC along with USG useful in differentiating benign diseases from malignancy.

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Original Article

Intraoperative Lavage in Peritonitis – Comparison between Saline and Metronidazole

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ABSTRACT

Background and Objectives: Peritonitis is a fairly common and challenging disease; we come across in the surgical practice. Operative treatment and intra-operative peritoneal lavage are the main stay of the treatment. Different types of fluids are used for peritoneal lavage. The objectives of this study are to compare the outcome in terms of, surgical wound infection, intra-abdominal abscess, sepsis, and hospital stay in saline peritoneal lavage group and metronidazole peritoneal lavage group in operated cases of peritonitis.

Materials and Methods: All patients who underwent laparotomy for peritonitis from February 2019 to May 2020 were studied, excluding patients younger than 15 years and older than 60 years. A total of 100 patients were studied, who were randomly divided into two groups receiving Saline IOPL and Metronidazole IOPL. Outcomes were compared between the two groups.

Results: There was a reduction in incidence of wound infection in metronidazole IOPL group by 14%, sepsis was reduced by 10%, and intra-abdominal abscess by 2%. Mortality was increased by 2% in the metronidazole lavage group. Mean hospital stay was lesser in the metronidazole lavage group by 1.8 days. However, none of these findings were found to be statistically significant.

Conclusion: There is a small improvement in the outcome when metronidazole is used for IOPL in peritonitis patients, but not up to statistically significant levels. The increased mortality in the metronidazole lavage group may be due to selection bias. There is no statistically significant difference in outcome between the saline group and metronidazole group.

Key words: Lavage, Metronidazole, Peritonitis

INTRODUCTION

Peritonitis is defined as inflammation of the serosal membrane that lines the abdominal cavity and the organs contained therein. Peritonitis usually occurs secondary to contamination of the peritoneal cavity by the gastro intestinal contents, either due to perforation of the hollow viscera or due to translocation of bacteria through the wall of ischemic gut.

Surgical closure of the perforation and intra-operative peritoneal lavage (IOPL) has been the cornerstone in the management of patients with peritonitis. Different types of fluids have been used for peritoneal lavage in peritonitis patients. These include, sterile water, warm saline, aqueous Povidone-iodine, and saline with antibiotics.

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Peritoneal lavage reduces the bacterial load, thereby reducing the incidence of post-operative surgical site infection and sepsis. Addition of antibiotics like metronidazole, tetracycline, netilmicin to the lavage fluid is being widely practiced in the treatment of peritonitis patients. Some studies have shown that there is no distinct advantage of adding antibiotics to the lavage fluid as therapeutic levels of the antibiotic are attained in the peritoneal fluid with intravenous injections.

In this study, peritonitis patients are divided into two groups randomly. In the first group of patients, warm saline is used for IOPL. In the second group, 200 ml of metronidazole is added to the saline for peritoneal lavage. Outcomes of both groups are compared to assess whether there is any advantage adding

Aims and Objectives of the Study

The objectives of the study were to compare the outcome in terms of, surgical wound infection, intra-abdominal abscess, and sepsis, hospital stay in saline peritoneal lavage group, and metronidazole peritoneal lavage group in operated cases of peritonitis metronidazole to the lavage fluid.

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MATERIALS AND METHODS

This comparative study of peritoneal lavage using saline versus metronidazole is based on 100 cases of peritonitis operated at Government Medical College, Siddipet, Telangana State during the period from February 2019 to May 2020.

Inclusion Criteria

All cases of peritonitis who underwent laparotomy were included in the study.

Exclusion Criteria

- Patients older than 60 years
- Patients younger than 15 years of age
- Patients coming with clinical features of peritonitis were assessed by thorough clinical examination. Diagnosis was confirmed by erect X-ray of the abdomen in most of the cases with the evidence of free gas under the diaphragm. USG abdomen was done in some cases. Investigations such as hemoglobin, total count, differential count, blood urea, and serum creatinine were done. Cases were randomly divided into two groups, each receiving plain saline peritoneal lavage and metronidazole lavage. Plain saline lavage group received IOPL with 2L of saline. Metronidazole lavage group received IOPL using 2L of saline mixed with 200 ml of metronidazole. Cases were followed up till the discharge or death of the patient. Post-operative complications – wound infection, intra-abdominal abscess, sepsis, fecal fistula, and death were noted. Post-operative hospital stay noted. Data were tabulated. Results of the two groups in terms of wound infection, intra-abdominal abscess, sepsis, fecal fistula, mortality, and post-operative hospital stay were compared using standard statistical tests. Results expressed as graphs and charts. Results are compared with other similar studies done in the past.

RESULTS

Hundred cases of peritonitis were studied. Fifty cases received plain saline peritoneal lavage and 50 received lavage using saline and metronidazole.

Cases studied were in the age group of 15–60 years. Highest number of cases was in the age group of 21–30 years (32%). Lowest number was in the age group of <20 years (2%) [Table 1].

Majority of cases were males. Males to female ratio - 6.14:1 [Table 2]

- The frequency of cause of peritonitis is as follows

The most common cause of peritonitis in this study was duodenal ulcer perforation (60%), followed by ileal (21%) and appendicular perforation (9%). Other causes were gastric perforation, ischemic bowel, traumatic jejunal perforation, and perforated Meckel's diverticulum [Table 3].

- Results of the operative procedure performed are as follows

In most of the patients perforation was closed primarily (78). Out of which 60 were duodenal perforations, 12 were ileal perforations, five were gastric perforations, and one was jejunal perforation. Resection and anastomosis of bowel were performed in 12 cases (eight ileal perforations, three ischemic bowels, and one perforated Meckel's diverticulum). Appendicectomy was done in nine cases. One patient with ileal perforation underwent ileostomy [Table 4].

In the saline lavage group incidence of wound infection was 40%. About 12% of the patients had intra-abdominal abscess. Sepsis was present in 28% of patients. About 6% of patients developed fecal fistula during the post-operative period. Mortality was 8% in this group [Table 5].

In the metronidazole lavage group incidence of wound infection was 26%. About 10% of the patients had intra-abdominal abscess. Sepsis was present in 18% of patients. About 6% of patients developed fecal fistula during the post-operative period. Mortality was 10% in this group [Table 6].

There was a 14% reduction in the incidence of wound infection in metronidazole lavage group when compared to saline lavage group. Incidence of intra-abdominal abscess reduced by 2% in metronidazole lavage group. About 10% reduction was seen in the incidence of sepsis in patients receiving metronidazole peritoneal lavage. There was no difference in the incidence of fecal fistula in either group. Mortality was higher in metronidazole lavage group by 2%. Chi-square test did not show any statistical significance of these apparent advantages of metronidazole lavage over saline lavage [Table 7].

The shortest post-operative hospital stay was 2 days where the patient died on 3rd post-operative day. The earliest discharge was after 7 days of hospital stay. The longest stay was 39 days postoperatively. Mean post-operative hospital stay in saline lavage group was 15.04 days and 13.22 days in metronidazole lavage group. However, the difference was statistically not significant.

DISCUSSION

The treatment of peritonitis is associated with a high morbidity and mortality. The usual treatment of the peritonitis consists of fluid replacement, nasogastric

Table 1: Age specific distribution of the cases

Age	No. of cases	Percentage
<20	2	2
21–30	32	32
31–40	30	30
41–50	23	23
51–60	13	13

Table 2: Sex distribution of the peritonitis cases

Sex	No. of cases	Percentage
Males	86	86
Females	14	14

Table 3: Causes of peritonitis

Cause	No. of cases	Percentage
Duodenal ulcer perforation	60	60
Ileal perforation	21	21
Appendicular perforation	9	9
Gastric perforation	5	5
Ischemic bowel	3	3
Traumatic jejunal perforation	1	1
Perforated Meckel's diverticulum	1	1

Table 4: Operative procedures performed

Procedure	No. of cases	Percentage
Primary closure of perforation	78	78
Resection and anastomosis	12	12
Appendicectomy	9	9
Ileostomy	1	1

Table 5: Outcomes in saline lavage group

Parameter	No. of cases	Total cases	Percentage
Wound infection	20	50	40
Intra-abdominal abscess	6	50	12
Sepsis	14	50	28
Fecal fistula	3	50	6
Death	4	50	8

Table 6: Outcomes in metronidazole lavage group

Parameter	No. of cases	Total cases	Percentage
Wound infection	13	50	26
Intra-abdominal abscess	5	50	10
Sepsis	9	50	18
Fecal fistula	3	50	6
Death	5	50	10

Table 7: Comparison of outcomes of saline lavage group and metronidazole lavage group

Parameter	Saline lavage group (%)	Metronidazole lavage group (%)	*P*-value
Wound infection	40	26	0.2
Intra-abdominal abscess	12	10	1
Sepsis	28	18	0.3
Fecal fistula	6	6	0.6
Death	8	10	1

suction, IV antibiotics, and operative intervention. Operation consists of suction of the fluid, which has collected in the peritoneal cavity, and definitive procedure for the pathology of the peritonitis (closure of perforation, closure bypass, resection, and anastomosis or appendicectomy, etc.). This is followed by peritoneal lavage and then the abdomen is closed with drain/drains.

Hundred patients were included in this study. Patients were randomly assigned into two groups: Saline lavage group and metronidazole lavage group. Patients in saline lavage group received IOPL with warm normal saline, while patients in metronidazole lavage group received IOPL with saline and metronidazole. Results were compared between the two groups.

Age

In this study, it was found that maximum number of cases was in the age group of 21–30 years. Least number of cases was in the age group of <20 years. Mean age of patients in this study was 37.25 years. This is comparable to the age distribution found by Khan *et al.* where maximum patients were in the age group of 31–40 years. Mean age was 37 years.

Patients younger than 15 years and older than 60 years were excluded from this study.

Sex Distribution

There was a male preponderance of cases in the present study, which is consistent with the values obtained by other studies.

Male to female ratio was 6.14:1.

Duodenal perforation was the leading cause of peritonitis in the present study, followed by ileal perforation and appendicular perforation. Gastric perforation, bowel ischemia, jejuna perforation, and perforation of Meckel's diverticulum were the less common causes of peritonitis.

Wound Infection

In the present study, there was 14% reduction in incidence of wound infection in the metronidazole lavage group. However, this difference is not statistically significant ($P = 0.2$). Similarly, Khan *et al.*[1] reported 20% reduction in incidence of wound infection, when superoxide solution was used for IOPL. On contrary, Schein *et al.*[2] did not find any difference in incidence of wound infection when chloramphenicol was used for IOPL.

Intra-abdominal Abscess

There was a 2% reduction in the incidence of post-operative intra-abdominal abscess in the metronidazole IOPL group. However, this is not statistically significant ($P = 1$). R. Fowler 48 in 1974 reported 16% reduction in the incidence of intra-abdominal abscess when cephaloridine was used for IOPL.

Sepsis

In this study, there was 10% reduction in the incidence of systemic sepsis in the metronidazole IOPL group. Statistically significant difference was not found in the incidence of sepsis between either group.

Fecal Fistula

Study did not find any difference in the incidence of post-operative fecal fistula in saline lavage group or metronidazole lavage group. In contrast to this study, Khan *et al*. (2009) reported 2.5% reduction in the incidence of fecal fistula in the study group, when superoxide solution was used for IOPL. This was not significant statistically.

Mortality

Mortality was 2% higher in the metronidazole IOPL group in this study. However, the difference is not statistically significant. Schein (1990) found no significant difference in mortality of patients treated with or without intraperitoneal lavage with chloramphenicol. Rambo (1972) also found no difference in the number of deaths when intraperitoneal irrigation with cephalothin was used. On the contrary McKenna *et al*. (1970) and Bhushan *et al*. (1975) found significant reduction in mortality in patients treated with antibiotic lavage.

Post-operative Hospital Stay

Mean post-operative hospital stay was 15 days in saline lavage group and 13.22 days in metronidazole lavage group. This improvement in the hospital stay is not statistically significant ($P = 0.17$). Khan *et al*. (2009) reported reduction in hospital stay by 1.5 days, which was not statistically significant. On the contrary, Vallance *et al*. (1985) found no improvement in the duration of hospital stay of patients treated with intraperitoneal lavage with chlorhexidine gluconate or Povidone-iodine when compared with those who received only saline lavage.

CONCLUSION

- Peritonitis is most common in the age group of 21–30 years (32%)
- There is a male preponderance with male:female ratio of 6.14:1
- Duodenal ulcer perforation (60%) is the most common cause of peritonitis, followed by ileal (21%), appendicular (9%), and gastric perforations (5%). Ischemic bowel (3%), perforation of Meckel's diverticulum (1%), and jejunal (1%) perforations are the rarer causes
- Primary closure of the perforation with omental patch is the most commonly performed operation (78%) followed by resection of the perforated segment of the bowel and end to end anastomosis (12%), appendicectomy (9%), and ileostomy (1%)
- There is 14% reduction in incidence of wound infection when metronidazole is used for IOPL. However, this is statistically not significant
- Incidence of intra-abdominal abscess is reduced by 2% in metronidazole lavage group, which is statistically not significant
- There is 10% reduction in systemic sepsis when metronidazole is used for IOPL. However, this is statistically not significant
- There is no difference in the incidence of post-operative fecal fistula whether metronidazole is used for IOPL or saline is used
- There is 2% increase in mortality when metronidazole is used for IOPL. This is not statistically significant
- Mean hospital stay is reduced by 1.8 days when metronidazole is used for IOPL. This is not statistically significant
- Addition of metronidazole to normal saline for IOPL has beneficial effects in terms of reduction in incidence of wound infection, intra-abdominal abscess, systemic sepsis and post-operative hospital stay. However, these are statistically not significant
- There is no statistically significant difference in the outcome between the saline group and metronidazole group

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Original Article

Prevalence of Pre-extensively Drug-resistant Tuberculosis and Extensively Drug-resistant Tuberculosis among Multidrug-resistant Tuberculosis Patients in South Tamil Nadu

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Abstract

Introduction: Drug resistance in tuberculosis (TB) is a growing global problem. The emergence of extensively drug-resistant TB (XDR-TB) strains is a significant roadblock in successfully implementing TB control programs. This further leads to high morbidity and mortality, especially in immunocompromised patients. The true scale of XDR-TB is unknown. Identification and observation of resistance patterns of XDR-TB strains may help clinicians manage multidrug-resistant TB (MDR-TB) cases.

Aims: This study aims to study the prevalence of pre-XDR and XDR-TB among the MDR-TB strains and clinical risk factors associated with XDR-TB in a tertiary care hospital in South Tamil Nadu.

Materials and Methods: This is a retrospective study conducted in a DR-TB Centre, Tirunelveli Medical College covering four South Tamil Nadu districts. We analyzed around 173 proven MDR-TB cases who were registered and initiated CAT IV regimen in our DR-TB Centre. Baseline second-line drug susceptibility testing for kanamycin and ofloxacin and the follow-up culture of pre-XDR and XDR patients from records were collected from August 2014 to July 2016 analyzed.

Results: Of the 173 patients with MDR-TB, 3 (2%) were XDR MTB strains. Thirty-three MDR-TB isolates (19%) were pre-XDR MTB strains and maximum resistance was observed to ofloxacin 82% (27/33). Socioeconomic status, migration history particularly to Mumbai (25%, *n* = 9), concomitant illness like diabetes mellitus (47%, *n* = 17), and previous intake of 2nd line drugs were significantly associated with the occurrence of XDR-TB.

Conclusions: This study showed the prevalence of XDR-TB compared to the "Global Report on surveillance and Response" which estimated that the prevalence of XDR among MDR-TB patients is 3.2%. MDR-TB cases need urgent and timely drug sensitivity reports for second-line ATT drugs to help the clinicians start proper drug combinations to treat MDR-TB patients and break the transmission chains.

Key words: Extensively drug resistant, Multiple drug resistant, *Mycobacterium tuberculosis*, Second-line drug resistance

INTRODUCTION

The emergence of pre-extensively and extensively drug-resistant tuberculosis (pre-XDR/XDR-TB) is the major hurdle for TB prevention and care programs, especially in developing countries like India. The less emphasis on universal access to laboratory techniques for the rapid diagnosis of TB and drug susceptibility testing (DST) makes the management of multidrug-resistant TB (MDR-TB) a challenge. Early detection of second-line anti-TB drugs resistance is essential to reduce transmission of pre-XDR/XDR-TB strains and adjusting the treatment regimen in MDR-TB.

The emergence of pre-extensively and XDR TB (pre-XDR/XDR-TB) is a significant obstacle for TB prevention in developing countries like India. The less focus on universal access to laboratory techniques for rapid TB diagnosis and DST challenges MDR-TB management. To reduce the transmission of pre-XDR/XDR-TB strains and

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adapt the MDR-TB treatment regime, early identification of second-line anti-TB drug resistance is crucial.[1] MDR-TB is a known phenomenon and is defined as the TB strain resistant to at least two first-line drugs such as rifampicin (RIF) and isoniazid. Pre-XDR TB is the MDR-TB strain that is resistant to either fluoroquinolone (FQ) or second-line injectable drug but not both. The MDR-TB strain that is resistant to any FQs and one of the second-line injectable drugs (capreomycin, kanamycin, or amikacin) is defined as XDR-TB.[2,3] Both XDR and pre-XDR TB are now posing concern on global efforts to control TB.

XDR-TB has been identified in 92 countries across the world according to a WHO report in 2012. India along with Russia and South Africa accounted for 45% of the total MDR-TB and RIF-resistant (RR-TB) cases in 2015 with an estimated 79,000 MDR-TB cases.[4] The exact prevalence of XDR-TB and its extent and magnitude is yet to be identified. Although the global incidence of MDR-TB is increasing, little data are available about the prevalence of XDR and pre-XDR-TB worldwide and in India. In India, the burden of TB is high, but the economic and resource constraints do not allow routine testing to FQ and second-line drug (SLD) resistance.[5] Unnecessary exposure to FQs and injectable aminoglycoside to treat bacterial infections other than TB may contribute to the evolution of resistance to these agents. In countries like India where TB is endemic, the registered practitioners must exercise utmost care while prescribing these drugs to patients in cases other than tuberculosis, keeping in mind the prevalence of drug resistance to these agents.

In 2015, only around 46% of the patients with MDR-TB had achieved treatment success and a 20% death rate was recorded. A poor outcome was reported in 9.5% of patients with XDR-TB.[6,7] Therefore, prevention and control of drug resistance are essential to reduce the death rate and improve treatment outcomes in MDR-TB cases. This study was designed to find out the prevalence of pre-XDR and XDR-TB among the MDR-TB strains and clinical risk factors associated with XDR-TB and create awareness about the community drug sensitivity patterns.

Aim

This study aims to study the prevalence of pre-XDR and XDR-TB among the MDR-TB strains and clinical risk factors associated with them in a tertiary care hospital in South Tamil Nadu.

MATERIALS AND METHODS

This is a retrospective study conducted in a DR-TB Centre, Tirunelveli Medical College covering four South Tamil Nadu districts. We analyzed around 173 proven MDR-TB cases who were registered and initiated CAT IV regimen in our DR-TB Centre. Baseline second-line DST for kanamycin and ofloxacin and the follow-up culture of pre-XDR and XDR patients from records were collected from August 2014 to July 2016 analyzed. The patients were grouped into primary MDR group, category I (XDR-TB) and category 2 (pre-XDR-TB). Sputum samples had been collected according to RNTCP guidelines. The culture was done on LJ medium and the identified *Mycobacterium tuberculosis* complex was subjected to sensitivity testing to SLDs kanamycin and ofloxacin. The patient's demographic data and migration history were obtained from the clinical records.

RESULTS

Of the 173 patients with MDR TB, 3 (2%) were XDR MTB strains. Thirty-three MDR-TB isolates (19%) were pre-XDR MTB strains that are strains are either resistant to ofloxacin (OFX 82%) or kanamycin (KM 18%). We observed maximum resistance to ofloxacin 82% (27/33). This may probably be due to the random use of quinolones by many registered and non-registered practitioners for common diseases. This highlights the problem in opting drug regimen to treat MDR cases. More than half (78%, $n = 28$) of these patients had a history of previous TB treatment. Nearly 22% of patients ($n = 8$) were primary MDR-TB. Among XDR-TB, all of them had a previous anti-TB therapy, with 67% of patients found to be diabetic, whereas in pre-XDR-TB, 42% of patients had diabetes. Socioeconomic status, migration history particularly to Mumbai (25%, $n = 9$), concomitant illness like diabetes mellitus (47%, $n = 17$), and previous intake of 2nd line drugs were significantly associated with the occurrence of XDR-TB. Only one of the patients enrolled was HIV seropositive (2.8%). HIV infection is not more common among drug-resistant TB patients than in the general population. Figure 1 depicts the analysis of pre-XDR and XDR-TB cases.

DISCUSSION

Early identification of SLD resistance plays a key role in TB control and management and also to optimize the treatment regimen composition. SLD resistance can impose a major economic burden in developing countries due to resource constraints and implications on short treatment regimens, new therapeutic agents, and new rapid diagnostic tools.[8] In the present study, 173 patients with MDR-TB were analyzed and the presence of pre-XDR and XDR TB strains was found in 19% and 2%, respectively, Figure 2. The percentage of pre-XDRTB was higher than XDR

strains and two SLDs OFX and KM were tested in our study. In Poland, the prevalence of pre-XDR-TB among MDR-TB patients is 12.1%, and in China, it is 31%.[9,10] The exact prevalence of pre-XDR and XDR-TB in India is not available and a few Indian studies report a prevalence rate of 2.4–33.3%.

Among the 33 pre-XDR-TB isolates, 27(82%) were resistant to OFX and 6 (18%) were resistant to kanamycin, Figure 3. This finding is similar to the study findings of Singhal *et al.* who also reported a higher resistance to OFX by the pre-XDR-TB isolates. The percentage of resistance in his study was 39% which is higher than the other studies ranging from 7.7% to 27.6%.[11] The increased resistance to ofloxacin highlights the problem in forming drug regimen to treat MDR cases. Similarly, the resistance to kanamycin in his study was 1.1%, and in our study, it is 18%. Various other studies report a prevalence rate ranging from 0.6% to 14.6%.[12] Myneedu *et al.* associates in their study showed 20.17% XDR-TB strains among a total of 223 MDR-TB strains. Global studies show a prevalence of 6.5% XDR stains in the USA, 10.3% in Germany, and 14.3% in Italy. In a 2010 WHO report, 58 countries reported the presence of XDR-TB strains among MDR-TB patients.[13] Apart from quinolones, kanamycin resistance pattern is a common finding ranging from 20% to 60% resistance documented in CDC and was seen in this study also (18%).[14]

In our study, 22% of the cases were primary MDR-TB cases and majority (78%) were previously treated for TB. This finding might indicate a significant public health threat given that there could be a progressive drug-resistant strain transmission in the population. Another interesting feature observed in our study was the migration history, especially to Mumbai where it showed 25% occurrence of XDR-TB, Figure 4. Concomitant illness like diabetes and previous intake of 2nd line drugs were also observed to be significantly associated with XDR-TB occurrence in this study, Figure 5. This may be due to the widespread and unchecked use of second-line anti-tuberculous drugs for other diseases like URTI and for urinary tract infections. Shah *et al.* in his study found that 70% of the total XDR-TB strains were resistant to SLD.[15] Studies also indicate that overcrowded/slum areas and high temperature and low altitude areas are at high risk of TB transmission and subsequent development of resistant strains.

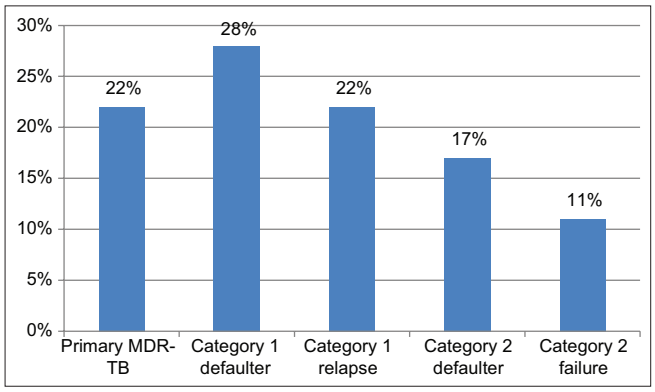

Figure 1: Analysis of pre-extensively drug-resistant (XDR) and XDR tuberculosis

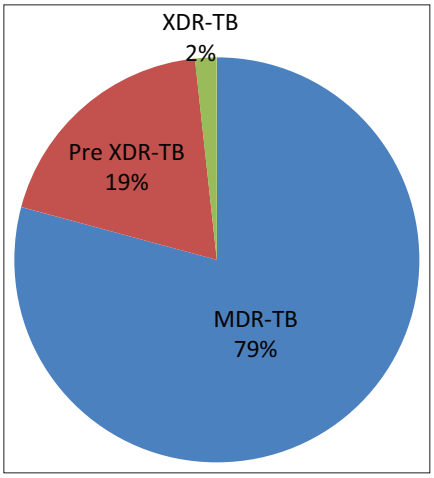

Figure 2: Pattern of drug resistance

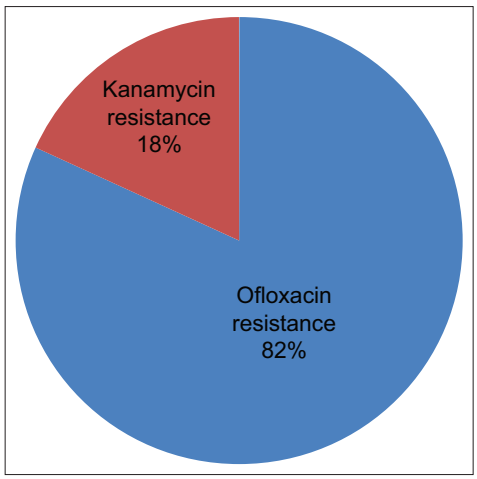

Figure 3: Percentage of resistance to second-line drug among pre-extensively drug-resistant tuberculosis

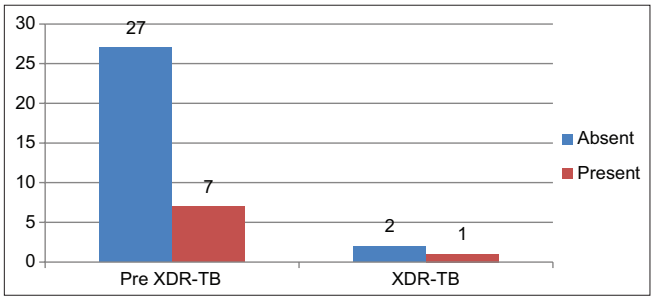

Figure 4: History of Mumbai residence

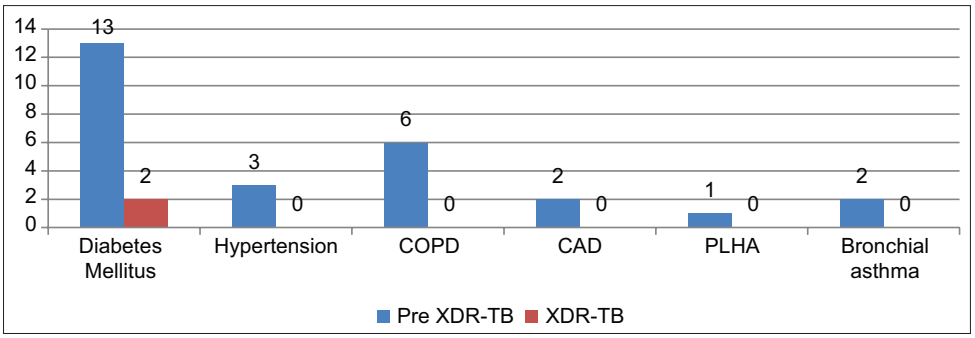

Figure 5: Comorbidities in pre-extensively drug-resistant (XDR) and XDR tuberculosis

Although our study showed a low prevalence of XDR-TB strains, the magnitude and distribution could not be estimated from the available data. Early diagnosis of resistance, appropriate therapy, and improved patient awareness for TB treatment play a crucial role in the control of MDR-TB and in interrupting the transmission chains. Future efforts should focus on strengthening of infrastructure for early diagnosis and treatment of MDR-TB and utilization of DOTS and DOTS plus strategy to increase community awareness, which can greatly avoid SLD resistance.

CONCLUSIONS

This study showed the prevalence of XDR-TB compared to the "Global Report on surveillance and Response" which estimated that the prevalence of XDR among MDR-TB patients is 3.2%. MDR-TB cases need urgent and timely drug sensitivity reports for second-line ATT drugs to help the clinicians start proper drug combinations to treat MDR-TB patients and break the transmission chains.

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Original Article

Study of Risk Factors Associated with Drug Resistant Tuberculosis

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Abstract

Introduction: There are many patient-specific factors, such as age, sex, alcohol abuse, poverty, HIV infection, smoking, substance abuse, a history of imprisonment, hospitalization, or recent immigration, all increase the probability of drug-resistant tuberculosis (DR-TB). However, although there are several risk factors for multi-DR-TB (MDR-TB), it should be noted that almost two-thirds of MDR-TB cases have never been previously been treated for TB or have none of these associated risk factors.

Aim: This study aims to study the risk factors associated with DR-TB in new cases.

Materials and Methods: In this retrospective study, 50 DR-TB patients were included, data such as demographic profile includes age, gender, occupation, comorbidities such as diabetes, alcoholism, chronic kidney disease, HIV and treatment history, and travel history were collected and analyzed.

Results: In 50 patients, the most common presenting complaint was cough (100%), patients with symptoms for more than 3 months were about 56%. In this study, the most common comorbidity was diabetes (21%). In our study also, majority was without any comorbidity (66.2%).

Conclusion: From the above study, it is concluded that there are some identifiable risk factors which will be associated with the development of primary DR-TB and they are non-specific since they are also associated with the development of drug-sensitive TB.

Key words: Drug-resistant tuberculosis, Risk factors, Universal drug susceptibility test

INTRODUCTION

Multidrug-resistant tuberculosis (MDR-TB) is emerging as a growing threat to TB control programs in many countries and accounts for 5% of all newly diagnosed patients worldwide.[1] The potentially serious impact of MDR-TB (TB strain resistant to at least isoniazid and rifampicin) has long been recognized;[2] however, the problem is of special concern because second-line drugs required for its treatment are often unavailable, are far more expensive than the first-line drugs, with only 65–75% efficacy, and have side effects that may require hospitalization.[3,4]

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Interrupting treatment with anti-TB medicines in an individual infected with TB allows some bacteria to remain alive, giving them a chance to develop resistance. MDR-TB can either occur due to inadequate treatment or direct contact with a MDR-TB patient.[5] Furthermore, MDR-TB is considered to be a main barrier to the control of TB in humans worldwide.[6] Numerous risk factors for the development of TB resistance have been established by the World Health Organization.[7] Many studies have identified risk factors associated with MDR-TB, including poor adherence to treatment, improper dosage, a short duration of treatment, and inadequate drugs.[8]

The literature shows that factors such as young age, migration, unemployment at the time of diagnosis, poor nutritional status (based on low body mass index), history of alcoholism, homelessness, and comorbidities, such as, diabetes, HIV/AIDS, and so on, are associated with MDR-TB.[9-11]

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Aim

This study aims to study the risk factors associated with DR-TB in new cases.

MATERIALS AND METHODS

This is a retrospective study done at DR-TB Centre, Department of Thoracic Medicine, Thiruvarur Medical College and Hospital, Tamil Nadu. The patients were selected for study from those who attending as outpatients for their follow-up or admitted as inpatients in the department of respiratory medicine from September 2020 to December 2020.

Inclusion Criteria

- All known newly diagnosed pulmonary TB patients with any form of drug resistance on treatment were included in the study.

Exclusion Criteria

The following criteria were excluded from the study:

- Previously treated TB patients
- Extrapulmonary TB patients
- Pregnancy
- Age <12 years.

Based on the criteria above, 50 DR-TB patients were selected for the study. Informed and written consent was obtained from all the patients. Data such as demographic profile include age, gender, occupation, comorbidities such as diabetes, alcoholism, chronic kidney disease, HIV and treatment history, and travel history were collected.

RESULTS

In the study 50 patients, majority was male (68%) patients and 50% of patients were between 40 and 60 years [Figures 1 and 2]. In the present study, the most common presenting complaint was cough (100%) which was productive in 96% of patients and fever was seen in 84% [Figure 3]. In this study, patients with symptoms for more than 3 months were about 56% [Figure 4]. In this study, the most common comorbidity was diabetes (21%). In our study also, majority was without any comorbidity (66.2%) [Figure 5].

DISCUSSION

India has the highest global burden of MTB and MDR-TB. Nearly half of the world's MDR-TB patients are from three countries, namely, India (27%), China (14%), and Russia (9%).[12] Indian survey of TB drug resistance in 2016 reports a lower incidence of MDR in treated (11.6% vs. 18%) and new cases (2.84% vs. 3.4%) in comparison with the global WHO 2019 report.[13] This study observed a gradual decline in MDR-TB from 5.06% in 2015 to 1.34% in 2018, although these data pertain to presumptive MDR-TB cases. Monoresistance to rifampicin and isoniazid also shows a decline from 2015 onward, pointing to the effectiveness of the Revised National TB Control Program in the state. About 60%–70% of our rifampicin-resistant TB is multidrug resistant, in close concordance with the global value of 78%.[14]

Our study results in concordance with Micheletti *et al.*[15] the most common signs and symptoms were productive cough (80.4%), weight loss (69.8%), and fever (41.3%). In this

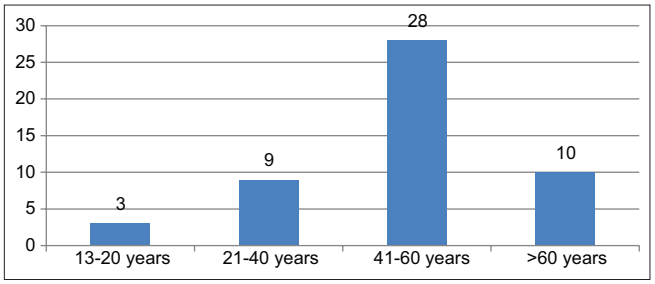

Figure 1: Distribution of age group

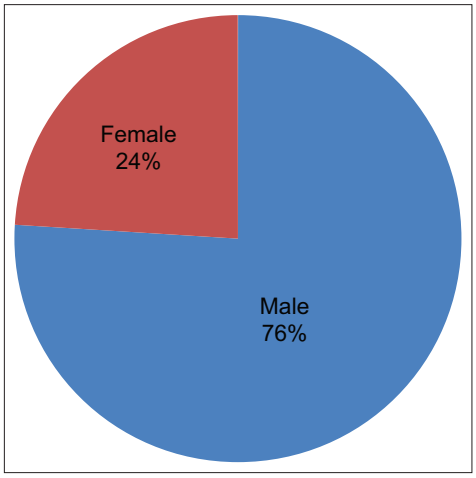

Figure 2: Distribution of gender

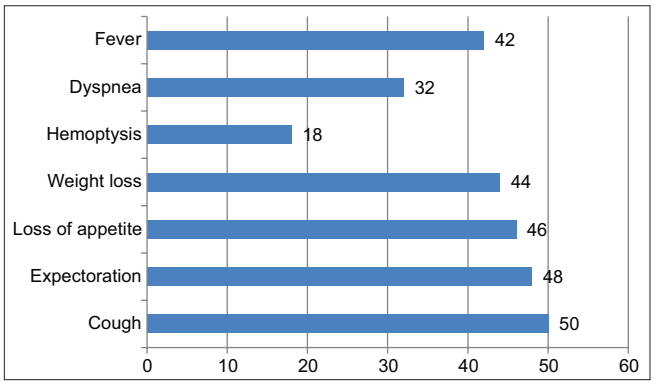

Figure 3: Distribution of symptoms

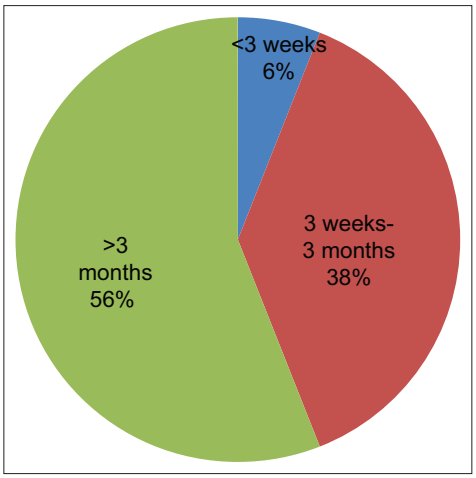

Figure 4: Distribution of duration of symptoms

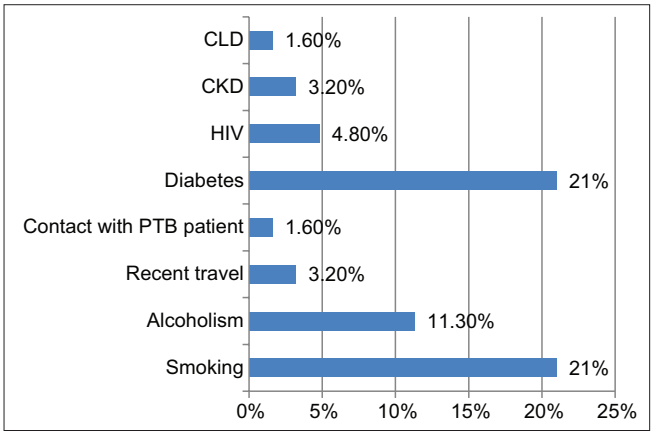

Figure 5: Distribution of risk factors

study, patients with symptoms for more than 3 months were about 54%. In Ricks *et al.*,[16] presentation with illness of long duration (>60 days) was a risk factor for the development of MDR-TB. In the current study, most common comorbidity was diabetes (21%). In Kang *et al.*,[17] DM was a relatively common comorbidity in DR-TB patients. However, in Micheletti *et al.*,[15] the most common comorbidity was HIV infection (26.2%) followed by diabetes mellitus (5.2%). Caminero[18] mentioned that high rate of primary MDR-TB in a general population with no identifiable risk factors for MDR-TB and suggested that in a high endemic area, targeting patients for MDR-TB based on the presence of risk factors are an insufficient intervention.

CONCLUSION

From the above study, it is concluded that there are some identifiable risk factors which will be associated with the development of primary DR-TB and they are non-specific since they are also associated with the development of drug-sensitive TB. Hence, risk factors based approach in evaluating TB patients for drug resistance is not useful in high endemic countries like India. Hence, it is necessary to follow universal drug susceptibility test principle as implemented by National TB Elimination Program to improve the favorable treatment outcomes and reduce the treatment failure and relapses.

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Original Article

Correlation of Vitamin D Levels in Normotensive and Preeclamptic Patients in Labor

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Abstract

Objective: The objective of the study was to evaluate maternal Vitamin D levels in term normotensive and preeclamptic patients in labor.

Materials and Methods: This was a case–control study carried out in the Department of Obstetrics and Gynaecology, CKM Hospital, Warangal. A total of 100 patients were divided into two equal groups (control and study groups of 50 each). Control group had women with singleton uncomplicated, term normotensive pregnant women in labor while the study group composed of term preeclamptic women in labor. A blood sample was collected by venepuncture. Serum 25 OHD (Serum 25 hydroxyl Vitamin D) concentrations were determined.

Results: Vitamin D levels were <15 ng/ml in 38 patients in the case group compared to 14 patients in the control group. Moreover, it was >15 ng/ml in 36 patients in the control group compared to 12 patients in the case group. This comparison of the Vitamin D (ng/ml) between the two groups shows that Vitamin D (ng/ml) is lower in case group which is statistically significant with $P < 0.001$. Comparison of Vitamin D based on severity of preeclampsia showed that as the severity of disease increases the vitamin level decreases which are evident from the comparison between preeclamptic and eclampic patient's Vitamin D levels which was statistically significant with $P < 0.001$.

Conclusion: From this study, Vitamin D deficiency is an independent modifiable risk factor for development of preeclampsia.

Key words: Preeclampsia, Vitamin D deficiency, Vitamin D

INTRODUCTION

Hypertensive disorders represent the most common medical complication of pregnancy affecting between 7 and 15% of all gestations and account for approximately a quarter of all antenatal admissions. According to the World Health Organization's (WHO) systemic review on maternal mortality worldwide, hypertensive disease remains a leading cause of direct maternal mortality.[1]

Hypertensive disorders are responsible for not only maternal deaths but also substantial morbidity for the pregnant women. Long-term impact of hypertension in pregnancy in the form of chronic hypertension and increased lifetime cardiovascular risk is also present. Hypertensive disorders also carry a risk for the baby.[1]

Hypertension and/or proteinuria are the leading single identifiable risk factor in pregnancy associated with stillbirth. Preeclampsia is strongly associated with fetal growth restriction, low birth weight, spontaneous or iatrogenic preterm delivery, respiratory distress syndrome, and admission to neonatal intensive care.[1]

Poor Vitamin D status, based on low circulating 25-hydroxy-Vitamin D (25 OHD) concentration, has been described in pregnant women in several countries. A lack of Vitamin D during pregnancy results in poor fetal and infant bone mineralization that may persist into later life. Low maternal Vitamin D has also been associated with an increased risk of preeclampsia. Vitamin D has direct influence on molecular pathways proposed to be important in the pathogenesis of preeclampsia. Serum 25OHD levels are associated with cardiovascular disease risk factors also. The placenta produces and responds to Vitamin D where Vitamin D functions as a modulator

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of implantation, cytokine production, and the immune response to infection.

Low Vitamin D levels have been associated with a wide range of adverse maternal and child health outcomes. One of them is preeclampsia according to few studies. Preeclampsia is a pregnancy specific syndrome that affects approximately 3–7% of first pregnancies.[1]

Several prospective studies have suggested that Vitamin D deficiency predisposes individuals to increased risk of incident hypertension, IHD, sudden cardiac death, or heart failure.

There is conflicting evidence whether hypovitaminosis D in pregnancy is associated with hypertension and preeclampsia.

Objective

The objective of the study was to evaluate maternal Vitamin D levels in normotensive and preeclamptic patients in labor.

Vitamin D insufficiency affects almost 50% of the population worldwide.[2] An estimated 1 billion people worldwide, across all ethnicities and age groups, have a Vitamin D deficiency (VDD).[2-4] This pandemic of hypovitaminosis D can mainly be attributed to lifestyle and environmental factors that reduce exposure to sunlight, which is required for ultraviolet-B (UVB)-induced Vitamin D production in the skin. Black people absorb more UVB in the melanin of their skin than do white people and, therefore, require more sun exposure to produce the same amount of Vitamin D.[5]

The high prevalence of Vitamin D insufficiency is a particularly important public health issue because hypovitaminosis D is an independent risk factor for total mortality in the general population.[6] Emerging research supports the possible role of Vitamin D against cancer, heart disease, fractures and falls, autoimmune diseases, influenza, type-2 diabetes, and depression. Many health-care providers have increased their recommendations for Vitamin D supplementation to at least 1000 IU.

A meta-analysis published in 2007 showed that Vitamin D supplementation was associated with significantly reduced mortality.[7]

Biology of the Sunshine Vitamin

Vitamin D is unique because it can be made in the skin from exposure to sunlight. Vitamin D exists in two forms. Vitamin D2 is obtained from the UV irradiation of the yeast sterol ergosterol and is found naturally in sun-exposed mushrooms.[4,8,9] UVB light from the sun strikes the skin, and humans synthesize Vitamin D3, so it is the most – natural‖ form. Human beings do not make Vitamin D2, and most oil-rich fish such as salmon, mackerel, and herring contain Vitamin D3. Vitamin D (D represents D2, or D3, or both) that is ingested is incorporated into chylomicrons, which are absorbed into the lymphatic system and enter the venous blood. Vitamin D that comes from the skin or diet is biologically inert and requires its first hydroxylation in the liver by the Vitamin D-25-hydroxylase (25-OHase) to 25(OH)D.[4] However, 25(OH)D requires a further hydroxylation in the kidneys by the 25(OH)D-1-OHase (CYP27B1) to form the biologically active form of Vitamin D 1,25(OH)2D. 1,25(OH)2D stimulates intestinal calcium absorption. Without Vitamin D, only 10–15% of dietary calcium and about 60% of phosphorus are absorbed. Vitamin D sufficiency enhances calcium and phosphorus absorption by 30–40% and 80%, respectively.[4]

Vitamin D receptor (VDR) is present in most tissues and cells in the body. 1,25(OH)2D has a wide range of biological actions, such as inhibition of cellular proliferation and inducing terminal differentiation, inhibiting angiogenesis, stimulating insulin production, inhibiting renin production, and stimulating macrophage cathelicidin production. The local production of 1,25(OH)2D may be responsible for regulating up to 200 genes 19 that may facilitate many of the pleiotropic health benefits that have been reported for Vitamin D.[4,8]

Vitamin D in Pregnancy

Introduction

Vitamin D has an increasingly recognized repertoire of non-classical actions such as promoting insulin action and secretion, immune modulation, and lung development. It, therefore, has the potential to influence many factors in the developing fetus. There is little information on Vitamin D intake in pregnancy and lactation and few studies on clinical outcomes. Some have suggested that the requirement for Vitamin D in these women may be up to 6000 iu/day 21 and the ideal Vitamin D regimen to prevent and treat Vitamin D insufficiency *in utero* is unknown.

VDD

Vitamin D and its active metabolite 1,25dihydroxyvitamin D (1,25(OH)2D) have classical actions of calcium balance and bone metabolism. Without sufficient 1,25(OH)2D, the intestine cannot absorb calcium and phosphate adequately, which leads to secondary hyperparathyroidism and a lack of new bone mineralization (rickets in children and osteomalacia in adults). Rickets is a childhood Vitamin D insufficiency and usually develops many months after delivery. However, the neonate is at risk of hypocalcemic tetany consequent on maternal hypovitaminosis D. Calcium levels are normal in utero when maternal Vitamin D is insufficient. However, when maternal calcium

delivery is interrupted at birth, the neonate may develop hypocalcaemia. While the developing fetus requires approximately 30 g of calcium, the maternal gut adapts and can overcome some Vitamin D insufficiency with increased calcium transport. VDD is common in northern Europe, especially in women with pigmented skin. In the general adult population, reduced Vitamin D concentrations are found in obese subjects. Prepregnancy obesity has been associated with lower levels of Vitamin D in both pregnant women and their neonates; 61% of women who were obese (body mass index [BMI] ≥30) before pregnancy were found to be Vitamin D deficient, compared to 36% of women with a prepregnancy BMI of less than.

Physiology

There are two forms of Vitamin D. Vitamin D3 (cholecalciferol) is produced from the conversion of 7-dehydrocholesterol in skin and Vitamin D2 (ergocalciferol) is produced in mushrooms and yeast. The biologically active form of Vitamin D is 1,25(OH)2D. This requires hydroxylation of Vitamin D in the liver to 25(OH) D (25-hydroxyvitamin D), which then undergoes renal hydroxylation to form 1,25(OH)2D. Although 25(OH)D has low biological activity, it is the major form of circulating Vitamin D. Serum 25(OH)D concentrations are generally thought to reflect nutritional status. Production of 1,25(OH)2D in the kidney is tightly regulated by plasma parathyroid hormone (PTH) as well as serum calcium and phosphate levels. The interaction of 1,25(OH)2D with nuclear VDRs influences gene transcription. Nuclear receptors for 1,25(OH)2D are present in a range of tissues including bone, intestine, kidney, lung, muscle, and skin. Similar to steroid hormones, 1,25(OH)2D acts through signal transduction pathways linked to VDRs on cell membranes. Major sites of action include intestine, bone, parathyroid, liver, and pancreatic beta cells. Its biological actions include increases in intestinal calcium absorption, transcellular calcium flux, and opening gated calcium channels allowing calcium uptake into cells such as osteoblasts and skeletal muscle. The biological effects of 1,25(OH)2D are diverse. It inhibits PTH secretion and adaptive immunity, while promoting insulin secretion and innate immunity. It also inhibits cell proliferation and stimulates their differentiation. The largest source of Vitamin D in adults is synthesis from solar radiation; ½ h of sunlight delivers 50 000 iu of Vitamin D with white-complexioned skin. Dietary intake of Vitamin D makes a relatively small contribution to overall Vitamin D status as there is little Vitamin D that occurs naturally in the food supply. Melanin absorbs UVB from sunlight and diminishes cholecalciferol production by at least 90%. Dietary Vitamin D is absorbed from the intestine and circulates in plasma bound to a Vitamin D binding protein. Preeclampsia and neonatal hypocalcemia are the most prevalent complications of maternal hypocalcaemia and are clearly associated with substantial morbidity. A statistical association of glucose intolerance and hypovitaminosis D has been demonstrated. Maternal Vitamin D is important to fetal bone development. Fetal lung development and neonatal immune conditions such as asthma may relate in part to maternal Vitamin D levels. Although it is not clear whether maternal Vitamin D supplementation will prevent these conditions, a strategy for supplementation and treatment of maternal VDD is proposed.

Maternal and fetal complications

Preeclampsia

There is conflicting evidence whether hypovitaminosis D in pregnancy is associated with hypertension and preeclampsia. In three studies, women who developed preeclampsia were found to have lower levels of Vitamin D than women who did not 26–28 with levels <50 nmol/l associated with a five-fold increased risk of severe preeclampsia.

Low levels in the first half of pregnancy were related to the risk of developing preeclampsia and the neonates of these mothers had a two-fold increased risk of having Vitamin D levels <37.5 nmol/l (VDD).

In a case–control study, women with severe preeclampsia before 34 weeks of gestation had reduced levels of Vitamin D compared to control women. Furthermore, women with early-onset severe preeclampsia and a small-for-gestational-age (SGA) infant had significantly lower Vitamin D levels than those with early-onset severe preeclampsia but non-SGA infants.

However, many studies have shown a weak or no relationship between Vitamin D and hypertensive disorders in pregnancy.

A Canadian study showed that women with low circulating maternal Vitamin D levels are more likely to have hypertension in pregnancy in the univariate analysis, but not the multivariate analysis.

Another study failed to show any association between Vitamin D levels and the development of preeclampsia, gestational hypertension, or preterm birth.

A similar study from the USA also failed to demonstrate an association between maternal first trimester Vitamin D levels and the subsequent development of preeclampsia after controlling for BMI.

However, two meta-analyses, including a meta-analysis of 31 studies, demonstrated that Vitamin D insufficiency was associated with preeclampsia and SGA infants.

Low birth weight

Maternal Vitamin D levels have been shown to positively correlate with birth weight centile.

In a study from Holland, women with VDD had a 2.4-fold increased risk of having an SGA baby.

Another study found that maternal Vitamin D levels of <37.5 nmol/l in the first half of pregnancy were associated with an adjusted odds ratio of 7.5 for SGA infants in white women, but not in black women.

Australian researchers found that mean birth weight was 200 g lower ($P < 0.001$) in babies of Vitamin D deficient mothers.

However, other studies demonstrated no relationship between maternal Vitamin D levels in the first trimester and birth weight but did demonstrate that low Vitamin D levels in late pregnancy were associated with reduced intrauterine long bone growth and lower gestational age at delivery.

Impaired glucose tolerance in pregnancy

Hypovitaminosis D is associated with impaired glucose tolerance and diabetes in the general population. However, the evidence for an association between low Vitamin D levels and gestational diabetes mellitus (GDM) is conflicting. Low concentrations of 25(OH)D have been related to the risk of developing type II diabetes mellitus (T2DM) through effects on insulin secretion and insulin sensitivity.

However, not all studies support these findings. The Third National Health and Nutrition Examination Survey (NHANES III) did not demonstrate an association between 25(OH)D levels and diabetes or insulin resistance in African Americans, in contrast to Caucasians and Mexican Americans.

In another study of European Caucasian subjects, insulin secretion and action were not associated with levels of 25(OH)D.

It is vital that such studies are controlled for obesity, a risk factor itself for VDD. GDM is considered to share the same pathogenesis as T2DM and similar associations between 25(OH)D and the development of GDM have been sought. Maternal 25(OH)D concentrations have been related to the risk of developing GDM in various cohorts.

Depending on the diagnostic criteria used, it has been suggested that GDM complicates up to 16% of pregnancies, although the true incidence can be much greater in some ethnic groups.

There are some data to suggest that the association between 25(OH)D levels and GDM risk is specific to ethnicity. In a majority non-Hispanic white population, 25(OH)D concentrations at 16 weeks of gestation were significantly lower in GDM subjects than in controls, whereas no association was found in Indian mothers where 25(OH) D concentrations were measured at 30 weeks of gestation.

Some studies have investigated more than one ethnic group using statistical techniques to correct for the effect of ethnicity, but none have been designed to describe the association in specific ethnic populations.

Conversely, a well-conducted study has found no association between maternal 25(OH)D and the development of GDM.

A meta-analysis of 31 studies demonstrated vitamin D insufficiency was associated with a higher risk of GDM.

Other complications

VDD (< 37.5 nmol/l) has been associated with a four-fold increased risk of primary cesarean section (caesarean section performed for the 1st time), 52 although this has not been demonstrated in all studies.

VDD is also associated with bacterial vaginosis in pregnant women.

In conclusion, hypovitaminosis D may be associated with hypertension, preeclampsia, and increased cesarean section rates. There are no randomized trials showing that Vitamin D supplementation alters these putative risks.

Neonatal hypocalcemic seizures

Neonatal Vitamin D levels are correlated with those of their mother, with maternal VDD increasing the risk of neonatal VDD.

In an Australian study, hypovitaminosis D was found in 15% of pregnant women and 11% of neonates.

VDD is a major cause of hypocalcemic seizures in neonates and infants.

Hypocalcemia is not uncommon in neonates and is a potentially severe problem.

Mothers of babies who suffer hypocalcemic seizures are more likely to be VDD (85%) than mothers of babies who do not (50%).

In another study from Egypt, all mothers of babies with hypocalcemic seizures had severe VDD.

Maternal VDD is a common, and potentially preventable, cause of neonatal hypocalcaemia. This is especially common in South Asian women.

Skeletal development and growth

Hypovitaminosis D is associated with impaired growth and bone development in the fetus.

Evidence is accruing to show that less profound maternal 25(OH)D insufficiency may lead to suboptimal bone size and density after birth without overt rachitic change.

This is likely to lead to an increased risk of osteoporotic fracture in later life.

A retrospective cohort study showed that children who had received supplements with Vitamin D in the 1st year of life had a significant increase in femoral neck bone density at the age of 8 years compared to the group that did not receive supplements. In a UK mother–offspring cohort, 31% of the mothers had circulating concentrations of 25(OH)D in late pregnancy of 27–50 nmol/l.

There was a positive association between maternal 25(OH) D concentration in late pregnancy and whole body bone mineral content and density, assessed using dual energy X-ray absorptiometry, in the offspring at 9 years of age. Furthermore, maternal UVB exposure and Vitamin D supplementation were associated with the bone mass of the child ($P < 0.05$), while lower levels of umbilical-venous calcium were also associated with lower childhood bone mass, 58 suggesting a possible role for placental calcium transport in this process. In addition, maternal UVB exposure during pregnancy was positively associated with whole body bone mineral content in the off spring at the age of 9 years in the Avon Longitudinal Study of Parents and Children, 59 although later analysis does not confirm these data.

Similar findings have come from another UK cohort.

The Southampton Women's Survey, in which neonatal bone area and bone mineral content were reduced in the female offspring of mothers who had 25(OH)D concentrations <33 nmol/l in late pregnancy.

These findings of altered neonatal bone mass have been confirmed by a Finnish mother–offspring cohort in which babies born to mothers with circulating 25(OH)D status belo the median (42.6 nmol/l) had reduced tibial bone mineral content and cross-sectional area, measured by peripheral quantitative computed tomography.

In a follow-up study, a deficit in tibial cross-sectional area was still observed at 14 months' follow-up, 62 despite the low Vitamin D group catching up with the other group for the bone mineral content. Evidence that 25(OH)D-related changes may be detectable early in gestation has come from the Southampton Women's Survey.

In this cohort, fetal distal femoral metaphyseal cross-sectional area was increased relative to femur length at 19 and 34 weeks of gestation in those babies whose mothers had low levels of circulating 25(OH)D, changes reminiscent of those seen in postnatal rickets. These findings suggest that the adverse consequences of maternal VDD for the offspring are manifest early in pregnancy. There are no data from randomized controlled trials to show benefit from maternal Vitamin D supplementation in terms of fetal or longer term growth of the child.

Fetal lung development and childhood immune disorders

Low maternal Vitamin D intake in pregnancy is associated with wheeze and asthma in the off spring.

Low cord blood 25(OH)D concentrations have been associated with respiratory syncytial virus bronchiolitis and respiratory infections.

There are plausible physiological mechanisms for an association between prenatal Vitamin D status and immune development. The metabolite 1,25(OH)2D has been shown in animal and *in vitro* models to have an immune-modulatory role and low levels of neonatal Vitamin D have been linked to childhood asthma.

Maternal Vitamin D supplementation is associated with cord blood gene expression of tolerogenic immunoglobulin such as immunoglobulin-like transcripts 3 and 4 (ILT3 and ILT4).71 Cord blood 25(OH)D is correlated with mononuclear cell release of IFN-γ and hence Th1 cell development.

More research is needed on the potential association between maternal Vitamin D in fetal lung development and childhood allergy; there are ongoing studies investigating long-term neonatal putative benefits of adequate maternal Vitamin D.

Screening for VDD in pregnancy

There are no data to support routine screening for VDD in pregnancy in terms of health benefits or cost effectiveness. There is an argument that some groups of women who are pregnant should have a screening test: for example, on the basis of skin color or coverage, obesity, risk of preeclampsia, or gastroenterological conditions limiting fat

absorption. As the test is expensive, offering it to all at-risk women may not be cost effective compared to offering universal supplementation, particularly as treatment is regarded as being very safe. At present, there are no data to support a strategy of measurement followed by treatment in the general female population.

Measurement of Vitamin D in a hypocalcemic or symptomatic woman as part of their management continues to be applicable. This includes women with a low calcium concentration, bone pain, gastrointestinal disease, alcohol abuse, a previous child with rickets, and those receiving drugs which reduce Vitamin D.

Supplementation and treatment in pregnancy

Daily Vitamin D supplementation with oral cholecalciferol or ergocalciferol is safe in pregnancy. The 2012 recommendation from UK Chief Medical Officers and NICE guidance state that all pregnant and breastfeeding women should be informed about the importance of Vitamin D and should take 10 μg of Vitamin D supplements daily.

Particular care should be taken over high-risk women. The recommendations are based on the classical actions of Vitamin D, although many of the non-classical actions of Vitamin D may be beneficial. As mentioned above, the review and meta-analysis by Aghajafari *et al*. found associations between Vitamin D insufficiency and risk of gestational diabetes, preeclampsia, bacterial vaginosis, and SGA infants.

Of course, this does not necessarily demonstrate that correction during pregnancy will reduce these risks.

Three categories of Vitamin D supplementation are recommended.

1. In general, Vitamin D 10 μg (400 units) a day are recommended for all pregnant women in accord with the national guidance. This should be available through the Healthy Start Programme
2. High-risk women are advised to take at least 1000 units a day (women with increased skin pigmentation, reduced exposure to sunlight, or those who are socially excluded or obese).

The RCOG has highlighted the importance of addressing suitable advice to these women. Seventy-eight women at high risk of preeclampsia are advised to take at least 800 units 79 a day combined with calcium.

Vitamin D may be inappropriate in sarcoidosis (where there may be Vitamin D sensitivity) or ineffective in renal disease. Deficient renal 1-α hydroxylation necessitates the use of active Vitamin D metabolites, such as 1α-hydroxycholecalciferol or 1,25-dihydroxycholecalciferol. Specialist medical advice should be sought in such cases. The limitation to therapy compliance mostly relates to the calcium which has a side effect of tasting of chalk, rather than the vitamin D element of oral therapy. It is often more appropriate to give Vitamin D alone for patient acceptability. However, this is limited by the availability of suitable agents; Vitamin D cannot be prescribed at low doses without calcium. 800-unit formulations of cholecalciferol without calcium are available. There may be particular benefits of Vitamin D/calcium supplementation in women at risk of preeclampsia.

Treatment

For the majority of women who are deficient in Vitamin D, treatment for 4–6 weeks, either with cholecalciferol 20 000 iu a week or ergocalciferol 10 000 iu twice a week, followed by standard supplementation, is appropriate. For women who require short-term repletion, 20 000 iu weekly appears to be an effective and safe treatment of VDD. A daily dose is likely to be appropriate to maintain subsequent repletion (1000 iu daily). In adults, very high doses of Vitamin D (300 000–500 000 iu intramuscular [IM] bolus) may be associated with an increased risk of fractures and such high doses are not recommended in pregnancy. A 2011 study demonstrated that supplemental doses of 4000 iu cholecalciferol a day were safe in pregnant women and most effective compared to the lower doses.

A comment piece in the lancet argued that routine supplementation of Vitamin D should be reserved for at-risk women rather than for all women.

This was on the basis of a large prospective cohort study showing no association between maternal serum Vitamin D levels and bone mineral content in the children. However, large, this was not randomized, did not consider supplementation and only looked at one indication.

Safety of Vitamin D

In pregnancy, there is enhanced intestinal calcium absorption. Vitamin D toxicity is manifested through hypercalcemia and hypercalciuria. Therefore, there is a hypothetical concern that when secondary hyperparathyroidism follows VDD, calcium given with Vitamin D may be associated with temporary hypercalcemia. However, this is self-limiting due to the associated hungry bone and has not been demonstrated to represent a clinical problem.

Opinion

Treatment of VDD women and Vitamin D supplementation is safe and is recommended for all women who are pregnant or breastfeeding. Low Vitamin D concentrations are present

in a significant proportion of the population. Women with pigmented or covered skin, obesity and immobility are at a higher risk. Low Vitamin D concentrations have been associated with a wide range of adverse maternal and offspring health outcomes in observational epidemiological studies. However, despite a dearth of interventional evidence supporting supplementation/treatment of Vitamin D in randomized controlled trial settings, it is generally accepted that supplementation/treatment is not harmful and may have some significant short- and long-term health benefits. Further research should focus on the potential benefits and optimal dosing of Vitamin D use in pregnancy.

Vitamin D and Preeclampsia

Vitamin D is a seco-steroid pro-hormone which, for biological activation, undergoes two successive hydroxylations, first to 25-hydroxyvitamin D (25(OH)D), a nutritional biomarker for Vitamin D status, and second to the active hormonal metabolite 1,25-dihydroxyvitamin D (1,25(OH)2D), that is, calcitriol. Calcitriol exerts the hormonal action through binding to nuclear VDRs, which are present throughout the body, including pregnancy-specific tissues such as the placenta and uterine placental bed (decidua). The placenta and decidua as well as other important target cells such as immune and endothelial cells have the molecular machinery for local production of calcitriol.

Preeclampsia is thought to originate in early pregnancy when the maternal immune system limits placental citriol can be considered a pregnancy-supporting factor that could work through several mechanisms to reduce preeclampsia risk, including a direct influence of calcitriol on implantation, placental invasion, and angiogenesis. It is also believed to be important in directing immune responses by dendritic cells and macrophages at the fetal-placental interface as well as immunological adaptation by the mother to reduce the risk of infection and inflammation.

Compared to normal pregnancies, Vitamin D metabolism is markedly altered in preeclampsia. This may be due to reduced placental 1α-hydroxylase activity resulting in lower circulating calcitriol concentrations compared to normotensive or chronically hypertensive pregnant women. Vitamin D status is reportedly lower in preeclamptic mothers at the time of diagnosis, but also before disease onset in some studies [Table 1].

MATERIALS AND METHODS

Source of Data

The study was conducted in pregnant patients in labor room, diagnosed as preeclampsia and normotensive patients in first stage of labor, of CKM Hospital, Warangal, between September 2019 and February 2020.

Method of Collection of Data (Including Sample Procedure if Any)

Study type: Comparative case–control study.

Inclusion Criteria

Case	Control
Age : 18–35 years of age	Age: 18–35 years of age
Singleton	Singleton
Preeclamptic patients in labor (defined as BP ≥140/90 mm Hg after 20 weeks of gestation and proteinuria ≥1+dipstick)	Uncomplicated Normotensive patients in labor

Exclusion Criteria

The following criteria were excluded from thr study:

- Patients who have taken Vitamin D prophylaxis.
- Patients with any other co-morbidities affecting Vitamin D levels.

METHODOLOGY

The women were included in the study on the basis of the inclusion and exclusion criteria were asked to give their consent for the test to be done for the purpose of this study.

The women were first screened for preeclampsia and accordingly included into _Case "and _Control" groups.

A blood sample was collected by venepuncture. Serum 25 OHD (serum 25 hydroxyl Vitamin D) concentrations were determined.

VDD defined as 25(OH)D levels below 15 ng/ml. (37.5 nmol/l).

Sample Size Estimation

Sample size is 100. The sample size was determined using the formula:

$n = 2(Z\alpha+Z\beta)^2\sigma^2/d^2$.

where,

n = sample size.

$Z\alpha = 1.96$ at 95% confidence interval.

$Z\beta = 1.2816$, at 90% power.

d = x1 - x2.

$\sigma = \sqrt{\sigma 1^2 + \sigma 2^2/2}$.

Cases – 50 patients diagnosed as preeclampsia in labor.

Controls – 50 normotensive patients in labor.

Statistical Methods

Independent –*t* test.

Pearson's Chi-square test.

OBSERVATION AND RESULTS

Comparison of the AGE between the two groups shows that AGE is higher in control group which is statistically not significant with $P = 0.542$. Hence, the first demographic factor age is comparable in cases and controls.

Comparison of the parity between the two groups shows that parity is statistically not significant with $P = 0.480$.

4B) Demographic factor – Period of Gestation

Comparison of the POG (Wks) between the two groups shows that POG (Wks) is higher in control group with a t value of 2.652 and is statistically significant with $P = 0.009$. The difference in the period of gestation in the cases and control was significant might be because of induction of preeclamptic patients in the earlier gestation than normotensive patients.

The maternal Vitamin D levels in the study group (cases) were relatively lower with a median value of 11.12 ng/ml as compared to 18.12 ng/ml in the control group. This difference in the median maternal Vitamin D levels of both the groups was found to be statistically significant with $P < 0.001$.

About 42% of the patients in the study group were found to be severely Vitamin D deficient (Vitamin D levels <10 ng/ml) as compared to 6% of the patients in the control group. This difference in the number of patients with severe VDD among the two groups was also statistically significant with $P < 0.001$

Vitamin D levels were <15 ng/ml in 38 patients in the case group compared to 14 patients in the control group. Moreover, it was >15 ng/ml in 36 patients in the control group compared to 12 patients in the case group. This comparison of the Vitamin D (ng/ml) between the two groups shows that Vitamin D (ng/ml) is lower in case group which is statistically significant with $P < 0.001$.

Comparison of Vitamin D based on severity of preeclampsia showed that as the severity of disease increases the vitamin level decreases which are evident from the comparison between preeclamptic and eclampic patient's Vitamin D levels which was statistically significant with $P < 0.001$ [Figures 1-4].

DISCUSSION

In our study, age and parity did not effect the Vitamin D levels. Hence, it is an independent risk factor for development of preeclampsia.

In our study, the difference in the period of gestation in the cases and control was significant might be because of induction of preeclamptic patients in the earlier gestation than normotensive patients.

Parameters	*P* value
Age	0.542
Parity	0.480
Gestational age	0.009

For this study, 100 women were selected and divided into two groups, the control group comprised 50 normotensive pregnant women, and the study group is comprised 50 diagnosed PE cases.

In our study, the cutoff for VDD taken was 15 ng/ml. Study done by Ringrose *et al.* has taken a cut off of 50 nmol/l (20 ng/ml).

In the contrast study by Shand *et al.*, the serum 25OHD concentration levels at the cutoff points of <37.5(15 ng/ml), <50, or <75 nmol/l.

Sample size	Cases		Controls
Robinson *et al.* (2010)	150	50	100
Ringrose *et al.* (2011)	187	78	109
Gupta *et al.* (2016)	100	50	50
Our study	100	50	50

In the present study, the serum Vitamin D levels were relatively lower with a median value of 11.12 ng/ml as compared to 18.12 ng/ml in the control group. This difference in the median maternal Vitamin D levels of both the groups was found to be statistically significant with $P < 0.001$. The supporting studies with our study were by Bodnar *et al.*, Ringrose *et al.*, Gupta *et al.*, and contrary to our study, were studies done by Shand *et al.*, Powe *et al.*

Study	Significance *P* value
Bodnar *et al.* (2007)	<0.05
Ringrose *et al.* (2011)	0.046
Shand *et al.* (2010)	0.21, 0.41
Gupta *et al.* (2016)	<0.001
Our study	<0.001

However, the limitations of this study were small sample size, and selection bias in selecting significant number of eclamptic patients.

Table 1: Number of cases and controls

Groups	Number
Cases	50
Controls	50

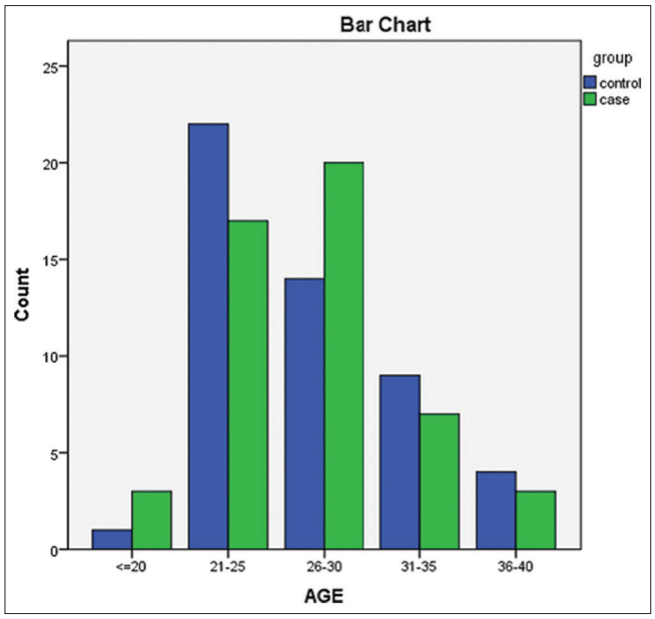

Figure 1: Demographic factors – age

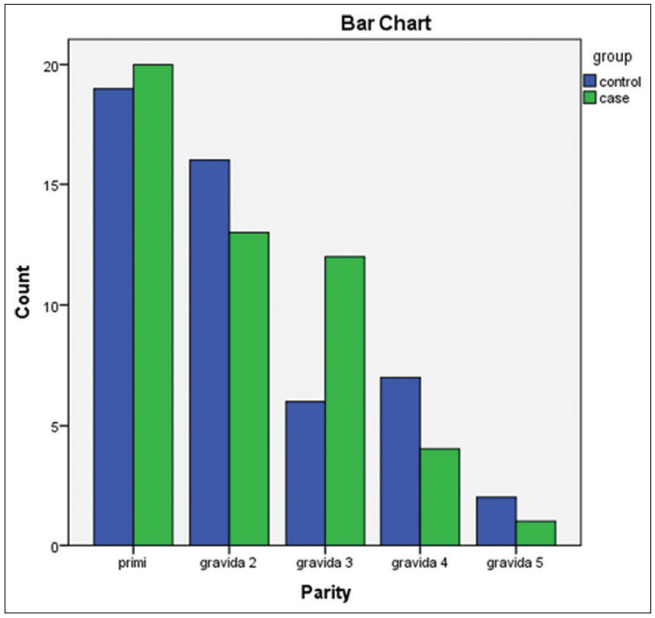

Figure 2: Demographic factor – parity

SUMMARY

Hypertensive disorders represent the most common medical complication of pregnancy affecting between 7 and 15% of all gestations and account for approximately a quarter of all antenatal admissions.

There is conflicting evidence whether hypovitaminosis D in pregnancy is associated with hypertension and preeclampsia.

Hence, this study deals with the levels of Vitamin D in preeclamptic patients compared to normotensive patients.

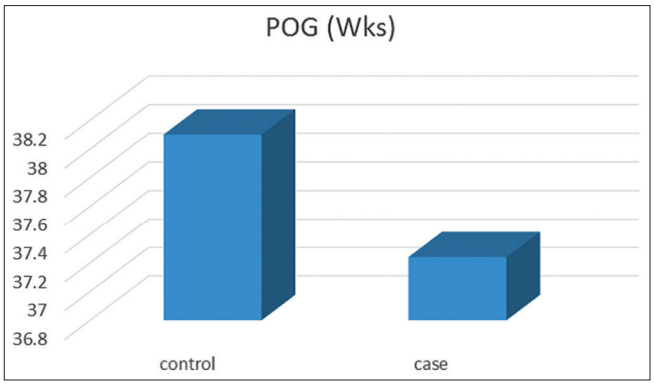

Figure 3: Demographic factor – period of gestation

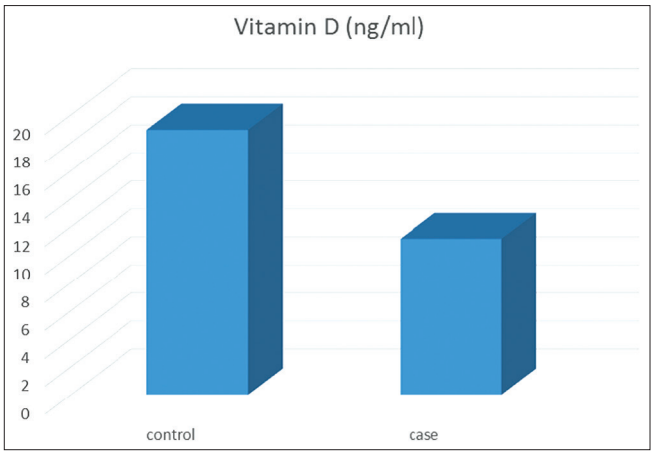

Figure 4: Vitamin D correlation

The study was conducted in pregnant patients in labor room, diagnosed as preeclampsia and normotensive patients in first stage of labor, of CKM Hospital, Warangal, between September 2019 and February 2020.

The women were first screened for preeclampsia and accordingly included into _Case "and _Control" groups. A blood sample was collected by venepuncture between of gestation. Serum 25 OHD (serum 25 hydroxyl Vitamin D) concentrations were determined. VDD defined as 25(OH) D levels below 15 ng/ml.

Cases – 50 patients diagnosed as preeclampsia in labor. Controls – 50 normotensive patients in labor.

Age, parity demographic features were comparable in both case and control groups. Period of gestation was higher in the control group might be because of induction of preeclamptic patients in the earlier gestation than normotensive patients.

Vitamin D levels were <15 ng/ml in 38 patients in the case group compared to 14 patients in the control group. Moreover, it was >15 ng/ml in 36 patients in the control group compared to 12 patients in the case group. This

comparison of the Vitamin D (ng/ml) between the two groups shows that Vitamin D (ng/ml) is lower in case group which is statistically significant with $P < 0.001$.

Comparison of Vitamin D based on severity of preeclampsia showed that as the severity of disease increases the vitamin level decreases which are evident from the comparison between preeclamptic and eclampic patient's Vitamin D levels which was statistically significant with $P < 0.001$.

CONCLUSION

From this study, VDD is an independent modifiable risk factor for development of preeclampsia.

Future research is needed to determine the effect of Vitamin D supplementation on the incidence of gestational hypertension and preeclampsia.

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Original Article

A Prospective Study on Maternal and Fetal Outcome in Gestational Diabetes Mellitus

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Abstract

Introduction: Gestational diabetes mellitus (GDM) is "Carbohydrate intolerance of variable severity with the onset and first recognition during the present pregnancy." Virtually, all new cases of diabetes in pregnancy are a transient form of type 2 diabetes.

Aims and Objectives of Study: The aim of this study was to study the risk factors associated with gestational diabetes and to evaluate effect of GDM on maternal and fetal outcome.

Materials and Methods: Descriptive study consecutive pregnant women diagnosed with GDM attending antenatal outpatient department (OPD) from January 2017 to September 2018 at the Department of Obstetrics and Gynaecology (OBG) of Kakatiya Medical College under Government Maternity Hospital Hanamkonda were enrolled for the study.

Conclusions: Consecutive pregnant women diagnosed with GDM attending antenatal OPD from January 2017 to September 2018 at the Department of OBG of Kakatiya Medical College under Government Maternity Hospital Hanamkonda were enrolled for the study.

Key words: Fetal outcome, Gestational diabetes mellitus, Macrosomia, Maternal outcome

INTRODUCTION

Gestational diabetes mellitus (GDM) is "Carbohydrate intolerance of variable severity with the onset and first recognition during the present pregnancy". Virtually, all new cases of diabetes in pregnancy are a transient form of type 2 diabetes. A small proportion of cases of *de novo* diabetes is found to persist after pregnancy. Most of these are type II diabetes mellitus (DM). However, rarely type I DM will arise during pregnancy simply as a matter of coincidence.[1]

GDM is a controversial clinical entity believed to be unmasking of a compensated metabolic abnormality characterized by a relative insulin deficiency and increased insulin resistance.

GDM is the special situation; as far as, the pregnancy is concerned, in which potential adverse effects on the fetus and mother is paramount importance and should be clearly identified.

Jarrett[2] wrote that GDM is non-entity whose only clinical association is with an increased risk of mother subsequently becoming diabetes.

Hunter and Milner stated that gestational diabetes is a diagnosis still looking for a disease whereas Beard and Hoet[3] concluded that GDM is a clinical entity associated with increased maternal and fetal morbidity. It has been demonstrated that perinatal and maternal morbidity among GDM can be reduced with application of systematic approach to identification and management of the disease.

Indian data on GDM is scant and does not give the actual picture. India falls under moderately risk group and with the advent of western lifestyle, incidence of type II DM is raising precipitously. Hence, number of women with GDM is also raising, hence the need for this study.

In spite of plenty of research papers over the years, still lot of controversies remain regarding type of screening universal or selective, which diagnostic test to follow and ideal cut-off levels. This study is done to find the risk

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factors associated with GDM and the effect of GDM on maternal and fetal outcome.

Aims and Objectives of Study

The aim of this study was as follows:

1. To study the risk factors associated with gestational diabetes
2. To evaluate effect of GDM on maternal and fetal outcome.

MATERIALS AND METHODS

Source of Data

1. All pregnant women were subjected to universal screening at 24–28 weeks of gestation with 75 g of glucose and 2 h plasma glucose. >140 mgs% is taken for diagnosis (as per diabetes and pregnancy study group India [DIPSI] guidelines which are a modified version of the World Health Organization [WHO]). After diagnosis, they were subjected to HbA1c. HbA1c is >6.5% the women which were excluded from the study. If negative, the test will be repeated in the third trimester (32–34 weeks of gestation)
2. Consecutive pregnant women diagnosed with GDM attending antenatal outpatient department from January 2017 to September 2018 at the Department of Obstetrics and Gynaecology of Kakatiya Medical College under Government Maternity Hospital Hanamkonda were enrolled for the study.

Study Design

This study was prospective study.

Statistical Data Analysis

Analysis of data will be done using descriptive statistics and association between qualitative characteristics will be done using Chi-square test.

Inclusion Criteria

Pregnant women diagnosed with GDM in second (24)- and third trimester (32–34weeks) were included in the study.

Exclusion Criteria

The exclusion criteria were excluded from the study:

1. Women with overt diabetes
2. Women with any other chronic medical disorders diagnosed before pregnancy.

Sample Size

Minimum 50 participants meeting inclusion criteria from January 2017 to September 2018 were included in the study.

Methods of Collection of Data

On enrollment patients, detailed history including age, marital period, family history, obstetric history (intrauterine device, abortions, and macrosomia), medical history, and body mass index (BMI) will be taken. All GDM patients were counseled regarding the diet therapy medical nutritional therapy (MNT) and regular self-monitoring of the blood sugar at home which is required for good perinatal and maternal outcome. Venous plasma glucose is checked after 2 weeks, if persistently 2 h postprandial blood sugar >120 mg% insulin will be started in consultation with a physician or endocrinologist.

Maternal and fetal outcome were analyzed by grouping the patients as follows

- Patients treated with MNT.
- Patients treated with MNT and insulin.

Table 1: Age distribution of the sample

Age group (in years)	Number	Percentage
<20	4	8
21–25	24	48
26–30	18	36
31 and above	4	8
Total	50	100

Table 2: Parity distribution of the sample

Parity	Number	Percentage
Primigravida	16	32
Gravida-2	17	34
Gravida-3	13	26
Gravid-4	03	0
Gravida-5	01	2%
Total	50	100

Table 3: Family history of GDM

Family history	Number	Percentage
Present	15	30
Absent	35	70
Total	50	100

GDM: Gestational diabetes mellitus

Table 4: History of Complications in previous pregnancy (in multiparous only)

Complications	Number (out of *n*=35)	Percentage
Abortion	16	45.71
Congenital anomaly	7	20.00
Previous H/O GDM	7	20.00
Preterm delivery	4	11.43
Macrosomia	3	8.57
IUD	3	8.57

GDM: Gestational diabetes mellitus; IUD: Intrauterine device

OBSERVATIONS AND RESULTS

Most of the sample belonged to the age group of 21–30, with 48% belonging to 21–26 years [Table 1].

Table 5: BMI

BMI (KG/m²)	Number	Percentage
<20.0	2	4
20.1–24.9	29	58
25.0–29.9	15	30
>30.0	4	8
Total	50	100

BMI: Body mass index

Table 6: Maternal complications

Complications	Number	Percentage
Polyhydraminios	6	12
Pre-eclampsia	4	8
UTI	4	8
Vaginitis	3	6
No complication	33	66
Total	50	100

UTI: Urinary tract infection

Table 7: Therapy advised

Therapy advised	Number	Percentage
Dietary modifications	33	66
Insulin	17	34
Total	50	100

Table 8: Gestational age at delivery

Gestational age	Number	Percentage
Preterm	13	26
Term	37	74
Total	50	100

Table 9: Mode of delivery

Mode of delivery	Number	Percentage
Full term vaginal delivery	20	40
Preterm vaginal delivery	8	16
Vaginal delivery (subtotal)	28	56
Elective LSCS	16	32
Emergency LSCS	6	12
Cesarean section (Subtotal)	22	44
Total	50	100

LSCS: Lower segment cesarean section

About 58% of the sample were primi or second parity [Table 2]. About 8% were grand multiparous.

About 30% of the sample had a positive family history [Table 3].

Out of 35 multigravid women had history of abortion [Table 4], 7 had history of congenital anomaly or GDM, 4 had preterm delivery, 3 had macrosomia, and 3 other had history of intra uterine death.

About 38% of the sample were obese [Table 5]. About 58% of the pregnant women were in the BMI range of 20.1–24.9.

Thirty-three pregnant women did not have any kind of complication [Table 6]. Of them six had polyhydromnios, four had pre-eclampsia, four had urinary tract infection (UTI), and three of them had vaginitis [Table 7].

Almost two-third of the sample was managed with dietary modifications and the remaining one-third were put on insulin [Table 8].

In the sample, 74% of the pregnancies continued beyond 37 weeks. The rest had preterm deliveries.

About 56% of the deliveries were vaginal deliveries [Table 9], 20 of 50 were full term, and 8 were preterm, 44% were cesarean sections, of which 16 of 50 were elective and 6 were emergency sections.

Primiparity with gestational diabetes were 2.18 times more likely to develop any kind of complications during their pregnancy than multiparity, but this difference was not significant statistically [Table 10].

Multiparity with GDM was found to be at higher risk of developing polyhydromnios and UTI, whereas primiparity was at higher risk for pre-eclamsia and vaginitis., but these were not statistically significant [Table 11].

It was observed that oral glucose tolerance test (OGTT) values had statistically significant moderately negative correlation with gestational age at delivery, that is, higher the OGTT values, earlier was the gestational age at delivery. Birth weights had moderate positive correlation with gestational age at delivery, that is, the longer the gestational age, the heavier was the baby at birth [Table 12].

Table 10: Maternal complications comparison with parity

Parity	Maternal Complication developed (%)	No maternal Complications developed	Total
Primiparity	7 (46.67)	8	15
Multiparity	10 (28.57)	25	35
Total	17	33	50

Chi-square=1.53; DF=1; *P*=0.216

OGTT values had moderately negative correlation with appearance, pulse, grimace, activity, and respiration (APGAR) scores, that is, with higher OGTT values, the APGAR score at 1 were low [Table 13]. Gestational age at delivery and birth weights was strongly positively correlated with APGAR scores, that is, APGAR scores tend to be higher with heavier babies and longer gestations.

DISCUSSION

Gestational diabetes is carbohydrate intolerance of various severity with onset or first recognitions during pregnancy. GDM is a risk factor for both mother and fetus. This risk increases proportionally to the maternal blood sugar concentration. Hence, we have to screen all antenatal patients with screening test between 24 and 28 weeks of gestation. In this study, we used 75 g OGTT as a one-step screening and diagnostic test. Early diagnosis of GDM reduces the perinatal morbidity and mortality [Table 14].

Green *et al*. showed that incidence of GDM was significantly greater for Chines (7.3%) and Hispanic (4.2%) women than for blacks. Indian populations is ethically prone to high prevalence of type 2 DM. ADA notice that 7% of all pregnancies are complicated by GDM. Anjalakshi *et al*., in their study of 800 pregnant women, diagnosed GDM by 75 g glucose irrespective of last meal timing and found no statistically significant difference between the plasma glucose levels of glucose challenge test and WHO glucose tolerance test (GTT).

Maternal age is an established risk factor for GDM Lao *et al*. [Table 15] which indicate that the risk of GDM become significantly and progressively increase from 25 years onward. In clinical practice, maternal age >25 years should be adopted instead of >35 years or 40 years as a risk factor for the development of GDM.

Seshiah *et al*. noted increase in the prevalence of GDM [Table 16] in their study and attributed it to increased BMI, as high maternal weight is associated with a higher risk of GDM. Moses *et al*. showed that GDM was present in 11.6% cases with positive family history.

Garner *et al*. showed that preeclampsia was twice as high in GDM [Table 17]. Older studies indicated a significant increase in incidence of preeclampsia, but recent studies like Nayor *et al*. questioned this. Hydraminos affects approximately 0.4–1.5% of all pregnancies. DM may be responsible for approximately 14% of all cases of polyhydraminos.

Sibai and colleagues reported that 9% of women spontaneously delivered before 35 weeks compared with 4.5% of non-diabetic women. In our study, preterm labor occurred among the GDM patients is 30%.

Table 11: Individual Maternal complications comparison with parity

Parity	Poly hydraminios	Pre-eclampsia	UTI	Vaginitis
Primi (*n* = 15)	2	2	1	2
Multi (*n* = 35)	4	2	3	1
Total	6	4	4	3
Chi-square	0.081	0.116	0.116	0.608
DF	1	1	1	1
P-value	0.776	0.733	0.733	0.436

UTI: Urinary tract infection

Table 12: Correlation of variables

Parameters	Age	Parity	BMI	OGTT	Gest Age	Birth weight	APGAR
Age	1						
Parity	0.262	1					
BMI	0.245	0.216	1				
OGTT	–0.043	0.111	–0.098	1			
Gestational Age	0.169	–0.062	0.108	–0.457	1		
Birth weight	0.104	–0.008	0.213	–0.171	0.375	1	
APGAR	0.075	0.008	0.154	–0.415	0.710	0.507	1

BMI: Body mass index; OGTT: Oral glucose tolerance test; APGAR: Appearance, pulse, grimace, activity, and respiration

Table 13: Significant correlations of variables

Sl. No	Variable-1	Variable-2	Correlation Coefficient (R)	*P*-value
1	Gestational age	OGTT	–0.457	0.001*
2	Birth weight	Gestational age	0.375	0.007*
3	APGAR	OGTT	–0.415	0.002*
4	APGAR	Gestational age	0.710	0.000*
5	APGAR	Birth weight	0.507	0.000*

OGTT: Oral glucose tolerance test; APGAR: Appearance, pulse, grimace, activity, and respiration

Table 14: Incidence of GDM in other studies

Author	Year	Incidence (%)
Coustan and Carpenter	1982	1.5
Green *et al.*	1990	4.5
Schmidt *et al.*	2001	7.2
Vinita das *et al.*	2002	4.0
Jali *et al.*	2011	16.0
Seshiah	2012	13.4
Kalra	2013	6.6

GDM: Gestational diabetes mellitus

Table 15: Age distribution of GDM in other studies

Age	Seshiah *et al.*[4] (%)	Jail (%)	Present study (%)
<20 years	14.5	7.7	8
21–24	13.7	26.9	48
25–29	19.5	36.5	36
30–34	25	19.2	8
>35		9.6	0

GDM: Gestational diabetes mellitus

Table 16: Risk factor for GDM

Risk factor	Seshiah *et al.* (%)	Jail (%)	Present study (%)
family history	-	76.9	30
BMI>25 kg/m^2	33.3	78.8	38
Age>30 years	30	28.8	8

BMI: Body mass index, GDM: Gestational diabetes mellitus

Table 17: Maternal complications in other studies

Author	Polyhydraminos (%)	Preeclampsia (%)
Jindal *et al.*	6.6	21
Usha Krishna	28	48
Present study	12	8

O'Sullivan *et al.* reported that the perinatal morality was 6.4% among GDM when compared to normal controls. In our study, 60% of GDM had APGAR score >8. All babies in GDM group had good APGAR due to good glucose control and prompt delivery and resuscitation.

In present study, among 50 GTT positive cases, 10 cases turned for follow-up. All the 10 cases were subjected to 75 g OGTT 6 weeks after delivery and GTT was normal in all four cases.

In present study, maternal mortality was nil. Perinatal mortality was also nil.

Neonatal deaths were 2%.

CONCLUSION

Indian women are more prone to gestational diabetes during pregnancy, hence the need for universal screening. For universal screening, the WHO recommended 75 g OGTT as a one-step screening and diagnostic procedure.

On March 14, 2007, Government of India order recommended universal screening at 24–28 weeks of pregnancy with 75 g OGTT. Venous blood glucose sample of 140 mg% or more is suggestive of GDM. One step procedure is less time consuming, economical, and feasible. The two-step procedure of screening with 50 g OGCT is not practical as the pregnant women have to visit the clinic twice and 3 or 4 blood samples are drawn, which is distressing to the patient.

DIPSI procedure is cost effective, without compromising the clinical equipoise and can be continued to diagnose GDM in our country.

During our study, detected GDM patients were closely monitored and treated with either insulin or diet plan which reduced the adverse obstetric and perinatal outcome.

The timely action in screening all pregnant women for glucose intolerance achieving euglycemia and ensuring adequate nutrition may prevent in all probabilities, the vicious cycle of transmitting glucose intolerance from one generation to another and also maternal and fetal complications.

SUMMARY

During January 2017 to September 2018, all antenanal patients at 24–25 weeks of gestation were subjected to screening for GDM by a single step screening and diagnostic 75 g OGTT, out of them, 50 antenatal women diagnosed as GDM were selected.

1. Majority of GDM patients were in age of 21–29 years
2. 38% of GDM patients had BMI >25 kg/m^2
3. 32% of GDM patients were primiparity
4. Family history of diabetes was present in 30% of GDM patients
5. Among GDM patients, 12% had polyhydramnious and 8% had UTIs
6. 17 out of 50 GDM patients are treated with insulin
7. Preterm delivery was seen in 26% of GDM patients
8. 44% of GDM patients underwent lower segment cesarean section, 56% had vaginal delivery
9. Among GDM patients, 12 babies had birth weight >3.5 kg
10. Neonatal complications observed were hypoglycemia, hyperbilirubinemia, and respiratory distress
11. Out of 50 GDM patients, 10 reverted back for follow-up and 75 g OGTT was normal.

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Original Article

Study of Red Cell Distribution Width in Heart Failure Patients

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Abstract

Introduction: Red cell distribution width (RDW) is a measurement of size variability of the red blood cells and has been shown to be a powerful predictor of prognosis in heart failure (HF) in the recent years. We sought to investigate the prognostic value and longitudinal pattern of RDW in patients with concomitant HF.

Aims: This study aims to study the relationship between RDW and HF assessed by echocardiography.

Materials and Methods: This is a prospective study was done on 50 patients with clinical diagnosis of HF. HF patients both with preserved and reduced ejection fraction (EF) were included in the study. RDW was measured with the use of an analyzer on the day of admission, ECG, ECHO, and chest X-ray were done and EF was calculated. HF was classified according to NYHA classification.

Results: Fifty patients with HF were studied and advancing age and male gender had increased association with HF. The mean RDW was 52.1 and ischemic heart disease was the most common cause of HF. Mean RDW in patients with EF < 54 was 55.68 with a SD of 6.1.

Conclusion: The study emphasizes that RDW can be used as a novel biomarker in HF at a low cost. Elevated RDW is associated with advanced stage of heart disease and correlates well with echocardiography findings in HF patients with reduced EF.

Key words: Anisocytosis, Echocardiography, Ejection fraction, Heart failure, Red cell distribution width

INTRODUCTION

Red cell distribution width (RDW) is the measure of variation in the size of erythrocytes and differentiates iron deficiency anemia from thalassemia trait. It is a simple, rapid, inexpensive, and straightforward hematological parameter that reflects the degree of anisocytosis *in vivo*. An increased RDW usually correlates to iron deficiency anemia.[1,2] RDW has been recently discovered as a new marker in cardiac failure. There are studies about the association of anemia and cardiovascular outcome in patients and the findings state that an increased RDW is associated with increased morbidity and mortality in chronic heart failure (HF) patients.[3] Scientific evidence suggests that RDW assessment also predicts the risk of adverse outcomes like hospitalization for acute decompensation or worsened left ventricular function in acute and chronic HF patients and is also a significant predictor of developing HF in otherwise normal individuals. There is no definite pathophysiology explaining this association and factors such as inflammation, nutritional deficiencies, and inadequate production of erythropoietin may be responsible.[4,5]

HF is a complex clinical syndrome, characterized by dyspnea and fatigue, impaired exercise tolerance, fluid retention, pulmonary and/or splanchnic congestion, ankle swelling, peripheral edema, elevated jugular venous pressure, and pulmonary crackles.[6,7] Several cardiac biomarkers including brain natriuretic peptide, N-terminal pro-BNP, and cardiac troponins have been identified as predictors of severity of HF. RDW has been studied in

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routine complete blood count in all patients admitted with the diagnosis of HF in the recent years.[8,9]

The biological interplay between impaired hematopoiesis and cardiac dysfunction may be present in HF patients and an increased RDW contributes to the worsening of HF. Overall, the longitudinal assessment of RDW changes overtime may be an efficient measure to predict the risk of development and progression of HF. In this study, we sought to investigate the prognostic value and longitudinal pattern of RDW in patients with concomitant HF.

Aims

This study aims to establish the relationship between RDW and HF assessed by echocardiography.

MATERIALS AND METHODS

This is a prospective randomized study done on 50 patients with clinical diagnosis of HF. The study was approved by the local ethics committee and informed consent was obtained from all patients before the start of the study. HF patients both with preserved and reduced ejection fraction (EF) were included in the study. Patients with liver disease, renal disease, anemia with hemoglobin <12 g/dl, hematological malignancy, or who had blood transfusion within the past 3 months were excluded from the study. For all patients, complete blood count with RDW was measured with the use of an analyzer on the day of admission. ECG, ECHO, and Chest X-ray were also done. The patients were classified according to NYHA functional classes of HF as follows:

Class I: No symptoms and no limitation in ordinary physical activity, for example, shortness of breath when walking, climbing stairs, etc.

Class II: Mild symptoms (mild shortness of breath and/or angina) and slight limitation during ordinary activity.

Class III: Marked limitation in activity due to symptoms, even during less than ordinary activity, for example, walking short distances (20–100 m). Comfortable only at rest.

Class IV: Severe limitations. Experiences symptoms even while at rest. Mostly bedbound patients.

EF was calculated using the formula EF= (SV/EDV)* 100, where SV = Stroke volume and EDV = End-diastolic volume.

RESULTS

Of the 50 study patients, majority of the study patients (22) were of the age group 51–60 years and 6 patients were above 61 years of age. About 64% of the patients were male and 34% were female. Incidence of HF is more with increasing age and male gender, Figures 1 and 2. The etiology of HF is depicted in Figure 3. The most common cause is ischemic heart disease (46%) followed by rheumatic heart disease (16%). Other causes of HF according to our study were cor pulmonale (12%), DCM idiopathic (10%), and two cases of calcific AS/AR and RVD (4%), and one case each of alcoholic cardiomyopathy, peripartum, Eisenmenger, and myocarditis (2%). HTN, DM, dyslipidemia, smoking, alcohol, and obesity were the

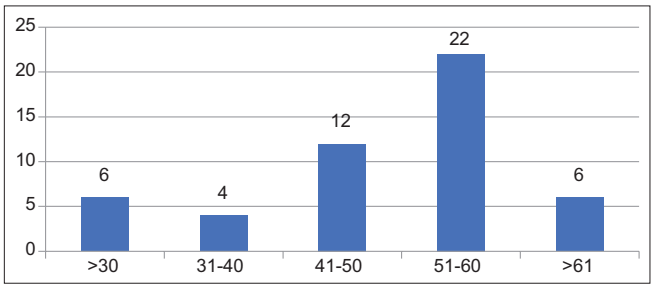

Figure 1: Age distribution

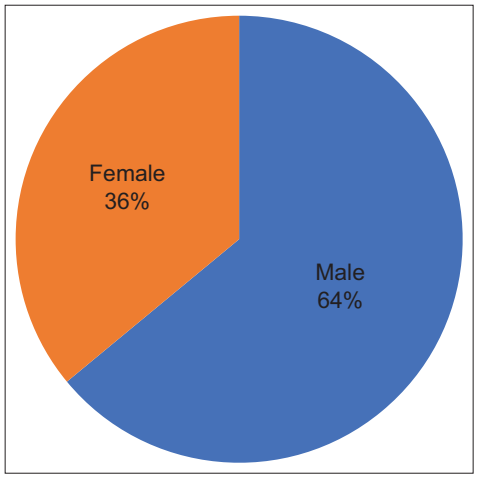

Figure 2: Gender distribution

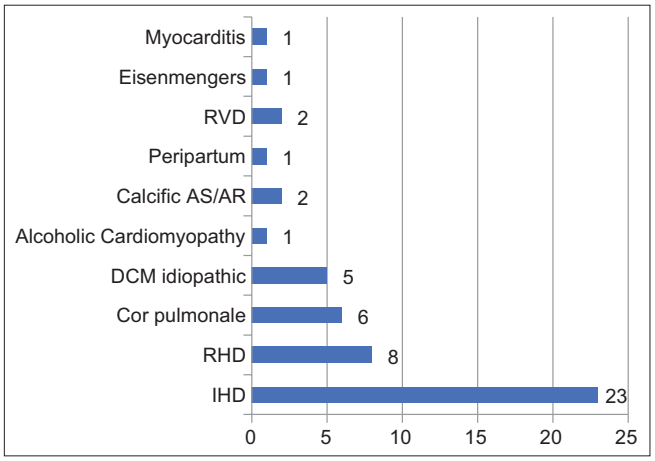

Figure 3: Etiology of heart disease

risk factors of HF as observed from our study, Figure 4. According to NYHA classification, 60% of the patients fell under Class III and 18% fell under Class IV. About 16% belonged to Class II and 6% fell under Class I classification, Figure 5. The mean RDW of each class of patients is shown in Figure 6. An increased mean RDW was observed in Class III (50.24 fL) and Class IV (62.48 fL) patients with a SD of 3.16 and 4.24, respectively (normal reference range of RDW – 39–46 fL). The total mean RDW is 52.1 with a SD of 5.14. A low EF < 54 was noticed in 66% of the patients, Figure 7. The mean RDW in patients with EF < 54 is 55.68 with a SD of 6.1, Figure 8. The findings indicate that an increased RDW is associated with low EF and high risk of HF.

DISCUSSION

Although a wide variety of biological markers have been used for morbidity and mortality prediction in patients with HF, many of them are still used only for research and not for clinical use. RDW, which is the variation in the size of erythrocytes, has been investigated as a new marker in cardiac diseases in the recent years. It can be done as a part of routine blood investigation and can reveal a lot about an underlying heart disease.[10] Conditions like impaired hematopoiesis can lead to a size heterogeneity of RBC volumes and play a role in the physiopathological interplay between anisocytosis and HF. Evidence states that both cell- and cytokine-mediated inflammatory pathways actively contribute to the development and progression of HF.[11] Inflammation is frequently associated with bone marrow dysfunction which can cause an increased production of circulating premature erythrocytes. Oxidative stress can also lead to deranged hematopoiesis by an excess reactive oxygen species production, all of which result in anisocytosis and alteration in RDW.[12,13] Impaired renal function in the elderly also can to anisocytosis and is an important determinant of adverse outcomes in patients with HF.

According to our study, advancing age and male sex are strong contributing factors for cardiac dysfunction. This finding is similar to the study findings of Lippi and Vigen who also demonstrated in their study about the association of advancing age and HF.[14] The reason for anisocytosis

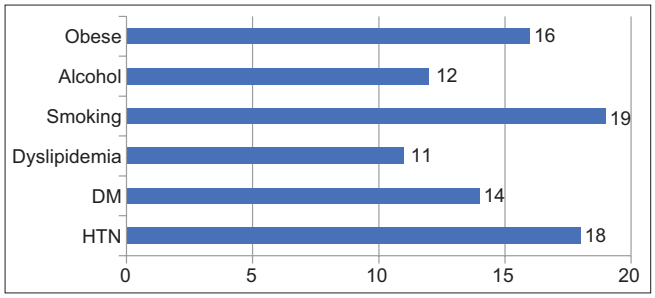

Figure 4: Distribution of risk factors

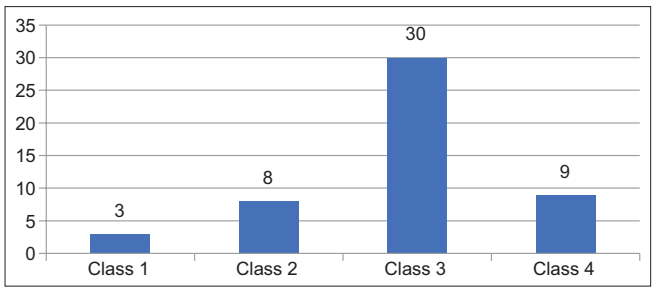

Figure 5: NYHA classification of heart disease

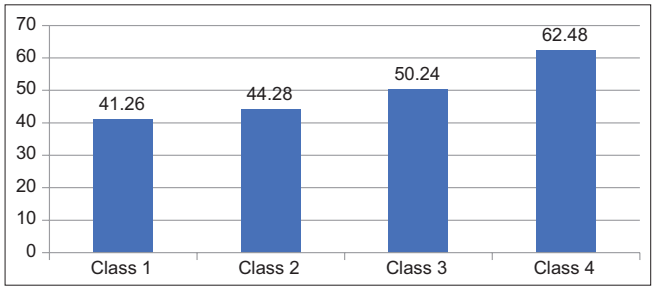

Figure 6: Mean red cell distribution width according to NYHA classification

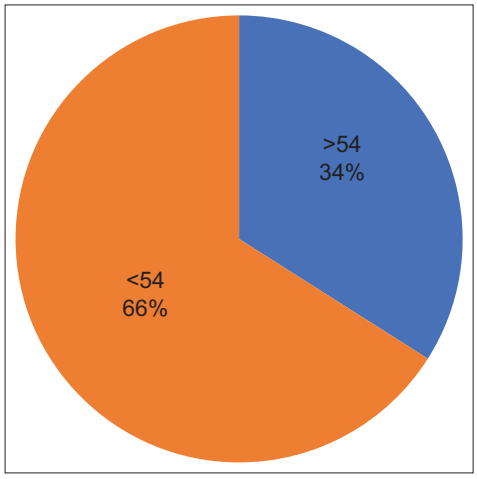

Figure 7: Percentage of ejection fraction

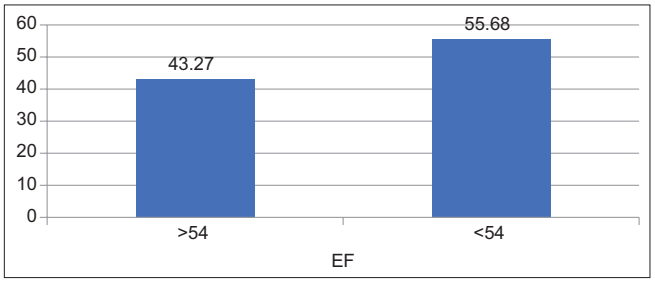

Figure 8: Elevated red cell distribution width is associated with low ejection fraction

with advancing age can be the result of multiple metabolic dysfunctions. All these conditions explain why RDW is a reliable marker of cardiac dysfunction. Anisocytosis may also play a direct role in the onset and progressive worsening of HF. The erythrocyte size heterogeneity signifies a reduced and severely impaired function of the essential corpuscular blood elements. RBCs are often characterized by lower deformability and decreased oxygen carrier capacity in conditions of high anisocytosis, contributing to reduced oxygenation of many peripheral tissues and cells (including cardiomyocytes), while abnormal erythrocytes may also actively participate in the pathogenesis of cardiac fibrosis through promotion or amplification of inflammation, cardiomyocyte stress, and apoptosis.[15]

In our study, an increased mean RDW of 50.24 and 62.48 was observed in Class III and Class IV HF patients, which indicates that altered RDW is a feature of advanced heart disease. Xanthopoulos *et al*. studied 218 patients who were admitted to the emergency department for acute HF and observed 1% increase in RDW up to 12 months after hospitalization.[16] A low EF usually signifies a LV dysfunction, cardiomyopathy, valvular defects, or cardiac muscle failure. In our study, a low EF of <54 was observed in 66% of the patients. Eroglu *et al*. in his study demonstrated that RDW was increased in patients with low EF.[17] The mean RDW of patients with EF < 54 was 55.68 in our study which indicates clearly that RDW can be a strong predictor of HF and a measure of prognostic outcome.

The limitation of this study is the small sample size and failure to assess RDW on a timely interval during the follow-up period.

CONCLUSION

RDW is reported as a component of the standard complete blood count and is significantly correlated with echo parameters for evaluation of HF. Elevated RDW is associated with advanced stage of heart disease and correlates well with echocardiography findings in HF patients with reduced EF. The study emphasizes that RDW can be used as a novel biomarker in HF. This simple test can be used as a marker of HF in the emergency room at a low cost. Further studies should be prompted for evaluating the association between RWD and outcomes of cardiac failure to improve understanding of the pathophysiology of HF. The degree of anisocytosis could also be used as an additional marker to identify these high-risk patients and improve treatment strategies in future.

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Original Article

Study on Vitamin-D Levels in Acute Ischemic Stroke

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Abstract

Introduction: Evidence suggests that Vitamin D deficiency is associated with an increased risk of ischemic stroke. Vitamin D is a neuroprotective prohormone, involved in the pathogenesis of cardiovascular disease. Recent studies have demonstrated the association between Vitamin D and stroke but the findings are inconsistent. In view of these discrepancies, we studied the association of Vitamin D levels with acute ischemic stroke using data from a population-based study.

Aim: The aim of the study was to evaluate the association between Vitamin D levels and acute ischemic stroke and assess the short-term outcome in these patients.

Methodology: A total of 50 acute ischemic stroke patients diagnosed with focal neurological signs or with acute infarct on CT brain were subjected to the study. Vitamin D levels in the range 30–100 ng/ml were defined normal, 10–30 ng/ml were defined insufficient, and <10 ng/ml were defined deficient.

Results: This prospective study included 50 patients of which 88% (44 patients) were male and 12% were female. A significant number of patients showed a deficiency in Vitamin D. There were no statistically significant differences regarding age and gender. No association was found between cholesterol and TGL with VIT D and there was no association between area of infarct with VIT D.

Conclusion: Vitamin D deficiency is an independent risk factor associated with the severity of cerebral ischemic stroke. Vitamin D supplementation should be used in the therapeutic management of cerebral stroke and screening for serum Vitamin D levels in routine investigations may identify the high-risk individuals and help in the prevention of serious disease events.

Key words: Cerebral ischemia, Inflammation, Ischemic, Stroke, Vitamin D

INTRODUCTION

Vitamin D is associated with calcium and phosphate homeostasis and musculoskeletal health.

It is one of the fat-soluble steroid hormones and is synthesized in the presence of ultraviolet light from 7-dehydrocholesterol in the epidermal layer of the skin.[1,2] Vitamin D also has a regulatory effect on the immune function and inflammation.[3] Poor Vitamin D status is a major public health problem that affects 30% of the patients worldwide. Many prospective studies have proved that a poor Vitamin D status can increase the risk of ischemic strokes.[4] The synthesis of Vitamin D requires two hydroxylation steps, the first being hydroxylation of inactive Vitamin D to 25-hydroxyvitamin D[25(OH) D] in the liver and then the conversion of 25-hydroxyvitamin D to biologically active form 1,25-dihydroxyvitamin D3 in the kidney by 1-α-hydroxylase (CYP27B) activity. Meta-analytic studies have shown that a decreased concentration of plasma 25(OH)D has an increased risk of occurrence of symptomatic ischemic stroke.[5,6]

Acute ischemic stroke has a heterogeneous origin marked by the sudden onset of focal neurological deficits. It is the major cause of disability and mortality across the world and is associated with unmodifiable risk factors such as age, genetics, sex, and modifiable risk factors including hypertension,

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diabetes mellitus (DM), dyslipidemia, sedentary lifestyle, and smoking.[7] Studies by Tarcin *et al.* in 2009 say that Vitamin D deficiency (VDD) is associated with an increased prevalence of CVS risk factors and endothelial dysfunction and is an independent risk factor of acute ischemic stroke.[8] Turetsky *et al.* and Park *et al.* in 2015 demonstrated in their study that hypovitaminosis D was independently associated with larger ischemic infarct volume and poor outcome. Low Vitamin D levels were also associated with calcium metabolism disorders, type 2 diabetes mellitus, autoimmune diseases, cardiovascular disease, stroke, multiple sclerosis, and some infectious diseases and cancers.[9,10]

Indian studies have also pointed to low 25(OH)D levels in Indian population in all age groups and regions, despite plenty of sunshine. Hence, our study aims to explore the association of Vitamin D deficiency/insufficiency with ischemic stroke and its risk factors.

Aim

The aim of the study was to evaluate the association between Vitamin D levels and acute ischemic stroke and assess the short-term outcome in these patients.

MATERIALS AND METHODS

A total of 50 acute ischemic stroke patients diagnosed with focal neurological signs or with acute infarct on CT brain were subjected to the. Only patients with acute onset of stroke were included in the study. Patients with chronic kidney disease, history of transient ischemic attacks, prior stroke, DM, HTN, and CAD were excluded from the study. Demographic, epidemiological, and clinical data including traditional stroke risk factors and the use of any therapeutic drug were obtained using a standard questionnaire at the admission of the individuals. The study began after obtaining written informed consent from all individuals and the study protocol was approved by the Institutional Ethics Committee. Serum levels of 25-hydroxyvitamin D levels were measured by chemiluminescence immunoassay technique. Vitamin D levels in the range of 30–100 ng/ml were defined normal, 10–30 ng/ml were defined insufficient, and < 10 ng/ml were defined deficient. Dyslipidemia was defined by the presence of one or more than 1 of the abnormal serum lipid concentration: Total cholesterol ≥ 200 mg/dL and triglycerides > 150 mg/dL.

RESULTS

This prospective study included 50 patients of which 88% (44 patients) were male and 12% were female. This indicates that the risk of occurrence of stroke is significantly associated with male sex but there is association with Vitamin D [Figure 1]. Most of the patients were of the age group >61 years (34%) and 15 patients (30%) belonged to the age group of 41–50 years. Only 6 patients (12%) were <40 years of age. There were no statistically significant differences regarding age [Figure 2]. According to the area of infarct, 34 patients (68%) had infarct in the middle cerebral artery (MCA), 6 cases (12%) in anterior cerebral artery (ACA), and 10 cases (20%) in posterior cerebral artery (PCA). The most common site of occurrence of infarct is the MCA but there was no association between area of infarct and Vitamin D [Figure 3]. The mean total cholesterol level was 212.34 mg/dL with a SD of 38.92 and the mean triglyceride level was 160.24 mg/dL with a SD of 42.24 [Figure 4]. Dyslipidemia was not associated with Vitamin D levels and stroke occurrence according to our study findings. Vitamin D levels were normal in 6 cases (12%), insufficient in 32 cases (64%), and deficient in 12 cases (24%) in our study [Figure 5]. This indicates that insufficient levels of Vitamin D can increase the risk of acute ischemic stroke.

DISCUSSION

Ischemic stroke has a clinical and socioeconomic effect on death and disability around the world. The etiology of

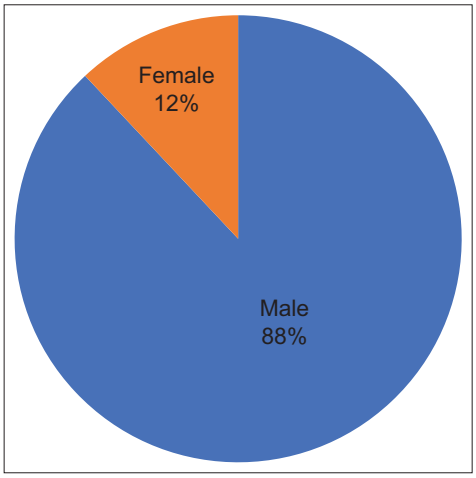

Figure 1: Sex distribution

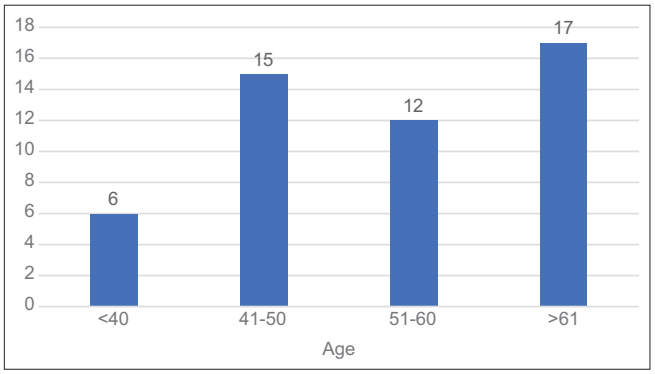

Figure 2: Age distribution

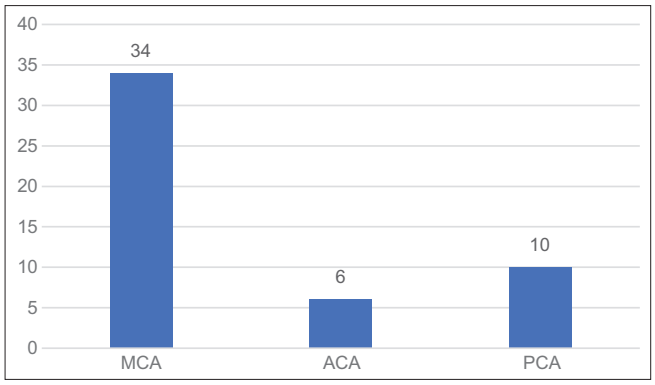

Figure 3: Distribution of area of infarct

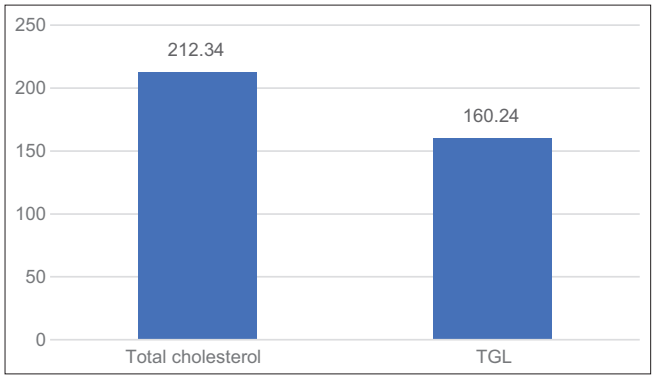

Figure 4: Distribution of lipid levels

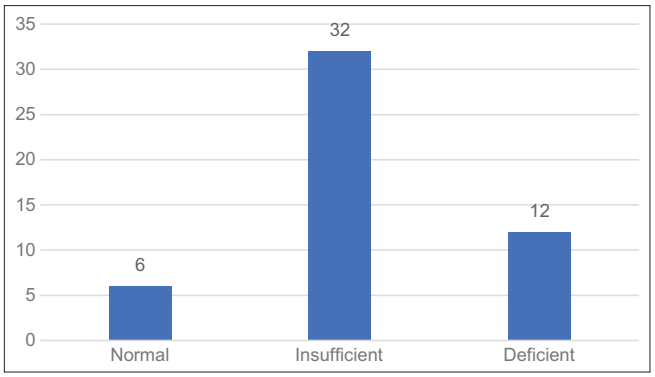

Figure 5: Distribution of vitamin D

ischemic stroke is heterogeneous and factors such as age, sex, genetics, hypertension, diabetes, sedentary lifestyle, and smoking may increase the risk of disease occurrence.[11] Studies have demonstrated the association between low levels of Vitamin D and acute stoke in patients.[12,13] Vitamin D has a vasoprotective potential and can slow down atherosclerosis, promote endothelial function, and reduce hypertension by suppressing the renin–angiotensin–aldosterone system. It is also linked to brain development and function and regulation of cerebrovascular physiology and a deficiency may lead to stroke and brain-related disorders.[14] In addition, Vitamin D also modulates smooth muscle cell proliferation, inflammation, and thrombosis and this vascular remodeling can result in stroke.

In the current study, there was no significant association between age group and gender with Vitamin D and no association was also found between the area of infarct and Vitamin D. Studies by Ponda and Zittermann *et al.* demonstrated in their study that Vitamin D deficiency was associated with dyslipidemia among stroke patients.[15,16] However, in our study, we did not find any association between TGL and cholesterol levels. A significant number (64%) of study patients (32 patients) had insufficient levels of Vitamin D in our study and 24% had Vitamin D deficiency. This result is in agreement with the other study findings and Vitamin D can be used as an independent marker of acute ischemic stroke. Studies by Pilz *et al.* in 2008 and Sun *et al.* in 2013 showed that low levels of 25(OH)D are consistent with ischemic stroke.[17] Poole *et al.*, in his study, found that 34 of 44 patients (77%) with stroke had low serum 25(OH)D levels (< 50 nmol/L) which were substantially lower than healthy elderly subjects.[18]

The results from our analyses suggest that low Vitamin D serum levels are a consequence of stroke. Limited Vitamin D production in the affected group may be because of reduced exposure to sunlight and quality of diet. The study findings of Brian *et al.* say that any benefit of Vitamin D supplementation is too mild to have an impact on stroke risk, unless the individuals are already severely Vitamin D deficient, as rightfully suggested by the VITAL trial investigators.[19] There are two proposed pathophysiological pathways leading to stroke: Vitamin D is involved in maintaining endovascular function directly and an indirect pathway where it regulates renin production through the renin–angiotensin–aldosterone system pathway, thereby attenuating hypertension. Hypertension and atherosclerosis are in general risk factors in stroke development but our study results did not link to TGL and total cholesterol levels. The main finding of the present study is that VDD can be considered as an independent marker associated with acute ischemic stroke.

The limitations of the study are the small sample size and failure to assess the levels of Vitamin D overtime to make sure if the levels remained stable. The exact dose of Vitamin D administration as a supplement in stroke patients was also not assessed.

CONCLUSION

Vitamin D deficiency is an independent risk factor associated with the severity of cerebral ischemic stroke according to our study results. The results suggest that Vitamin D supplementation should be used in the

therapeutic management of cerebral stroke. Further prospective studies are needed to establish the appropriate therapeutic dose of Vitamin D in stroke patients. Screening for serum Vitamin D levels in routine investigations may identify the high-risk individuals and help in the prevention of serious disease events.

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