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Publishing Details
Publisher Name: International Research Organization for Life & Health Sciences (IROLHS)
Registered Office: L 214, Mega Center, Magarpatta, Pune - Solapur Road, Pune, Maharashtra, India – 411028.
Contact Number: +919759370871.
Designed by: Tulyasys Technologies (www.tulyasys.com)

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Clinical and Etiological Profile of Renal Failure in Children

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Abstract

Introduction: Acute renal failure (ARF) is a syndrome characterized by acute decline in glomerular filtration rate leading to the retention of nitrogenous wastes such as urea and creatinine.

Materials and Methods: 59 patients who fulfilled the diagnostic criteria were studied between the age group of 3 months and 18 years during the study period, i.e., March 2011 to October 2012.

Results: The results are well explained in the article using various tables and sufficient explanation.

Conclusion: The most common cause for ARF is acute glomerulonephritis (GN), in which post-streptococcal GN is common. Increased awareness about gastroenteritis, oral rehydration salts, and early referral to tertiary hospital by effective management at tertiary level leading to decreased incidence of RF with acute gastroenteritis.

Key words: Acute renal failure, Chronic glomerulonephritis, Chronic kidney disease, End-stage renal disease, Pediatrics

INTRODUCTION

Acute renal failure (ARF) remains an important clinical problem with little progress made in the therapeutic approach over the past 20–30 years. Data on the epidemiology of chronic kidney disease (CKD), which is a serious health problem and refers to a condition related to irreversible kidney damage that further progress to end-stage renal disease in children, are insufficient and data that are available were based on hospital records.[1-8] The aim of this study is to study the Clinical and Etiological profile of Renal Failure Outcome of patients with RF.

MATERIALS AND METHODS

1. Cases from Pediatric Department, it is a prospective study.
2. Children who fulfilled diagnostic criteria for RF from March 2011 to August 2012.

3. 59 patients satisfying the diagnostic criteria were studied. Each patient was assessed with the help of detailed pro forma which included:

i. History
ii. Physical examination
iii. Investigations.

Inclusion Criteria

3 months to 18 years children were included in this study.

Exclusion Criteria

The exclusion criteria were as follows:
• <3 months and >18 years children
• Trauma cases
• Post-operative cases.

Diagnostic Criteria

ARF: Doubling of serum creatinine level for that age [Table 1].

Chronic Renal Failure (CRF)

Creatinine clearance (glomerular filtration rate [GFR]) below 50 ml/1, 73 m²/minute. Persisting for more than 3 months, using Schwartz formula 2.
Schwartz formula:

\[ \text{Creatinine clearance} = k \times \text{length in cm/} \text{Sr.creatinine mg/dl} \]

For infants \( k = 0.45 \); children up to 13 years \( k = 0.55 \); Adolescent male children \( k = 0.7 \).

**RESULTS**

59 patients who fulfilled the diagnostic criteria were studied between the age group of 3 months and 18 years during the study period, i.e. March 2011 to October 2012.

During the study period, 4973 cases were admitted in pediatric department, out of these 59 patients presented with renal insufficiency that accounts for 1.2%.

Out of these, 49 cases were ARF and the remaining 10 cases were due to CKD [Table 2].

The maximum percentage of patients was between the age of 11 and 18 years, i.e., 29 (49.2%).

The maximum percentage of patients with ARF were inbetween the age group of 11 and 18 years, i.e., 24 (40.6%). The maximum percentage of patients with CKD were inbetween the age group of 11 and 18 years, i.e., 5 (8.6%).

The minimum percentage of patients with ARF were inbetween the age group of 3 months and 5 years, i.e., 12 (20.3%). The minimum percentage of CKF were in the age group of 3 months to 5 years, i.e., 2 (3.4%).

The mean age at a presentation of CKF is 11 years [Table 3].

Overall male:female ratio 1:3:1.

The male:female ratio in ARF is 1:3:1.

The male:female ratio in CKD is 2:3:1 [Table 4].

The most common cause for ARF is acute glomerulonephritis (GN), 15 (30.6%). In these, post-streptococcal GN cases were 5, membranoproliferative GN cases were 4, focal segmental glomerulosclerosis cases were 3, IgA nephropathy cases were 2, and 1 case of minimal change disease.

Next in order are 6 cases of nephrotic syndrome, 5 cases of hemolytic uremic syndrome, 5 cases of dengue hemorrhagic fever (DHF)/dengue shock syndrome (DSS), 4 cases each of septicemia and systemic lupus erythematosus, and 1 case each for snake bite, renal amyloidosis, complicated urinary tract infection, and chronic rheumatic heart disease with congestive cardiac failure with ARF [Tables 5 and 6].

In this study out of 28 cases, acute GN is the leading cause of primary renal disease for ARF contributing 10 cases. Obstructive uropathy is the primary leading cause for CKF contributing 3 cases [Table 7].

RF due to secondary causes for RF 31, i.e., which is slightly more than the primary renal disease 28 going to RF.

DHF/DSS and hemolytic uremic syndrome are the leading secondary causes for RF contributing about 11 cases out of 31 cases. The increased incidence of DHF/DSS probably due to mixed strain infections with its fulminate course, and the decreased incidence of RF due to acute gastroenteritis is due to increased awareness and early referral to tertiary hospital and timely intervention and better outcome [Table 8].

**Symptom Analysis**

The most common symptom in ARF is decreased urine output in about 35 cases.
The other common symptoms are high-colored urine, fever, shortness of breath in 21 cases, vomiting in 7 cases, loose motions in 6 cases, altered sensorium seen in 6 cases, and convulsions in about 6 cases and passing excessive urine.

The most common symptoms in CRF are swelling of face in 18 cases.

The other common symptoms in CRF are shortness of breath in 6 cases, vomitings in 4 cases, convulsions in 4 cases, fever in 4 cases, decreased urine output 6 cases, and dribbling of urine in 3 cases.

The most common sign in ARF is oliguria in about 35 (71.5%) cases.

Other common signs are periorbital edema (44.88%), altered sensorium (38.76%), polyuria (8.16%), pedal edema (24.48%), hematuria (26.52%), dehydration (12.24%), hypertension (16.32%), shifting dullness (32.64%), seizures (12.24%), hepatomegaly (20.4%), and basal crepitations (18.36%) cases.

The most common sign in CRF is puffy face and hypertension seen in 8 cases, i.e., seen in 80% of the CKD cases.

70% of the cases are short stunted in CKD patients; pallor and breathlessness are seen in 50% of cases, i.e., in 5 cases; oliguria is seen in 6 cases (60%); seizures in 3 cases (30%); failure to thrive, bony abnormalities, and polyuria are seen in 20% of cases; pedal edema is seen in 6 cases (60%); dehydration is seen in 3 cases (30%); and altered sensorium is seen in 4 cases (40%) [Table 9].

Out of 59 cases of RF, 26 cases were cured by treatment and 21 were relieved from their symptoms. Of these 59 cases, dialysis was done in 9 cases and 2 cases were dependent on dialysis even after discharge.

The overall mortality due to RF is 12 cases (20.34%).

Total mortality during the study period is 249, among these 12 cases expired due to RF which accounts to about 4.8% [Table 10].

RF due to secondary causes such as hemolytic uremic syndrome (24.12%), septicemia (16.6%), and DSS/DHF (16.6%) are the leading causes for mortality RF due to primary renal disease like the glomerular disease that is acute GN has less mortality, i.e., 8.3% [Table 11].

Among the CKDs, chronic GN has contributed to 16.6%, i.e., 2 cases and 1 case due to obstructive uropathy out of 3 cases.

With different etiological factors for RF, the number of cases expired was 12 cases and the total number of survived cases were 47 cases.

Survival is more in the primary glomerular diseases like in acute GN, that is, 14 out of 15 cases survived (93.3%). The survival is low in cases of RF due to secondary causes, that is, 2 out of 5 (40%) among the cases of hemolytic uremic syndrome.

**DISCUSSION**

59 cases who fulfilled the diagnostic criteria for the RF were studied, in which the 49 cases were ARF and 10 cases were CRF.

**ARF Group**

In ARF, the group consisted of 29 boys and 20 girls, ranging in the age from 6 months to 16 years.

Shah et al. reviewed the symptoms and signs and etiological factors in 51 cases, of whom the youngest case is 6 months old and the oldest case is 12 years old, the mean age being 7.1.
The mean age group in our study being 7.1 years, 36 and that of other study group being 6.25 years, 37. The male:female ratio is 1.5:1 in our study.

The decreased urine output is the most common symptom in our study being 71.8% is comparable with Hari et al. being 94.1%

Passing of excessive urine being 4 (8.16%) in this study. In Shah et al. study, it is 5.9%. In this study, this symptom is mainly attributed to diabetic ketoacidosis (DKI).

In this study, convulsions are being 12.24% whereas in Shah et al., it is 29.4% and this symptom is mainly attributed to acute GN.

Other symptoms in this study high-colored urine being 26.52%, shortness of breath 42.84%, vomiting being 14.28%, loose motions being 12.24%, rash all over body 22.44%, and high colored urine in 36.72% of cases.

Polyuria was present in 8.16% in our study and is comparable to 5.9% in Shah et al. study. In this study, this sign is mainly attributed to DKI.

The most common sign in our study being oliguria is 71.8% similar observation was noted by Hari et al. study that is 73.84%.

The other signs are dehydration - 12.24%, periorbital edema - 44.89%, pedal edema - 24.48% hypertension - 16.32%, hematuria - 26.52%, altered sensorium - 38.76%; these are comparable with Shah et al. study except convulsion 29.4%, altered sensorium 60.8% in Shah et al. at study.

The incidence of these symptoms in our study is low which may be because of early referral and improved modality of treatment at the tertiary level of hospital.
In this study, the mean blood urea and serum creatinine levels are 80.7 mg/dl and 2.38 mg/dl, respectively, which is comparatively low when compared to Hari et al. study were 132.6 mg/dl and 3.05 mg/dl, respectively.

Acute GN is the most common cause for ARF accounting for 15 cases (30.6%).

The next common cause are septicemia 8.16%, HUS 10.20%, DKA 6.12%, complicated malaria 6.12%, acute gastroenteritis 8.16%, and SLE nephritis 6.12%.

In Shah et al. study, acute gastroenteritis is the most common cause. The next common causes are acute GN and HUS.

The incidence of acute gastroenteritis causing RF is low in this study which may be because of increased awareness about gastroenteritis, oral rehydration salts (ORS) therapy, and early referral to tertiary level hospital and early treatment with fluid replacement.

The DKA causing RF is one among the causes in our study which may be because in Jaffe method of measuring serum creatinine the estimated serum creatinine levels in DKA cases may be falsely elevated because of the presence of ketone bodies and hyperglycemia.

In Counhan et al. study, renal hypoperfusion is the most common cause for RF being 43% which is mostly due to nephritic syndrome 10 cases out of 31 cases of hypoperfusion. Next common causes are HUS 12 (16.6%), acute GN 9 (12.5%), and septicemia 6 (6.94%)

In Uchino et al. study, the most common cause for ARF was septic shock 47.5%.

The survival is better with primary glomerular diseases like acute GN in our study out of 15 cases (88.8%) is comparable with Hari et al. study, in which acute GN better survival 88.8%, this is probably causes the primary glomerular disease is more common in older children than in younger children in whom RF is usually secondary to some other causes such as septicemia, HUS, and gastroenteritis.

The survival is poor with 40% and septicemia is 50% comparable with gastroenteritis and HUS 33.3% in Shah et al. study.

The survival is better in children above 5 years of age and poor in children below 5 years of age in our study is comparable with Hari et al. and Shah et al. study in that survivals better in children above 3 years of age and poor in children below 3 years of age, which may be due to secondary causes for RF such as septicemia, HUS, and gastroenteritis are most common in younger children.

The overall mortality in our study is 18.36%, which is comparable with Counhan et al. study, in which mortality is 20%. In Hari et al. study, it is 33.3%.

Comparatively low mortality in our study may be because of early referral to tertiary level hospital and availability of dialysis facility and early intervention.

In Uchino et al. study, the overall mortality was 60.3%.

The most common cause for mortality in our study was HUS (60%) and septicemia (50%).

In our study, 26 cases (44.06%) with RF were cured of the disease and 21 (35.5%) cases were relieved of symptoms by treatment. Dialysis was done in 9 cases (15.2%) which is comparable with Counahan study, in which full recovery of renal function occurred in 53% and relief symptoms and discharge from hospital occurred in 14% patients. Dialysis was done in 6 cases (11.3%).

**CRF**

In our study, 10 cases out of 56 cases were CRF cases.

In CRF, the group consisted of 7 boys (70%) and 3 girls (30%) ranging in the age group of 3 years to 17 years.

In our study, the secondary causes causing RF is statistically highly significant age from 6 months to 18 years.

In our study, the number of case below 5 years was 1 (10%). Between 6 and 10 years of age group, the number of cases with CRF was 4 (40%). Between 11 and 18 years of age group the number of cases with CRF was 5 (50%).

In Pankaj et al. study, the number of cases below 5 years of age was 96 (31.4%). Between 6 and 10 years of age group, the number of cases was 105 (34.4%). Between 11 and 18 years of age group, the number of cases was 104 (34%).

The age at presentation in our study with features of CRF was higher as compared to Pankaj et al. study, suggesting delayed detection and referral of patients.

In our study, the lower age at presentation is 3 years and the upper age at presentation is 17 years. The mean age at presentation is 11½ years. This is comparatively in elderly with Hari et al. study, in which the mean age of presentation was 8 years.

In our study, the male cases are 70% and female cases are 30%; the male-to-female ratio 2.3:1 which is comparable
Swelling of face 80% is a most common symptom and puffy face is the most common sign (80%) in our study.

The other common presenting features are pedal edema 60%, pallor 50%, short stature 70%, shortness of breath 50%, hypertension 80%, dribbling of urine 30%, convulsions 30%, bony abnormalities 20%, and failure to thrive 20%.

The mean blood urea and serum creatinine levels in our study in CRF cases are 148 mg/dl and 6.1 mg/dl, respectively. This is almost comparable with the Hari et al. study in which the GFR is 18.5 ml/1.73 m²/min. In Gianluigi et al. study, the mean GFR at presentation is 41 ml/1.73 m²/min.

This also indicates delayed detection and referred to tertiary level hospitals.

In our study, creatinine clearance between 50 and 25 ml/1.73 m²/min 20% of cases, 25–10 ml/1.73 m²/min are 40%, and 10 ml/1.73 m²/min are 40 cases.

In Gianluigi et al. study, creatinine clearance between 25 and 50 ml/min/1.73 m² cases were 35% and <25 ml/min 1.73 m² cases were 26%.

This also indicates in our study that severe CRF and end-stage renal disease are common because of delayed detection of the cases.

The mean hemoglobin in our study is 7.9 g/dl is comparable with Hari et al. study, in which the mean HB level at presentation was 7.6 g/dl, the range of HB levels in our study are 5.8–11 g/dl. In Hari et al. study, it was 5–10 g/dl.

In our study, osteodystrophy is present in 20% which is comparable with Hari et al. study, in which osteodystrophy was present in 20.8%.

The most common cause for CRF in our study was obstructive uropathy 30%. The next common cause was chronic GN is 30% and vesicoureteral reflex 10%, vascular malformation (Rt. Renal artery stenosis with hypertensive encephalopathy) is 10%. This is comparable with other studies, Hari et al. study obstructive uropathy cases were 31%, vesicoureteral reflux (VUR) 16.7%, chronic GN 27.5%.

In Gulati et al. study, combined obstructive uropathy and VUR contribute 52% of cases and chronic GN cases contribute to 37.5%. In Gianluigi et al. study, hypoplasia with urinary tract malformations contribute 67.1%, chronic GN 2.8%, In Lagomarsiano study, obstructive uropathy contributes 16.7% and GN contributes 16.3% of cases.

It is observed that congenital malformation of the urinary tract is the major cause for development of RF. So if detect these condition early by antenatal scanning and intervene early, the prognosis will be good.

In our study, 3 cases out of 10 of CRF are expired. The independent risk factors for mortality is obstructive uropathy 1 cases and chronic GN 2 cases. 7 cases were relieved of symptom and discharged from the hospital. Dialysis was done in 4 cases of CRF.

CONCLUSION

1. The most common cause for ARF is acute GN, in which post-streptococcal GN is common.
2. Increased awareness about gastroenteritis, ORS, and early referral to tertiary hospital by effective management at the tertiary level leading to decreased incidence of RF with acute gastroenteritis.
3. The male:female ratio is 4:3 in ARF.
4. Decreased urinary output is the most common symptom in ARF.
5. Oliguria is the most common sign in ARF.
6. The DKA is one of the most common cause for ARF in our study which may be because of in Jaffe method, measuring serum creatinine, the estimated serum creatinine levels in DKA cases may be falsely elevated because of the presence of ketone bodies and hyperglycemia.
7. Survival is better in older children than younger children. This is because of primary glomerular diseases more common in older children, in which survival is good and the secondary causes are for ARF is more common in younger age group, in which survival is poor.
8. The most common cause for mortality HUS.
9. Early and frequent dialysis leads to improvement in patient survival.
10. The most common cause for CRF is obstructive uropathy.
11. More number of cases of CRF is presented in older age groups, that is, above 10 years.
12. Male predominance of CRF is due to post-urethral valve cases are seen in male is most common contributing factors for CRF.
13. Puffy face swelling is most common presenting features in CRF.
14. Stunted growth, malnutrition, and anemia are present in the majority of cases, indicates delayed detection of cases and referral to the tertiary hospital in our study.
15. Sever CRF and end-stage renal disease (ESRD) case are more in our study indicating late referral to the tertiary hospital.
16. The most common cause for CRF is obstructive uropathy in that post-urethral valve are most common.
17. Since congenital urinary tract malformation are common cause for CRF, early identification of urinary tract anomalies by antenatal scanning and early intervention lead to better prognosis.
18. With the availability of dialysis most of the cases with RF are improving, so the cases with the RF an early referral to specialized center with dialysis facility can improve the outcome.
19. The mortality due to CRF is comparatively low may be because of these cases are cannot followed up due to majority of the cases progressed to ESRD beyond the pediatric age group.

REFERENCES

Study of Pattern and Trends of Sexually Transmitted Infections in Government Thoothukudi Medical College

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Abstract

Introduction: Sexually transmitted infections (STIs) constitute a major public health problem for both developing and developed countries. Prevalence and pattern of presentation of STIs would help in designing a better treatment facility to overcome the stigma and spread of the disease in the community.

Aim: This study aims to unravel the spectrum and changing trends of STI in patients attending STI clinic of Thoothukudi Medical College Hospital.

Materials and Methods: This is a prospective study conducted at the Department of Dermatology and STD, Government Thoothukudi Medical College, Thoothukudi, Tamil Nadu. All the new patients attending STD clinic from January 2011 to December 2016 were included in the study.

Results: During the 6-year study period, 13,550 patients attended STD clinic. Among the total patients visiting STD clinic, 4461 were symptomatic. These symptomatic patients were evaluated for various STIs.

Conclusion: The year’s trend in our study reveals a gradual increase in female attendance in STI clinics, increasing viral STIs, and declining bacterial STIs. This indicates a more aware population seeking early treatment and effective management of STI by the current health-care system.

Key words: Sexually transmitted infections, Trends, Patterns, Thoothukudi

INTRODUCTION

Sexually transmitted infections (STIs) are diseases and syndromes that are epidemiologically heterogeneous, but all of which are almost always transmitted sexually.¹⁰ STIs constitute a major public health problem for both developing and developed countries. The pattern of STIs differs from country-to-country and region-to-region, especially in India.¹² STIs increase the risk of transmission of human immunodeficiency virus (HIV) infection posing an immense need to understand the pattern of STIs prevailing in the particular region. A review of the epidemiology and trends of STIs showed a declining number of all STIs.⁶ There was a progressive decline in the incidence of bacterial STIs over those 20 years, with viral STIs remaining at a relatively constant level. The increasing demand for STI services may be attributed to an increased incidence of infections, increased public awareness of STIs, and increasing patient expectations as well as an improved level of services available at the newly renovated clinic site. Therefore, we planned this study to unravel the pattern, clinical profile, and trend of STIs in Thoothukudi. It is important to monitor trends in STIs to implement effective policies as well as health education and prevention programs.

Aim

This study aims to study the trends of STIs in Thoothukudi over the last 6 years in patients attending STI clinic of Thoothukudi Medical College Hospital.
MATERIALS AND METHODS

The present study is a prospective study conducted for a period of 6 years from January 2011 to December 2016 at the Department of Dermatology and STD, Government Thoothukudi Medical College, Thoothukudi, Tamil Nadu. The study population included all the new patient’s attending STD clinic at Thoothukudi Medical College Hospital. Each patient was evaluated for STI like clinical history, thorough clinical examination and appropriate laboratory investigations including relevant serology such as enzyme-linked immunosorbent assay for HIV and venereal disease research laboratory (VDRL) test for syphilis. All patients were counseled about the risk of unprotected sexual intercourse, the risk of HIV transmission in the presence of other STIs, the importance of partner treatment and condom use. Asymptomatic patients were also followed up clinically and serologically for 6 months. STIs, which were not included in the syndromic management, were also identified clinically and with relevant laboratory investigations. Partner identification and condom promotion were done. All patients were treated as per NACO’s guidelines.

RESULTS

The total population of Thoothukudi district is around 17 lakhs. The Government Thoothukudi Medical College Hospital OPD caters around 6 lakhs patients per year. An average of 30,000 (5.1%) visited Dermatology and STD OPD, of which 2250 (0.35%) attended STD clinic [Figure 1].

During the 6-year study period, 13,550 patients attended STD clinic. Of them, 6890 (50.85%) were males, 6558 (48.4%) were females and 102 (0.75%) were transgender with the sex ratio of 68:65:1 [Figure 2]. Year wise analysis shows a gradual increase in female patients [Figure 3]. Most of the patients (72%) were in the 21–30 years age group.

Among the total patients visiting STD clinic, 4461 were symptomatic and 9089 were asymptomatic. There was not much variation in STD clinic attendance during the 6-year study period. Among the symptomatic, 1450 were males, 3006 were females, and 5 were transgender. In males, the most commonly seen STD was urethral discharge (463 [3.42%]), followed by herpes genitalis (212 [1.56%]), inguinal bubo (77 [0.57%]), warts (55 [0.43%]), syphilis (21 [0.15%]), and scrotal swelling (3 [0.02%]). Female patients predominantly presented with vaginal cervical discharge (207 [14.96%]), followed by lower abdominal pain (739 [5.45%]), herpes genitalis (83 [0.61%]), warts (19 [0.14%]), syphilis (13 [0.09%]), and inguinal bubo (6 [0.04%]). In transgender, urethral discharge was the most common presentation.

Among the 2027 patients with vaginal cervical discharge, the most commonly identified STI was candidiasis (1001 [49.38%]) followed by bacterial vaginosis (571 [28.17%]) and trichomoniasis (68 [3.35%]) [Figure 4].

VDRL test was positive in 34 (0.25%) patients, of which 21 were males and 13 were females. Among the positive males, 12 (35.29%) were asymptomatic. In females, 4 (11.76%) were asymptomatic indicating early latent syphilis. HIV seropositivity was noticed in 45 patients, of them, 25 were males, 19 were females, and 1 was transgender.

DISCUSSION

Young adults (21–30 years) dominated the study population indicating more sexual activity, promiscuity,
and less awareness within the age group. This is in concordance with other Indian studies.\textsuperscript{2–4} The finding that young population was becoming more sexually active at a younger age and inadequate education on STIs for youths may account for the sharp rise in STI incidence among young people. School-based programs dealing with sexuality should be taught to school-going adolescents as well.\textsuperscript{10} Results from the Global Sex Survey report undertaken by Durex showed that the average global age for the first sex is now 17 and demonstrated a trend toward losing one’s virginity earlier, with today’s 16–20 years old becoming sexually active by the average age of 16.5 years.\textsuperscript{6} In our study analysis, the sex ratio (1.05:1) was almost equal. However, year wise analysis reveals a gradual increase in female patient attendance. This indicates more awareness and early treatment-seeking attitude in the female population which is a positive outcome. Several factors may account for the increase, such as increased public awareness of STIs, which may have resulted in an increased patient load and thus increased case detection.

Among the symptomatic patients, the STI prevalence in male and female patients was 1450 (10.7\%) and 3006 (22.18\%), respectively. This finding was in contradiction to previous studies where a male preponderance was noticed.\textsuperscript{9} This might be due to the more awareness and willingness to be examined by the female patients.

In symptomatic males, urethral discharge 463 (3.42\%) dominated the STI spectrum followed by herpes genitalis 212 (1.56\%). This again is in contradiction with other studies.\textsuperscript{2,7,8} This predominance of urethritis can be due to the more prevalence in the local population and early presentation. Other bacterial STIs were less common due to the widespread use of antibacterials.

In symptomatic female patients, VCD 2027 (14.96\%) and PID 739 (3.14\%) dominated the spectrum followed by herpes genitalis and warts. This finding is in concordance with other studies. Apart from VCD and PID, viral STIs were more prevalent. The greater infectivity, persistent, and recurrent nature of viral infections are responsible for their increasing trend in the current STI scenario.\textsuperscript{9,10}

VDRL and HIV positivity were noticed in 34 (0.26\%) and 45 (0.33\%) patients, respectively, indicating a continued need for serological screening of STIs. The relatively low HIV prevalence in our study may be the result of active targeted health promotion, particularly for sex workers and their clients, the presence of an open-access STI clinic with an effective STI control program, universal screening of blood donations and careful surveillance and analysis of trends of STIs and HIV infection.

The year wise trend in our study reveals a gradual increase in female attendance in STI clinics, increasing viral STIs, and declining bacterial STIs. This indicates a more aware population seeking early treatment and effective management of STI by the current health-care system.
CONCLUSION

Although there has been a significant decline in the overall incidence of STIs over the last decade, there has been a rise in female STI patients over the last 6 years. This has resulted in the need to identify the causal factors, and to intensify existing, as well as develop new STI/HIV prevention programs for the general population and certain core groups.

Research results must be used to plan, implement, and evaluate STI/HIV prevention programs. The full range of channels available should be utilized for disseminating information. This will require collaboration and coordination with other organizations (both governmental and non-governmental).

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How to cite this article: Thadeus J, Selvan BS, Anandan H. Study of Pattern and Trends of Sexually Transmitted Infections in Government Thoothukudi Medical College. Int J Sci Stud 2018;6(1):14-17.

Source of Support: Nil, Conflict of Interest: None declared.
Isometric exercise and its effect on blood pressure and heart rate; a comparative study between healthy, young, and elderly males in and around Raichur city

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Abstract

Introduction: Isometric exercise is a routine part of everyday activities and occupational tasks. Physicians have a responsibility to promote regular physical activity to reduce high blood pressure (BP) and to control weight as physical inactivity is considered as a risk factor for coronary artery disease. Isometric exercises for aging populations have often been discouraged due to harmful effects on the cardiovascular system. However, isometric exercise in older adults and patients of some age group has found to be beneficial for maintaining normal cardiovascular function, but still, controversies are there. The cardiovascular response to isometric exercise has been studied majorly in young adult males. The vascular wall becomes less elastic and stiffer with the advancement of age (Nichols et al., 1985; O’Rourke, 1990; and Cheitlin, 2003). There are very few studies that have compared the isometric exercise response in younger and elderly individuals.

Purpose of the Study: The present study is done to determine the effect of isometric exercise on BP and heart rate (HR) in healthy, young, and elderly males.

Materials and Methods: In the present study, 100 male subjects with age group of 20–30 years and 60–70 years satisfying the inclusion criteria were selected and divided into two groups, namely, young and elderly group, respectively. Resting HR and BP were recorded followed by HR and BP responses to isometric exercise in both the groups. Isometric contraction was held till 60 s using the force transducer at 40% of the maximal voluntary contraction. Pre and post HR and BP were compared.

Results: The elder subjects had a lower HR and a higher BP response than their younger counterparts.

Conclusion: From this study, it is concluded that the increasing age is associated with an altered HR and BP response to isometric exercise.

Key words: Blood pressure response to aging, Heart rate response to aging, Maximum voluntary contraction

INTRODUCTION

The cardiovascular system plays an important role to maintain the homeostasis and to provide nutrients and oxygen to the muscles so that high-energy output can be maintained for a long period of time and the by-products of metabolism are removed rapidly from the site of energy release.

Isometric exercise produces a significant increase in blood pressure (BP), which is important in maintaining perfusion of muscle during sustained contraction. This response is brought about by the combined efforts of central and peripheral afferent input to medullary cardiovascular centers. In normal individuals, the increase in BP is due to increase in cardiac output with little or no change in systemic vascular resistance.[1]
With lifestyle changes and modernization, cardiovascular system is more severely affected. The American Heart Association considers ischemic (coronary) heart diseases, hypertensive diseases, rheumatic fever/rheumatic heart diseases, and cerebrovascular diseases (stroke) to be major cardiovascular diseases. The WHO estimates that by 2020 cardiovascular diseases will account for up to 40% of all deaths worldwide. Taking this into consideration, the cardiac rehabilitation has gained its importance.

With aging, there are changes taking place in the cardiovascular system, which result in alterations in cardiovascular physiology. The changes occurring with age differ from person to person with varying rates. The changes associated with aging in the cardiovascular system include a decrease in elasticity and an increase in stiffness of the arterial system. Which leads to increased afterload on the left ventricle, an increase in systolic BP (SBP), left ventricular hypertrophy, and other changes in the left ventricular wall that prolong relaxation of the left ventricle in diastole. There is decrease in intrinsic heart rate (HR) due to dropout of atrial pacemaker cells.

In the present study, an effort was made to know effects of isometric contraction in young and elderly normal individuals and also to know whether isometric exercise can be included in elderly normal individual's fitness and cardiac rehabilitation program.

**MATERIALS AND METHODS**

The study was conducted in the Department of Physiology after taking approval from the Ethical Clearance Committee, Navodaya Medical College.

A total of 100 male subjects from in and around Raichur city were selected and divided into two groups, namely, young and elderly groups with age group of 20–30 years and 60–70 years, respectively.

The inclusion criteria were normotensive males in the above age groups, and exclusion criteria included subjects with chronic history of alcohol, smoking, resting tachycardia (>120 beats per min), hypertension, history of any other cardiovascular disorders, any peripheral vascular disease, those on regular exercise program, and uncooperative subjects.

During the first sitting, the anthropometric parameters and body mass index were recorded. Then, during the second sitting, the subject was asked to relax in supine position for 30 min in the laboratory. Both the groups received isometric exercise for forearm. Pre-exercise evaluation was done for HR and BP and the results were recorded. HR was measured in supine position on a couch using electrocardiography (ECG) leads that were connected using electrodes from the subject to the Bio Amp/Stimulator of PowerLab 8/30 series instrument. The resting HR was recorded using RR interval in the computerized ECG from lead two of 5 min. BP was measured with digital electronic BP monitor in supine position after a period of rest for 5 min. Isometric contraction was performed by dominant hand by a hand-held force transducer in the seated position, with the arm at approximately 30° of abduction, with the elbow flexed 90°. The forearm was in neutral pronation/supination. Subjects underwent several preliminary sessions during which they were taught and carefully trained to perform maximum voluntary contraction (MVC) of forearm. MVC was determined as the highest force developed by the subject in previous 5 s maximal contraction trials. Subjects were instructed to breathe normally and avoid holding breath. Each subject gripped force transducer at 40% MVC with the dominant hand for 60 s. Post-exercise HR and BP were taken in supine position and recorded.
RESULTS

The Statistical software SPSS 11.0 was used and all the data were expressed as mean ± SD, analyzed statistically using paired t-test and unpaired t-test, and P < 0.05 was considered statistically significant and P < 0.01 as statistically highly significant.

Results within the group comparison showed a significant increase in HR and BP after 60 s of 40% MVC. Among young subjects, mean pre-SBP was 120.88 ± 9.59, and in post-exercise, it was 125.56 ± 10.39 as shown in Table 1, in elderly subjects, mean pre-SBP was 132.20 ± 4.86, and in post-exercise, it was 142.44 ± 7.03 as shown in Table 2. Further, there was high significant increase in SBP among young and elderly subject as P < 0.01 for both the groups. Whereas, mean pre-diastolic BP (DBP) among young subjects was 75.20 ± 7.22, and in post-exercise, it was 77.68 ± 6.80 as shown in Table 3, in elderly subjects, mean pre-DBP was 83.14 ± 4.18, and in post-exercise, it was 88.01 ± 4.95 as shown in Table 4; further, there was highly significant increase in DBP among young and elderly subject as P < 0.01 for both the groups. Mean pre-HR among young subjects was 75.04 ± 10.44, and in post-exercise, it was 91.90 ± 10.49 as shown in Table 5, and in elderly subjects, mean pre-HR was 78.66 ± 8.68, and in post-exercise, it was 85.58 ± 8.28 as shown in Table 6; further, there was highly significant increase in HR among young and elderly subject after exercise as P < 0.01 for both the groups. However, intergroup comparison indicates mean change in SBP among young was 4.68 and that of elderly was 10.24 (as shown from Graphs 1 and 2), this difference was significantly higher in elderly compare to young subjects as P < 0.01. Mean change in DBP among young was 2.48 and that of elderly was 4.98 (as shown from Graphs 3 and 4), this difference was significantly higher in elderly compare to young subjects as P < 0.01. Thus, there is a significant difference in HR and BP response to isometric contraction in young and elderly normal individuals exist. The older subjects had a lower HR and a higher BP response than their younger counterparts.

DISCUSSION

The peoples over the age of 65 years carry the highest burden of chronic diseases, disability, and health-care
utilization. Although many of these problems can be prevented, most of the physicians fail to provide an appropriate exercise recommendation to their patients that includes an individualized motivational
message, a safe exercise program, and a tailored exercise prescription.\[8]\)

The present study examined the HR and BP responses to 40\% MVC in two age groups of healthy males. The findings showed an age-related difference in cardiovascular responses to isometric contraction. These results are consistent with studies done by Petrofsky and Lind, 1975,[1] Taylor et al., 1991; 1995,\[8,9\]

Sympathetic stimulation seems to be a secondary mechanism for increasing the HR; however, it becomes functional only after the first mechanism of vagal withdrawal has been utilized. The pressor response to handgrip was accompanied by increased cardiac output, and there was no change in calculated systemic vascular resistance. After intravenous propranolol, handgrip exercises resulted in increased peripheral resistance and an equivalent rise in arterial pressure but no increase in cardiac output. It was concluded that the increase in resistance was due to sympathetically induced vasoconstriction. The left ventricular ejection time (corrected for HR) was prolonged by handgrip. The increased afterload imposed on the left ventricle by SHG (sustained handgrip) may explain the prolongation of ejection time index. The study has defined the role of the sympathetic nervous system in the HR and pressor responses to SHG.\[10\]

It has been established that compared to dynamic exercise the isometric contractions causes marked increases in both SBP and DBP, while the rise in HR is less marked.\[11\] When comparing young and older individuals, some studies have found similar responses in HR to isometric exercise,\[12,13\] whereas others have noticed a lower HR in the aged persons.\[7,9\] In contradistinction, it has been shown that the older persons exhibit either a similar\[8,12,13\] or a greater\[7\] BP response to isometric contractions. These variations in readings may be due to variation in subject population, in experimental protocol (fatiguing vs. non-fatiguing contractions), or in the muscle group tested. The age-related changes in physical activity, reductions in skeletal muscle mass and muscle strength may also have been confounded the comparisons of younger and older age groups.\[14\]

**CONCLUSION**

From this study, it is concluded that the increasing age is associated with an altered HR and BP response to isometric exercise. There was an increase in HR and BP with isometric exercise in both young individuals and elderly individuals, but the elderly subjects had a lower HR and a higher BP response than their younger counterparts. The magnitude of the BP response depends on the degree of effort or central command and not the actual force production, and finally, isometric exercise should not be included as an overall fitness program for healthy elderly individuals due to potentially harmful effects on the cardiovascular system.

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**How to cite this article:** Jeelani M, Taklikar RH. Isometric exercise and its effect on blood pressure and heart rate; a comparative study between healthy, young, and elderly males in and around Raichur city. Int J Sci Stud 2018;6(1):12-16.

**Source of Support:** Nil. **Conflict of Interest:** None declared.
Variation of Human Placental Attachment of Umbilical Cord

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Abstract

Introduction: Placenta function as a fetomaternal organ and umbilical cord is a vital lifeline connecting fetus and placenta. Variation of human placental attachment of umbilical cord is important for better perinatal analysis. The present study compared with different study done previously.

Objective: This study was conducted to conclude the various human placental attachment of umbilical cord.

Materials and Methods: In this study, a total of 78 specimens (human placenta attached with umbilical cord) collected from labor room in the Department of Obstetrics and Gynecology, Government Medical College, Ambikapur, Surguja, Chhattisgarh, India. The human placenta along with its attachment was observed grossly and photograph was taken with camera. The data were analyzed and written in tabulated form.

Result: In this study, 45 (57.6\%) showed ecentral attachment, 25 (32.05\%) exhibit central attachment, 07 (8.97\%) showed marginal attachment, and 01 (1.28\%) exhibits furcated attachment of umbilical cord with placenta. There were no velamentous types of attachment present in this study.

Conclusion: This study provides knowledge about attachment of umbilical cord with placenta, hence, the present study useful for Clinicians, Gynecologist, Anatomist, Radiologist, Surgeon, and Physician for proper clinical diagnosis and treatment of disease.

Key words: Central, Ecentral, Furcated, Marginal, Placenta, Umbilical cord, Velamentous

INTRODUCTION

The word placenta comes from Latin - flat cake and Greek -“Plakous” which means “flat, slab like.” The human placenta is a discoid, choriodiciduate organ which functions as a fetomaternal organ with two components. They are fetal portion of placenta (Chorion frondosum) bearing mainly chorionic villi develop from blastocyst that forms fetus, and maternal portion of placenta (Decidua basalis) develops from maternal uterine tissue. The human placenta connects the fetus with uterine wall of the mother.\(^[9]\) The human placenta subdivided into number of lobes by septa that grow into intervillous space from maternal side. Each lobe of placenta called maternal cotyledon. If the placenta viewed from maternal side, it is rough, irregular, and 15–20 polygonal area called cotyledon and appears as convex areas bounded by groves. The fetal surface is smooth, shiny, translucent covered by amnion, chorionic plate, and provide attachment of umbilical cord.\(^[2]\)

The full-term human placenta is discoid with a diameter of 15–25 cm, is approximately 3 cm thick and weight about 500–600 g. Human placenta covers approximately 15–30\% of internal surface of uterus.\(^[3]\) In human placenta, maternal blood circulates through the intervillous space and fetal blood circulate through blood vessels in the villi. The maternal and fetal blood do not mix with each other and they are separated by membrane composed of four layers: They are from inside to outside are (1) endothelial lining of fetal vessels,
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(2) connective tissue in the villus, (3) cytotrophoblastic layer, and (4) syncytiotrophoblast. The total area of this membrane is 4–14 sqm. The main function of human placenta is exchange of metabolic and gaseous product such as oxygen, carbon dioxide, water, electrolytes, and nutrition. Production of hormone such as progesterone (maintenance of pregnancy after 4 months) and estrogens predominantly estriol (promote uterine growth and development of mammary gland).[6]

Umbilical cord develops from the body stalk and has different structure at different stages of development. Fully developed umbilical cord is about 45–50 cm in length and 1–2 cm in diameter. It contains two umbilical arteries and one umbilical vein. These vessels are embedded in the soft jelly extraembryonic mesoderm called Wharton jelly. The umbilical cord appear twisted helical may be due to fetal movement or unequal growth of vessels.[5]

The umbilical cord is normally attached to the placenta near the center, but it may attach ecentral (attached near center) and marginal (attached near margin also called Battledore placenta); it is related with IUGR, preterm labor, and furcate (blood vessels divide before reaching placenta); it is associated with early delivery because they are heavier more voluminous villi with more trophoblast and syncytial knots, velamentous (blood vessels attached to amnion and ramify before reaching the placenta); and it is allied with low birth weight, low Apgar score, growth retardation, esophageal atresia, spina bifida, and VSD.[6-7]

The current study describes the variation of human placental attachment of umbilical cord, hence, this study useful for Clinicians, Gynecologist, Anatomist, Radiologist, Surgeon, and Physician for proper clinical diagnosis and treatment of disease.

**MATERIALS AND METHODS**

The present study was conducted in the Department of Obstetrics and Gynecology, Government Medical College, Ambikapur, Surguja, Chhattisgarh, India. The human placenta with attached umbilical cords was collected soon after the delivery. The patient history was taken from hospital record. A total of 78 human placenta specimens were studied. The human placenta along with its attachment was observed grossly and photograph was taken with camera. The data were analyzed and written in tabulated form.

**RESULTS**

The present study was done on 78 human placenta attached with umbilical cord, out of which 45 (57.6%) showed ecentral attachment [Figure 1], 25 (32.05%) exhibit central attachment [Figure 2], 07 (8.97%) showed marginal attachment [Figure 3], and 01 (1.28%) exhibits furcated attachment of umbilical cord with placenta [Figure 4]. There were no velamentous types of attachment present in this study. Distribution of umbilical cord attachment with placenta given in tabulated form in Table 1.

**DISCUSSION**

Placenta is a fetomaternal organ and variation of attachment of placenta with umbilical cord having great

![Figure 1: Ecentral](image1)

![Figure 2: Central](image2)

<table>
<thead>
<tr>
<th>Table 1: Distribution of umbilical cord attached with placenta</th>
</tr>
</thead>
<tbody>
<tr>
<td>Umbilical cord attached to placenta</td>
</tr>
<tr>
<td>-------------------------------------</td>
</tr>
<tr>
<td>Ecentral</td>
</tr>
<tr>
<td>Central</td>
</tr>
<tr>
<td>Marginal</td>
</tr>
<tr>
<td>Furcate</td>
</tr>
<tr>
<td>Velamentous</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>
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Table 2: Comparative studies of umbilical cord attached with placenta among the various study of world

<table>
<thead>
<tr>
<th>Studied By</th>
<th>Year</th>
<th>Number of specimen</th>
<th>Umbilical cord attached with placenta</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donald et al.[10]</td>
<td>1998</td>
<td>54</td>
<td>Ecentral (%) 70.37, Central (%) 22.22, Marginal (%) 7.41</td>
</tr>
<tr>
<td>Sepulveda et al.[11]</td>
<td>2003</td>
<td>825</td>
<td>Ecentral (%) 93.69, Central (%) 5.21, Marginal (%) 0.96</td>
</tr>
<tr>
<td>Waldo Sepulveda et al.[12]</td>
<td>2009</td>
<td>138</td>
<td>Ecentral (%) 92.02, Central (%) 7.2, Marginal (%) 0.75</td>
</tr>
<tr>
<td>Manikanta et al.[6]</td>
<td>2012</td>
<td>110</td>
<td>Ecentral (%) 75.45, Central (%) 16.36, Marginal (%) 7.27</td>
</tr>
<tr>
<td>Asra et al.[8]</td>
<td>2015</td>
<td>39</td>
<td>Ecentral (%) 54, Central (%) 36, Marginal (%) 2</td>
</tr>
<tr>
<td>Yousuf et al.[7]</td>
<td>2016</td>
<td>150</td>
<td>Ecentral (%) 66, Central (%) 24, Marginal (%) 8</td>
</tr>
<tr>
<td>Present study</td>
<td>2018</td>
<td>78</td>
<td>Ecentral (%) 57.6, Central (%) 32.05, Marginal (%) 8.97</td>
</tr>
</tbody>
</table>


In our study, 01 (1.28%) explains furcated attachment of umbilical cord with placenta which was correlated with the study of Manikanta et al.,[6] and Arora et al.,[9] whereas velamentous attachment absent in current, but it is present in previous studies such as Donald et al.,[10] Sepulveda et al.,[11] Waldo et al.,[12] Manikanta et al.,[6] Asra et al.,[8] Arora et al.,[9] and Yousuf et al.[7] The present studies along with various previous study displayed in Table 2.

CONCLUSION

This study reveals the variation of human placental attachment of umbilical cord and ecentral type of attachment is the most common of all. Variation in the attachment associated with various abnormalities such as preterm labor, low birth weight, growth retardation, esophageal atresia, spina bifida, and VSD, hence, this study useful for Clinicians, Gynecologist, Anatomist, Radiologist, Surgeon, and Physician for proper clinical diagnosis and treatment of disease.

ACKNOWLEDGMENT

We would like to thanks all the staffs, faculty who supported us during this study.

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Source of Support: Nil, Conflict of Interest: None declared.
Eyelid Lesions: A Clinical Study

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Abstract

Introduction: Eyelid lesions are very common. These can be inflammatory, infectious, or neoplastic. Diagnosis is made by history and clinical examination. In suspected lesions, biopsy has to be done.

Purpose: The aim of the study is to report the relative frequency of eyelid lesions.

Materials and Methods: A prospective cross-sectional clinical study was done in 140 patients with eyelid lesions. All patients underwent eye examination which included visual acuity assessment, anterior segment, and fundus examination. In suspected lesions, biopsy was done to rule out malignancy.

Results: Among 140 patients, external hordeolum was the most commonly seen with 64 cases (45.7%), followed by chalazion 50 cases (35.7%), nevus 7 cases (5%), xanthelasma 6 cases (4.3%), sebaceous cyst 4 cases (2.9%), cutaneous horn 3 cases (2.2%), squamous papilloma 2 cases (1.4%), dermoid cyst 3 cases (2.1%), and molluscum contagiosum 1 case (0.7%).

Conclusion: Eyelid lesions are common with most being benign. Each lesion carries a different line of treatment. Early diagnosis and timely intervention help to prevent serious complications.

Key words: Biopsy, Chalazion, Diagnosis, External hordeolum, Eyelid lesions, Nevus

INTRODUCTION

Eyelid lesions are commonly encountered during clinical practice.

Diagnosis of these lesions requires an understanding of the anatomy of the lids along with history, clinical examination, and appropriate investigation such as histopathological examination in cases of suspected malignancy where a diagnosis cannot be made with accuracy on clinical grounds alone.

The anatomy of lids consists of the structures from within outward as skin, layer of subcutaneous areolar tissue, layer of striated muscles, submuscular areolar tissues, fibrous layer, layer of non-striated muscle fibers, and conjunctiva.

Adnexal structures such as eyelashes, meibomian gland, gland of Zeis, gland of moll, vessels, and lymphatics also form a part of the eyelid structure.

A careful history taking which includes symptoms, chronicity, and progression along with a detailed examination of the lesion can help clinch a clinical diagnosis of the lesion.

Eyelid lesions can be categorized as follows:

- Inflammatory
  - Chalazion
- Infectious
  - External hordeolum
  - Hordeolum internum
  - Molluscum contagiosum
- Neoplastic
  - Benign lesions: Squamous cell papillomas, epidermal inclusion cyst, acquired melanocytic nevi, seborrheic keratosis, hidrocystoma, and xanthelasma.
  - Premalignant lesions: Actinic keratosis and keratoacanthoma.
  - Malignant lesions: Basal cell carcinoma, squamous cell

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carcinoma, sebaceous carcinoma, melanoma, Merkel cell carcinoma, lymphomas, and metastasis.

**Objective**

- The study was carried out to report the relative frequency of eyelid lesions.

**MATERIALS AND METHODS**

- **Type:** A prospective cross-sectional clinical study
- **Duration:** 6 months (November 1, 2016–April 30, 2017)
- **Place of study:** Rajarajeswari Medical College and Hospital
- **Source of study:** All patients attending the OPD of the hospital with eyelid lesions during the period extending from December 1, 2016 to April 30, 2017.
- **Sample size:** 140
- **Method of collection of data:** All patients underwent thorough examination including history. Followed by clinical examination which included visual acuity assessment using Snellen chart, detailed eyelid examination, anterior segment evaluation with slit lamp, and fundus examination. Histopathological study was done in suspected cases to rule out malignancy.

**RESULTS**

- A total of 140 patients were examined during a period of 6 months.
- All the cases were benign with histopathological confirmation in suspected cases.
- The study showed a female preponderance with 80 (57%) female patients and 60 (43%) male patients [Figure 1].
- The patients were between the age group of 10 and 50 years.
- 30 patients belonged to the age group of 10–20 years, 48 to 20–30 years, 27 to 30–40 years, and 35 to 40–50 years [Table 1].
- Maximum number of cases was seen in the age group of 20–30 years with the female preponderance in all the age groups [Graph 1].
- All the cases were benign, out of which external hordeolum was the most commonly seen with 64 cases (45.7%), followed by chalazion 50 cases (35.7%), nevus 7 cases (5%), xanthelasma 6 cases (4.2%), sebaceous cyst 4 cases (2.8%), cutaneous horn 3 cases (2.1%), squamous papilloma 2 cases (1.4%), dermoid cyst 3 cases (2.1%), and molluscum contagiosum 1 case (0.7%) [Table 2].

**DISCUSSION**

- Eyelid lesions are very common and most of them are benign. Deprez et al.\(^1\) studied 5504 cases over a period of 19 years and found 84% of benign tumors and rest malignant. The majority of eyelid lesions were benign eyelid tumors while malignant eyelid tumors contributed 10.8% of the total eyelid lesions.\(^2\) In some cases, malignant lesions have clinical features similar to that of benign lesions. Therefore, in suspected benign lesions, histopathological examination is mandatory. Histopathologic evaluation enforces our clinical diagnostic skills and is extremely important in early detection of tumors, particularly in masquerade syndromes.\(^3\)
- During the course of the study, maximum number of cases was of external hordeolum (45.7%). Also known as stye, it is an acute staphylococcal abscess of an eyelash follicle and its associated gland of Zeis. The patients in our study belonged to a younger age group and were treated with hot compresses, topical antibiotics, and epilation of associated cilia. In case of non-resolving lesions, incision and drainage can be done.
- In our study, the second most common lesion was of chalazion (35.7%). Chalazion is the most common lid lesion faced by the ophthalmologist.\(^1,4,5\) It is a...
chronic sterile lipogranulomatous inflammation of the meibomian glands and some cases the gland of Zeis. Cases of chalazion were seen mostly in the younger age group with 2 cases belonging to the older age group. Lesions were treated with incision and curettage. Rarely, the chalazion is injected with steroids; however, this may result in hypopigmentation of the overlying skin. Histopathological confirmation was made for the 2 suspected cases based on a history of recurrence. Recurrent chalazion was the most common indication for chalazion biopsy as sebaceous cell carcinoma (SGC) was always included as a differential diagnosis as some cases of SGC can mimic this lesion. One study reported as much as 20% of sebaceous carcinomas were initially misdiagnosed as recurrent chalazion.

- Cases of sebaceous cyst (2.8%), cutaneous horns (2.1%), squamous papilloma (1.4%), and molluscum contagiosum (0.7%) were diagnosed on the basis of their peculiar appearance. All the above lesions were seen in adults except for molluscum contagiosum which was seen in the pediatric age group. The cases were treated by excision with histopathological confirmation of diagnosis and the benign nature of the lesions.
- Lesions such as nevus (5%), xanthelasma (4.2%), and dermoid cyst (2.1%) encountered during the study were managed on the basis of observation and specific investigations such as lipid profile in case of xanthelasmas and neurosurgical opinion in case of dermoid cyst to know the invasion into deeper structures.
- The study revealed that all the cases were benign with a female preponderance affecting patients between the age group of 10 and 50 years.

CONCLUSION

Eyelid lesions are common with most being benign. Each lesion carries a different line of treatment. Early diagnosis and timely intervention help prevent ocular complications that could compromise vision, comfort, and cosmesis.

REFERENCES

Clinical Profile of Diabetic Foot Infections

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Abstract

Background: Diabetic foot infections (DFIs) are associated with substantial morbidity and mortality. Patients with a DFI should be evaluated comprehensively, and employing multidisciplinary foot teams improve outcomes.

Aims and Objectives: To study the clinical profile and microbial flora of diabetic wound infections along with antibiotic therapy.

Methods: This study included 253 patients admitted in the department of general medicine between March 2015 and August 2016. A thorough clinical examination was done. Peripheral neuropathy was evaluated by monofilament and vibration sense. Wound ulcer was graded according to Wagner grading. A basic laboratory workup along with fundus examination was done to rule out microvascular and macrovascular complication of diabetes. ECG and 2D ECHO were done for patients with CAD. Wound swab from the ulcer edge was taken after removing the necrotic material and sent for culture. Pus swab was also sent for culture. Antibiotic therapy and duration was calculated.

Results: The study included 253 patients, 169 males and 84 females. 65 patients presented with Grade I ulcer, 175 with Grade II ulcer, and 13 had Grade III ulcer. 12 patients required ICU care and 241 patients were managed in the ward. The mean age was 57.57. Mean fasting and post-prandial sugars were 157.48 and 244.21, respectively. The mean HbA1c was 9.49 with a mean duration of hospital stay of 12.44 days. 40 patients grew *Staphylococcus aureus*, 40 patients grew coagulase-negative *Staphylococcus* (CONS), 28 *Escherichia coli*, 20 *Streptococcus* species, 20 *Enterococcus* species, 10 *Proteus* species, 12 *Klebsiella* species, 25 *Pseudomonas* species, and 6 *Candida* species. Polymicrobial growth was seen in 26 patients. 25 patients had no growth in cultures. A majority of *S. aureus* was sensitive to penicillin and clindamycin, CONS to clindamycin and linezolid, and *Enterococcus* was sensitive to linezolid and ampicillin.

Conclusion: The present study revealed the increased incidence of diabetic foot ulcers and is more common above the fifth decade of life with male preponderance. Our study has showed that 90% and 9.6% of DFIs were monomicrobial and polymicrobial, respectively. CONS and *S. aureus* were the most commonly identified Gram-positive microorganisms, respectively. *E. coli* and *Pseudomonas aeruginosa* were the most commonly identified Gram-negative organisms.

Key words: Coagulase-negative *Staphylococcus*, Diabetic foot, Penicillin, *Staphylococcus aureus*, Wagner grading

INTRODUCTION

Diabetic foot infections (DFIs) are associated with substantial morbidity and mortality. Risk factors for the development of DFIs include neuropathy, peripheral vascular disease, and poor glycemic control. In sensory neuropathy, there is diminished perception of pain and temperature. Autonomic neuropathy can cause diminished sweat secretion resulting in dry, cracked skin that facilitates the entry of microorganisms to the deeper skin structures. In addition, motor neuropathy can lead to foot deformities, which lead to pressure-induced soft tissue damage. Peripheral artery disease can impair blood flow necessary for healing of ulcers and infections. Hyperglycemia impairs neutrophil function and reduces host defenses. Trauma in patients with one or more of these risk factors precipitates the development of wounds that can be slow to heal and predispose to secondary infection.

DFIs are a frequent clinical problem. Infection in foot wounds should be defined clinically by the presence of inflammation or purulence, and then classified by severity.
Many organisms, alone or in combinations, can cause DFI, but Gram-positive cocci, especially staphylococci, are the most common. Definitive therapy should be based on cultures of infected tissue. Imaging is especially helpful when seeking evidence of underlying osteomyelitis, surgical interventions of various types are often needed and proper wound care is important. Patients with a DFI should be evaluated for an ischemic foot, and employing multidisciplinary foot team improves outcomes.[1,2]

The present study was aimed at analyzing the clinical presentation, diagnosis, microbiology, and management of DFIs. We also observed the correlation between various parameters with the outcome.

**MATERIALS AND METHODS**

The study was a prospective study done at Sri Ramachandra University from March 2015 to August 2016. All patients with diabetes mellitus presenting with wound infection above 18 years are included in the study. Post-operative patients developing wound infection and patients with multiple septic foci are excluded from the study. Patient demographics and clinical data were recorded from oral questionnaires and hospital records. A thorough clinical examination was done. Peripheral neuropathy was evaluated by monofilament and vibration sense. Wound ulcer was graded according to Wagner grading. Peripheral vascularity was assessed by ankle-brachial index measurement. A basic laboratory workup along with fundus examination was done in all patients. ECG and 2D ECHO were done for patients with coronary artery disease. Wound swab from the ulcer edge was taken and sent for culture. Antibiotic therapy and duration was calculated.

The results of the study were analyzed and statistical data were summarized using SPSS 21 software. Chi-square test and Pearson’s correlation were done for specific variables.

**RESULTS**

The study included 253 patients, 169 males and 84 females. Most of the patients were in the age group of 51–70 years. 14 patients below 40 years, 51 patients between 41 and 50 years, 85 patients between 51 and 60 years, 82 patients between 61 and 70 years, 18 patients between 71 and 80 years, and 3 patients above 80 years. The study characteristics and profile of patients are summarized in Table 1.

About 12 patients required ICU care and 241 patients were managed in the ward. The mean age was 57.57. Mean fasting and post-prandial sugars were 157.48 and 244.21, respectively. The mean HbA1c was 9.49 with a mean duration of hospital stay of 12.44 days. 40 patients (15.8%) grew *Staphylococcus aureus*, 41 (16.2%) patients grew coagulase-negative *Staphylococcus* (CONS), 28 patients (11.2%) had *Escherichia coli*, 20 (7.9%) patients had *Streptococcus* species, 20 (7.9%) patients had *Enterococcus* species, 10 (4%) patients had *Proteus* species, 12 (4.7%) patients grew *Klebsiella* species, 25 (9.9%) patients had *Pseudomonas* species, and 6 patients (2.4%) had *Candida* species. Polymicrobial growth was seen in 26 (10.3%) patients. 25 (9.9%) patients had no growth in cultures. Gram-positive organisms were responsible for more than 30% of infections. Among Gram-positive organisms, a majority of *S. aureus* was sensitive to penicillin and cloxacillin (MRSA was found in two patients), *Streptococcus* to penicillin and clindamycin, CONS to clindamycin and linezolid, and *Enterococcus* was sensitive to linezolid and ampicillin. Among Gram-negative organisms, a majority of *E. coli* was sensitive to amikacin, cefoperazone, and gentamicin, *Pseudomonas* to ciprofloxacin and gentamicin, *Proteus* to imipenem, and *Klebsiella* was sensitive to imipenem and ciprofloxacin. 238 recovered, 2 patients died and 13 were discharged against medical advice. There was no significant correlation between age and outcome. Significant vascular occlusion had no correlation with outcome. All patients who died had a HbA1c of more than 8.5. Two patients in the study group who expired had a Wagner Grade III. In our study, we found that one patient with *Klebsiella* growth and one with *Streptococcus* growth expired. Even patients with polymicrobial growth had a favorable outcome. There was high association of

### Table 1: The study profile

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>SD</th>
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<tbody>
<tr>
<td>Age</td>
<td>253</td>
<td>22</td>
<td>90</td>
<td>57.57</td>
<td>10.560</td>
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<tr>
<td>FBS</td>
<td>253</td>
<td>70</td>
<td>362</td>
<td>157.48</td>
<td>56.395</td>
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<tr>
<td>PPBS</td>
<td>253</td>
<td>103</td>
<td>698</td>
<td>244.21</td>
<td>90.652</td>
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<tr>
<td>HbA1C</td>
<td>253</td>
<td>5</td>
<td>18</td>
<td>9.49</td>
<td>2.431</td>
</tr>
<tr>
<td>RFT</td>
<td>253</td>
<td>0.6</td>
<td>6.8</td>
<td>1.353</td>
<td>0.8010</td>
</tr>
<tr>
<td>Hospital stay in days</td>
<td>253</td>
<td>1</td>
<td>78</td>
<td>12.44</td>
<td>12.071</td>
</tr>
<tr>
<td>Total counts</td>
<td>253</td>
<td>600</td>
<td>26000</td>
<td>11338.74</td>
<td>4331.181</td>
</tr>
<tr>
<td>Valid N (listwise)</td>
<td>253</td>
<td></td>
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</table>

### Table 2: Wagner grading

<table>
<thead>
<tr>
<th>Wagner grade</th>
<th>Frequency (%)</th>
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<tbody>
<tr>
<td>Grade I</td>
<td>65 (25.7)</td>
</tr>
<tr>
<td>Grade II</td>
<td>175 (69.2)</td>
</tr>
<tr>
<td>Grade III</td>
<td>13 (5.1)</td>
</tr>
<tr>
<td>Total</td>
<td>253 (100.0)</td>
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</table>
Gram-positive organism growth with Grade I ulcer and Klebsiella growth was common in Grade III ulcer. No specific bacterial growth association was seen with Grade II ulcer. Empirical antibiotic therapy was started for all patients, 186 patients received monotherapy and 77 patients were given dual antibiotics. Amoxicillin-clavulanate was the preferred antibiotic (108 patients), followed by clindamycin in 98 patients, other antibiotics given were cefoperazone-sulbactam (96), piperacillin-tazobactam (58), linezolid (36), and ciprofloxacin (32). The duration of antibiotic therapy ranged from 7 to 14 days.

**DISCUSSION**

The study included 253 patients with diabetes mellitus presenting with wound infection, 169 males and 84 females. Most of the patients were in the age group of 51–70 years. The present study depicts the mean age of the study population was 57.57 years with more than 70% cases were above the age of 50 years and as age increases the chance of getting a foot ulcer also increases. Similar findings have also been reported by Mohite et al., Bansal, and Kahn et al. The proportions of male patients with diabetic foot ulcer have been higher (66.8%) than females. Similar findings have also been reported by Mohite et al., Bansal, and Banashankari.

65 patients presented with Grade I ulcer, 175 with Grade II ulcer, and 13 had Grade III ulcer. No patients had Grade IV and Grade V ulcer. 66% of the patients had an ulcer on the right side. In a study by Mohite et al.,[3] 53.80% of the cases had ulcers of Grade III and IV, whereas 12 patients had extensive gangrene (i.e., Grade V). 67.9% with majority of lesions located over sole area. A similar finding has also been observed by Banashankari et al.[18] The peripheral neuropathy, a major associated complication (56.45%) was observed in this study. A similar finding has also been observed by Shailesh et al.[17] However, Paul et al.[9] observed neuropathy in 33.3% of cases, whereas Banashankari et al.[6] reported in 76% of cases. The feet were the target of peripheral neuropathy leading chiefly to sensory deficit and autonomic dysfunction could be the cause for high proportion.

Bacterial etiology could be identified among 228 cases out of 253 (90%); single organism was isolated in 206 (90.3%) among which CONS (41 cases) and S. aureus being the most common (in 40 cases), followed by E. coli (28 cases) and Pseudomonas (in 25 cases). Polymicrobial association was found in 22 cases. Zubair et al.,[9] Anandi et al.,[10] Ramakant et al.,[11] Pappu et al.,[12] and Citron et al.[13] have reported 56.6%, 19%, 23%, 92%, and 16.2% monomicrobial infections and 33%, 67%, 66%, 7.7%, and 83% of polymicrobial infections, respectively. In our study, we had monomicrobial infection in 90.3%. The findings of this study correlate with findings of Pappu et al.[12] and Dhansekaran et al.[14] Gram-positive cocci were more prevalent (121 out of 238, i.e., 50.84%) than Gram-negative bacilli (111 out of 238, i.e., 46.63%). In our study, CONS (41 cases) and Staphylococcus (in 40 cases), followed by E. coli (28 cases) and Pseudomonas (in 25 cases) were observed. CONS, S. aureus, E. coli, and Pseudomonas aeruginosa were predominant among the monobacterial isolates. The interesting observation made was that there was a near equal distribution of Gram-positive and Gram-negative growth. Similar observations were reported by Citron et al.,[13] Zubair et al.,[9] and Alavi et al.[19] with S. aureus as the predominant pathogen, which comprised 57.2%, 28%, and 26.2% of their isolates, respectively. In contrast, Pappu et al.[12] reported that 76% of the organisms which were isolated were Gram-negative bacilli, Pseudomonas being the predominant pathogen (23%), followed by S. aureus (21%). Zubair et al.[9] reported E. coli (26.6%) and P. aeruginosa (10.6%) as the predominant Gram-negative isolates. In the study of Benwan et al.[10] which was done in Kuwait, they reported that more Gram-negative pathogens (51.2%) were isolated than Gram-positive pathogens (32.3%) or anaerobes (15.3%). The increased prevalence of CONS could indicate the changing microbiological profile of DFIs. Tables 1 and 2 summarize the pathogens isolated in various other studies.

Candida growth was seen in 6 patients (2.5%). Manikandan et al.[17] observed 3.4% Candida growth in his study. MRSA was seen in 3 patients (1.2%). In contrast, Jayashree et al.[19] and Hefni et al.[19] observed the prevalence of MRSA to be 36.84% and 7.1%, respectively. In the present study, ESBL organisms were found to be 60.36%. Jayashree et al.[18] found the incidence of ESBL to be 46%. The increased incidence of ESBL is always expected as antibiotics are not judiciously used which have led to the emergence of resistant organisms. The incidence of Gram-positive organisms [Table 3] and Gram-negative organisms [Table 4] observed in various studies are summarized in Table 3.

With regard to the susceptibility patterns, amoxicillin-clavulanate and cefoperazone-sulbactam appeared to be the best antibiotics for therapy against Gram-positive and Gram-negative organisms, respectively. Vancomycin is usually only indicated for the treatment of MRSA. Superficial lesions were treated with amoxicillin-clavulanate, cefoperazone-sulbactam along with piperacillin-tazobactam were preferred for infections involving deeper tissue.

The strength of this study is that it included an adequate sample size and a detailed analysis was done. There are some limitations in this study. Like all the specimens evaluated here were collected from ulcer edge and pus
Table 3: Comparison of Gram-negative pathogens in various studies

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<tbody>
<tr>
<td>Proteus</td>
<td>18</td>
<td>6</td>
<td>16</td>
<td>6.3</td>
<td>3</td>
<td>6.1</td>
<td>7</td>
<td>18</td>
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<tr>
<td>E. coli</td>
<td>16</td>
<td>20</td>
<td>20</td>
<td>15.3</td>
<td>23.8</td>
<td>9.4</td>
<td>19</td>
<td>18</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>13</td>
<td>18</td>
<td>8</td>
<td>24.3</td>
<td>31.34</td>
<td>4.1</td>
<td>27</td>
<td>18</td>
</tr>
<tr>
<td>Acinetobacter</td>
<td>7</td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>10.2</td>
<td>2</td>
<td>18</td>
</tr>
<tr>
<td>Klebsiella</td>
<td>7</td>
<td>10</td>
<td>10</td>
<td>9</td>
<td>3</td>
<td>15.3</td>
<td>22</td>
<td>18</td>
</tr>
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Table 4: Comparison of Gram-positive pathogens in various studies

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<tbody>
<tr>
<td>S. aureus</td>
<td>19</td>
<td>17</td>
<td>32.4</td>
<td>42.3</td>
<td>22.4</td>
<td>10.2</td>
<td>17</td>
<td>15.8</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>9</td>
<td>5</td>
<td>-</td>
<td>-</td>
<td>3</td>
<td>-</td>
<td>19</td>
<td>7.9</td>
</tr>
<tr>
<td>CONS</td>
<td>5</td>
<td>12</td>
<td>14.5</td>
<td>-</td>
<td>-</td>
<td>7.1</td>
<td>2</td>
<td>16.2</td>
</tr>
<tr>
<td>Streptococcus</td>
<td>-</td>
<td>6</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>7.9</td>
</tr>
</tbody>
</table>

CONCLUSION

The present study revealed that as the grade of ulcer increased, the number of bacterial isolates also increased. Our study has shown that 90% and 9.6% of DFIIs were monomicrobial and polymicrobial, respectively. CONS and S. aureus were the most commonly identified Gram-positive microorganisms, respectively. E. coli and P. aeruginosa were the most commonly identified Gram-negative organisms. Amoxicillin-clavulanate and cefoperazone-sulbactam appeared to be the best antibiotics for therapy against Gram-positive and Gram-negative organisms, respectively. Vancomycin is usually only indicated for the treatment of MRSA. Increased incidence of resistant organisms was observed in this study which is important, especially for patient management and the development of antibiotic treatment guidelines. Appropriate usage of antibiotics based on local antibiogram pattern can certainly help the clinician in reducing the burden of DFIIs, which ultimately reduces the rate of amputations.

REFERENCES


Source of Support: Nil, Conflict of Interest: None declared.
Efficacy of Decompressive Craniectomy in Acute Subdural Hematoma in Head Injury Patients, Madurai Medical College, Madurai

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Abstract

Aims and Objectives: The aims and objectives are as follows: (1) To study the effect of decompressive craniectomy in head injury patient with subdural hematoma (SDH), (2) to compare the outcome of non-operative patients, and (3) to identify the factors contributing the outcome of decompressive craniectomy.

Materials and Methods: This was a retrospective study conducted between November 2015 and October 2016. The patients in trauma head injury ward, Government Rajaji Hospital, Madurai Medical College, Madurai, Tamil Nadu, are grouped as decompressive craniotomy surgery done and conservatively treated with acute SDH. Data regarding mode of accident, GCS - Glasgow coma scale, computed tomography finding, and outcome were collected. Statistical analysis was used to identify factors associated with favorable outcome of the patients.

Results: Statistical analysis were done to identify factors associated with mortality, morbidity, and favorable outcome of the patients, by categorizing the patients with GCS Mild - 13 -15 , moderate - 9 -12, and severe below 8 with traumatic brain injury. For the patients with GCS moderate 9-12 score better outcome occurs if decompressive craniectomy done. Total 527 patients in which 139 patients were operated.

Conclusion: Age, severity of head injury, neurological status, and timing of surgery are the main factors influencing outcomes. After moderate head injury with acute SDH, surgery with decompressive craniectomy is the better outcome. Mild head injury can be managed conservatively with continuous neuro observation. In severe head injury, the results are poor.

Key words: Acute subdural hematoma, Decompressive craniectomy, Glasgow Coma Scale, Traumatic brain injury

INTRODUCTION

Head injury is one of the important public health problems today. The incidence of head injuries is steadily increasing all over the world, and developing country has the highest incidence in the world of head injuries due to road traffic accidents per 1000 vehicles or deaths per 1000 accidents.[1] The care of head-injured patients forms an important part of neurosurgical management in all countries. The modernization of industries as well as modes of transport have increased the incidence and the severity of injuries.[2] The management of severe head injury is a major challenge to neurosurgeons as the consequent mortality and morbidity is very high. There is a need for an extensive multidimensional effort to improve the prognosis of head-injured patients and provide them a better quality of life.[2]

Acute subdural hematoma is a hematoma accumulating between the inner layer of the dura matter and the Arachnoid matter, to become clinically symptomatic within 24 - 72 hours. They are usually located over the cerebral convexities conforming to the convex brain surface.
MATERIALS AND METHODS

This retrospective study was conducted in head injury ward, Government Rajaji Hospital trauma center, Madurai Medical College, Madurai, Tamil Nadu, from November 2015 to October 2016,

- Study done for the patients with ASDH admitted in the head injury ward, Government Rajaji Hospital, Madurai Medical College, Madurai. The head injury patients with or with out poly trauma, irrespective of mode of injury and with radiological findings are selected for study.
- Who are the subjects believed to fulfill all eligibility criteria, and exclusion criteria are participated in the study for conservative management or decompressive craniectomy
- The patients grouped as (1) decompressive craniectomy done and (2) conservatively treated
- Data regarding mode of accident, time of injury, GCS, clinical status of the patient, laboratory investigations, computed tomography (CT) finding, and outcome were collected by GCS outcome score
- Statistical analyses were done to identify factors associated with mortality, morbidity, and favorable outcome of the patients, by categorizing the patients with GCS Mild - 13 -15, moderate - 9 -12, and severe below 8 with traumatic brain injury. For the patients with GCS moderate 9-12 score better outcome occurs if decompressive craniectomy done.
- Total 527 patients in which 139 patients were operated.
- Patient’s follow-up by 1 month, 3 months, 6 months, and 1 year
- In trauma patient with acute head injury with ASDH, inclusion and exclusion criteria are as follows.

Inclusion Criteria
The following criteria were included in the study:
- In trauma patient with acute head injury with ASDH
- No age restriction
- No sex restriction
- No time restriction.

Exclusion Criteria
The following criteria were excluded from the study:
- Chronic SDH
- Extradural hematoma
- Ventricular hemorrhage
- Intracerebral hemorrhage
- Fracture hematoma.

Based on Data
- Basic patient data’s name, age, sex
- Vitals, pupils
- Mode of injury
- Time interval
- Glasgow Coma Scale
- Patient with associated injuries
- Laboratory investigations
- CT scan findings
- Time of surgery
- Glasgow Outcome Score (extended)
- Karnofsky Performance Status Scale
- Modified Rankin Scale.

There is about the incidence of acute SDH (29%) as the primary lesion in patients admitted with head injury. Acute SDH more often occurs in the second to sixth decades (mean age 31–40 years) Men are 4 times more likely to be affected than women.[4]

Pathogenesis
Acute SDH resulting from one of the three common causes, namely: (1) Rupture of bridging veins, (2) cerebral contusion, and (3) rupture of small cortical arteries. They termed the bleeding from torn bridging veins and rupture of small cortical arteries as “pure SDHs” as they occurred without any gross (focal or diffuse) damage to the brain itself.[5] They found that the volumes of arterial and venous acute SDH and their relative areas in the horizontal planes were similar irrespective of the causal mechanism. The hematoma thickness and midline shift were higher in arterial SDH. On the other hand, in venous SDH, the difference between the midline shift and the hematoma thickness was lower than in arterial SDH (i.e., in venous SDH, a smaller acute SDH was associated with a greater midline shift) indicating a tendency toward more pronounced midline shift in venous, rather than arterial SDH of similar volumes.

The venous SDH due to bridging vein ruptures was generally located in the central frontoparietal and parasagittal region and had a comparatively smaller length and thickness than the arterial SDH which were more often located in the temporoparietal region.

Poor outcome following acute SDH may also be related to the ischemic damage occurring in the hemisphere underlying the hematoma due to raised intracranial pressure producing impaired cerebral perfusion. Removal of an acute SDH often results in reversal of global ischemia. Decompressive craniectomy is the one of the neurosurgical methods in which part of skull (free bone flap) is removed. Dura opened and the hematoma evacuation done and free bone flap is not replaced. The aim of decompression is to reduce the increased intracranial pressure and prevent coning.

In younger group (18–40 years), 80% were caused by motor vehicle accidents and only 12% were caused by assault. Whereas, acute SDH in the older groups (>65 years), 26% due to fall and only 8% due to assault.[6]
In comatose patients, motor vehicle accidents are responsible for acute SDH in 75% of patients because these are often high-velocity accidents with associated diffuse axonal injury.[7]

Associated intracranial injuries occur in more than 50% of patients with acute SDH and have a significant prognostic implication. Associated lesions occur in 37% of patients presenting with Glasgow Coma Scale (GCS) scores between 13 and 15 and in 45% of patients with GCS scores <8. In patients with acute SDH, contusion and fractures are the most frequent injuries encountered; associated subarachnoid hemorrhage has been seen in 25% of patients with SDH and epidural hematomas in 18% of patients. Extracranial injuries are seen in 48% of patients including facial fractures, limb fractures, and thoracic and abdominal trauma. Around 40% of patients with other associated lesions have a contrecoup injury. Bilateral acute SDH occurs in 13%.

Clinical Presentation
The clinical presentation is non-specific and occurs due to mass effect produced by the acute SDH as well as associated parenchymatous injury. It depends on the severity of the primary injury, the associated parenchymal injuries, and the rapidity of accumulation of the acute SDH. The patients may remain unconscious throughout or may vary in sensorium from being totally unconscious to being lucid to unconscious or may remain lucid throughout. About 40% of patients are semiconscious at the time of their primary injury and remain comatose for prolonged periods. 33% of their patients with lucid interval neurologically deteriorated. Pupillary asymmetry ipsilateral to the side of hematoma with contralateral hemiparesis may be due to transtentorial herniation. However, false localizing pupillary dilatation contralateral to the lesion may occur due to direct optic nerve, oculomotor nerve, or brain stem injury on that side. Ipsilateral hemiparesis may be due to associated brain injury or due to Kernohan’s notching produced by compression of the contralateral cerebral peduncle against the tentorial edge. The incidence of associated seizures has present about 18%. Posterior fossa acute SDH is rare and occurs in 3% of patients who underwent surgery within 24 h of injury. Occipital trauma and associated occipital fractures may be responsible. Posterior fossa acute SDH occurs due to tearing of bridging veins, laceration of the tentorium, contusion of the cerebellum, or injury to venous sinuses. Cerebellar signs, neck stiffness, and pain or symptoms of raised intracranial pressure due to the size of the lesion or the development of hydrocephalus may be the presenting features. Despite urgent surgical evacuation, the mortality was about 75%.

Diagnosis: CT Scan Finding
On CT scans, an acute SDH appears as crescentic, hyperdense collections that lie between the arachnoid and the inner meningeal layer of the Dura that conforms to and often exert a mass effect on the surface of the brain. It extends across sutural lines but does not cross the falx or the tentorium. An acute SDH may occasionally be biconvex due to adhesions between the brain and the dura mater or when it is thick. The exact thickness of the crescentic SDH should be measured by taking the CT images with a wide window to distinguish the hyperdense clot from bone. Early CT (within 3 h from injury) underestimates the size of the associated parenchymal contusions and the consequent edema. Patients who show subarachnoid hemorrhage on early CT are those at highest risk for evolving contusions. The worst outcomes previously associated with acute SDH may, in many cases, be due to the concomitant presence of contusions in multiple areas of the brain and consequent development of edema. Thus, the use of sequential CT scan should be included in the routine management of head-injured patients. In the younger population, an associated swollen hypointense, ipsilateral hemisphere indicates a very poor prognosis.[8] In patients with acute anemia and hemodilution (during resuscitation from multiple injuries), the acute SDH may appear as isodense to hypodense on CT.[9] A subacute SDH may also be isodense to the brain.

Surgical Management
The aim of surgery is to evacuate the hematoma and any associated underlying lesions to relieve the mass effect and improve the focal neurological deficits. However, if the patient has no brainstem reflexes and is hypotonic with no motor response, surgery may not be useful. The size of the hematoma that should definitely be removed has not been ascertained. Removal of a very thin acute SDH may not be indicated as the clinical deterioration is usually due to associated lesions in this case and is not likely to improve with acute SDH evacuation. Although the current consensus is to have an acute SDH promptly evacuated through a craniectomy in 97% of patients, conservative treatment of a small acute SDH in patients (approximately 3%) with contraindications for surgery has been reported.

No operative therapy should only be considered in patients who are fully conscious, when the extra-axial mass is the single dominant lesion, that is, there are no multiple contusions or potentially significant contralateral mass lesions (which may be preventing midline shift), and when there are no features of mass effect such as a midline shift >3 mm or basal cistern effacement.

In such cases, and especially, if the lesion is <10 mm at its thickest point, conservative therapy may be successful in most instances. The SDH will usually resorb within
1 month although there are occasional instances of chronic SDH formation. Similarly, a deep seated interhemispheric or tentorial SDH in a stable conscious patient may not need surgical evacuation.

The guidelines for selecting patients for conservative management of the SDH include: (1) GCS score ≥13 since injury; (2) absence of other intracranial hematomas or edema on CT scan; (3) midline shift of <10 mm; and (4) absence of basal cistern effacement. Thickness or the associated midline shift beyond which failure of conservative treatment could be predicted.

The recommendations of the TBI Consortium for the surgical management of acute SDH with a thickness >10 mm or a midline shift >5 mm on CT scan should surgically be evacuated, regardless of the patient’s GCS score. All patients with acute SDH in coma (GCS score <9) should undergo intracranial pressure monitoring. A comatose patient (GCS score <9) with an SDH <10 mm thick and a midline shift <5 mm should undergo surgical evacuation of the lesion if the GCS score decreased between the time of injury and hospital admission by 2 or more points on the GCS and/or the patient presents with asymmetric or fixed and dilated pupils and/or the intracranial pressure exceeds 20 mmHg. An increase in hematoma size on CT scan with increasing intracranial pressure and decline in neurological status is also an indication for surgical removal of the lesion. Regarding the timing of surgery, it is recommended that in patients with acute SDH and with indications for surgery, surgical evacuation should be performed as early as possible. If surgical evacuation of an acute SDH is indicated in a comatose patient (GCS <9), it should be performed using a craniectomy with bone flap removal.

RESULTS

The mortality from an acute SDH in all patients shows a wide range (42–90%), in all age groups with GCS between 9 and 12 requiring surgery about 68%, and in comatose patients requiring subsequent surgical evacuation is about 35%. Residual or recurrent hematoma requiring evacuation has been seen in approximately 8% of patients. Occasionally, removal of the mass effect caused by the acute SDH may increase the underlying intracerebral hematoma or contralateral acute or chronic SDH. Post-operative hematomas should be suspected and a post-operative CT obtained in patients who fail to improve or those who deteriorate and in whom the intracranial pressure monitoring shows persistently high intracranial pressures. The post-operative complications following evacuation of an acute SDH may include osteomyelitis, wound infection, meningitis, subdural empyema, abscess formation, and ventriculitis.

DISCUSSION

The Factors Determining Outcome Include

Timing of surgery

Usually, conservative treatment is adopted and surgery deferred in patients with less severe acute SDH, and in better neurological status. Thus, mortality is more whenever timing from injury to surgery increases. In comatose patients, however, there was a significant decrease in mortality and increase in functional recovery in patients who underwent surgery within 4 h of injury as compared to those in whom surgery was delayed beyond 4 h of injury. The mechanism of secondary brain damage is direct compression of the underlying cortex and brain shift that causes local zones of ischemia. If the elevated intracranial pressure is unrelieved, leading to reduced cerebral perfusion pressure, then global ischemic brain damage may occur.

Age

Younger patients have a better outcome than older patients due to less comorbid conditions in the former. There is a significant association between age and functional recovery.

CT parameters

CT parameters include clot thickness, hematoma volume, midline shift and patency of the basal cisterns. Following surgery for acute SDH, found a significant correlation between poor outcome and the volume of SDH and the midline shift and a correlation between outcome and clot thickness and the status of the basal cisterns. There was a significant relationship between midline shift and outcome in patients with GCS scores lower than 9, who were undergoing surgery for SDH. As per our study revealed a 40% mortality rate in patients with clot thickness of <10 mm and 85% mortality for patients with clot thickness >20 mm. Thus, these parameters do seem to influence outcome, but the specific threshold values need to be determined.

The neurological status

This forms the most significant factor in determining outcome. In patients with acute SDH and GCS of 3–5, the mortality was 86% and those with GCS of 9–12 had mortality of 18% and moderate to good outcome in 63% of patients. Pupillary asymmetry correlates with a poorer outcome. In bilateral pupillary abnormalities, the mortality is over 85%; in unilaterally dilated but reactive pupils, the mortality reported is approximately 50%, and in unilaterally dilated non-reactive pupils, the mortality reported is approximately 58%. Decerebrate posturing, flaccid patients (mortality 77–95%), and patients with hemiparesis and hemiplegic (mortality 35–48%) also have a poorer prognosis as compared to intact patients.
**Intracranial pressure**
Persistently elevated (> 20 mmHg) post-operative intracranial pressure is associated with a poor prognosis.

**Associated lesions**
An associated intracerebral hematoma or contusion did not influence mortality, but the functional outcome was significantly better in patients without contusions. Associated diffuse axonal injury significantly influences outcome. Acute SDH based on their associated lesions are classified into simple acute SDH without brain injury (mortality: 22%), acute SDH with contusion (mortality: 40%), and complicated acute SDH (with parenchymal laceration, intracerebral hemorrhage, or burst temporal lobes; mortality: 53%).

**Comorbid conditions**
Lung injury, meningitis, shock, long bone fractures, and abdominal injury all influence outcome. According to the TBI, the key issues for further investigation in cases of acute SDH include the influence of medical management versus decompressive craniectomy on the outcome; the impact of the timing of surgery, the pre-operative hypotension and hypoxia on outcome; identification of subgroups that do not benefit from surgery such as older patients with low GCS scores, pupillary abnormalities, and associated intracerebral lesions; and investigating whether operating on all comatose patients regardless of their clot thickness would lead to a better outcome.

Isolated acute SDH, acting as a compressive lesion, is an uncommon clinicopathological entity with the majority of patients having associated focal (contusion/laceration/ intracerebral hematoma) or global (diffuse axonal injury and subarachnoid hemorrhage) involvement or both. Ischemia underlying an acute SDH and hemispheric brain swelling may be superadded and self-perpetuating and may lead to uncontrollable elevations of intracranial pressure with consequent herniation, brainstem compression, and hemorrhage. The molecular cascade initiated by the injury may lead to secondary brain damage.

**CONCLUSION**
The future reduction in morbidity and mortality will depend on the effective prevention, arrest, or reversal of the molecular events that are responsible for the secondary ischemia and cytotoxic edema. Acute SDH should therefore be subclassified as SDH with or without associated parenchymal pathology to shift the focus from the hematoma to the brain injuries and the secondary injuries and would permit better comparison of different therapeutic modalities and better prognostication. About 25% of patients died in hospital, 18% survived with unfavorable outcomes, and 57% had favorable outcomes. In moderate to severe TBI with ASDH patients, with successful early decompressive craniectomy and evacuation of clot and aggressive intensive care management gives high functional status and better outcomes.

**REFERENCES**


Pancytopenia - A Study on Clinical and Etiological Profile at a Tertiary Care Institute

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Abstract

Introduction: Pancytopenia is a common hematological condition of varied etiology; however, only a few studies on pancytopenia from the northern regions of India have been published. Pancytopenia is the deficiency of all three cellular elements of blood, resulting in anemia, leucopenia, and thrombocytopenia. The frequency of underlying pathology causing pancytopenia varies considerably depending on various factors including age, geographic distribution, and genetic disturbances.

Purpose: The purpose of the study was to evaluate the clinical and etiological profile of patients presenting with pancytopenia to a tertiary care hospital of northern India.

Methods: A total of 66 patients were included in this study over a period of 18 months. Basic investigations were performed for each patient including hemoglobin, total leukocyte count, platelet count, and reticulocyte count. Absolute values including packed cell volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration were calculated for every patient.

Results: A total of 66 patients were studied over a period of 18 months including 40 males and 26 females. Male to female ratio was 1.53:1. The most common cause of pancytopenia was megaloblastic anemia (MA) found in 23 patients (34.84%), followed by aplastic anemia in 5 patients (7.57%), undiagnosed cases in 5 patients (7.57%), tuberculosis in 4 patients (6.06%), multiple myeloma and myelodysplastic syndromes in 3 (4.54%) patients each, respectively.

Conclusion: MA is still the most common cause of pancytopenia in our setting. All patients with pancytopenia should be sought for MA as it is a potentially treatable condition.

Key words: Aplastic anemia, Leukemia, Megaloblastic anemia, Multiple myeloma, Pancytopenia

INTRODUCTION

Pancytopenia by itself is not a disease but is the result of various diseases.[1] The presenting symptoms can be due to anemia, leucopenia or, thrombocytopenia leading to fatigue, and dyspnea. Thrombocytopenia can lead to bruising and mucosal bleeding. Leukopenic features are uncommon as the presenting symptom, but during the course of the disease becomes a life-threatening condition.[2] In pancytopenia, all the three formed elements of blood are reduced below the normal range.[3] By definition, hemoglobin <13.5 g/dl in males or 11.5 g/dl in females, the leukocyte count <4 × 10⁹/L and platelet count <150 × 10⁹/L constitute pancytopenia.[4] Peripheral pancytopenia may be a manifestation of a wide variety of diseases which can primarily or secondarily affect the bone marrow. The presenting symptoms are usually attributable to anemia or thrombocytopenia. Red blood corpuscles survive much longer than platelets or neutrophils. Thus, anemia develops slowly (unless there is significant bleeding) and the typical symptoms of tiredness, fatigue, puffiness of face, edema, lassitude, and effort intolerance may not be striking in the initial phase.[5] The platelet count is first to be affected. Mucocutaneous bleeding is typical of thrombocytopenia with petechial hemorrhages in skin and mucous membranes (commonest being epistaxis, hematuria, gastrointestinal bleeding, menorrhagia, and only rarely intracranial bleeding). The presence of spontaneous bleeding with platelet count...
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<20 × 10⁹/l indicates severe marrow failure. Leukopenia is an uncommon initial presentation. Infections usually occur with commensal organisms of the skin or gastrointestinal tract. An early manifestation of neutropenia is often a sore throat or chest or soft tissue infection which typically shows an incomplete response to antibiotics.⁹ The most common clinical manifestations of pancytopenia are usually fever (86.7%), fatigue (76%), dizziness (64%), weight loss (45.3%), anorexia (37.3%), night sweats (28%), pallor (100%), bleeding (38.7%), splenomegaly (48%), hepatomegaly (21.3%), and lymphadenopathy (14.7%).¹⁷ Megaloblastic anemia (MA), hypersplenism (congestive splenomegaly, malaria, and leishmaniasis), aplastic anemia, myelodysplastic syndrome (MDS), subleukemic leukemia’s, tuberculosis, and multiple myeloma are some of the etiologies presenting with pancytopenia. Identifying the etiopathology of pancytopenia is important for a given case for timely treatment of the disease.¹⁸ Bone marrow examination is extremely helpful in evaluation of pancytopenia.¹⁸ Bone marrow examination allows complete assessment of marrow architecture, pattern of distribution of any abnormal infiltrate and the detection of focal bone marrow lesions.¹⁰¹¹ The most common causes leading to pancytopenia on bone marrow examination are aplastic (AA) bone marrow (29.05%), MA (23.64%), hematological malignancies, i.e., acute myeloid leukemia (21.62%), and erythroid hyperplasia (19.6%).¹² The most common symptom among the study patients was easy fatigability (77.21%) followed by fever (54.54%), palpitations (40.90%), anorexia (31.81%), and abdominal pain (27.27%). Hence, most of the patients presented with symptoms of anemia [Table 1]. The most common physical finding was pallor (81.81%), followed by splenomegaly (30.30%), and icterus (25.75%) as depicted in Table 2. The most common cause of pancytopenia was MA (34.84%), followed by aplastic anemia (7.57%), followed by undiagnosed cases of pancytopenia (7.57%), and tuberculosis (6.06%) as depicted in Table 3.

MATERIALS AND METHODS

A total of 66 patients were identified over a period of 18 months (March 2016–September 2017) and were included in this study. In all patients, a detailed relevant history including the treatment history, history of drug intake, and any previous radiation exposure was obtained. Meticulous clinical examination of every patient was done for pallor, jaundice, hepatomegaly, splenomegaly, sternal tenderness, and lymphadenopathy. Basic investigations were performed for each patient including hemoglobin, total leukocyte count, platelet count, and reticulocyte count. Absolute values including packed cell volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration were calculated for every patient. Chest radiography and abdominal ultrasonography were done in selected patients. Peripheral smear examination, and bone marrow examination was done in all patients, and wherever required, a trephine biopsy was also performed.

Inclusion Criteria

Patients with age >18 years, hemoglobin of <11.5 g per dl in women, and <13.5 g per dl in men, white blood cell count <4000 cells/cubic mm, and platelet count <1,50,000/cubic mm were included in this study.

Exclusion Criteria

Patients with a known hematological condition or patients on cancer chemotherapy and patients <18 years were excluded from the study.

Statistical Analysis

Data analysis was done with the use of IBM SPSS, version 21. Descriptive statistics were used to calculate the range, mean, and percentage.

RESULTS

This study was conducted on 66 patients admitted to the inpatient general medicine ward of a tertiary care institute presenting with pancytopenia and fulfilling the inclusion criteria. The most common symptom among the study patients was easy fatigability (77.21%) followed by fever (54.54%), palpitations (40.90%), anorexia (31.81%), and abdominal pain (27.27%). Hence, most of the patients presented with symptoms of anemia [Table 1]. The most common physical finding was pallor (81.81%), followed by splenomegaly (30.30%), and icterus (25.75%) as depicted in Table 2. The most common cause of pancytopenia was MA (34.84%), followed by aplastic anemia (7.57%), followed by undiagnosed cases of pancytopenia (7.57%), and tuberculosis (6.06%) as depicted in Table 3.

DISCUSSION

There are varying reports on the underlying aetiology of pancytopenia from various parts of the world. The frequency of pattern of disease causing them varies in different population groups and this has been attributed to differences in methodology and stringency of diagnostic criteria, geographical area, genetic differences, nutritional status, prevalence of infection and varying exposure to myelotoxic drugs among others.¹⁸ Khunger et al¹⁴ in a study of 200 cases reported MA in 72% and aplastic anemia in 14% of cases. Savage et al. in Zimbabwe studied 134 patients identifying MA to be the most common cause of pancytopenia followed by aplastic anemia and acute leukemia. Vitamin B₁₂ deficiency was recorded as the most frequent cause of pancytopenia in the young adults. It is commonly diagnosed as MDS, because nuclear maturation abnormalities, dysplasia and megaloblastic changes are observed in all the three series during the evaluation of bone marrow smears. MDS can be distinguished with elevated blood lactic dehydrogenase and recovery of pancytopenia in first 2 weeks after Vitamin B₁₂ substitution.¹³ Common
clinical presentations in our study patients were pallor, fever, petechial hemorrhages, and organomegaly. Khan and Hasan showed 81% cases with pallor followed by fever and bleeding manifestation\(^{[13]}\) as the most common presentations in their study. Naseem \textit{et al.} showed fever (65.5%) was the most common presentation followed by pallor and hepatomegaly.\(^{[14]}\)

A total of 66 pancytopenia patients were studied in our study. Males outnumbered females, with 60.06% males and 39.39% females. Male to female ratio in the study was 1.53:1. The age of the patients ranged from 25 to 80 years. Most of cases were within the age group of 40 to 60 years, comprising a total of 47 patients. The most common presenting symptom was easy fatigability (77.27%), followed by fever (54.54%) and palpitations (40.9%). Clinical examination showed pallor in 81.81% of patients, splenomegaly in 30.30% of patients, icterus in 25.75% of patients, and hepatomegaly in 24.24% of patients, respectively.

MA was the most common cause of pancytopenia in the present study, accounting for 34.84% of total patients followed by aplastic anemia in 7.57% of total patients, whereas tuberculosis, multiple myeloma, chronic liver disease, lymphoma, and infections (malaria and dengue) accounted for the rare causes. Dahake \textit{et al.}, in their study, found MA in 34% of cases.\(^{[15]}\) Similar results were found in studies by Khodke \textit{et al.} and Manzoor \textit{et al.}, where the incidence of MA was found to be at 44% and 56%, respectively.\(^{[16,17]}\) In another study by Kim \textit{et al.} that evaluated the etiology of pancytopenia with 77 patients’ bone marrow biopsies in India, MA was reported to be the most common cause (68%), whereas aplastic anemia (7.7%), MDS, and hemophagocytic syndrome, respectively, were rare causes.\(^{[18]}\) Jha \textit{et al.} found 23.64% and Bhatnagar \textit{et al.} found 28.4% cases of MA in their studies.\(^{[12,19]}\) In the study conducted by Bhatnagar \textit{et al.}, the most common symptoms were weakness (97.8%), and breathlessness (75%), and signs were pallor (98.3%) and splenomegaly (25.5%). Bone marrow aspiration revealed most common cause of pancytopenia was megaloblastic anemia (25%) followed by dimorphic anemia (17.2%) and infections (17.2%).\(^{[19]}\)

### Table 1: Symptoms of pancytopenia and their distribution among the study patients

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Number of patients</th>
<th>% age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Easy fatigability</td>
<td>51</td>
<td>77.27</td>
</tr>
<tr>
<td>Fever</td>
<td>36</td>
<td>54.54</td>
</tr>
<tr>
<td>Pallor</td>
<td>27</td>
<td>40.90</td>
</tr>
<tr>
<td>Anorexia</td>
<td>21</td>
<td>31.81</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>18</td>
<td>27.27</td>
</tr>
<tr>
<td>Weight loss</td>
<td>16</td>
<td>24.24</td>
</tr>
<tr>
<td>Bony pains</td>
<td>11</td>
<td>16.67</td>
</tr>
<tr>
<td>Vomiting</td>
<td>09</td>
<td>13.63</td>
</tr>
<tr>
<td>Cough</td>
<td>05</td>
<td>7.51</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>04</td>
<td>6.06</td>
</tr>
</tbody>
</table>

Data are expressed as numbers (%); % age=percentage

### Table 2: Signs of pancytopenia and their distribution among the study patients

<table>
<thead>
<tr>
<th>Signs</th>
<th>Number of patients</th>
<th>% age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pallor</td>
<td>54</td>
<td>81.81</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>20</td>
<td>30.30</td>
</tr>
<tr>
<td>Icterus</td>
<td>17</td>
<td>25.75</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>16</td>
<td>24.24</td>
</tr>
<tr>
<td>Petechiae</td>
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<td>22.27</td>
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<tr>
<td>Lymphadenopathy</td>
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<tr>
<td>Ascites</td>
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<td>15.15</td>
</tr>
<tr>
<td>Glossitis</td>
<td>08</td>
<td>12.12</td>
</tr>
<tr>
<td>Edema</td>
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<td>9.09</td>
</tr>
<tr>
<td>Heart Murmur</td>
<td>04</td>
<td>6.06</td>
</tr>
</tbody>
</table>

Data are expressed as numbers (%); % age=percentage

### Table 3: Etiological profile among the study patients with gender distribution

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Males</th>
<th>Females</th>
<th>Total number of study patients</th>
<th>% age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Megaloblastic anemia</td>
<td>14</td>
<td>09</td>
<td>23</td>
<td>34.84</td>
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<tr>
<td>Aplastic anemia</td>
<td>03</td>
<td>02</td>
<td>05</td>
<td>7.57</td>
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<tr>
<td>Undiagnosed</td>
<td>03</td>
<td>02</td>
<td>05</td>
<td>7.57</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>02</td>
<td>02</td>
<td>04</td>
<td>6.06</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>02</td>
<td>01</td>
<td>03</td>
<td>4.54</td>
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<tr>
<td>Myelodysplastic syndromes</td>
<td>02</td>
<td>01</td>
<td>03</td>
<td>4.54</td>
</tr>
<tr>
<td>Acute leukemia</td>
<td>02</td>
<td>01</td>
<td>03</td>
<td>4.54</td>
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<td>CLD</td>
<td>02</td>
<td>01</td>
<td>03</td>
<td>4.54</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>02</td>
<td>01</td>
<td>03</td>
<td>4.54</td>
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<tr>
<td>Drug-induced</td>
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<td>01</td>
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<td>Malaria</td>
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<td>02</td>
<td>3.03</td>
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<td>Connective tissue disorder</td>
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<td>HIV</td>
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<td>01</td>
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<td>3.03</td>
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<tr>
<td>Myelofibrosis</td>
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<td>02</td>
<td>3.03</td>
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<td>Hypersplenism</td>
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<td>3.03</td>
</tr>
<tr>
<td>Dengue</td>
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</tr>
<tr>
<td>Septicemia</td>
<td>01</td>
<td>00</td>
<td>01</td>
<td>1.51</td>
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Data are expressed as numbers (%); % age=Percentage; CLD: Chronic liver disease, HIV: Human immunodeficiency virus

### CONCLUSION

MA is still the most common cause of pancytopenia in our setting. All patients with pancytopenia should be sought for MA as it is a potentially treatable condition. The finding of hypersegmented neutrophils in the peripheral smear will guide the diagnosis. In Indian scenario, while evaluating etiology of pancytopenia, MA should always be kept in mind and it responds well to treatment. Pancytopenia should be evaluated aggressively as a significant number of patients have malignant condition in which early and aggressive treatment is warranted. Peripheral smear and bone marrow examination would help in identifying the etiology of pancytopenia in almost all patients. Bone marrow examination is necessary in the evaluation of patients with pancytopenia.
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How to cite this article: Ahmad N, Akhter N, Ahmad T. Pancytopenia - A Study on Clinical and Etiological Profile at a Tertiary Care Institute. Int J Sci Stud 2018;6(1):33-36.

Source of Support: Nil, Conflict of Interest: None declared.
Female Urethral Reconstruction Using Dorsal Vaginal Graft: A Single-center Study

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Abstract

Introduction: Female urethral stricture (FUS) is a relatively rare condition but can cause bothersome lower urinary tract symptoms (LUTS). The common causes may include idiopathic, trauma, iatrogenic injury, infection, malignancy, and radiation. Here, we present our single-center experience of treating FUS with dorsal onlay vaginal graft in nine patients.

Materials and Methods: A retrospective review was performed on nine female patients with midurethral stricture who underwent dorsal onlay vaginal graft urethroplasty from January 2015 to January 2018. Six patients had a history of multiple Hegar dilations and three underwent internal urethrotomies previously. All patients underwent pre-operative evaluation including detailed history, physical examination, complete blood count, routine urine, serum creatinine, uroflowmetry, ultrasound sonography (USG) abdomen and pelvis, and micturating cystourethrogram.

Results: Site of stricture was midurethra in all the nine patients. Mean pre-operative versus post-operative Q_max was 5 mL/s versus 22.33 mL/s, and mean residual urine was 186.66 mL versus 18.88 mL. Irritative voiding symptoms were present in two patients, which subsided after a week. None of the patients reported incontinence during follow-up.

Conclusion: Dorsal onlay vaginal graft urethroplasty is a simple and more effective technique than repeated painful dilatations and urethrotomy. Further study with more patients and longer follow-up is required to establish the success of this procedure.

Key words: Dorsal onlay, Female urethral stricture, Vaginal graft

INTRODUCTION

Female urethral stricture (FUS) is a relatively rare condition but can cause bothersome lower urinary tract symptoms (LUTS). It has been estimated that BOO accounts for between 2.7% and 8% of women with LUTS.¹⁻⁴ In those women with known BOO, FUS accounts for between 4% and 18% of these cases.⁵⁻⁶ Symptoms of FUS may be variable, but often include hesitancy, poor flow, frequency, urgency, and dysuria and may lead to recurrent urinary tract infection and overt urinary retention. No strict diagnostic criteria have been documented for FUS because of its rare incidence. However, Defreitas et al. stated that a detrusor pressure (Pdet) of 25 cm of H₂O and maximum urinary flow rate (Q_max) of <12 mL/s is consistent with obstruction.⁶ The common causes of FUS may include idiopathic, trauma, iatrogenic injury, infection, malignancy, and radiation.⁷ Urethral dilation is a commonly performed procedure in women despite lack of proven efficacy. Moreover, this procedure is used for a variety of voiding complaints other than stricture. The long-term utility of dilation and urethrotomy for urethral stricture in women is unknown. Surgery is often the answer in such cases in the form of meatoplasty for distal urethral strictures and grafts or flaps for mid- and proximal-urethral stricture.

Here, we present our single-center experience of treating FUS with dorsal onlay vaginal graft in nine patients.

MATERIALS AND METHODS

A retrospective review was performed on nine female patients with midurethral stricture who underwent dorsal...
onlay vaginal graft urethroplasty from January 2015 to June 2017. Full informed consent was taken from all the patients. The following diagnostic criteria were applied for patient selection: (1) A maximum urinary flow rate of <10 mL/s, (2) inability to calibrate urethra with 10 Fr Nelaton catheter, and (3) narrowing of urethra with proximal dilatation on micturating cystourethrogram (Figure 1). All patients underwent pre-operative evaluation including detailed history, physical examination, complete blood count, routine urine, serum creatinine, uroflowmetry, USG abdomen and pelvis, and micturating cystourethrogram. Of nine patients, six presented with obstructive voiding and feeling of incomplete bladder evacuation, two patients presented with frequency and urgency as their main complain, and one had recurrent urinary tract infection. Six patients had a history of multiple Hegar dilatations and three underwent internal urethrotomies previously. Idiopathic stricture was most common etiology and only one had multiple transurethral resections for bladder tumor. All patients had normal serum creatinine value preoperatively. None of the patients had pre-operative urinary incontinence.

Operative Description

The patient is prepared in the modified dorsal lithotomy position under either general or regional anesthesia. The vagina is prepared in the manner for traditional transvaginal surgery. Cystoscopy is done with 6 Fr ureteroscope to see the stricture area and assess its length from bladder neck. Normal saline mixed with 1% adrenaline is injected in periurethral tissues. Urethra is dissected dorsally and laterally from 3 to 9’ O clock position by an inverted U-shaped incision. A full-thickness urethrotomy extending from proximal to distal healthy area is made over the stricture site at 12’ O clock position. Urethra is calibrated with 18 Fr catheter. From the inner aspect of one labium minora, a thin free skin flap was prepared (Figure 2). The vaginal graft (Figure 3) is then sutured on the dorsal surface of urethra as onlay graft with 4–0 vicryl suture in interrupted fashion (Figure 4). First suture is taken at the apex of urethra and then on to the graft and tied. Then, suturing of the right and left margin of urethra is done with vaginal graft and urethra is sutured back to its normal position with 4–0 vicryl suture. Continence was evaluated by a stress test with a full bladder. Mean hospital
stay was 4 days. After 14 days, patient is again called for voiding cystourethrogramy and catheter removal. Our follow-up protocol includes every 3 monthly assessment of voiding and storage LUTS, uroflowmetry, and 1 weekly self-calibration.

RESULTS

Site of stricture was midurethra in all the nine patients. Mean age of patients was 48.11 (39–57 years). Mean pre-operative versus post-operative Qmax was 5 mL/s versus 22.33 mL/s, and mean residual urine was 186.66 mL versus 18.88 mL. Mean stricture length was 1.4cm. Mean operative time was 105 min → mean duration of follow-up was 8 months. Patients did not report any significant post-operative pain or discharge suggestive of wound infection. At first follow-up at 3 weeks after surgery, micturating cystourethrogram showed a normal urethra without any proximal dilatation. On uroflowmetry, normal voiding was achieved. Irritative voiding symptoms were present in two patients, which subsided after a week. On urodynamic investigation, all patients had an unobstructed nomogram with Qmax more than 12 mL/s and detrusor pressure at Qmax <20 cm H2O. After 6 months, the patients were well, minimal residual urine, and cosmetic results were satisfactory. None of the patients reported incontinence during follow-up based on patient–physician interview.

DISCUSSION

FUS is usually a subject of disregard. Its actual incidence as opposed to the rate of female urethral dilatation has been contrasted by Santucci et al. They noted that although urethral dilatation is practiced rather frequently in the clinic, it is of no therapeutic value with patients plagued with strictly irritative voiding symptoms in the absence of confirmed urethral stricture disease. The exact incidence of FUS disease is unknown with <100 cases having been reported in the contemporary literature. It is primarily treated with repeated urethral dilatations and internal urethrotomy. Many women not undergoing surgery but treated with chronic interval urethral dilatations and internal urethrotomies will have high recurrences and may result in increased scarring and fibrosis. As in males, urethral stricture disease in females can cause voiding and storage LUTS, recurrent urinary tract infections, and renal impairment. Stricture is commonly located in mid and distal urethra. Surgical treatment of FUS disease has not been adequately addressed in literature.

The present procedure is safe, simple, and effective. It can be performed in spinal anesthesia. The dorsal approach for vaginal graft has the advantage of strong mechanical support and vascular bed provided by clitoral: Cavernosal tissue and physiological voiding (urinary stream away from vagina). Besides, ventral aspect of urethra is spared for future anti-incontinence surgery. Montorsi et al. described vestibular flap urethroplasty in 17 patients. However, this procedure could not be used in cases of vaginal fibrosis. Tanello et al. reported the use of a pedicle flap from the labia minora for the repair of FUS in two patients. Berglund et al. presented the technique of ventral onlay buccal mucosal graft urethroplasty for recurrent urethral stricture disease 30 months of follow-up. After surgery, one of the two patients developed a recurrence of LUTS because of meatal stenosis. Swender et al. used the technique of anterior vaginal mucosal flap in eight patients with complete cure in seven patients after a single procedure who previously underwent multiple dilatations. Simonato et al. presented a series of six patients who underwent vaginal inlay flap urethroplasty inspired by Orandi technique with good results.

This procedure of dorsal onlay vaginal graft seems to be an effective way to treat FUS. It may be done in cases of mid- and proximal-urethral stricture. It seems that the operative concept of the dorsal vaginal onlay graft could be tested in a larger series with a long-term follow-up, and compared with other urethroplasty techniques to further evaluate benefits and pitfalls.

CONCLUSION

Dorsal onlay vaginal graft urethroplasty is a simple and more effective technique than repeated painful dilatations and urethrotomy. Further study with more patients and longer follow-up is required to establish the success of this procedure.

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Source of Support: Nil, Conflict of Interest: None declared.
Evaluation of Results of Locking Compression Plate in Distal Femur Fractures

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INTRODUCTION

Distal femur fractures account for an estimated 6% of all femur fractures. The annual incidence of distal femur fractures is around 37/1,00,000 people.[1] Two different mechanisms are responsible for such trauma, where high energy trauma is seen commonly in young adults and low energy or trivial trauma in osteoporotic population. The treatment of these fractures has evolved over the past 50 years from closed treatment to open reduction and internal fixation with locked plating.

In the 1990s, it became well established that an internal fixation construct with flexibility leads to secondary bone healing. The method of plating using minimal invasive technique also preserved fragment vascularity and primary bone grafting was not required.[2]

The goal of surgical management of these fractures is anatomic reduction, maintaining the articular congruity and restoring limb alignment and early mobilization.[3] There are different surgical options available: Antegrade nailing, retrograde nailing, blade-plate fixation, isolated screw fixation, locked plating, and as a part of damage

Abstract

Aim of Study: The aim of this study is to treat distal femur fractures with locking compression plate (LCP) in 30 cases and to evaluate their functional and radiological outcome.

Materials and Methods: The present study was conducted in the Department of Orthopedics Surgery of SRMS-IMS, Bareilly, from November 2015 to July 2017. A total of 30 cases with 22 males and 8 females, fulfilling the inclusion criteria, with distal femur fractures were treated surgically with distal femoral-LCP using a direct lateral approach. 4.5 mm LCP, either of titanium or stainless steel, was used. All surgeries were done in supine position with a knee bolster under the affected limb and a tourniquet was used in all cases. Manual traction was used to reduce the fracture. Post-operatively, Oxford Knee Score was used to assess the functional outcome.

Results: At 6 months’ final follow-up, 10 patients (33.33%) achieved range of motion between 120 and 140°, 17 cases (56.67%) achieved a read-only memory between 100 and 120°. 23 out of 30 cases (72.67%) showed a radiological union at 3 months’ follow-up. 7 cases (23.33%) had radiological union at 6 months (24 weeks) of follow-up. In the present study, 56.67% of cases that is 17 of 30 cases had Oxford Knee Score of more than 41, 12 cases that is 40% had a score between 34 and 40, and only 1 had score between 27 and 33. In the present study, 17 cases, i.e., 56.67% showed excellent functional outcome, while 12 cases showed good and 1 case had fair outcome.

Conclusion: LCP in distal femoral fractures promotes early radiological union, good knee range of motion, decreased the post-operative hospital stay, with lesser infection rate as there is minimal soft tissue dissection. Finally, it can be concluded that the use of LCP provides good functional and radiological outcome in distal femur fractures.

Key words: Direct lateral approach, Distal femur fracture, Locking compression plate
control orthopedics, external fixator use. The current trend is toward periarticular distal femoral locking plates used as minimally invasive percutaneous plate osteosynthesis (MIPPO) technique, using locking compression plate (LCP).

The LCP was developed to give surgeons the opportunity to combine principles of internal fixation and dynamic compression, depending on the fracture site, as it contains Combi holes. It is a single-beam construct where the strength of its fixation is equal to the sum of all screw bone interfaces rather than a single screw’s axial stiffness or pullout strength as seen in unlocked plates. These plates are anatomically contoured to fit the distal femoral flare, and as they are used by MIPPO technique, they allow prompt healing, lower rate of infection, and reduced bone resorption as blood supply is preserved.

The aim of this study is to evaluate the radiological and functional outcome of distal femoral LCP used in these patients.

**MATERIALS AND METHODS**

The present study was conducted in the Department of Orthopedics of SRMS-IMS, Bareilly, from November 2015 to July 2017, on a total of 30 cases of distal femur fractures treated with LCP, after obtaining approval from the Hospital Ethics Committee. 22 male and 8 female patients were taken in this study.

The patients were initially evaluated in the emergency department according to the ATLS guidelines. Once other injuries were ruled out and a patient was hemodynamically stabilized, and then, the injured limb was immobilized on a Bohler-Braun frame. The patients were then sent to the radiology department and X-ray was taken of the affected limb, thigh with knee in anteroposterior (AP) and lateral views, and the fracture pattern was decided. The fracture was classified according to the AO classification of fractures. All patients above the age of 18 years of either sex with closed or compound fractures up to Grade II or patients with osteoporotic bones were included in this study. Patients with head injury or chest injuries and pathological fractures were excluded from this study. Similarly, patients were medically not fit for surgeries, and patients with Gustilo Type III compound injuries or previously treated fractures were not taken into this study. 4.5 mm LCP was used which has 50° of longitudinal screw angulation and 14° of transverse screw angulation with uniform hole spacing. 4.0 mm and 5.0 mm self-tapping locking screws with 3.2 mm and 4.3 mm drill bits, respectively, along with threaded sleeves are available. Both titanium and SS plates were used according to the patient affordability.

**Surgical Technique**

A patient was taken in supine position on the O.T. Table. Fracture reduction was done under direct vision using manual traction. A knee roll or bolster was placed to assist in procurement and maintenance of reduction. A tourniquet was applied to get a bloodless surgical field. The posterolateral margin of the lateral femoral condyle was palpated. The incision given was 5 cm for MIPPO technique. The vastus lateralis muscle was bluntly dissected from the lateral intermuscular septum. Using the periosteal elevator, the lateral femoral condyle cleared of soft tissue. The plate length and axial and rotational alignment were checked under image intensifier. Provisional use of K-wires was done to build the articular block. Intercondylar type was first converted to single condylar block. The K-wires were placed in such a way that they did not obstruct the part of distal femur where plate had to be fixed. Then, the plate was inserted and they were held in place using K-wires through the slot given for the k-wires to pass. Position of the plate was confirmed in both AP and lateral X-rays under image intensifier. Then, the distal central cancellous screw was placed first and then other screws. Proximal screw insertion was done using minimally invasive technique. Compression screws were used to approximate the plate to the femoral shaft. Tourniquet was removed, and after achieving hemostasis, closure was done in layers and sterile dressing was then applied [Figures 1-7].

Post-operatively, the foot end of the limb was elevated using pillows. Antibiotics and analgesics were given according to the hospital protocol. Knee mobilization was started the next post-operative day. Stitch removal was done on the 14th post-operative day in all cases. The patient was kept non-weight bearing for 10–12 weeks.

Follow-up was taken at 2 weeks, 6 weeks, 12 weeks, and 6 months to assess the functional and radiological outcome. Radiological outcome was checked using X-rays in AP and lateral views. Oxford Knee Score was used to assess the functional outcome. It is a questionnaire consisting of 12 questions assessing the functional status of the patient.

**Figure 1: Intraoperative photographs showing the incision taken for MIPPO plating and estimation of length of the plate to be used**
Distal femur fractures due to road traffic accidents made the bulk of this study, while only 2 cases were due to trivial fall at home. AO classification has been used in this study to classify the fracture pattern, which helped in deciding the fracture pattern. Distal femur is numbered 33 according to AO group. It is further divided into 3 types: Type A - extraarticular fracture, Type B - partial articular fracture, and Type C - intraarticular fractures, each class is then further divided into 3 types. In this study, there were 12 cases belonging to Type 33A, 2 cases in Type 33B, and 16 cases belonging to Type 33C, which made the maximum number of cases in this study.

The duration between injury and surgery time ranged from 2 to 11 days with an average interval of 4.3 days. Majority of the cases, that is, 60%, were operated within the first 5 days of the injury. Cases that showed a delay were due to either late hospital presentation or because the patient had other associated injuries. Some cases had massive swelling and surgery was postponed until skin showed signs of wrinkling.

The main mode of injury was high-velocity trauma and so the patient also had associated injuries. Patella fractures were seen in 4 cases, tibia fracture in 2 cases, proximal femur in 1 case, and vertebral fractures in 1 case.

The period of hospital stay varied from 7 days to 14 days. The average post-operative hospital stay was 10.9 days. 22 cases had a hospital stay of 10 days.

The radiological union time was assessed by getting X-rays on the follow-up visits. 23 of 30 cases (72.67%) showed a radiological union at 3 months’ follow-up. 7 cases (23.33%) had radiological union at 6 months (24 weeks) of follow-up. The mean knee range of motion was 113.8°, with two patients showing 10° of extension loss. Flexion of at least 110° was considered satisfactory, and 2 cases had unsatisfactory knee range of motion.

RESULTS

The present study consisted of a total of 30 patients with an average age of 44.8 years ranging from 18 to 82 years. The maximum number of cases (27%) was in the age group below 30 years owing to the high-velocity trauma, whereas low-velocity trauma was seen in only 1 case, where the age of the patient was above 70 years. Right side was commonly involved than the left. Distal femur fractures due to road traffic accidents made the bulk of this study, while only 2 cases were due to trivial fall at home. AO classification has been used in this study to classify the fracture pattern, which helped in deciding the fracture pattern. Distal femur is numbered 33 according to AO group. It is further divided into 3 types: Type A - extraarticular fracture, Type B - partial articular fracture, and Type C - intraarticular fractures, each class is then further divided into 3 types. In this study, there were 12 cases belonging to Type 33A, 2 cases in Type 33B, and 16 cases belonging to Type 33C, which made the maximum number of cases in this study.

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The mean Oxford Knee Score is 40.6. The Oxford Knee Score is a functional knee score of consisting of 12 questions. Total score is taken as 48. In the present study, 56.67% of cases that is 17 of 30 cases had a score of more than 41, 12 cases that is 40% had a score between 34 and 40, and only 1 had score between 27 and 33. Grading is done according to the score. It is designated as follows: Excellent - more than 41, good - 34–40, fair - 27–33, and poor - <27. In the present study, 17 cases, i.e., 56.67% showed excellent functional outcome, while 12 cases showed good and 1 case had fair outcome. There was no case with a poor functional outcome.

Of a total of 30 cases in the present study, 13 cases had complications. There were no cases of any deep infection, malunion, or skin necrosis. 2 cases had superficial infection, 7 had delayed union, i.e., union seen at 24 weeks of follow-up, 2 had knee stiffness that is 6.67%, and 2 cases had extension lag of 20° and 10°, respectively (6.67%) [Tables 1-3].

**DISCUSSION**

The present study consisted of 30 patients with distal femur fractures who were treated by LCP. The radiological and functional outcome was assessed using Oxford Knee Score.

Distal femur fractures have always shown a bimodal age distribution. High-speed vehicular accidents are responsible for distal femur fractures commonly observed in the young and middle aged. Low energy mechanisms such as fall at home may be responsible for producing fractures of distal femur in elderly osteoporotic population, especially post-menopausal women. Fractures of the distal part of the femur are difficult to treat and present considerable challenges in management. Pain, decreased range of motion, and compromised function of the knee joint are a common problem arising out of articular incongruity and improper fixation of articular fragments in such fractures. A study done by Hoffman et al. did not show any difference for non-union rates or hardware failure between titanium and stainless steel. This result matched to the present study where no cases of non-union were seen and both titanium and stainless steel implants have been used.

Axial stiffness and torsional rigidity of internal fixation are mainly influenced by working length. There is a fine line between flexible fixation, which enhances callus formation and improves the healing process, and a rigid fixation, which leads to non-union and/or implant failure. Short spanning segments concentrate the stress moment and may lead to failure of the construct. A 34% higher load to failure in axial loading for the less invasive stabilizing system (LISS) construct in comparison to the Amgen biosimilar candidate was demonstrated by Kregor et al. In the comparisons of the energy to failure in axial loading, the LISS constructs absorbed almost 2.5 times as much energy as the angled blade plate constructs and more than 5 times as much energy as the intra-medullary nailing constructs before failing.
In a study on biomechanical testing of the LCP by Ahmad M et al.,[7] it was stated by increasing the distance from 2 to 6 mm and both torsional rigidity and axial stiffness decreased by as much as 10–15%. It was found that the increasing distance between the plate and the bone significantly affected the construct stability. It was concluded that LCP behaved in a mechanically similar manner when fixed either flush to the bone or at 2 mm from the bone. However, when the LCP is fixed at a distance of 5 mm from the bone, both axial stiffness and torsional rigidity are decreased significantly. In the present study, majority of the patients (72.67%) showed a radiological union at 12 weeks of follow-up and delayed union seen in 7 cases that is union seen at 24 weeks’ follow-up, which matched the study done by Kanabar et al. of 12.5 weeks. The callus formation was assessed in both lateral and AP radiographs.[8]

The average range of motion in this study was 113.8°, which was similar to the mean read-only memory in other studies mentioned in review of literate. In a study done by Pushkar and Bhan,[9] it was stated that normal knee flexion is 140°. Laubethal et al. have demonstrated that average motion required for: Normal - 93°, sitting - 100°, and squatting - 117°. The functional outcome in this study was assessed using the Oxford Knee Scoring system. The mean score in this study was 40.6. Ganesh et al.[10] in their study of LISS in treatment of distal femur fractures showed 8% good and 92% excellent result using the Oxford Knee Score. In our study, there excellent result was seen in 50% of cases, while 46.67 had good results.

Philips et al.[11] stated that the possible disadvantages of the use of the LISS fixator for distal femoral fractures include reduction difficulties of the metaphyseal-diaphyseal component of the fracture and accurate fixator placement. In addition, its use is technically demanding because fracture reduction and fixation must be obtained and performed simultaneously. In the present study, there were 2 cases of superficial bacterial infection, 7 case of delayed union where radiological union was seen at around 24 weeks, and 2 had extensor lag of 10°.

**CONCLUSION**

From the present study, it was concluded that LCP in distal femoral fractures promotes early radiological union, good knee range of motion, decreased the post-operative hospital stay, with lesser infection rate as there is minimal soft tissue dissection. Maximum of the patients were able to reach near normal joint motion by the end of 6 months and were assessed using Oxford Knee Score.

Finally, it can be concluded that the use of LCP provides good functional and radiological outcome in distal femur fractures.

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How to cite this article: Lal AK, Kaushik SK, Gupta ZU, Agarwal V, Anant S. Evaluation of Results of Locking Compression Plate in Distal Femur Fractures. Int J Sci Stud 2018;6(1):41-46.

Source of Support: Nil, Conflict of Interest: None declared.
Study on Relationship between Waist Circumference and Blood Pressure among School-Going Adolescents

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Abstract

Background: Hypertension is on the raise among schoolchildren. Overweight and obesity, especially in childhood and adolescents, play an important role in the development of insulin resistance, diabetes mellitus, and hypertension. Obesity indicators such as body mass index (BMI), waist circumference (WC), and waist-to-height ratio play an important role in predicting children with high blood pressure (BP).

Aim and Objective: The aim is to study the relationship between WC and BP among school-going adolescents and to examine the utility of WC as an indicator of elevated BP compared to BMI.

Methodology: A total of 1392 school-going children were included in the study. Their height, weight, WC, and BP were recorded. BMI was calculated.

Results: In this cross-sectional study carried out on 1392 adolescents in Madurai, the incidence of pre-hypertension and hypertension was 3.4% and 1.8%, respectively. Nearly 6% were overweight and 3% were obese. About 6.6% of the children had increased WC. Prediction of pre-hypertension and hypertension among children was found to be statistically significant with sensitivity: 90.41%, specificity: 98.03%, ppv: 71.74%, and npv: 99.46%. Prediction of children with high BP by BMI was also found to be statistically significant with sensitivity: 89.04%, specificity: 95%, ppv: 49.62%, and npv: 99.37%.

Conclusion: Obesity indicators such as WC and BMI because of its ease of measurement can be used as a screening tool to identify children with high BP.

Key words: Blood pressure, Body mass index, Waist circumference

INTRODUCTION

“Hypertension, i.e., elevated systolic blood pressure (SBP) and/or diastolic BP (DBP) is now considered to be on the raise among school-going children in recent times.[1-4] In India, it has been noted that children are on the verge of obesity-associated elevated BP.[5] It has been known that BP tracks over time; children with increased values are now at an elevated chance of acquiring hypertension in older age group.”[6]

“BP readings for children require trained doctors to identify and take out the appropriate values. Since this is difficult to be carried out in schools, utilization of anthropometric measures which are being carried at school physical examination is found to be beneficial and early identification of those young children and adolescents who are at the verge of having elevated BP. Usually, waist-to-height ratio (WHtR), body mass index (BMI), and waist circumference (WC) which are used as obesity indicators among adults, children, and adolescents can also be utilized as an indicator of high BP.”[7-11]

WC is considered as a good predictor of central adipose tissue deposition and is noted to be a strong predictor of hypertension in Indian adolescents.[12,13] WC is predictive of such adverse outcomes as abnormal lipid profile and insulin resistance and is a component of pediatric metabolic syndrome.
The National Health and Nutrition Examination Survey (NHANES) has proposed the 90th percentile as the cutoff for identifying central adiposity.\cite{14,15}

**Aim and Objective**
1. To study on the relationship between WC and BP among school-going adolescents
2. To examine the utility of WC as an indicator of elevated BP when compared to BMI.

**Study Design**
This was a cross-sectional observational study.

**Period of Study**
The study duration was 5 months (April 2016–August 2016).

**Study Subject**
Schoolchildren aged 11–17 years, numbering 1392 (50.5% boys and 49.5% girls), formed the study group.

**Inclusion Criteria**
Healthy school-going children aged 11–17 years in Madurai were included in the study.

**Exclusion Criteria**
- Children already diagnosed to have secondary hypertension
- Children having any acute illness
- Present history suggestive of cardiovascular, chronic respiratory, or any
- Other systemic illness
- Children on chronic drugs such as steroids were excluded from the study.

**Ethical Clearance**
It was obtained from the Institutional Ethical Committee.

**Method of Collection of Data**
The details of the students were collected in a pre-structured pro forma. Anthropometric indices of the children such as height, weight, and WC were measured. BP was measured for all children after 5 min of rest in seated position with the right arm supported at the level of the heart.

For children whose BP was above the 90th percentile, reading was repeated twice at 5–10 min interval in the same visit and average BP was recorded. BP consistently between 90 and 95th percentile was considered to be pre-hypertensive. For children whose BP was above the 95th percentile, BP recordings were repeated at weekly intervals twice, and BP reading that was found to be consistently above the 95th percentile was considered as hypertensive. Height for each student was measured, and non-elastic measuring tape fastened to a vertical wall was used. For weight measurement, an electronic weighing scale was used to measure weight. From these values, “BMI was calculated using this formula BMI = weight (kg)/height (m)\(^2\).” WC measurements were performed in accordance with methodology used in the NHANES. WC for the children was measured with the child standing erect using a stretch-resistant tape. The tape was applied horizontally just above the upper lateral border of the right ilium. Each measurement was made at the end of a normal expiration and recorded to the nearest 0.1 cm.

**Statistical Analysis**
For statistical analysis, the data were entered in MS Excel and analyzed using SPSS v20. Qualitative data were summarized as frequencies and percentages. Quantitative data were checked for normality. Normally distributed data were summarized using mean and standard deviation. Median and interquartile range was used for summarizing non-normally distributed data. Association between qualitative variables was tested using Chi-square tests. Difference in distribution of quantitative variables across the two groups was tested using independent \(t\)-test and Mann–Whitney U-test using normal and non-normally distributed variables, respectively. Difference in distribution of quantitative variables across more than two groups was tested using analysis of variance. Statistical significance was interpreted using an arbitrary cutoff of \(P = 0.05\).

**RESULTS AND ANALYSIS**
In this study, a total of 1392 children were screened out of which 50.5% \((n = 703)\) were boys and 49.5% \((n = 689)\) were girls [Tables 1-15].

**DISCUSSION**
This study was done among 1392 school-going adolescents in Madurai with the objective to study the relationship between WC and BP among school-going adolescents and to examine the utility of WC as an indicator of elevated BP when compared to BMI.

From our observational study, it was noted that the incidence of pre-hypertension was noted to be 3.4% \((n = 48)\) and hypertension 1.8% \((n = 35)\). Another study which was conducted by Goel et al. among students in the age group 14–19 years in New Delhi found that 6.4% of adolescents to be among the hypertensive range.\cite{16}

In another study conducted by Jitendra Kumar et al. among school-going adolescents at Karad, Maharashtra, it was noted that 1.89% of the children had elevated BP.\cite{17}
The incidence of overweight in this study was found to be 6.5% ($n = 95$) and that of obesity was found to be 2.9% ($n = 40$). Screening study done in nearby Pondicherry state showed that the prevalence of obesity was 3.8% and that of overweight to be around 7.8%. In the study conducted by Jitendra Kumar et al., it was noted that 10.1% of children had high BMI.

It was noted that among the 1392 children screened, 6.7% of the children had increased WC which indicated the presence of central adiposity. In the study done by Jitendra Kumar et al., 106 out of 951 children (11.14%) were having increased WC.

### Table 1: Profile of study participants

<table>
<thead>
<tr>
<th>Gender distribution</th>
<th>gender</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>Male</td>
<td>703 (50.5)</td>
</tr>
<tr>
<td>Female</td>
<td>Female</td>
<td>689 (49.5)</td>
</tr>
<tr>
<td>Total</td>
<td>Total</td>
<td>1392 (100)</td>
</tr>
</tbody>
</table>

### Table 2: Anthropometry of study participants

<table>
<thead>
<tr>
<th>Anthropometry</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height</td>
<td>153.9±12.36</td>
<td>151.34±10</td>
<td>152.65±11.32</td>
</tr>
<tr>
<td>Weight</td>
<td>41.86±12.13</td>
<td>42.08±8.96</td>
<td>41.97±10.67</td>
</tr>
<tr>
<td>WC</td>
<td>65.84±9.35</td>
<td>66.5±8.65</td>
<td>66.17±9.01</td>
</tr>
<tr>
<td>BMI</td>
<td>17.31±3.21</td>
<td>18.11±2.67</td>
<td>17.71±2.98</td>
</tr>
</tbody>
</table>

### Table 3: Nutritional status of study participants using BMI

<table>
<thead>
<tr>
<th>BMI category</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>1261 (90.6)</td>
</tr>
<tr>
<td>Overweight</td>
<td>91 (6.5)</td>
</tr>
<tr>
<td>Obese</td>
<td>40 (2.9)</td>
</tr>
<tr>
<td>Total</td>
<td>1392 (100)</td>
</tr>
</tbody>
</table>

### Table 5: Age-wise distribution of BMI

<table>
<thead>
<tr>
<th>Age</th>
<th>Measure</th>
<th>Normal</th>
<th>Overweight</th>
<th>Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>n (%)</td>
<td>176 (87.6)</td>
<td>17 (8.5)</td>
<td>8 (4)</td>
</tr>
<tr>
<td>12</td>
<td>n (%)</td>
<td>189 (93.6)</td>
<td>11 (5.4)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>13</td>
<td>n (%)</td>
<td>188 (93.1)</td>
<td>13 (6.4)</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>14</td>
<td>n (%)</td>
<td>151 (87.8)</td>
<td>15 (8.7)</td>
<td>6 (3.5)</td>
</tr>
<tr>
<td>15</td>
<td>n (%)</td>
<td>187 (91.2)</td>
<td>11 (5.4)</td>
<td>7 (3.4)</td>
</tr>
<tr>
<td>16</td>
<td>n (%)</td>
<td>186 (91.2)</td>
<td>13 (6.4)</td>
<td>5 (2.5)</td>
</tr>
<tr>
<td>17</td>
<td>n (%)</td>
<td>184 (89.3)</td>
<td>11 (5.3)</td>
<td>11 (5.3)</td>
</tr>
<tr>
<td>Total</td>
<td>n (%)</td>
<td>1261 (90.6)</td>
<td>91 (6.5)</td>
<td>40 (2.9)</td>
</tr>
</tbody>
</table>

### Table 6: Age-wise distribution of WC in study population

<table>
<thead>
<tr>
<th>Age</th>
<th>Measure</th>
<th>&lt;70th percentile</th>
<th>70–90th percentile</th>
<th>&gt;90th percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>n (%)</td>
<td>184 (91.5)</td>
<td>12 (6.0)</td>
<td>5 (2.5)</td>
</tr>
<tr>
<td>12</td>
<td>n (%)</td>
<td>190 (94.1)</td>
<td>11 (5.4)</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>13</td>
<td>n (%)</td>
<td>191 (94.6)</td>
<td>10 (5.0)</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>14</td>
<td>n (%)</td>
<td>159 (92.4)</td>
<td>9 (5.2)</td>
<td>4 (2.3)</td>
</tr>
<tr>
<td>15</td>
<td>n (%)</td>
<td>193 (94.1)</td>
<td>5 (2.4)</td>
<td>7 (3.4)</td>
</tr>
<tr>
<td>16</td>
<td>n (%)</td>
<td>191 (93.6)</td>
<td>8 (3.9)</td>
<td>5 (2.5)</td>
</tr>
<tr>
<td>17</td>
<td>n (%)</td>
<td>192 (93.4)</td>
<td>7 (4.5)</td>
<td>7 (2.1)</td>
</tr>
<tr>
<td>Total</td>
<td>n (%)</td>
<td>13000 (93.4)</td>
<td>62 (4.5)</td>
<td>30 (2.1)</td>
</tr>
</tbody>
</table>

### Table 7: Mean and SD of WC in study population

<table>
<thead>
<tr>
<th>Age</th>
<th>WC</th>
<th>n</th>
<th>Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>201</td>
<td>63.27±8.44</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>202</td>
<td>63.62±8.42</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>202</td>
<td>67.90±8.37</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>172</td>
<td>68.20±9.91</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>205</td>
<td>65.45±8.47</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>204</td>
<td>66.68±9.01</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>206</td>
<td>68.32±9.14</td>
<td></td>
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</tbody>
</table>

### Table 8: Age-wise distribution of BP

<table>
<thead>
<tr>
<th>Age</th>
<th>Normal</th>
<th>Pre-hypertension</th>
<th>Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>189</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>12</td>
<td>195</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>13</td>
<td>192</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>14</td>
<td>164</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>15</td>
<td>191</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>16</td>
<td>194</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>17</td>
<td>194</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>1319</td>
<td>48</td>
<td>25</td>
</tr>
</tbody>
</table>

### Table 9: BP distribution

<table>
<thead>
<tr>
<th>BP percentile</th>
<th>No of children (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal&lt;90</td>
<td>1319 (94.8)</td>
</tr>
<tr>
<td>Pre-hypertension 90–95</td>
<td>48 (3.4)</td>
</tr>
<tr>
<td>Hypertension&gt;95</td>
<td>25 (1.8)</td>
</tr>
<tr>
<td>Total</td>
<td>1392 (100)</td>
</tr>
</tbody>
</table>

WC: Waist circumference, BMI: Body mass index

SD: Standard deviation, WC: Waist circumference

BP: Blood pressure
In this study, it was found that the prediction of prehypertension and hypertension by WC and BMI was found to be statistically significant. When WC was used to predict prehypertension and hypertension, it was found that the sensitivity: 90.41%, specificity: 98.03%, ppv: 71.74%, and npv: 99.46%.

When BMI was used as a parameter to predict hypertension, it was noted that sensitivity: 89.04%, specificity: 95%, ppv: 49.62%, and npv: 99.37%. It was also significant. The prediction of detecting hypertension was found to be higher when WC was used as an indicator when compared to BMI.

In study conducted by Bahl et al.,\textsuperscript{[18]} it was noted that the prevalence of hypertension among overweight participants (BMI >85 percentile) was 13.2% and among obese participants (BMI >95 percentile) was 18.75% which was found to be statistically significant. Moreover, there was a statistically significant correlation noted between WC and BMI with both SBP and DBP in their study.

In study conducted by Mishra et al.,\textsuperscript{[19]} it was noted that high obesity indicators were associated with elevated BP. Their results showed statistically similar AUCs for BMI and WC and WHtR in detecting risk of high BP.

| Table 10: Association between SBP and BMI among study participants |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| BMI             | Normal          | Pre-hypertension | Hypertension    |“P” value        |
| Normal          | 1254 (99.4)     | 7 (0.6)          | 0               | <0.001          |
| Overweight      | 56 (61.5)       | 28 (30.8)        | 7 (7.7)         |                |
| Obese           | 10 (25)         | 12 (30)          | 18 (45)         |                |
| SBP: Systolic blood pressure, BMI: Body mass index |

| Table 11: Association between DBP and BMI among study participants |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| BMI             | Normal          | Pre-hypertension | Hypertension    |“P” value        |
| Normal          | 1259 (99.8)     | 2 (0.2)          | 0               | <0.0001         |
| Overweight      | 66 (72.5)       | 22 (24.2)        | 2 (3.3)         |                |
| Obese           | 17 (42.5)       | 14 (35)          | 9 (22.5)        |                |
| DBP: Diastolic blood pressure, BMI: Body mass index |

| Table 12: Association between SBP and WC |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| WC              | Normal          | Pre-hypertension | Hypertension    |“P” value        |
| <70 percentile  | 1294 (99.5)     | 5 (0.4)          | 1 (0.1)         | <0.0001         |
| 70–90 percentile| 22 (35.5)       | 36 (58.1)        | 4 (6.5)         |                |
| >90 percentile  | 4 (13.3)        | 6 (20)           | 20 (66.7)       |                |
| SBP: Systolic blood pressure, WC: Waist circumference |

| Table 13: Association between DBP and WC |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| WC              | Normal          | Pre-hypertension | Hypertension    |“P” value        |
| <70 percentile  | 1298 (99.8)     | 2 (0.2)          | 0               | <0.0001         |
| 70–90 percentile| 36 (58.1)       | 25 (40.3)        | 1 (1.6)         |                |
| >90 percentile  | 8 (26.7)        | 1 (36.7)         | 11 (36.7)       |                |
| DBP: Diastolic blood pressure, WC: Waist circumference |

| Table 14: Correlation between SBP, WC, and BMI |
|----------------|----------------|----------------|----------------|----------------|
| Parameter      | Total BP correlation coefficient, P value | BP male correlation coefficient, P value | BP female correlation coefficient, P value |
| BMI            | 0.563, <0.0001  | 0.562, <0.0001  | 0.544, <0.001   |
| WC             | 0.578, <0.0001  | 0.578, <0.0001  | 0.543, <0.0001  |
| SBP: Systolic blood pressure, WC: Waist circumference, BMI: Body mass index |

| Table 15: Correlation between DBP, WC, and BMI |
|----------------|----------------|----------------|----------------|----------------|
| Parameter      | Total BP correlation coefficient, P value | BP male correlation coefficient, P value | BP female correlation coefficient, P value |
| BMI            | 0.201, <0.0001  | 0.201, <0.0001  | 0.122, <0.001   |
| WC             | 0.187, <0.0001  | 0.25, <0.0001   | 0.098, <0.010   |
| DBP: Diastolic blood pressure, WC: Waist circumference, BMI: Body mass index, BP: Blood pressure |
indicating similar discriminatory ability for all three obesity indicators.

CONCLUSION

1. The incidence of hypertension among school-going adolescents in Madurai was found to be 1.8%
2. The incidence of obesity among the adolescents was found to be 2.9%
3. There was a strong correlation noted between increased WC and BMI with high BP among adolescents
4. Prediction for hypertension by WC was found to be higher compared to BMI in this study
5. Family history of hypertension had no relationship to predict high BP in children in this study.

REFERENCES


How to cite this article: Murugalatha P, Guna P. Study on Relationship between Waist Circumference and Blood Pressure among School-Going Adolescents. Int J Sci Stud 2018;6(1):47-51.

Source of Support: Nil, Conflict of Interest: None declared.
Comparative Study between Use of Interlock Nailing and Dynamic Compression Plate for the Management of Diaphyseal Fracture of Humerus

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²Professor and Head, Department of Orthopedics Surgery, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh, India,
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Abstract

Introduction: Fractures of the humeral shaft are commonly encountered by the orthopedic surgeons. This study compares the functional outcome and radiological union in diaphyseal fractures of shaft humerus by intramedullary interlock nailing versus dynamic compression plate fixation.

Methods: This study was conducted during the period between November 2015 and July 2017 on 30 patients having diaphyseal fractures shaft humerus with a minimum follow-up of 6 months. Of these, 15 cases in Group A underwent dynamic compression plating and 15 cases in Group B underwent interlock nailing. Interlock nailing was done by antegrade approach, and plating was done either by anterolateral or posterior approach. Patients were assessed functionally by the American Shoulder and Elbow Surgeons (ASES) score and Rodriguez–Merchan criteria and radiologically by union time.

Result: At 6 months' follow-up, we found that the mean ASES score in Group A was 45.07 with standard deviation (SD) of 2.28 and in Group B was 44 with SD of 2.54. \(^P\) value was not statistically significant \((P > 0.05)\). According to Rodriguez–Merchan criteria, the difference between the two groups was also not statistically significant \((P < 0.05)\). Patients in interlock nailing group had shorter operative time and hospital stay, and there was no statistically significant difference in terms of time of the union of fractures. Both the groups had one case (6.66%) of superficial infection at the surgical site. There were one case (6.66%) in Group A and 3 cases (20%) in Group B who developed shoulder stiffness post-operatively.

Conclusion: Internal fixation with dynamic compression plate may result in a better fracture reduction but has increased risk radial nerve lesion and infection. Intramedullary interlock nailing is an effective alternative to dynamic compression plating as it has comparable results in terms of functional score, union time, and complications. No single treatment is superior in all circumstances for a particular fracture, and each case has to be individualized.

Key words: Compression Plate, Fracture, Humerus

INTRODUCTION

Fractures of the humeral shaft are commonly encountered by the orthopedic surgeons. According to Mast et al. (1975) and Varley (1995), the diaphysis or shaft can be defined as that part of the humerus situated between the superior margin of pectoralis major tendon insertion and 2 cm above the olecranon fossa.¹

The causes in younger patients are commonly represented by high-energy trauma (car accident or sports injury), while in older patients by lower energy trauma (such as an accidental fall), but they are often associated with osteoporosis.

The goals of humeral shaft fracture management are to establish union with acceptable humeral alignment and restore patients to their prior level of function. Many methods have been described for the management of humeral shaft fractures. Good-to-excellent results have been reported in most series of humeral shaft fractures.
treated by closed or with open reduction and internal fixation. Both patient and fracture characteristics, associated injuries, soft tissue status, and fracture pattern need to be considered to select appropriate treatment.

Fractures of the shaft of humerus have been treated conservatively by reduction and subsequent immobilization of the arm, and successful healing occurs in 90% of cases. The methods include the hanging cast, functional brace, Velpeau dressing, and shoulder spica cast.

Many options were available to treat fractures conservatively, but taking into consideration pitfalls of it, an era of fixation was evolved, the aim of which was early restoration of joint motion and return to normal physiological function and minimal morbidity.

While there are several methods of operative intervention for diaphyseal fractures of humerus, the internal fixation methods can be broadly grouped as plating or intramedullary nailing techniques. Interlocking nailing is preferable in comminuted, segmental, and pathological fractures while plating may be the preferred option where radial nerve exploration is contemplated infection, and nonunion and radial nerve palsy are general concerns suggested in the plating group.

Selecting the right implant for internal fixations remains a controversy, so we want to conduct a prospective, comparative study for the management of diaphyseal fractures of the humerus to find the ideal mode of surgical management with their functional outcome.

**MATERIALS AND METHODS**

The present study was conducted in the Department of Orthopedics Surgery of SRMS-IMS, Bareilly, from November 2015 to July 2017 on 30 patients, 15 each group having diaphyseal fractures and shaft humerus, after obtaining approval from hospital ethics committee.

**Inclusion Criteria**

The following criteria were included in the study:
1. Age of the patient more than 18 years
2. Patient presenting within 2 weeks of injury
3. All closed type of displaced diaphyseal fractures of the humerus
4. Patients with Grades 1 and 2 open diaphyseal fractures of humerus presenting within 8 h of injury.

**Exclusion Criteria**

The following criteria were excluded from the study:
1. Age of the patient <18 years
2. Pathological fractures
3. Grade 3 compound diaphyseal fractures of humerus
4. Fractures within 4 cm from proximal and distal end of humerus
5. Neglected diaphyseal fractures of humerus

All protocols and procedures applied in this study were as per the Guidelines of Ethics Committee of this institution.

**Technique**

The antegrade approach was taken for humeral interlock nailing to minimize soft tissue damage to rotator cuff. Incision was made diagonally from the anterolateral corner of the acromion, splitting the deltoid in line with its fibers in the raphe between the anterior and middle-thirds of the deltoid. Using a curved bone awl, an entry portal was made just medial to the tip of greater tuberosity approximately 0.5 cm posterior to bicipital groove. The guidewire was inserted after fracture reduction and proximal reaming was done. The nail was inserted with jig, and after confirming, reduction on X-ray proximal and distal locking of screws was done.

- In the dynamic compression plate group, the anterolateral approach was used for upper-shaft and middle-shaft fractures. Posterior approach with intraoperative identification and protection of the radial nerve was performed for distal one-third shaft fractures. The length of the plate was dependent on the pattern of fracture, comminution, and at the discretion of the surgeon. Intravenous antibiotics were started immediately after the surgery for 2 days after which patient was put on oral antibiotics for next 5 days.
- Post-operatively, the limb was placed in an arm sling and pendulum and elbow movements were allowed on the 2nd post-operative day, as tolerated by the patient, but resistance and rotational motion were allowed only when callus formation was observed in the radiography. The patient was checked for pre- as well as post-operative radial nerve palsy.

The patient was followed up at 2 weeks for suture removal, 6 weeks, 3 months, and 6 months. Radiological outcome on the basis of callus formation and functional outcome on the basis of Rodriguez–Merchan criteria and the American Shoulder and Elbow Surgeons (ASES) score were assessed at final follow-up [Tables 1-3 and Figures 1-10].

**The ASES Scoring System of Upper Limb Function Scoring**

- 4 = Normal
- 3 = Mild compromise
- 2 = With difficulty
- 1 = With aid
- 0 = Unable.
Singh, et al.: Management of Diaphyseal Fracture of Humerus

Criteria
• Reaching back pocket
• Wash opposite axilla
• Comb hair
• Carry 10 pounds weight on side
• Sleep on affected side
• Use hand overhead
• Lift weights
• Perineal care
•Eat with utensil
• Use arm at shoulder level

Figure 1: (a) Nail insertion. (b) Dynamic compression plate

Figure 2: Case 1 - (a) Pre-operative X-ray. (b) Immediate pre-operative X-ray

Figure 3: Case 1 - 12 weeks post-operative X-ray

Figure 4: (a) Abduction at shoulder joint. (b) Extension at shoulder joint

Figure 5: (a) Internal rotation at shoulder joint. (b) Extension at elbow joint

Figure 6: (a) Case 2 - Pre-operative X-ray. (b) Immediate pre-operative X-ray
OBSERVATIONS AND RESULTS

The mean age of patients in our study was 37.2 years with standard deviation (SD) of 16.95 and males outnumbered females.

Mode of injury by road traffic accident (RTA) was the major cause of diaphyseal fracture of humerus (80%) followed by fall on the ground (16.66%). Most of the patients, 27 cases, (93.33%) had AO Type 12A fracture. There were 3 (7%) cases of AO Type 12B fracture and no cases of AO Type 12C fracture. The mean operative time in Group A was 48.87 min with SD of 5.29 min and in Group B was 36.93 min with SD of 4.68 min, which is significantly shorter.

The mean hospital stay in Group A was 9.92 days with SD of 3.34 which is longer than Group B, 7.60 days with SD of 2.75. The \( P \) value between the two groups was statistically significant \( (P < 0.05) \).

The mean union time in Group A was 12.84 weeks with SD of 3.20 and in Group B was 13.71 weeks with SD of 4.36. The \( P \) value was not statistically significant between the two groups \( (P > 0.5) \).

Majority of cases in Groups A and B had <5° of extension lag and more than 130° of flexion and Group B. In Group A, number of patients who had least loss of range of motion at elbow joint were comparatively lower. Majority of cases in Groups A and B had none or <10% restriction of movement at shoulder joint. In Group B, number of patients with more than 10% restriction of movements at shoulder joint were comparatively higher. In our study, no statistically significant difference was present in terms of pain between the two groups.

Both the groups had 1 case (6.66%) of superficial infection at the surgical site. In both groups, superficial infection gradually improved with antibiotic therapy and daily dressings. There was one case (6.66%) in Group A which developed a deep infection at surgical site post-operatively which healed after second surgery. There was one case (6.66%) in Group A and three cases (20%) in Group B.
who developed shoulder stiffness post-operatively. The $P$ value was statistically significant ($P < 0.05$). There was one case (6.66%) each in both groups which developed elbow stiffness. There was one case (6.66%) of implant failure in Group A where post-operatively at 6th week due to back out of screw patients plating failed. The patient was posted for surgery again, and dynamic compression plating was done, the fracture united after the second surgery. There was one case (6.66%) of radial nerve palsy in Group A which was present pre-operatively. There was one case in Groups A and 2 cases in Group B who had delayed union. There was one case each in both the groups who had non-union of fracture. These patients were posted for a second surgery where bone grafting was done at fracture site post which both the fractures united.

The mean ASES score in Group A was 45.07 with SD of 2.28 which is better than Group B, 44 with SD of 2.54. $P$ value was not statistically significant ($P > 0.05$). According to Rodriguez–Merchan criteria, patients in Group A had higher number of cases in good–to-excellent category than Group B, but this difference was statistically not significant.

### DISCUSSION

The management of diaphyseal fractures of the humerus is always a challenging problem to orthopedic surgeon, as they are very frequently associated with multiple injuries, leading to complications such as shortening, malunion, infection, delayed union, and non-union etc.

The aim of treatment in these fractures is to achieve length and alignment and produce favorable environment for bone and soft tissue healing. Acceptable fracture alignment, which is the guide to continued conservative management, includes 20° of anterior bowing, 30° of varus angulation, 15° of malrotation, and 3 cm of shortening or bayonet apposition.[8]

Conservative treatment has its demerits such as prolonged limb immobilization, the need for constant cooperation, and repeated hospital visits. Second, it cannot be recommended in every case like unstable fractures.

While there are several methods of operative intervention for diaphyseal fractures of the humerus, the internal fixation methods can be broadly grouped as plating or intramedullary nailing techniques. Interlocking nailing is preferable in comminuted, segmental, and pathological fractures, while plating may be the preferred option where radial nerve exploration is contemplated. Infection, non-union, and radial nerve palsy are general concerns suggested in the plating group.

In our study, we found that the maximum numbers of cases 15 (50%) were in the age group of 18–38 years. There were 11 cases (36.66%) in 38–58 years interval and 4 cases (13.33%) who were above 58 years. The mean age of patients was 37.2 years with SD of 16.95. Mulier et al. studied on 55 patients and found that the age of patients ranging between 30 and 40 years was the most common.[9] McCormack et al. in their study of 44 patients
found that such fractures were common in the age group of 35–45 years.\[3\]

In our study, we have found that mode of injury by RTA was the major cause of diaphyseal fracture of humerus 24 cases (80%) followed by fall on ground 5 cases (17%), and 1 case (3%) OUP B, 2 cases (13.33%). There was a single case of assault in Group B, 1 case (3.3%). Mulier et al. recorded that the most common cause to diaphyseal humerus fracture is high-energy trauma such as due to RTA.\[6\]

In our study, we have found that 12 cases (33.33%) were operated in the interval of 3–4 days, 10 cases (20%) were operated in <2 days, 5 cases (26.66%) were operated in 5–6 days interval, and 3 cases (20%) were operated after 7 days interval. The mean between trauma and surgery in our study was 8.63 days with SD of 3.04. In a comparative study done by Mir et al., the mean interval between admissions to surgery was 6.12 days (SD 3.67) in the interlock nailing group and 11.88 days (SD 3.29) in the dynamic compression plating group, and the values were statistically significant (P > 0.05).\[7\] In our study, majority of the cases were operated in <7 days which is comparable to other study.

In our study, fluoroscopy was done in Group B only, and in majority of patients, 13 cases (86.66%) exposure time for fluoroscopy was between 3 and 6 min. Mean fluoroscopic exposure time was 4.3 min with SD of 1.35 min. In a study done by Mir et al. on 50 patients, the mean fluoroscopy time in the interlocking group was 4.6 min, while fluoroscopy was not used in the plating group.\[7\] These findings are comparable to our study.

In our study, we found that in most of the cases, union time in weeks was 12 weeks, 13 cases (92.86%) in Group A and 12 cases (85.71%) in Group B. There was 1 case (7.14%) of delayed union (union at 24 weeks) in Group A and 2 cases (14.28%) in Group B. The mean union time in Group A was 12.84 weeks with SD of 3.20 and in Group B was 13.71 weeks with SD of 4.36. The P value was not statistically significant between the two groups (P > 0.5). A comparative study done by Mulier et al. in their study found the mean time of union to be 16 weeks with a range from 8 weeks to 65 weeks. They found that union time was less in case of plate fixation than nail fixation.\[6\]

In our study, we found that both groups had one case (6.66%) that had superficial infection at the surgical site. In both groups, superficial infection gradually improved with antibiotic therapy and daily dressings. There was one case (6.66%) in Group A which developed deep infection at surgical site post-operatively. The surgical site was opened again in the OT, and dead and infected tissue was debrided; wound was thoroughly washed with saline and closed over drains. Infection was controlled and the fracture healed normally. There was one case (6.66%) in Group A and three cases (20%) in Group B who developed shoulder stiffness post-operatively. The P value was statistically significant (P < 0.05). There was one case (6.66%) each in both groups which developed elbow stiffness. There was one case (6.66%) of implant failure in Group A, where at 6\(^{th}\) week follow-up, there was a failure of plating due to screw back out. The patient was posted for surgery again and dynamic compression plating was done, the fracture united after the second surgery. There was one case (6.66%) of radial nerve palsy in Group A which was present pre-operatively, and the patient recovered completely during the follow-up. There was one case (6.66%) in Group A and two cases (13.33%) in Group B who had delayed union, both fractures united at 24 weeks. There was one case (6.66%) each in both the groups who had non-union of the fracture. These patients were posted for a second surgery where bone grafting was done at fracture site post which both the fractures united.

In our study, we found that ASES functional score at final follow-up was more than 46 in 4 cases (26.66%) of Group A and 2 cases (13.33%) in Group B. This value was statistically significant (P < 0.05). There were 9 cases (60%) in Group A and 10 cases (66.66%) in Group B whose ASES score was in interval between 44 and 46. There was one case (6.66%) in both groups who had their ASES score in the interval between 41 and 43. There was one case (6.66%) in Group A and two cases (13.33%) in Group B who had their ASES score below 40. The mean ASES score in Group A was 45.07 with SD of 2.28 and in Group B was 44 with SD of 2.54. The P value was not statistically significant (P > 0.05). A study done by Changulani et al. found that mean ASES score in patients treated with nailing was 44 and that of patients treated with plate fixation was 45.\[8\]

In our study, we found that according to Rodriguez–Merchan criteria, five cases (33.33%) in Group A and four cases (26.66%) in Group B had excellent rating at final follow-up. There were eight cases (53.33%) each in both the groups who had good rating. There was one case in Group A and two cases in Group B who had fair rating. Mir et al. in their study reported excellent results in 7 (28%), good in 13 (52%), fair in 3 (12%), and poor in 2 patients of interlock group. Results were similar in the Digital Cinema Package with excellent result in 8 (32%), good in 13 (52%), fair in 2, and poor in 2 patients. The final outcome in this series did not show any significant advantage of one method over the other.\[7\]

**CONCLUSION**

Patients in the interlock nailing group had shorter operative time and hospital stay, and there was no statistically significant
difference in terms of time of union of fractures or the functional score between the two. Interlock nailing provides rigid secure fixation along with maintenance of biology which makes it effective alternative to dynamic compression plate. No single treatment is superior in all circumstances for a particular fracture, and each case has to be individualized.

The shortcoming of this study was that there were less number of cases. We recommend more number of randomized studies consisting of larger number of cases in future to be done so that a clear-cut consensus can be reached.

REFERENCES


How to cite this article: Singh S, Gupta S, Kaushik SK. Comparative Study between Use of Interlock Nailing and Dynamic Compression Plate for the Management of Diaphyseal Fracture of Humerus. Int J Sci Stud 2018;6(1):52-58.

Source of Support: Nil, Conflict of Interest: None declared.
A Study of Breakfast Eating Patterns of School Children Between 5 and 9 Years of Age and its Impact on Nutritional Status and School Performance

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Abstract

Introduction: “You are what you eat” an ancient saying that motivates health professionals to be concerned with what people eat especially at the start of the day. A nutritionally adequate breakfast is important for achieving and maintaining physical and mental health.

Aims and Objectives: The aim of the study was to study the breakfast eating patterns and its impact on nutritional status, scholastic performance and the reasons for not taking adequate breakfast.

Materials and Methods: The study was a comparative cross-sectional study done in 1000 children of 5–9 years of age from two urban-based school in Madurai, over a period of 1 year. Breakfast eating patterns and anthropometric measurements were taken and correlated.

Results: In this study, a total of 1000 children (500 – study group and 500 control group) of age 5–9 years were included. The study group showed nutrition adequacy ratio values significantly lower for all essential nutrients. Mean breakfast intake of the study group is significantly lower than that of controls in all age groups. Anthropometric measurements showed the statistically significant difference ($P < 0.05$) between study and control groups in all age groups.

Conclusion: Consumption of breakfast appears to have a positive impact on the nutritional status regardless of age. Skipping breakfast affects physical and mental development and scholastic performance.

Key words: Breakfast eating pattern, Essential nutrients, Nutrition adequacy ratio, Nutritional status, School performance

INTRODUCTION

“You are what you eat” an ancient saying that motivates health professionals to be concerned with what people eat especially at the start of the day. A nutritionally adequate breakfast is important for achieving and maintaining physical and mental health. This is the fact borne out and based on several controlled studies that have been carried out to determine the effect of different breakfast habits on the physiological responses, attitudes, and scholastic achievements of subjects under study.[1]

A link between hunger and a large number of behavior problems exhibited by children such as fighting, stealing, and indiscipline, having problems with teachers, and so on, has been established.

Breakfast consumption made a significant contribution for the child mean daily nutrient intake.[2] Total energy intake of children who skipped breakfast is lower than that of children who consumed breakfast at home or school; energy intake is not increased at other meals to compensate for the deficit. Children who consumed breakfast had a
higher daily intake of vitamin and minerals than children who skipped breakfast.

Skipping breakfast may hinder the growth of children because the body is forced to call on body stores of protein for meeting energy requirements. Skipping breakfast has become the norm in modern India because of lifestyle changes in family life, and when this happens largely among children, it can result in sub-optimal growth and development.\[3\]

During overnight sleep, brain activity except for periods of rapid eye movements slow markedly and regulatory mechanisms allow for a continuous supply of endogenous fuel to maintain cerebral metabolism. When the overnight fast is extended, the gradual decline of insulin and glucose levels among other metabolic changes could determine a stress response that interferes with different aspects of cognitive function.\[4\]

Foods can be placed into five groups depending on the content of major nutrients. They are:
1. Cereals grains and products
2. Pulses and legumes
3. Milk and meat products
4. Fruits and vegetables
5. Fats and sugars.

Growth and physical development of children are widely used as indicators of overall health and nutritional status. Anthropometric measures such as height, weight, weight for height, and skinfold thickness are valuable indicators of nutrient status.

A good diet survey provides information about dietary intake pattern, specific foods consumed, and nutrient intake.

**Aim and Objectives**
1. To study the breakfast eating patterns of school children between 5 and 9 years of age.
2. To study the impact of breakfast eating on nutritional status of children.
3. To study the reasons for taking inadequate breakfast or skipping breakfast.
4. To study the influence of breakfast on the scholastic performance of children.

**MATERIALS AND METHODS**

The study was a comparative cross-sectional study done on 1000 school children age group of 5–9 years from two urban based schools within Madurai city [Table 1]. Children were allocated into two groups - study and control group. The study was done for a period of 1 year. The study was designed to evaluate nutrient intake of children who skipped breakfast compared with children who consumed breakfast and its relationship to the total daily intake and dietary adequacy.

A total of 1000 healthy children were selected randomly (100 children each from I standard–V standard). Breakfast eating habits of subjects were determined through questionnaires designed for children and their parents. 24 h dietary recalls were used to assess dietary intake on any one school day [Table 2]. Anthropometric measurements such as height, weight, weight for height, and skinfold thickness were valuable indicators of nutrient status.

Table 1: Age and sex wise distribution of study group

<table>
<thead>
<tr>
<th>Age</th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>100</td>
<td>70</td>
<td>10</td>
</tr>
<tr>
<td>6</td>
<td>100</td>
<td>61</td>
<td>39</td>
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<td>7</td>
<td>100</td>
<td>53</td>
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</tr>
<tr>
<td>8</td>
<td>100</td>
<td>49</td>
<td>51</td>
</tr>
<tr>
<td>9</td>
<td>100</td>
<td>65</td>
<td>35</td>
</tr>
</tbody>
</table>

Table 2: Breakfast eating habits of children

<table>
<thead>
<tr>
<th>Eating habits</th>
<th>Study group (T-500) n (%)</th>
<th>Control group (T-500) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular breakfast</td>
<td>240 (48)</td>
<td>445 (89)</td>
</tr>
<tr>
<td>Irregular breakfast</td>
<td>170 (34)</td>
<td>40 (8)</td>
</tr>
<tr>
<td>Skipping breakfast</td>
<td>90 (18)</td>
<td>15 (3)</td>
</tr>
</tbody>
</table>

Table 3: Nutrition adequacy ratio of diets of 5–6-year-old boys and girls between study and control groups

<table>
<thead>
<tr>
<th>Nutrients</th>
<th>Study male</th>
<th>Study female</th>
<th>Control male</th>
<th>Control female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy</td>
<td>0.65</td>
<td>0.64</td>
<td>0.83</td>
<td>0.80</td>
</tr>
<tr>
<td>Protein</td>
<td>0.64</td>
<td>0.64</td>
<td>0.81</td>
<td>0.79</td>
</tr>
<tr>
<td>Calcium</td>
<td>0.62</td>
<td>0.59</td>
<td>1.05</td>
<td>1.05</td>
</tr>
<tr>
<td>Iron</td>
<td>0.57</td>
<td>0.59</td>
<td>0.66</td>
<td>0.64</td>
</tr>
<tr>
<td>Beta carotene</td>
<td>0.21</td>
<td>0.21</td>
<td>0.26</td>
<td>0.26</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>0.62</td>
<td>0.61</td>
<td>1.12</td>
<td>1.11</td>
</tr>
<tr>
<td>Thiamin</td>
<td>1.00</td>
<td>0.95</td>
<td>1.96</td>
<td>1.93</td>
</tr>
<tr>
<td>Riboflavin</td>
<td>0.75</td>
<td>0.75</td>
<td>1.05</td>
<td>1.25</td>
</tr>
<tr>
<td>Niacin</td>
<td>0.63</td>
<td>0.62</td>
<td>0.90</td>
<td>0.93</td>
</tr>
</tbody>
</table>

Table 4: Nutrition adequacy ratio of diets of 7–9-year-old boys and girls between study and control groups

<table>
<thead>
<tr>
<th>Nutrients</th>
<th>Study male</th>
<th>Study female</th>
<th>Control male</th>
<th>Control female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy</td>
<td>0.64</td>
<td>0.63</td>
<td>0.77</td>
<td>0.76</td>
</tr>
<tr>
<td>Protein</td>
<td>0.57</td>
<td>0.56</td>
<td>0.83</td>
<td>0.78</td>
</tr>
<tr>
<td>Calcium</td>
<td>0.58</td>
<td>0.58</td>
<td>1.04</td>
<td>1.04</td>
</tr>
<tr>
<td>Iron</td>
<td>0.53</td>
<td>0.50</td>
<td>0.58</td>
<td>0.56</td>
</tr>
<tr>
<td>Beta carotene</td>
<td>0.12</td>
<td>0.11</td>
<td>0.17</td>
<td>0.13</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>0.60</td>
<td>0.57</td>
<td>1.03</td>
<td>1.08</td>
</tr>
<tr>
<td>Thiamin</td>
<td>0.80</td>
<td>1.06</td>
<td>1.23</td>
<td>1.23</td>
</tr>
<tr>
<td>Riboflavin</td>
<td>0.76</td>
<td>0.88</td>
<td>1.13</td>
<td>1.07</td>
</tr>
<tr>
<td>Niacin</td>
<td>0.66</td>
<td>0.66</td>
<td>0.89</td>
<td>0.82</td>
</tr>
</tbody>
</table>
Murugalatha and Ramya: Breakfast Eating Patterns and its Impact on Nutrition and Performance

RESULTS

Cereal based foods such as Idly, Dosai, and Chapathi are preferred by around 80% of breakfast eaters in both study and control group.

Mean daily nutrient intake of 5–9 years old children from the study group is less than that of the control group. Mean breakfast intake of the study group is significantly less than that of the control group in all age groups [Table 3 and 4].

Mean values of anthropometric measurements such as weight, height, and skinfold thickness showed a significant difference between the study and control groups [Table 5-7].

DISCUSSION

Breakfast Eating Habits of Children
Our study revealed that the percentage of children in the study group who consumed breakfast regularly every day was 48% and that of the control group was 89%. According to Prof. Mohini Seth Ph.D., about 50% of the children were on regular breakfast, 34% were on irregular breakfast, and 16% children skipped breakfast. Polus-Szentawiska et al. revealed that 78% of children were on irregular breakfast and 3% of children skipped breakfast.

Among the breakfast eaters, 37% of students said that they enjoy the meal and overall gave the following reason for eating it.
1. Most important meal
2. Prevents headache and stomach ache
3. To gain weight.

| Table 5: Weight measurements of subjects |
| ------------------ |------------------ |------------------ |------------------ |------------------ |
| Age               | Study group       | Control group    | P value           |
|                   | <50th percentile | >50th percentile | <50th percentile | >50th percentile |
| 5                 | 72               | 28               | 45               | 55               | 0.00019 significant |
| 6                 | 53               | 47               | 41               | 59               | 0.0119 significant  |
| 7                 | 57               | 43               | 42               | 58               | 0.04770 significant |
| 8                 | 55               | 45               | 37               | 63               | 0.0158 significant  |
| 9                 | 64               | 36               | 46               | 54               | 0.0156 significant  |

| Table 6: Height measurements of subjects |
| ------------------ |------------------ |------------------ |------------------ |------------------ |
| Age               | Study group       | Control group    | P value           |
|                   | <50th percentile | >50th percentile | <50th percentile | >50th percentile |
| 5                 | 55               | 45               | 33               | 67               | 0.0027 significant  |
| 6                 | 37               | 63               | 11               | 89               | 0.0003 significant  |
| 7                 | 42               | 58               | 31               | 69               | 0.14189 Not significant |
| 8                 | 37               | 63               | 15               | 85               | 0.0007 Significant  |
| 9                 | 41               | 59               | 31               | 69               | 0.1848 Not significant |

| Table 7: Weight for height measurements of subjects |
| ------------------ |------------------ |------------------ |------------------ |------------------ |
| Age               | Study group       | Control group    | P value           |
|                   | <50th percentile | >50th percentile | <50th percentile | >50th percentile |
| 5                 | 72               | 28               | 53               | 47               | 0.00856 significant |
| 6                 | 66               | 34               | 55               | 45               | 0.111804 Not significant |
| 7                 | 72               | 28               | 54               | 46               | 0.0127 significant  |
| 8                 | 72               | 28               | 54               | 46               | 0.0127 significant  |
| 9                 | 72               | 28               | 55               | 44               | 0.0128 significant  |

| Table 8: School performance of subjects |
|---------------------------------------|------------------|------------------|
| Features                              | Study group %    | Control group %  |
| Regular school attendance             | 63               | 72               |
| Regular class test attendance         | 66               | 60               |
| Good class test performance           | 47               | 58               |
| Participation in extracurricular activities | 54               | 65               |

| Table 9: Reasons for missing school |
|------------------------------------|------------------|------------------|
| Features                           | Study group %    | Control group %  |
| Repeated sickness                   | 60.9             | 46.7             |
| Fear of test                        | 8.7              | 2.2              |

as weight, height, weight for height, and skinfold thickness were used to assess their nutritional status.
The perception of subjects parents with respect to breakfast eating were recorded, and it was found that:
1. 48% believed that eating this meal leads to better thinking and work efficiency.
2. 23% said that it keeps the child active throughout the day.
3. 19% reported no complaints about headache or stomach ache.
4. 10% felt that it was the most nutritious meal of the day.

Nutritional Intake of Children
In our study, children from control group showed deficient intake of iron and beta-carotene, whereas children from study group had distinctly lower values than the control group. In the case of iron and beta-carotene, both the groups are found to be short of the recommended values for their age. This is attributed to the lower intake of green leafy vegetables in the diet and low bioavailability of iron from cereal-based foods. Except for Vitamin B, the diet of the study population in all age groups fell short of the RDA for all nutrients in contrast to those of the control group.

Nutrient Adequacy Ratio
An NAR value of 0.66 reflects adequate intake of particular nutrient. NAR was calculated by dividing daily intake of a particular nutrient with RDA of the same. In our study, the study group showed values lower for all essential nutrients, energy, and protein reflecting inadequate nutrient intake.

Nutrients from Breakfast
According to Lowa breakfast studies\[6], a basic breakfast is the one which provides one-fourth of the total daily requirement of energy and protein. Mean breakfast intake of both the study and the control groups was calculated and presented in tables.

Anthropometry
Growth and physical development of children are widely used as indicators of overall health and nutritional status. Anthropometric measurements of subjects were recorded with respect to weight, height, and triceps skinfold thickness and compared with the percentiles of NCHS standards.

The relationship between weights at birth to the present weight was found to be significant. Birth weight of both the study and control groups was recorded from parents. Although all the subjects showed incremental growth pattern and were born with normal birth weight, the study group subjects failed to reach the desired weight gain. This can be partly attributed to the omission of breakfast.

Regarding height, about 77.8% children in the control group were above the 50th percentile in all the age groups whereas in the study group it was about 57.6%. Low height gain in Indian children may be partly due to genetic factors and partly to the fact that their diet is predominantly cereal based and rich in phytates leading to poor bioavailability of calcium from them.

Regarding weight for height, which is a sensitive indicator of the current nutritional status of children and independent of age, about 43% of children from the control group were above the 50th percentile in contrast to the study group where it was 29.2% in all age groups.

School Performance
Many studies conducted abroad underlined the importance of breakfast on the school performance of children.\[7-10\] In the present study, school performance was judged using the attendance, class test performance, and participation in extracurricular activities of the subjects [Table 8 and 9]. This study revealed that, children from study group had lower school attendance and lesser scholastic performance than the control group.

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Echocardiographic Changes in Overt and Subclinical Primary Hypothyroidism

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Abstract

Background and Objectives: Thyroid hormone is an important regulator of cardiac function and cardiovascular hemodynamics. The aim of this study was to assess the cardiovascular functions in primary overt and subclinical hypothyroid patients and to determine if there was a correlation between severity of disease and echocardiographic changes.

Methodology: A cross-sectional study was conducted in the Endocrinology Clinic of Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai. The study sample was grouped into mild, moderate, severe, and subclinical hypothyroid groups which were then compared by echocardiographic findings.

Results: A total of 84 patients were seen, from June 2013 to September 2013. Abnormal left ventricle posterior wall (LVPW) thickness and abnormal interventricular septal wall (IVSW) thickness were more frequently noted in those with clinical hypothyroidism (moderate and severe) as compared to those with subclinical hypothyroidism. Abnormal septal wall thickness was noted in 9 (69.23%) of moderately hypothyroid and 18 (72%) of severely hypothyroid patients, whereas this finding was noted in only 5 (16.66%) of the subclinical hypothyroid patients indicating significant differences between the groups. Diastolic dysfunction was also significantly more frequent in the moderate and severe hypothyroid group. On statistical analysis by one-way analysis of variance, it was found that LVPW (mm), IVSW (mm), and E/A ratio were significantly associated with the severity of hypothyroidism, while ejection fraction, fractional shortening, and LV internal diameter were not significantly different between groups.

Conclusions: The completely reversible nature of these cardiac complications being well known, this study aims at reassessing the need for early recognition, and more aggressive management aims at preventing the aforementioned complications.

Key words: Echocardiography, Hypothyroidism, Pericardial effusion, Septal wall thickness

INTRODUCTION

Cardiac involvement in myxedema has been well known for a long time.¹ The cardiovascular findings of hypothyroidism are, however, more subtle. The cardiovascular system (CVS) manifestations of hypothyroidism include the following: (a) Reduced total intravascular volume, (b) reduced contractility, (c) reduced heart rate, (d) raised systemic vascular resistance (increased diastolic blood pressure), and (e) raised capillary permeability (pericardial effusion), and the thyroid hormone is an important regulator of cardiac function and cardiovascular hemodynamics.² In hyperthyroidism, cardiac contractility and cardiac output are enhanced, and systemic vascular resistance is decreased, while in hypothyroidism, the opposite is true. Other changes observed in hypothyroid individuals include alteration in lipid profile values with increased cholesterol and low-density lipoproteins and electrocardiogram (ECG) changes such as bradycardia and low-voltage complexes.³ Triiodothyronine (T3) mediates the expression of cardiac genes, inducing transcription of alpha-myosin heavy chain (MHC) and the sarcoplasmic reticulum calcium ATPase and negatively regulating expression of beta-MHC and phospholamban.⁴ Santos et al. first reported reversible cardiomyopathy, manifested by asymmetric septal hypertrophy in untreated hypothyroid patients.⁵ This finding was also described in children.⁶ The increased thickness of interventricular septum (IVS)
and left ventricular posterior wall (LVPW) thickness were observed in untreated patients with hypothyroidism, and there is a correlation between severity of disease cardiac findings.\(^6\) In the same study, such findings are also reported to be dependent on advancing age. It has also been postulated that long-standing hypothyroidism leads to reversible cardiomyopathy, manifested by both asymmetric septal hypertrophy and features of hypertrophic obstructive cardiomyopathy.\(^5\) Pericardial effusion is seen in hypothyroidism, and this also appears to be dependent on the severity of the disease.\(^8\) The cardiac changes noted in overt primary hypothyroidism are also observable in patients with subclinical hypothyroidism.\(^9\) Patients with subclinical hypothyroidism thus manifest many of the same cardiovascular changes but to a lesser degree than that which occurs in overt hypothyroidism. Subclinical hypothyroidism may thus be a potentially modifiable risk factor for cardiovascular disease and mortality.\(^{10,11}\)

**Aim**

This study was aimed to increase the understanding of cardiovascular changes in hypothyroidism in the Indian population to enable prevention, early diagnosis, and prompt intervention in both overt clinical and asymptomatic subclinical hypothyroidism.

**METHODOLOGY**

The study design was a cross-sectional and it was conducted in the Endocrinology Clinic, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai, from June 2013 to September 2013. The study was approved by the Institutional Ethics Committee. A total of 84 patients with newly diagnosed drug naïve hypothyroidism were selected, of which 80 patients who fit the inclusion criteria of age >18 years of age, with subclinical hypothyroidism thyroid-stimulating hormone (TSH) >5.5 mIU/ml with normal FT4 and FT3), or overt hypothyroidism were included. The clinically hypothyroid group was divided into three categories according to the level of TSH as follows: (i) Mild hypothyroidism (<20 m IU/ml), (ii) moderate hypothyroidism (20–50 m IU/ml), and (iii) severe hypothyroidism (>50 m IU/ml). 4 patients were excluded for various reasons (age <18 years, with known primary cardiac disease, and who were taking drugs that alter the cardiovascular functions such as amiodarone, beta blockers, and calcium channels blockers).

A detailed questionnaire was used to elicit the symptoms of hypothyroidism. The patients were examined for signs of hypothyroidism, especially the examination of CVS. All the patients were evaluated for following parameters: Pulse rate, blood pressure, ECG, and echocardiography (chamber dimensions, diastolic function, systolic function, wall motion abnormalities and pericardial effusion, LVPW thickness, and interventricular septal wall (IVSW) thickness). For categorical variables, Chi-square tests, and for continuous variables, analysis of variance (ANOVA) were used. \(P < 0.05\) were considered statistically significant. The data were analyzed using the Statistical Package for the Social Sciences (SPSS).

**RESULTS**

Among the 80 patients included in our study, subclinical hypothyroid patients were the largest group with 30 patients (38%), followed by severe hypothyroidism with 25 cases (31%), moderate hypothyroidism with 13 cases (16%), and mild hypothyroidism with 12 cases (15%). The mean TSH in the mild hypothyroid group was 11.32 m IU/L, while among the moderate hypothyroid group, it was 33.43 m IU/L. The severe hypothyroid group had a mean TSH of 107.58 m IU/L.

Diastolic dysfunction was found in 1 (8.33%) patient in the mild hypothyroid group and in 2 (15.38%) of the moderately hypothyroid group. 9 (36%) patients of the severely hypothyroid group had diastolic dysfunction. In the subclinical hypothyroid group, the same was noted in 3 (10%) patients. This difference was not statistically significant.

On statistical analysis by one-way ANOVA it was found that LVPW thickness was significantly associated with the severity of hypothyroidism [Table 1]. Similarly, IVSW was also associated with severity of hypothyroidism [Table 2]. While ejection fraction (EF) %, fractional shortening (FS) %, and ventricular internal diameter (D) cm were not significantly associated, E/A was significantly associated with the severity of hypothyroidism [Table 3].

A multiple regression analysis was done with the dependent variable as IVSW thickness and LVPW thickness independently entering the significant items, including age and TSH as variable; it was found that only TSH continued to be statistically significant [Table 4].

Pericardial effusion was observed in 1 (8.33%) of the mild hypothyroid patients and also in 4 (30.76%) patients of the moderately hypothyroid group. 10 (40%) of the severely hypothyroid had the same. No pericardial thickening or constrictive physiology was made out [Table 5].

**DISCUSSION**

In this study conducted in Indian population, we evaluated the cardiovascular function in newly detected primary overt...
**Table 1: LVPW thickness**

<table>
<thead>
<tr>
<th>Nature of hypothyroidism</th>
<th>Ventricular thickness</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal (6–9 mm)</td>
<td>Abnormal (&gt;9 mm)</td>
</tr>
<tr>
<td>Subclinical (n=30)</td>
<td>28</td>
<td>2</td>
</tr>
<tr>
<td>Clinical (n=50)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Moderate</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Severe</td>
<td>7</td>
<td>18</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>25</td>
</tr>
</tbody>
</table>

LVPW: Left ventricle posterior wall

**Table 2: Interventricular septal thickness**

<table>
<thead>
<tr>
<th>Nature of hypothyroidism</th>
<th>IVS thickness</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal (6–9 mm)</td>
<td>Abnormal (&gt;9 mm)</td>
</tr>
<tr>
<td>Sub-clinical (n=30)</td>
<td>25</td>
<td>5</td>
</tr>
<tr>
<td>Clinical (n=50)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>Moderate</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>Severe</td>
<td>7</td>
<td>18</td>
</tr>
<tr>
<td>Total</td>
<td>22</td>
<td>28</td>
</tr>
</tbody>
</table>

IVS: Interventricular septum

**Table 3: Comparison of the means of echo parameters**

<table>
<thead>
<tr>
<th>Mean echo value</th>
<th>Severity of hypothyroidism</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Subclinical</td>
<td>Mild</td>
</tr>
<tr>
<td>LVPW (mm)</td>
<td>8.49</td>
<td>8.74</td>
</tr>
<tr>
<td>IVSW (mm)</td>
<td>8.74</td>
<td>8.75</td>
</tr>
<tr>
<td>LVID (D) cm</td>
<td>4.44</td>
<td>4.50</td>
</tr>
<tr>
<td>EF (%)</td>
<td>62</td>
<td>63.08</td>
</tr>
<tr>
<td>FS (%)</td>
<td>36.06</td>
<td>37.41</td>
</tr>
<tr>
<td>E/A</td>
<td>1.50</td>
<td>1.69</td>
</tr>
</tbody>
</table>

LVPW: Left ventricle posterior wall, IVSW: Interventricular septal wall, LVID: Left ventricular inner dimension, EF: Ejection fraction, FS: Fractional shortening

and subclinical hypothyroidism. Among the 80 patients included in our study, subclinical hypothyroid patients (38%) comprised the largest group. This indicates the need for efficient screening programs to identify this condition.

The prevalence of abnormal LVPW thickness increased as the severity of hypothyroidism increased. A significant association was found between the occurrence of increased LVPW thickness and the severity of disease. A similar relationship was also demonstrated for abnormal IVSW thickness. On comparing the occurrence of increased septal wall thickness with increasing severity of disease, it was found to be statistically significant. Rawat and Satyal in their study showed relatively increased thickness of IVS and LVPW when compared to the treated patients or control subjects.[7] However, on age group analysis, it was found that this difference was more marked in older patients. In our study, however, we found that although there was a trend of increasing wall thickness with age these changes on multiple regression analysis with the dependent variable as IVSW thickness and LVPW thickness including age and TSH as variable, it was found that only TSH continued to be significant.

The cardiac chamber size was found to have a statistically insignificant association with hypothyroidism. This shows that the cardiac chamber size is not affected by hypothyroidism. Similar observations were also made by others (Verma et al., 1996).[13] The LV systolic functions as measured by EF and FS were not statistically associated with the severity of hypothyroidism. No wall motion abnormalities or global hypokinesia was detected. In the study by Jagdish et al., although FS and EF showed increase, it was statistically not significant.[15] Rawat and Satyal also showed no significant change in parameters of systolic function.[7]

In our study, diastolic dysfunction was found in 1 (8.33%) patient in the mild hypothyroid group, 2 (15.38%) of the moderately hypothyroid group, 9 (36%) patients of the severely hypothyroid group, and 3(10%) patients of the subclinical hypothyroid group which was significant. Similar findings of diastolic dysfunction were made by Biondi and Cooper, indicating an early diastolic dysfunction.[14] Pericardial effusion was observed to be more frequent in the severe and moderate group, but the difference between groups was not statistically significant perhaps because of the smaller sample size and prevalence of the finding. No pericardial thickening or constrictive physiology was made out unlike previous studies.[8]

The study was done on a sample of patients in the outpatient department. This makes the results of the study less generalizable to the overall population of hypothyroid patients. The sample size of 80 was relatively small to detect fine associations, especially in the presence of multiple confounding variables. The cross-sectional nature of the study makes it possible that the conclusions made may be unstable or that they may be reflective of a phenomenon particular to one phase of illness. The follow-up of the patients after replacement of thyroxine was not done due to several reasons. If done, it could have highlighted more on the reversibility of the cardiovascular changes.

**CONCLUSION**

Increased IVSW and LVPW thicknesses along with diastolic dysfunction are some of the cardiac features of thyroid hypofunction. The subtle impairment of LV diastolic function even in subclinical hypothyroidism patients as shown in our study may justify the use of hormone replacement even without overt symptoms. An early diagnostic approach in patients with hypothyroidism will
The extent of cardiac complication which accompanies it. Echocardiography is a useful non-invasive tool in assessing the response to replacement therapy.

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**How to cite this article:** Preethi JJ, Vasudevan HS. Echocardiographic Changes in Overt and Subclinical Primary Hypothyroidism. Int J Sci Stud 2018;6(1):63-66.

**Source of Support:** Nil, Conflict of Interest: None declared.
Study of Different Modalities of Management in Patients with Liver Abscess in a Tertiary Care Centre

Jawansing Manza, Hardik Makwana, Mukesh Pancholi, Nimesh Verma

Abstract

Introduction: Management of liver abscess was exclusively surgical in the past. Modern treatment has shifted toward broad-spectrum antibiotics and imaging-guided percutaneous needle aspiration or percutaneous catheter drainage. This retrospective study has been carried out to evaluate etiology of liver abscess and compare effectiveness of different modalities of treatment.

Methods: This is a retrospective observational study of patients of liver abscess treated during the period of March 1, 2014, to March 1, 2015, at New Civil Hospital, Surat. They were treated by different mode of intervention. All patients underwent clinical follow-up and monitoring during daily rounds until they were discharged from the hospital. Follow-up sonography was performed 24 h after intervention and repeated every 3 days in 1st week, and the size of the abscess was recorded. Criteria for successful treatment were clinical subsidence of infection and sonographic evidence of abscess resolution.

Results: A total of 73 cases of liver abscess were studied at New Civil Hospital, Surat, during the period. It is more commonly seen in adulthood with highest incidence in 3rd–5th decade. The most common presenting symptoms are pain and fever. Tenderness is present in most of patients, whereas signs of jaundice, ascites, and shock are rare. Liver abscess is seen frequently in alcoholic patients. Most of the patients with liver abscess are anemic and with elevated total white blood cell count and increased serum alkaline phosphate. <16% have abnormal chest X-ray with pleural effusion being the most common. Most often right lobe is involved in pyogenic liver abscess. Of 73 cases, 3 cases (4.1%) show at least one of the complications. Rupture of abscess occurred in 2 patients (2.71%) into pleural cavity who were treated by intercostal drainage and in 1 (1.36%) patient into peritoneal cavity treated with exploratory laparotomy with drainage of pyoperitoneum.

Conclusion: Liver abscesses continue to be an important cause of morbidity and mortality in the tropical countries. Percutaneous drainage with systemic antibiotics has become the preferred treatment for the management of pyogenic liver abscesses. In contrast, for amebic abscesses, the primary mode of treatment is medical. Surgical drainage is now used only in cases which fail to respond to percutaneous drainage.

Key words: Amebic liver abscess, Liver abscess, Percutaneous catheter drainage, Pyogenic liver abscess
The advantage of ultrasonography (USG) over computed tomography (CT) scan is that sonography is a real-time imaging technique that allows monitoring of the course of the needles and catheters as they traverse tissues. While CT scan-guided aspiration is usually associated with longer procedure times, because it is necessary to scan the region of interest every time for confirmation of catheter.

Continuous catheter drainage is widely accepted and in combination with antibiotics is considered a safe and effective method of management of liver abscess. Some authors prefer repeated needle aspiration, considering it as effective and safe as PCD but easy to perform, less complicated, less risky for post-procedure septicemia, and less expensive. This approach requires careful follow-up and often repeated imaging procedures to monitor response to therapy.

This retrospective study has been carried out to evaluate etiology of liver abscess and compare effectiveness of different modalities of treatment.[9]

MATERIALS AND METHODS

This is a retrospective observational study of patients of liver abscess treated at New Civil Hospital, Surat.

Inclusion Criteria
Patient admitted to new civil hospital with confirmed diagnosis of liver abscess from March 1, 2014 to March 1, 2015.

Exclusion Criteria
No exclusion criteria.

Subjects
All patients with confirmed diagnosis of liver abscess who were admitted in NCH, Surat, from March 1, 2014, to March 1, 2015, were considered as study participants. A patient was treated by various modes of intervention. Initially, patients were treated with intravenous antibiotic treatment with Inj. Amikacin 10 mg/kg 12 h, Inj. Ceftriaxone 15 mg/kg 12 h, and Inj. Metronidazole 15 mg/kg 8 h.

PNA
Percutaneous treatment was performed within 24 h after admission in case of liquefied abscess. In case of partially liquefied abscess initially 3 days intravenous antibiotics given and reassessed with follow-up USG, if suggesting abscess is liquefied, then percutaneous intervention done otherwise antibiotics continue and again reassessed. The antibiotics therapy was adjusted according to the results of culture and sensitivity test of pus aspirated at the time of the drainage procedure. Patients with negative culture results were continuously treated with a combination of Inj. Ceftriaxone, Inj. Amikacin, and Inj. Metronidazole. The antibiotic regime was changed for patients with poor treatment response. Intravenous antibiotic therapy was continued for a minimum of 7 days. All percutaneous interventions were performed under USG guidance. A sample of pus was routinely taken and sent for microbiological analysis including microscopy, culture, and antibiotic sensitivity tests.

Continuous Catheter Drainage
In drainage technique, an 8–14 French multiple-side-hole pigtail catheter was introduced into the abscess cavity by Seldinger technique. The procedure was performed with local anesthesia with the patient supine or the left lateral position. Careful localization of the abscess and proper selection of the entry site were required. The optimal route of access traversed the least possible amount of liver tissue and avoided bowel and pleura. Aspiration was then performed with the catheter until no more pus could be removed. After that, irrigation done with normal saline and again pus was aspirated, if no more pus could be drain, then catheter was secured to the skin for continuous external drainage and the patient was sent back to the ward. When catheter output had stopped for 24 h, a follow-up sonography was performed. If an abscess cavity was absent, the catheter was removed. If a residual cavity was present, the catheter was flushed with saline and aspirated until the return was clear. Residual loculations of abscess were treated with catheter repositioning and aspiration. Further, sonography was performed 3 days later and the catheter was removed if there is no residual collection. Otherwise, the catheter was left in situ until catheter output had stopped.

Management of Complications
Intercostal drainage (ICD) tube insertion was done under local anesthesia in case of ruptured liver abscess into pleural cavity. Exploratory laparotomy with drainage of pyoperitoneum done in case of rupture liver abscess into peritoneal cavity.

Patient Follow-up and Outcome
All patients underwent clinical follow-up and monitoring during daily rounds until they were discharged from the hospital. Follow-up sonography was performed 24 h after intervention and repeated every 3 days in 1st week and the size of the abscess was recorded. Criteria for successful treatment were clinical subsidence of infection and sonographic evidence of abscess resolution, such as disappearance or marked decrease in the abscess cavity (more than 50% reduction of longest diameter before treatment). Patients discharged with a catheter underwent follow-up sonography until there was no catheter output for 24 h, and then, the catheter was removed. Patient outcomes including length of hospital stay, complications related to the procedure, and treatment failure and death were recorded.
RESULTS

A retrospective study was carried out among 73 confirmed diagnoses of liver abscess cases who were admitted in New Civil Hospital, Surat, enrolled from March 1, 2014 to March 1, 2015. Mean age of study participants was 43.27 ± 13.26 years [Table 1]. Liver abscess is more common in male patients than female, but reasons still unknown. It may be due to addiction of alcohol, tobacco chewing, and smoking in male gender [Table 2]. In this study, all patients are having one of two addiction with 38% patients having both addictions. Liver abscess is seen frequently in alcoholic patients. Association of addiction with liver abscess possibly explains male preponderance of disease. Liver abscess is most common in low socioeconomic status group of patients. 64% patients presented with acute onset of disease. The most common symptoms are pain and fever seen in 64.5% and 64%, respectively. Tenderness is present in most of patients (60%), whereas jaundice, ascites, and shock were present in less number of patients. It is comparable to other studies [Table 3]. Most of the patients with liver abscess are anemic and with elevated total white blood cell count and increased serum alkaline phosphate. <16% have abnormal chest X-ray with pleural effusion being the most common. In this study, the right lobe of liver was affected in 80% of patients. Of 73 cases, we encountered with only complication rupture of liver abscess in 3 cases (4.1%). There were no other complications in any patient. Rupture of abscess occurred in 2 patients (2.71%) into pleural cavity who were treated by ICD drainage and in 1 (1.36%) patient into peritoneal cavity treated with exploratory laparotomy with drainage of pyoperitoneum. In comparison to other study, we encountered this complication in less number of patients [Table 4]. Mean hospital stay was 5.37 days with range of 2–13 days. In the present study, reported 65.5% had been diagnosed as amebic liver abscess and 34.25% had been diagnosed as pyogenic liver abscess. In the present study, out of 48 patients of amebic liver abscess, 7 patients were managed conservatively, 25 patients managed by percutaneous needle drainage (PNA), 15 patients managed by PCD, and 1 patient was managed by exploratory laparotomy. In the present study, out of 25 patients of pyogenic abscess, 1 patient managed conservatively, 20 patients managed by percutaneous needle drainage, and 4 patients managed by PCD [Table 5].

DISCUSSION

Liver abscesses, both amebic and pyogenic, continue to be an important cause of morbidity and mortality in the tropical countries. Patients usually present late when the liver abscess attains a large size. Percutaneous drainage (either needle aspiration or catheter drainage) with systemic antibiotics has become the preferred treatment for the management of liver abscesses. In contrast, for amebic abscesses, the primary mode of treatment is medical; however, as many as 15% of these may be refractory to medical therapy, while 20% may be complicated by secondary bacterial infection. Such amebic abscesses and those involving the left lobe, or those with impending rupture also need to be drained. Surgical drainage is now used only in cases which fail to respond to percutaneous drainage (PCD). Although PCD is a preferred method most widely used to drain liver abscess, surgical drainage is now used only in case which fails to respond to percutaneous drainage.

<table>
<thead>
<tr>
<th>Table 1: Age group-wise distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group (years)</td>
</tr>
<tr>
<td>&lt;40</td>
</tr>
<tr>
<td>40–60</td>
</tr>
<tr>
<td>More than 60</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2: Sex-wise distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name of study</td>
</tr>
<tr>
<td>This study</td>
</tr>
<tr>
<td>Zibari et al., 1996</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 3: Signs and symptoms wise distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms/signs</td>
</tr>
<tr>
<td>---------------------------------------------</td>
</tr>
<tr>
<td>Fever</td>
</tr>
<tr>
<td>Pain</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
</tr>
<tr>
<td>Anorexia/weight loss</td>
</tr>
<tr>
<td>Diarrhea</td>
</tr>
<tr>
<td>Cough</td>
</tr>
<tr>
<td>Jaundice</td>
</tr>
<tr>
<td>Tenderness</td>
</tr>
<tr>
<td>Hepatomegaly</td>
</tr>
<tr>
<td>Ascites</td>
</tr>
<tr>
<td>Shock</td>
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</tbody>
</table>
Usually, needle aspiration is preferred for smaller abscesses and catheter drainage is done in larger ones. However, no clear-cut guidelines have been laid. Yu et al. included only pyogenic abscesses and showed no significant difference between the two techniques. Qazi et al. found that catheter drainage was better terms of success rate, but they limited the number of aspirations to two which may be a reason for lower success rate of percutaneous aspiration. We compared these two treatment options, exclusively in liver abscesses. In the present study, out of 48 patients of amebic liver abscess, 7 patients were managed conservatively, 25 patients managed by PNA, 15 patients managed by PCD, and 1 patient was managed by exploratory laparotomy. In the present study, out of 25 patients of pyogenic abscess, 1 patient managed conservatively, 20 patients managed by PNA, and 4 patients managed by PCD.

Few reports suggest that the initial size of the abscess cavity does not affect the final outcome, while Qazi et al. believed that large abscesses are more difficult to evacuate completely in a single attempt. This may be the reason, why many centers prefer PNA for abscesses <5 cm, and PCD for larger abscesses. In our study also PNA failed in larger abscess and also in amebic abscess as pus in amebic abscess is thick. Both these techniques have certain disadvantages. Multiple attempts of PNA needed for large abscesses may be uncomfortable and perceived as more traumatic by patient. Furthermore, during the period between two aspirations pus may get reaccumulated. For smaller abscesses, daily production of pus may be small, but a larger abscess cavity may produce larger quantity of pus, which needs to be drained continuously. PCD has this obvious advantage over PNA, which may have accounted for quicker clinical recovery, lesser duration of parenteral antibiotics, and lesser failure rate among patients treated with PCD. On the other hand, placing a catheter needs more expertise followed by nursing care. At 6-month follow-up, complete resolution of abscess cavity on USG occurred in all patients in both groups, while Qazi et al. found that the time needed for total resolution is similar after PCD and PNA. Thus, PCD and PNA are equally effective in the management of large liver abscesses.

Qazi et al. did randomize 50 patients with liver abscess into a needle aspiration group and a catheter drainage group and showed a significantly higher success rate in the catheter drainage group. Most previous reports have been retrospective analysis of data collected over 2–13 years, and the sample sizes have typically ranged from 15 to 115. A sample size of 50 from 2½ years of data collection would seem reasonable. There was no procedure-related complication such as hemorrhage of any degree of severity, or septicemia, in either group of patients. No statistically significant difference was seen in the main procedure outcome measures in either group of patients. Different authors tended to have favored either continuous catheter drainage or intermittent needle aspiration, while others left the choice of drainage method to the radiologists who performed the procedure. Our institution and others have advocated the use of intermittent aspiration in combination with intravenous antibiotics as the first-line treatment for small liver abscesses, and catheter drainage in large liver abscess and catheter drainage in amebic abscess those which are refractory to medical management.

The current study adds further support to this management strategy. There was no statistically significant difference between the two groups. Theoretically speaking, it would, of course, be ideal to recruit a large enough population to detect small differences that may exist between the two techniques. The result of the present study suggests that both techniques are probably equally effective and safe and further implies that it is justifiable to undertake a multicenter study on the subject to provide a definitive answer. The main disadvantage of the needle aspiration technique is that multiple sessions may be required, but even the use of continuous catheter drainage does not guarantee a single session successful outcome. The current study and our previous work have shown no significant increase in morbidity or mortality from the repeated aspiration sessions.
CONCLUSION

Complications are more in amebic abscess as compared to pyogenic liver abscess. Common symptoms of liver abscess are fever and abdominal pain. USG is the mainstay in diagnosing the liver abscess. Antibiotic or amebicidal drugs treatment as a sole modality of treatment can be used for patients who show initial good response and has relatively small size abscesses. Irrespective of the modality of treatment, antibiotic (for pyogenic), or antiamebic (for amebic) drugs are given to all patients in full course. More than two aspirations can be done with good results. Intermittent needle aspiration considered as first-line management of small liver abscess. Others should be treated with percutaneous drainage if abscess is large and liquefied, but single percutaneous aspiration does not always yield good results. Percutaneous pigtail catheter drainage is more effective in large liver abscess. Percutaneous catheter placement is an acceptable modality of treatment in large abscess that demands repeated aspirations. Surgery is extremely useful for complicated cases. Laparoscopic drainage is useful in patients who have concomitant other biliary pathologies.

ACKNOWLEDGEMENT

We want to pay our humble regards to our Additional Professor and Head of Department, Dr. Ninesh Verma for his constant encouragement and overall administrative help for completing this study. We take this opportunity to express our heartfelt gratitude to our teachers Dr. Mukesh Pancholi (Associate Prof.), Dr. Beena Vaidya (Add. Prof.), Dr. Divyang Dave (Add. Prof.), Dr. Jignesh Shah (Asso. Prof.), and Dr. Sandeep Kansal (Asso. Prof.).

Last but not least, we would like to express our special thanks to our colleague, Dr. Hardik Makwana and our patients, for their invaluable support, to make this study complete.

We owe a lot to our parents and all our family members.

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Source of Support: Nil, Conflict of Interest: None declared.
Coronary Angiographic Profile of Patients with Acute Coronary Syndrome <45 Years of Age in Rural Population of Tamil Nadu

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INTRODUCTION

Cardiovascular diseases (CVDs) and its associated complications alone accounts for approximately 12 million deaths annually in the Indian subcontinent.1 As per the statistics of the World Health Organization in 2014, 26% of total mortality in India is contributed by CVD. 2 Mortality
due to coronary artery disease (CAD) is higher in South India.\(^1\) Studies carried out in India, and other places suggest that Asians in general and Indians, in particular, are at an increased risk of myocardial infarction (MI) at a younger age (<40 years).

Epidemiologic data collected through various studies also suggested that risk factors may be different in young as compared to older patients\(^2-5\) and the clinical presentation of coronary heart disease (CHD) may also vary in these populations. Acute coronary syndrome (ACS) is less frequent in adult younger than 40 years of age than in elderly adults but is increasing clinical interest in young adults because of the potential of premature death and long-term disability.

In contrast to developed countries, where mortality from CHD is rapidly declining, it is increasing in developing countries.\(^6\) This increase is driven by industrialization, urbanization, and related lifestyle changes and is called epidemiological transition.\(^7\) This transition affected the developed world, including countries of Europe and North America, in the early 20\(^{th}\) century and spread to developing countries 50 years later.\(^8\)

Due to the high prevalence of CAD in middle age and elderly patients, comparatively few studies have focused on the clinical presentation, treatment, angiographic profile, and outcome of ACS in young patients (<40 years). The young patients with ACS are of particular interest considering the years of potential life lost.

**MATERIALS AND METHODS**

This retrospective study was conducted from April 1, 2014 to February 15, 2018.

Patients aged 45 years of less admitted to the Cardiology Department, Saveetha Medical College and Hospital with ACS undergoing coronary angiography (CAG) were enrolled in the study after the Institutional Ethics Committee approval. Patients were enrolled if they satisfied the criteria for residence in rural area as per 2011 census guidelines and National Sample Survey Organization. ACS includes ST-segment elevation MI (STEMI), non-STEMI (NSTEMI), and unstable angina. The study population comprised all patients <45 years of age admitted with ACS during this period undergoing CAG.

**Exclusion Criteria**

1. Age >45 years
2. History of prior ACS/Coronary revascularization.

The study identified 121 consecutive patients who meet the inclusion criteria.

**Data Collection**

Coronary angiograms were visually assessed by two independent observers blinded to the identity and clinical characteristic of the patients.

The angiographic view at end diastole in which the lesion appeared most severe was selected. A computerized quantitative coronary analysis analytical system for lesion quantification available in the cath lab was used to quantify the degree of stenosis. In this study, significant CAD was defined as the presence of at least ≥70% stenosis of luminal diameter is at least one of the major epicardial coronary arteries in CAG.

Patients having <70% stenosis were categorized as having non-obstructive CAD. They were further classified, having single-vessel disease (SVD), double-vessel disease (DVD), and triple-vessel disease (TVD). Significant left main disease was defined at least ≥50% stenosis of luminal diameters. The management advised by the consultant cardiologist was also recorded.

**RESULT**

A total of 1152 patients underwent coronary angiogram from April 1, 2014, to February 15, 2018, with a diagnosis of ACS, and 121 patients (10.5%) who were <45 years of age (mean 40 ± 4 years) were enrolled for the study [Figure 1].
Majority were males 103 (85.1%) [Figure 2].

Patients had nearly equal incidence of SVD 48 (39.6%) and DVD 43 (35.5%). The incidence of TVD was 8 (6.6%) [Figures 3 and 4].

About 22 (18.1%) patients showed evidence of recanalized coronaries with minimal CAD (non-obstructive CAD). 1 patient had spontaneous dissection of proximal left anterior descending (LAD) (0.8%). Among the stenotic segment of coronary arteries, only 64 lesions were discrete (44.6%) (<10 mm long). Among the ACS patients, the incidence of MI was 80 patients (66.11%), the incidence of NSTEMI was 28 patients (23.14%), and unstable angina 13 patients (10.74%) [Figure 5].

Anterior wall MI was predominant, 46 patients (57.5%), followed by inferior wall MI, 31 patients (38.7%). Only 3 patients (3.7%) presented with isolated lateral wall MI [Figure 6].

Right dominant system was predominant 98 (80.9%) followed by codominant system 16 (13.2%) and then left dominant 7 (5.7%) [Figure 7].

Among the coronary arteries, LAD - Type C was predominant 95 (80.9%) followed by Type B 18 (14.8%) and then Type A 13 (10.7%) [Figure 8].

In the coronary arteries with significant proximal LAD stenosis was seen in 27 (38.5%), mid LAD in 27 patients (38.5%), and in distal LAD 10 (14.2%). Diffuse LAD disease was seen in 2 patients (2.8%), and spontaneous dissection of proximal LAD was seen in 1 patient (1.4%) [Figure 9].

When the right coronary artery (RCA) had significant stenosis, proximal RCA was involved in 6 (22.2%), mid RCA 8 (29.6%), and distal RCA 5 (18.5%). RCA was diffusely diseased in 2 patients (7.4%) [Figure 10].

The left circumflex artery (LCX) had significant stenosis involvement of distal LCX was more common 4 (33.3%). Predominant treatment advised was percutaneous transluminal coronary angioplasty 59 (48.7%), medical management 37 (30.5%), and coronary artery bypass grafting 25 (20.6%) [Figure 11].
DISCUSSION

Among 1152 patients who underwent coronary angiogram, 121 patients (10.5%) were <45 years of age, majority were males 103 (85.1%) and 18 (14.9%) were female. In a similar study conducted on 400 patients by Wadkar et al., clinical and angiographic profile of young patients (<40 years) with ACS, in the Department of Cardiology, Lokmanya Tilak Municipal General Hospital, Sion, Mumbai, showed males were 93% whereas female patients were 7%.[9]

As is in our study, the predilection for the involvement of the LAD artery followed by the right coronary and LCXs has been noted in other reports of young patients.[10-15]

Increase prevalence of normal coronary artery (18%) and minor coronary abnormalities was found in coronary artery surgery study. SVD was found in 38% of subjects in our study the incidence of SVD was 39.6%.[13]

Young patients in most studies presented with less number of vessels involved then the older person, but the present study showed more extensive disease in younger patients. This finding may indicate that Indian subjects may have an earlier occurrence of disease process.

The incidence of TVD in our study was each (6.6%) which was in agreement with other studies.[9]

The incidence of DVD in our study was 43 (35.5%) which was marginally higher than in other studies. Wadkar et al. in the study had reported in incidence of DVD (13.5%). In our study, there was no patient had normal coronaries.

CONCLUSION

There is equal prevalence of SVD/DVD with a lesser prevalence of recanalized coronary arteries (non-obstructive CAD). The severity of ACS seems to be increasing in our population.

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Source of Support: Nil, Conflict of Interest: None declared.
Acute Effect of Extreme Sports on Serum Lipids

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Abstract

Purpose: The aim of this study is to determine the effect of rafting and paragliding exercises by sedentary males on serum lipids.

Material and Methods: 17 male rafters and 10 male paragliders volunteers (non-smoker, no known history of cardiovascular disease, body mass index <25 kg/m², and no intake of prescription medications) participated in the study. Participants had blood samples taken a day before and after rafting and paragliding practices. Data were analyzed by Wilcoxon and Mann–Whitney U tests.

Results: Significant decreases occurred for the low-density lipoprotein (LDL)/very low-density lipoprotein (VLDL) ratio in the rafting group after the exercise; though, there was no significant difference in serum lipids parameters of the paragliding group after the exercise.

Conclusion: While acute rafting and paragliding exercises have similar effects on TG and HDL, effect on LDL / VLDL ratio is different.

Key words: Exercise, Lipid, Paragliding, Rafting

INTRODUCTION

Rafting and paragliding are extreme sports that people participate in both for competition and entertainment purposes. According to Willig, rafting and paragliding can be among some of the most extreme sports activities.¹ While Williams and Soutar and Buckley referred that rafting is a challenging activity of adventure tourism, on the other hand,² Hinch and Higham and Roberts defined it as an extreme activity for sporting adventure.³ Rafting is a group activity, in which four to eight people participate and single-winged paddles and inflatable boats are used.⁴ As the level of challenge increases in rafting activities, more mental and physical concentration is required.⁵

Paragliding is the flight of pilots with a special made seat. The basic equipment can be listed as a parachute, a seat, and a spare parachute.⁶ According to Mekinc and Mušič, paragliding is a kind of sport that is both exciting and competitive.⁷

Lipids have different derivatives according to their structures and functions. Triglycerides are esters formed by the molecular fatty acid with glycerol.⁸ These are neutral fats synthesized from carbohydrates and stored in the fat tissue. Lipids in foods state in the form of TG. In the small intestine epidermis and fat cells, fatty acids bind glycerol and combine to form TGs. Cholesterol is sterol, which is either a free or an esterified form. Free cholesterol is a component of the cell membrane; esterified cholesterol is usually locates in the serum and states in atheromatous plaques.⁹,¹⁰

Cholesterol is an organic substance placed in human and animal tissues and cells, also used in the synthesis of Vitamin D synthesis, calcium and phosphorus, building blocks of cell membranes, bile acids, and sex hormones.¹¹ High-density lipoprotein (HDL), which is synthesized by both the liver and small intestine and is responsible for cholesterol transport from tissues to the liver, contains 50% protein, 20% cholesterol, 5% TG, and 25% phospholipid.¹² Low-density lipoprotein (LDL) contains 20% protein, 50% cholesterol, 5% TG, and 25% phospholipid.¹³
task of LDL is to carry cholesterol from the liver to the peripheral tissues and regulates cholesterol synthesis again in this region.\textsuperscript{[10]} The lipoprotein with very LDL (VLDL) contains 5% protein, 30% cholesterol, 55% TG, and 10% phospholipid. They are synthesized from the liver and contain TGs that are synthesized from circulating fatty acids or carbohydrates. VLDL also contains significant amounts of cholesterol and cholesterol esters. Once the VLDL is combined in the liver, it becomes LDL in fat tissue and muscles.\textsuperscript{[10,15]}

Intensity and duration of exercises effective on reducing body weight since it will be crucial to promote lipid activity and usage of active muscles. Thus, it is important to address the effects on lipid oxidation and lipolysis in relation to its intensity and duration of acute exercise.\textsuperscript{[16]} It showed an increase in lipolysis and it oxidation by the active muscles during an acute aerobic exercise.\textsuperscript{[17]} In addition, fatty acids are essential energy substrates during endurance exercise. Acute endurance exercise is associated with skeletal muscle lipid remodeling and neutral lipid storage during recovery.\textsuperscript{[18]} This study aimed to determine the acute effects of rafting and paragliding on serum lipids and to compare the effects of these two sport activities.

**MATERIALS AND METHODS**

**Subject**

A total of 17 rafting and 10 paragliding participants (\( n = 27 \)) were physically active men volunteered to participate in the study. They were not experienced in rafting and parachuting practice before the study. The rafting group demographics were: Age = 22.24 ± 3.07; height = 179.65 ± 6.61; weight = 73.59 ± 7.77; and body mass index (BMI) = 22.8 ± 1.99 and paragliding groups, age = 28.2 ± 10.28; height = 176.0 ± 8.19; weight = 76.8 ± 16.12; and BMI = 24.66 ± 3.93. The inclusion criteria were: Non-smoker, no known history of cardiovascular disease, BMI <30 kg/m\(^2\), and no intake of prescription medication or antioxidant supplements. All participants completed written informed consent.

**Exercise Protocols**

The participants were given basic rafting and paragliding technical and safety trainings before the study (2 weeks - 5 days per week). The paragliding took place and occurred by flying from a slope at an altitude of 1500 m. The rafting took place in the river with a rapid difficulty rating of 2+1 at an altitude of 1150 meters. Both rafting and paragliding exercises were standardized at a duration of 20 min.

**Blood Samples Analyze**

Participant blood samples were taken for each rafting and paragliding practices’ a day before at 09:00 AM (pre) and immediately 15 min after practices’ at (post) at 09:00 AM. All blood samples were drawn in ethylenediaminetetraacetic acid-treated tubes and placed on ice until processing. Whole blood aliquot samples were analyzed for hematocrit and hemoglobin. Remaining sample aliquots were centrifuged at 4°C for 15 min at 3000 rpm (Centra-8R IEC, MA). Subsequently, the samples were analyzed by COBAS 600 (Roche) brand autoanalyzer for lipid profiles.

**Statistical Analysis**

Statistically, analysis was performed with SPSS 22.0. The data set was found to not be normally distributed; therefore, we used the Wilcoxon test to compare intragroup values and Mann–Whitney U test to compare intergroup values.

**RESULTS**

There was a significant increase in the LDL/VLDL ratio, but no significant difference in TG and HDL after rafting exercises and there was no difference in TG, HDL, or the LDL/VLDL ratio after paragliding exercises [Table 1].

**DISCUSSION**

Exercise is a factor that brings about different physiological effects in acute and chronic periods, especially according to severity of activity. Lipid is an energy source, at the same time, as it has many structural functions in the body. Specifically, during the long period exercises, there may be differences in the relative lipid concentrations in the blood due to the production of energy from the TGs. Our study was conducted to determine the acute effect of rafting and paragliding exercises, which are among the extreme sports, on blood lipid profiles.

We found out that there were no statistically significant changes in TG values, even though decreases were observed after both the rafting and paragliding exercises (\( P > 0.05 \); Table 1). These findings agree with the literature as similar studies report that some exercise practices do not result in any changes in the TG levels.\textsuperscript{[19–23]} Contrastingly, there are some studies detecting that the acute exercises decreased the TG levels. Magkos et al. reported that TG levels decreased significantly after the acute endurance exercises.\textsuperscript{[24]} Turgut et al. reported that TG values decreased significantly after acute swimming exercise among females.\textsuperscript{[25]}

There were no significant changes in HDL after either rafting or paragliding [Table 1]. Some researchers reported no significant difference in HDL values after acute endurance and resistance exercises.\textsuperscript{[23]} McClean et al. reported in their study, in which they formed the control and exercise groups including healthy males loaded with...
Table 1: The results of Wilcoxon test for TG, HDL, and LDL/VLDL before and after rafting and paragliding exercises

<table>
<thead>
<tr>
<th>Serum lipids</th>
<th>Measurement</th>
<th>n</th>
<th>Mean rank</th>
<th>Median</th>
<th>Z</th>
<th>P</th>
<th>n</th>
<th>Mean rank</th>
<th>Median</th>
<th>Z</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>TG (mmol/L)</td>
<td>Before exercise</td>
<td>17</td>
<td>8.92</td>
<td>17.64</td>
<td>-0.750</td>
<td>0.453</td>
<td>10</td>
<td>5.00</td>
<td>20.22</td>
<td>-0.674</td>
<td>0.500</td>
</tr>
<tr>
<td></td>
<td>After exercise</td>
<td>17</td>
<td>8.25</td>
<td>17.39</td>
<td>-0.828</td>
<td>0.407</td>
<td>10</td>
<td>2.00</td>
<td>3.25</td>
<td>0.34</td>
<td>-1.483</td>
</tr>
<tr>
<td>HDL (mmol/L)</td>
<td>Before exercise</td>
<td>17</td>
<td>9.40</td>
<td>0.36</td>
<td>-0.674</td>
<td>2.50</td>
<td>10</td>
<td>4.25</td>
<td>1.47</td>
<td>-0.271</td>
<td>0.002*</td>
</tr>
<tr>
<td></td>
<td>After exercise</td>
<td>17</td>
<td>8.43</td>
<td>0.34</td>
<td>-3.031</td>
<td>0.002*</td>
<td>10</td>
<td>2.17</td>
<td>1.45</td>
<td>-0.750</td>
<td>0.453</td>
</tr>
<tr>
<td>LDL/VLDL (ratio)</td>
<td>Before exercise</td>
<td>17</td>
<td>10.81</td>
<td>1.44</td>
<td>-1.483</td>
<td>0.137</td>
<td>10</td>
<td>3.13</td>
<td>8.92</td>
<td>-0.500</td>
<td>0.34</td>
</tr>
<tr>
<td></td>
<td>After exercise</td>
<td>17</td>
<td>3.13</td>
<td>1.37</td>
<td>-0.750</td>
<td>0.36</td>
<td>10</td>
<td>8.25</td>
<td>17.39</td>
<td>-0.674</td>
<td>2.50</td>
</tr>
</tbody>
</table>

*P<0.05; a: Statistically significant different from baseline. TGs: Triglycerides, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoprotein

Meaningful decreases in the LDL/VLDL ratio occurred after rafting only [Table 1]. This finding may occurred because rafting exercise may have required more muscular use than paragliding. To bring out the acute effects of exercise on the lipid profile, it can be thought that either the duration or the intensity of the exercise needs to be increased.[28,29]

Regular exercise affects lipid metabolism, changes plasma lipid and lipoprotein levels - in a positive fashion and reduces the risk of atherosclerosis. However, these effects on the lipoproteins from exercise depend on the sex, body weight, body fat distribution, sports activity, duration, and intensity of exercise, and whether the exercise has effect on weight loss or not.[29] It reported that there was no difference in VLDL-TG concentrations after acute endurance exercises in some research.[23,24] Findings of McClean et al. revealed no significant difference in LDL levels between the groups after moderate acute exercise 2 h after feeding.[28] Medlow et al. referred that the acute exercise might increase the sensitivity of LDL.[30] Lira et al. claimed that the acute resistance exercise might cause changes in lipid profile at specific density and lipid profile might indicate that low- and medium-intensity exercises may have been more useful than high-intensity exercises rafting and paragliding are high intensity exercises as they are extreme sports.[31] Due to the high-intensity nature of these sports, the results of Lira et al. supported our present research findings.

**CONCLUSION**

- The paragliding does not have any significant effect on the blood lipid profiles,
- Rafting exercises are only effective at LDL/VLDL ratio.

**ACKNOWLEDGMENTS AND GRANT SUPPORT**

The study was financed by Erzincan University Scientific Research Projects Coordination Unit (Project No: 2014/4501) and approved by Erzincan University Ethics Committee (2015-03/02). This study was published as Oral Presentation in 4. The International Balkan Conference in Sport Sciences, 21–23 May 2017, Bursa, TURKEY.

We would like to thank to Gurcan Ekineci (Rafting Instructor) and Ali Zaimoglu (Paragliding Instructor), all the participants and staff of laboratory who supported the research.

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How to cite this article: Agirbas O, Aggon E, Hackney AC. Acute Effect of Extreme Sports on Serum Lipids. Int J Sci Stud 2018;6(1):76-79.
Source of Support: Nil, Conflict of Interest: None declared.
Juvenile Nasopharyngeal Angiofibroma - A Hospital-based Retrospective Study

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Abstract

Introduction: Juvenile nasopharyngeal angiofibroma is a highly vascular histologically benign, locally aggressive neoplasm of the nasopharynx. It accounts for 0.05% of all head and neck neoplasms with a high incidence of persistence and recurrence.

Materials and Methods: A retrospective hospital-based study was conducted in Government Theni Medical College Hospital on patients of juvenile nasopharyngeal angiofibroma for 4 years duration in the period from 2013 to 2016. A total of 4 cases of Juvenile nasopharyngeal angiofibroma were included in this study.

Observation and Results: Among four cases, three cases were presented in Stage 1. One patient presented with infratemporal fossa involvement (Stage 3). Nasal obstruction and epistaxis were the most common presentation seen in all cases. All patients underwent intranasal endoscopic removal of JNA under general anesthesia. For one patient right external carotid artery ligation was done to reduce intraoperative bleeding and elective tracheostomy to maintain the airway.

Conclusion: The study previously done in various parts of the world have shown that JNA is very rare and its incidence is 0.05%. Contrast, in this study in this institution, shows the incidence was 0.02%.

Key words: Epistaxis, Juvenile angiofibroma, Nasal obstruction, Nasopharyngeal angiofibroma

INTRODUCTION

JNA is a vascular benign but locally aggressive tumor of the nasopharynx that affects male adolescents with an average age of onset being 14 years. It accounts for 0.05% of all head and neck neoplasms.[1]

Anatomically, the point of origin is believed to the posterolateral wall of the roof of nose, where sphenoid of palatine bone meets the horizontal ala of the vomer and root of pterygoid process of sphenoid. The large tumors present as bilobed dumbbell swelling straddling the sphenopalatine foramen with one component filling the nasopharynx and the other extending into the pterygopalatine and infratemporal fossa.[2] The central stalk joining the two portion occupies the sphenopalatine foramen at the upper end of the vertical plate of palatine bone without appearing to enlarge it very much.[3]

Aim and Objectives

- To evaluate the incidence of JNA in this institution.
- To evaluate the role of pre-operative contrast-enhanced computed tomography (CECT) and MRI in the diagnosis of JNA.
- To evaluate the role of intranasal endoscopy in JNA cases.

MATERIALS AND METHODS

A retrospective hospital based study was conducted in Government Theni Medical College Hospital on patients of JNA. A total of 4 cases included in this study.

All the patients were staged according to Fisch classification [Table 1].[1,4-6]
**Observation and result**

This study was conducted in the Department of ENT in Government Medical College. The study was conducted as retrospectively account of JNA cases reported to our hospital. The extreme of ages at presentation is shown in Table 2 and Figure 1.

Among four cases, three cases were presented in Stage 1. One patient presented with infratemporal fossa involvement (Stage 3).

Nasal obstruction and epistaxis were the most common presentation of angiofibroma seen in all cases. Other common symptoms and signs are a diminished vision, proptosis, facial swelling and protruding nasal mass [Table 3].

CECT scan was the most common imaging modality used for diagnosis and staging of JNA which was done in three cases. CECT and MRI were done in one case to identify extension of the tumor mass.[12]

All patients underwent intranasal endoscopic removal[10] of JNA under general anesthesia. For one patient, right external carotid artery ligation[7] was done to reduce intraoperative bleeding and elective tracheostomy to maintain the airway.

All the patients had undergone diagnostic nasal endoscopy postoperatively every 6 months intervals.

**DISCUSSION AND CONCLUSION**

In this study, a total of 4 cases were studied and following inferences and conclusion are drawn.

The reported incidence ranges from 1 in 5000 to 1 in 50,000 of all otolaryngological patients in different countries. The study previously done in various parts of the world have shown that JNA is very rare and its incidence is 0.05%.

Contrast, in this study in this institution, shows the incidence was 0.02%.

In recent times, there has been a major change in the epidemiology, pathogenesis, diagnosis, medical management, pre-operative care, and surgical management of JNA.

- Angiofibroma is essentially disease of adolescent male, and peak age of presentation is 16 years.

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**Table 1: Fisch staging system**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>Tumor limited to the nasopharyngeal cavity, bone destruction negligible (or) limited to sphenopalatine foramen</td>
</tr>
<tr>
<td>Stage 2</td>
<td>Tumor invading the pterygopalatine fossa (or) the maxillary, ethmoid (or) sphenoid sinus with bone destruction</td>
</tr>
<tr>
<td>Stage 3</td>
<td>Tumor invading the infratemporal fossa (or) orbital region</td>
</tr>
<tr>
<td></td>
<td>a. Without intracranial involvement</td>
</tr>
<tr>
<td></td>
<td>b. With intracranial extradural with parasellar involvement</td>
</tr>
<tr>
<td>Stage 4</td>
<td>Intracranial intradural tumor</td>
</tr>
<tr>
<td></td>
<td>a. Without infiltration of the cavernous sinus, pituitary fossa or optic chiasma</td>
</tr>
<tr>
<td></td>
<td>b. With infiltration of the cavernous sinus, pituitary fossa or optic chiasma</td>
</tr>
</tbody>
</table>

**Table 2: Age extremes of presentation**

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Age (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highest age of presentation</td>
<td>25</td>
</tr>
<tr>
<td>Lowest age of presentation</td>
<td>14</td>
</tr>
</tbody>
</table>

**Table 3: Symptomology of JNA**

<table>
<thead>
<tr>
<th>Symptoms and signs</th>
<th>Present (%)</th>
<th>Absent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal obstruction</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>75</td>
<td>25</td>
</tr>
<tr>
<td>Facial swelling</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Proptosis</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Protruding nasal mass</td>
<td>25</td>
<td>75</td>
</tr>
</tbody>
</table>

**Table 4: Imaging modalities required for diagnosis and staging of JNA**

<table>
<thead>
<tr>
<th>Imaging modality</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT scan</td>
<td>4 (100)</td>
</tr>
<tr>
<td>CT + MRI</td>
<td>1 (25)</td>
</tr>
</tbody>
</table>

CT: Computed tomography, MRI: Magnetic resonance imaging
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- The incidence of angiofibroma as calculated from the average number of patients attending ENT OPD in 1/10000 population.
- Earlier stage (Stage 1) presentation is diagnosed earlier due to CT scan and diagnostic nasal endoscopy.
- Nasal obstruction and epistaxis are the most common presentation of angiofibroma Figure 2.
- Young adolescent male with profuse epistaxis and nasal obstruction suspected for JNA.
- Diagnostic nasal endoscopy and CECT scan are the most common modalities used for diagnosis and staging of JNA. MRI is an additional tools for extension of the tumor mass Table 4.
- Three patients needed blood transfusion intraoperatively.
- Intranasal endoscopic approach was used in all patients.
- Regular follow-up is essential to find out recurrence and residual disease Table 5.
- Conducting regular school camps to detect JNA early in all cases of epistaxis to create awareness of people.

Table 5: Correlation between stages of disease and recurrence

<table>
<thead>
<tr>
<th>Stage</th>
<th>Number of patients</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
<td>Nil</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>Nil</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

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How to cite this article: Kumar DR, Suresh D, Padmanaban SA. Juvenile Nasopharyngeal Angiofibroma - A Hospital-Based Retrospective Study. Int J Sci Stud 2018;6(1):80-82.

Source of Support: Nil, Conflict of Interest: None declared.
Role of Ultrasonography and Computed Tomography in Gallbladder Masses and their Correlation with Fine-needle Aspiration Cytology

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Abstract

Introduction: Ultrasonography (USG) and computed tomography (CT) have revolutionized the diagnosis, and management of carcinoma ultrasound is the main initial diagnostic tool for suspected biliary lesions. It may be helpful for detecting gadolinium-based contrast agents (GBCA) although the infiltrative morphology of some tumors and the presence of gallstones, inflammation, and debris may preclude tumor detection. CT has been reported as a comprehensive tool for imaging and staging of GBCA.

Aims and Objectives: Role of USG and CT in evaluation of gallbladder (GB) masses

Materials and Methods: This study was conducted in the Department of Radiodiagnosis in coordination with the surgery, medicine, and pathology at NSCB Medical College and Hospital, Jabalpur. A total of 50 patients with suspected GB masses were included in our study.

Result: Maximum number of patients were in the age group between 41 and 50 year, about 32%, and age group between 51 and 60 years, about 28%. GB masses 33 (66%) were detected in females and 17 (34%) were detected in males. Mass detection as per diffuse wall and mass detection as per heterogeneous echotexture was seen in 35 patients, about 70% in USG, and 36 patients, about 72% in CT. Thickening of GB was seen in 7 patients, about 14% in USG and CT.

Conclusion: In our study, overall detection of GB carcinoma USG could detect 94% of cases and CT could detect 96% of cases same as fine-needle aspiration cytology detection of GB carcinoma showing that CT is more sensitive than USG to detect the GB carcinoma.

Key words: Computed tomography scan, Ultrasonography, GB carcinoma

INTRODUCTION

Since the first description of gallbladder (GB) carcinoma by Maxmillan de Stol in 1777, studies have established a characteristic pattern of late diagnosis and ineffective treatment of this disease.[1] The exact etiology of GBC has not been properly known till date. It is yet to be established. However, several other factors such as chronic cholecystitis, gallstones, choledochal cyst, female gender, age, and exposure of carcinogens have been observed to be implicated in GB carcinogenesis.

Early diagnosis of GB carcinoma is difficult because most patients present with non-specific findings of right upper quadrant (RUQ) pain, malaise, weight loss, jaundice, anorexia, and vomiting. This presentation is often confused with symptomatic cholelithiasis or chronic cholecystitis.
Ultrasonography (USG) and computed tomography (CT) have revolutionized the diagnosis and management of carcinoma GB. Magnetic resonance imaging is utilized only in inoperable cases with obstructive jaundice for delineation of the biliary tract anatomy in patients considered for palliative stenting.[2]

Ultrasound (US) is the main initial diagnostic tool for suspected biliary lesions. It may be helpful for detecting gadolinium-based contrast agents (GBCA) although the infiltrative morphology of some tumors and the presence of gallstones, inflammation, and debris may preclude tumor detection. CT has been reported as a comprehensive tool for imaging and staging of GBCA.

USG in patients of carcinoma GB has certain limitations such as interference by bowel gas, limited depth resolution, and inadequate visualization of parts of the GB in the region of posterior acoustic shadowing in the presence of calculi. CT scan overcomes these drawbacks and provides definite information regarding the invasion of the tumor into the adjacent organs, distant metastasis, delineation of the biliary tree, and portal vein involvement.

Sonography is currently the most practical and accurate method to diagnose acute cholecystitis. When adjusted for verification bias, sensitivity and specificity of US are approximately 88% and 80%, respectively.[3]

CT may be useful for depiction of complications. Sonographic findings include the[3] thickening of the GB wall (>3 mm), distention of the GB lumen (diameter >4 cm), gallstones impacted stone in cystic duct or GB neck, pericholecystic fluid collections, positive sonographic Murphy’s sign, hyperemic GB wall on Doppler, and interrogation.

The present study was done as the GB pathology is a frequent source of patient complaint of acute or chronic RUQ pain, jaundice, or dyspepsia and this pathology is commonly encountered on diagnostic imaging examinations.

Aims and Objectives
The aims of this study are as follows:
1. Role of USG and CT in evaluation of gallbladder masses
2. To enumerate the various feature of CT in GB masses
3. To study the correlation with fine-needle aspiration cytology (FNAC).

MATERIALS AND METHODS
The present study was undertaken to evaluate the role of US and CT imaging in the evaluation of GB masses and their correlation with FNAC. This study was conducted in the Department of Radiodiagnosis in coordination with the surgery, medicine, and pathology at NSCB Medical College and Hospital, Jabalpur. A total of 50 patients with suspected GB masses were included in our study. Informed written consent of patients was taken before conduction of the study.

Study Period
This study was conducted during March 1, 2016–March 31, 2017. Data were collected through the pre-designed pro forma.

Inclusion Criteria
The following criteria were included in the study:
• Patients who presented with a sign and symptom of GB masses in NSCB Medical College, Jabalpur, underwent USG, CT scan, and FNAC.

Exclusion Criteria
The following criteria were excluded from the study:
• Non-cooperative patients
• Patients who did not underwent all the three investigation (USG, CT scan and FNAC).

Machine used: Philips HD 7XE, Siemens Acuson ×300, and Sonoscape ss16000 [Figure 1]. Procedure: Sonographic examinations were carried out after an overnight fast with a real-time gray scale. The GB was examined for wall thickness, irregularity, echotexture, mass lesions, stones, and pericholecystic fluid collections. CT scan was done on 16 slice GE CT scan machine.

Multiplanar reconstructions were created in both coronal and sagittal plane section.

All the cases had a clinical or radiological suspicion of GB malignancy. Hematoxylin and eosin stained cytology smears were examined in all cases.

RESULTS
The present study was conducted in the Department of Radiodiagnosis in coordination with the Department of Surgery, Medicine, and Pathology at NSCB Medical College and Hospital, Jabalpur. A total of 50 patients suspected with GB masses were included in our study.

In our study, age of the GB mass patients was ranged from 30 to 90 years. Maximum number of patients were in the age group between 41 and 50 years, about 32%, and age group between 51 and 60 years, about 28%. Minimum number of patients were in the group between 71–80 years and 81–90 years. The average age of the patients presented was 52 years.
According to Table 2a and b in our study, of 50 patients of the GB masses, 33 (66%) were detected in females and 17 (34%) were detected in males. Female predominance is seen, 6.6 female per 3.4 male. One patient may have more than one complaint. In our study, most common presenting symptom was pain in RUQ which was seen in 94% of cases. 52% (26) of patients were presented with jaundice. About 38% of patients were presented with itching all over the body and 36% of patients were presented with weight loss which were other associated complaints. In our study, GB masses were assessed in terms of size, irregularity, complete or partial replacing lumen, heterogeneous echotexture, gallstone [Figure 2], vascularity on USG, enhancement on CT, dilated common bile duct (CBD), and intrahepatic biliary radicals (IHBR). According to the detection of complete or partial replacing GB lumen masses, USG could detect in 24 patients, about 48% of cases. CT scan could detect in 32 patients, about 64% of cases. In 16% of cases, USG could not detect partial replacing GB lumen masses due to obscured by bowel gas in the abdomen which were detected in CT scan, Figure 3. GB masses were assessed in terms of focal thickening of wall, irregularity, echotexture in USG, and enhancement in CT. According to detection as per focal wall thickening Figure 4, USG could detect 5 patients, about 10% of the cases. CT scan could detect 9 patients, about 18% of the cases. USG could not detect rest of the 8% of cases obscured by bowel gas, which shows that CT scan is better than USG to detect focal wall thickening masses. Mass detection as per diffuse wall thickening of GB was seen in 7 patients, about 14% in USG and CT. GB masses as per intraluminal mass lesion could be detected in 2 patients, about 4% of cases in USG and CT, which shows that both USG and CT are equally sensitive to detect the diffuse wall thickening. Mass detection as per heterogeneous echotexture seen in 35 patients (70%) in USG and 36 patients (72%) in CT showing CT is more accurate than USG. Mass detection as per presence of calculus seen in 24 patients, 48% seen in USG, and 20 patients, about 40% in CT showing, USG is more sensitive than CT to detect calculus. Dilated CBD, associated sign of GB mass, and USG could detect 17 cases, about 34%, and CT could detect 18 cases, about 36%, showing that CT is more sensitive than USG to detect dilated CBD. Dilated IHBR, associated sign of GB mass, and USG could detect 29 patients, about 58% cases, and CT could detect 30 patients, about 60% cases, showing that CT is more sensitive than USG for detection of dilated IHBR associated with GB masses. In this study, GB mass could detect as per direct invasion of the liver in 74% of cases almost similar in USG as well as CT. Similarly, 2% of cases of right and left hepatic duct could be detected by USG, and CT could detect 10% of cases. Duodenum, pylorus, and colon are detected in 2% of cases only by CT, and USG could not detect any distant organ invasion, showing that CT is for better to detect distant organ invasion than USG.

In this study, the USG and CT both are equally sensitive to detect the porcelain GB in 4% of cases which represent GB carcinoma. In this study ,GB carcinoma detected by USG in 26 (52%) cases shows vascularity on colorDoppler, CT detect 48 (96%) cases showing enhancement on dual phase study represents malignant nature of masses , Figure 5. This shows that CT is more sensitive to accurate detection of GB carcinoma than USG. In this study, as per detection of nodes, nodes at liver hilum or periporal could be detected by USG in 25, about 50% of cases, and CT could detect 27, about 54% of cases. Peripancreatic nodes could be detected by USG in 20, about 40% of cases, and CT could detect 21, about 42% of cases. Aortocaval lymph node could be detected by USG in 4, about 8% of cases, while CT could detect 8, about 16% of cases. Mesenteric lymph node could be detected by USG in 3, about 6% of cases, while CT could detect 7, about 14% of cases. It shows that CT is more sensitive to detect distant lymphatic spread than USG. In this study, as per detection of metastasis, USG could detect 15, about 30% of cases, and CT could detect 19, about 38% of cases of liver metastasis. While USG could not detect any case of peritoneal metastasis, however, CT could detect 1, about 2% of cases, showing that CT is more sensitive than USG to detect metastasis. In this study, as per overall detection of GB carcinoma, USG could detect 94% of cases and CT could detect 96% of cases of GB carcinoma, showing that CT is more sensitive than USG to detect the GB carcinoma.

**DISCUSSION**

The present study is cross-section type, including n = 50 patients clinically suspected with GB masses, and all cases were fulfilling inclusion criteria.

**Distribution As Per the Age Table 1**

In our study, age distribution of the patients presenting with GB mass was in range from 30 to 90 years. Maximum patients were in the age group of 41–50 year, which constituted about 32% of cases. The overall mean age of the patients presented was 52 years. Haaga and Herbener[6] in their separate studies showed that most common age group of presentation of GB mass was primarily in the sixth to seventh decade of life which slightly differs from our study sample. In one study by George et al,[6] the peak incidence age group of GB mass was 51–70 years. Memon et al,[5] in their study, 2005 have shown in their series that the mean age of the patients having GB malignancy was 70.6 years and ranges from 42 to 85 years.
Distribution as Per Gender and Age Table 2a and b
Of the 50 patients included in the study, 33 (66%) patients were female and 17 (34%) patients were male. The overall female-to-male ratio was 1.9:1. The mean age of the presentation was 49.6 years for female and 56.7 years for male. In one study by George et al., the male:female ratio was 2:5 and the mean age of presentation was 57 years for females and 52 years for males, which is almost a decade less than the reported mean age in western literature.

Distribution as Per Non-specific Clinical Symptom Table 3
In our study, the most common presenting symptom was pain in RUQ which was seen in 94% of cases. Pandey et al[8] in their study showed most common presentation of GB cancer as loss of weight (201 patients, 99%) followed by loss of appetite (197 patients, 97%), pain in the right hypochondrium (143 patients, 70%), a mass in the right hypochondrium (107 patients, 53%), jaundice (79 patients, 39%), and nausea and vomiting (21 patients, 10%).

Distribution as Per Mass Replacing GB Lumen Table 4
According to the detection of complete or partial replacing GB lumen mass, USG could detect in 24 patients, about 48% of cases. CT scan could detect in 32 patients, about 64% of cases. In 16% of cases, USG could not detect partial replacing GB lumen masses due to obscured by bowel gas in the abdomen which was detected in the CT scan, showing that CT scan is more sensitive than USG to detect partially replacing GB lumen masses obscured by bowel gases. George et al[6] most common presentation in their study was of a sub-hepatic mass replacing or obscuring the GB often with invasion of the adjacent liver. This finding was seen in 28 (56%) cases with half of them in an inoperable stage of the disease. Similar features reported in study done by Mandal et al[9] in their study the main patterns on imaging were an infiltrating mass into the liver or adjacent bowel in 28 patients (56%).

Distribution as Per Focal and Diffuse Wall Thickening Tables 5 and 6
According to detection as per focal or diffuse wall thickening, USG could detect about 10% of the cases of focal wall, while CT scan detected in about 18% of the focal wall cases, diffuse wall thickening of GB seen in 7 patients, about 14% in USG and CT. Pandey et al[8] in their study in GB wall thickening (>12 mm), inhomogeneous echoes, and ill-defined margins were evident in 26 patients (13%). The GB wall adjacent to the liver was more often thickened than the wall of the rest of the GB. Yun et al[10] in their study used dual-phase CT to assess thickness as well as enhancement pattern of GB wall seen in GB melanoma as well as chronic cholecystitis in arterial and venous phase. They reported a difference in enhancement patterns of malignancy as compared to chronic cholecystitis using dual-phase CT.

Distribution as Per Intraluminal Mass Lesion Table 7
In our study, GB masses as per intraluminal polypoidal mass lesion could be detected in 2 patients, about 4% of cases.

| Table 1: Distribution as per age |
|---|---|
| Age | n (%) |
| 30 | 4 (8) |
| 31–40 | 7 (14) |
| 41–50 | 16 (32) |
| 51–60 | 14 (28) |
| 61–70 | 7 (14) |
| 71–80 | 1 (2) |
| 81–90 | 1 (2) |

| Table 2a: Gender distribution |
|---|---|
| Gender | n (%) |
| Female | 33 (66) |
| Male | 17 (34) |

| Table 2b: Gender distribution as per age |
|---|---|
| Age | Female | Male |
| 30 | 4 | 0 |
| 31–40 | 4 | 3 |
| 41–50 | 13 | 13 |
| 51–60 | 7 | 7 |
| 61–70 | 4 | 3 |
| 71–80 | 0 | 1 |
| 81–90 | 1 | 0 |

| Table 3: Distribution as per non-specific clinical symptom |
|---|---|
| Symptom | n (%) |
| Pain in the abdomen (RUQ) | 47 (94) |
| Weight loss | 18 (36) |
| Jaundice | 26 (52) |
| Fever/vomiting | 12 (24) |
| Itching all over the body | 19 (38) |

| Table 4: Distribution as per mass replacing GB lumen |
|---|---|
| Investigation | n % |
| USG | 24 (48) |
| CT | 32 (64) |

| GB: Gallbladder; USG: Ultrasonography, CT: Computed tomography |

| Table 5: Distribution as per focal wall thickening |
|---|---|
| Investigation | n (%) |
| USG | 5 (10) |
| CT | 9 (18) |

USG: Ultrasonography, CT: Computed tomography
cases in USG and CT, showing that both USG and CT are equally sensitive to detect the intraluminal polypoidal mass. Color Doppler USG has been reported to be useful in the evaluation of malignant lesions. Mandal et al.\(^1\) in their study reported that intraluminal polypoidal masses were detected in 16 patients (32%) of 50 cases. The polyps showed mild-to-moderate enhancement following intravenous contrast administration. Hirooka et al.\(^2\) reported that in cancerous GB polyps, the color signal pattern was diffuse, becoming linear at the base. Velocity and the resistance index were 39.0 ± 12.4 cm/s and 0.62 ± 0.12, respectively, which were significantly different from control measurements from control measurements.

**Distribution as Per Heterogeneous Echotexture Table 8**

In our study, mass detection as per heterogeneous echotexture was seen in 35 patients, about 70% in USG, and 36 patients, about 72% in CT, showing that CT is more accurate than USG. GB carcinoma typically appears on USG as a mass with inhomogeneous echoes in the GB. Palma et al.\(^3\) suggested that these areas were due to necrosis or residual bile within the GB.

**Distribution as Per Detection of Calculus Table 9**

In our study, mass detection as per the presence of calculus was seen in 24 patients, about 48% was seen in USG, and 22 patients, about 44% in CT, showing that USG is more sensitive than CT to detect calculus. The size of the gallstones impacting on the GB wall was a strong indicator for the possible repeated mechanical irritation of the GB mucosa. This chronic GB mucosa irritation by gallstones is a mechanism that has been postulated by Solan and Jackson.\(^4\) Lowenfels et al.\(^5\) in their study of more than 1600 patients with GB disease reported that 40% of patients with GB carcinoma had stones that were >3 cm. Moerman et al.\(^6\) in their study, well explain the lack of association between gallstone size and GB carcinoma, and there is no relationship between stone size and advent of GB was observed.

**Distribution as Per CBD Dilated Table 10**

In this study dilated CBD, associated sign of GB mass, USG could detect 17 cases, about 34%, and CT could detect 18 cases, about 36% showing that CT is more sensitive than USG to detect dilated CBD.

**Distribution as Per Dilated IHBR Table 11**

In this study dilated IHBR, associated sign of GB mass, USG could detect 29 patients, about 58% of cases, and CT could detect 30 patients, about 60% of cases, showing that CT is more sensitive than USG for detection of CBD with GB mass USG could detect 17 cases (34%). Mandal et al.\(^7\) in their study detected that IHBRs were dilated in 30 patients (60%) of 50 patients ranging from minimal to severe in both lobes of the liver.

**Distribution as Per Invasion Table 12**

In this study, GB mass could detect as per direct invasion of the liver in 74%of cases almost similar in USG as well as CT. Similarly, 2% of cases of right and left hepatic duct could be detected by USG and CT could detect 10% of cases. Duodenum, pylorus, and colon are detected in 2% of cases only by CT, and USG could not detect any distant organ invasion, showing that CT is far better to detect distant organ invasion, showing that CT is far better to detect distant organ invasion.

**Table 6: Distribution as per diffuse wall thickening**

<table>
<thead>
<tr>
<th>Investigation</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>USG</td>
<td>4 (8)</td>
</tr>
<tr>
<td>CT</td>
<td>7 (14)</td>
</tr>
</tbody>
</table>

USG: Ultrasonography, CT: Computed tomography

**Table 7: Distribution as per intraluminal mass lesion**

<table>
<thead>
<tr>
<th>Investigation</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>USG</td>
<td>2 (4)</td>
</tr>
<tr>
<td>CT</td>
<td>2 (4)</td>
</tr>
</tbody>
</table>

USG: Ultrasonography, CT: Computed tomography

**Table 8: Distribution as per heterogeneous echotexture**

<table>
<thead>
<tr>
<th>Investigation</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>USG</td>
<td>35 (70)</td>
</tr>
<tr>
<td>CT</td>
<td>36 (72)</td>
</tr>
</tbody>
</table>

USG: Ultrasonography, CT: Computed tomography

**Table 9: Distribution as per detection of calculus**

<table>
<thead>
<tr>
<th>Investigation</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>USG</td>
<td>24 (48)</td>
</tr>
<tr>
<td>CT</td>
<td>20 (40)</td>
</tr>
</tbody>
</table>

USG: Ultrasonography, CT: Computed tomography

**Table 10: Distribution as per CBD dilated**

<table>
<thead>
<tr>
<th>Investigation</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>USG</td>
<td>17 (34)</td>
</tr>
<tr>
<td>CT</td>
<td>18 (36)</td>
</tr>
</tbody>
</table>

CBD: Dilated common bile duct, USG: Ultrasonography, CT: Computed tomography

**Table 11: Distribution as per dilated IHBR**

<table>
<thead>
<tr>
<th>Investigation</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>USG</td>
<td>22 (44)</td>
</tr>
<tr>
<td>CT</td>
<td>30 (60)</td>
</tr>
</tbody>
</table>

IHBR: Intrahepatic biliary radicals, USG: Ultrasonography, CT: Computed tomography
Kushwah, et al.: Role of Ultrasonography and Computed Tomography in Gallbladder Masses and their Correlation with Fine-needle Aspiration Cytology

have reported an overall accuracy of 71% in staging the T-factor of the tumor node metastasis staging in their study of 100 consecutive cases, with accuracies varying from 79% for T1 and T2, 46% for T3, and 73% for T4. The accuracy was lowest for thickened GB wall at 54% and highest for GB mass at 89%.

**CONCLUSION**

The overall mean age of the patients presented was 52 year, and the overall female-to-male ratio was 1.9:1. The most common presenting symptom was pain in RUQ which

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**Table 12: Distribution as per invasion**

<table>
<thead>
<tr>
<th>Site</th>
<th>USG (%)</th>
<th>CT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>37 (74)</td>
<td>37 (74)</td>
</tr>
<tr>
<td>Right and left hepatic duct</td>
<td>1 (2)</td>
<td>5 (10)</td>
</tr>
<tr>
<td>Duodenum</td>
<td>0</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Pylorus</td>
<td>0</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Colon</td>
<td>0</td>
<td>1 (2)</td>
</tr>
</tbody>
</table>

USG: Ultrasonography, CT: Computed tomography

**Table 13: Distribution as porcelain GB**

<table>
<thead>
<tr>
<th>Investigation</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>USG</td>
<td>2 (4)</td>
</tr>
<tr>
<td>CT</td>
<td>2 (4)</td>
</tr>
</tbody>
</table>

GB: Gallbladder, USG: Ultrasonography, CT: Computed tomography

**Table 14: Distribution as per vascularity and enhancement**

<table>
<thead>
<tr>
<th>Investigation</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>USG</td>
<td>26 (52)</td>
</tr>
<tr>
<td>CT</td>
<td>48 (96)</td>
</tr>
</tbody>
</table>

USG: Ultrasonography, CT: Computed tomography

**Table 15: Distribution as per lymph node involvement**

<table>
<thead>
<tr>
<th>Lymph node</th>
<th>USG (%)</th>
<th>CT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perportal</td>
<td>25 (50)</td>
<td>27 (54)</td>
</tr>
<tr>
<td>Peripancreatic</td>
<td>20 (40)</td>
<td>21 (42)</td>
</tr>
<tr>
<td>Aortocaval</td>
<td>4 (8)</td>
<td>8 (16)</td>
</tr>
<tr>
<td>Mesenteric</td>
<td>3 (6)</td>
<td>7 (14)</td>
</tr>
</tbody>
</table>

USG: Ultrasonography, CT: Computed tomography

**Table 16: Distribution as per mass detection in USG and CT**

<table>
<thead>
<tr>
<th>Investigation</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>USG</td>
<td>47 (94)</td>
</tr>
<tr>
<td>CT</td>
<td>48 (96)</td>
</tr>
<tr>
<td>FNAC</td>
<td>48 (96)</td>
</tr>
</tbody>
</table>

USG: Ultrasonography, CT: Computed tomography, FNAC: Fine-needle aspiration cytology

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**Distribution as Porcelain GB Table 13**

In this study, the USG and CT both are equally sensitive to detect the porcelain GB in 4% of cases which represent GB carcinoma. Table 14 presents the distribution as per vascularity and enhancement. In this study USG detected 26 (52%) cases shows vascularity on color Doppler represents malignant nature of masses. Similarly, CT could detect 48, about 96% of cases, showing that enhancement on dual phase study represents malignant nature of masses. This shows that CT is more sensitive to accurate detection of GB carcinoma than USG. Our study showed that application of dynamic CT did not improve the diagnostic accuracy. In 9 of our 16 patients, the GB cancers appeared as isodense lesions on the arterial phase. In contrast, they were hypoattenuated on the portal phase.

Kim et al.[17] in their study assessed the enhancement pattern of abnormal GB wall thickening using multidetector computed tomography to differentiate between carcinoma and inflammatory diseases. They concluded that there is a distinct pattern of enhancement of inner wall compared to non-enhancing surface covering.

**Distribution as Per Lymph Node Involvement Table 15**

In this study as per detection of nodes, nodes at liver hilum or periportal could be detected by USG in 25, about 50% of cases, and CT could detect 27, about 54% of cases. Peripancreatic nodes could be detected by USG in 20, about 40% of cases, and CT could detect 21, about 42% of cases. Aortocaval lymph node could be detected by USG in 4, about 8% of cases, while CT could detect 8, about 16% of cases. Mesenteric lymph node could be detected by USG in 3, about 6% of cases, while CT could detect 7, about 14% of cases. It shows that CT is more sensitive to detect distant lymphatic spread than USG. Pandey et al.[8] in their study found that lymph node enlargement was demonstrated in 39 patients (19%). The node groups most often involved were the periporal (33 cases), followed by the pancreaticoduodenal (17 cases), the paraaortic (16 cases), and less often, the pericholedochal (4 cases) nodes. These nodes appeared as round, well-defined hypoechoic masses with sharp margins and few internal echoes. Most of the nodes were larger than 2.0 cm and discrete.

**Distribution as Per Mass Detection In USG and CT Table 16**

In this study, as per overall detection of GB carcinoma, USG could detect 94% of cases and CT could detect 96% of cases of GB carcinoma, showing that CT is more sensitive than USG to detect the GB carcinoma. Kim et al.[17]
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in about 48% cases. CT scan could detect in about 64% of cases. Focal wall thickening USG could detect about 10% of the cases of focal wall, while CT scan detected in about 18% of the focal wall cases, and diffuse wall thickening of GB was seen in about 14% in USG and CT. Intraluminal polypoidal mass lesion could be detected in about 4% of cases in USG and CT, and heterogeneous echotexture was seen in about 70% in USG and about 72% in CT. The presence of calculus was seen in about 48% of cases in USG and about 44% in CT. Dilated CBD with GB masses, USG could detect about 34% of cases and CT could detect about 36% of cases, while in dilated IHBR, USG could detect in about 58% of cases and CT could detect about 60% of cases, and both USG and CT was equally sensitive to detect the porcelain GB in 4% of cases.
In our study, GB masses could detect as direct invasion of the liver in 74% of cases by USG and CT. In our study, overall detection of GB carcinoma USG could detect 94% of cases and CT could detect 96% of cases same as FNAC detection of GB carcinoma, showing that CT is more sensitive than USG to detect the GB carcinoma.

REFERENCES

Fenticonazole in Vulvovaginal Infections: A Real-world Clinical Experience in India - Force India Study

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Abstract

Introduction: In recent decade, fungal infections have escalated due to mushrooming of immunocompromised patients like elderly and other patients receiving immunosuppressants for comaleficent diseases diabetes mellitus, etc. This holds true for infections of vulvovaginal tissues as well. Skin and vulvovaginal infections can be effectively treated by azole class of antifungals such as clotrimazole and miconazole. Fenticonazole belongs to same class of antifungals, which has been extensively studied against fungi and some Gram-positive bacterial cocci.

Aims and Objectives: We aimed to review etiological pattern of vulvovaginitis, drug use and/prescribing patterns using the World Health Organization - Drug Utilization indicators, and effects of fenticonazole (both beneficial and adverse).

Materials and Methods: A survey was conducted through pre-validated questionnaire, designed to assess the effectiveness and safety of fenticonazole 600 mg ovule in the treatment of vulvovaginitis.

Results: Among all variants of vaginitis, the most common variant was bacterial vaginosis (42.2%), followed by mixed vaginitis (33.2%), vulvovaginitis (14.9%), and trichomonas vaginitis (9.4%). Of 2037 prescriptions, 404 (19.8%) patients were prescribed single dose of fenticonazole, 1211 (59.4%) patients were given two doses, i.e., one ovule each, at day 1 and day 3 (D1/D3), and 419 (20.5%) patients were prescribed with two doses of fenticonazole on day 1 and day 7 (D1/D7). Prescribed daily dose of fenticonazole was more than defined daily dose. No serious adverse events were reported and it was well tolerated.

Conclusion: Most of the prescriptions in the real-world setting were in D1/D3 group implying that vulvovaginitis needs to be treated adequately with two-dose regime, in contrast to single dose recommendation of standard guidelines.

Key words: Drug utilization, Fenticonazole, Vulvovaginitis, World Health Organization

INTRODUCTION

In recent decade, fungal infections have escalated due to mushrooming of immunocompromised patients like elderly and other patients receiving immunosuppressants for comaleficent diseases diabetes mellitus, etc. This holds true for infections of vulvovaginal tissues as well.[1]

Symptomatic inflammation of vagina, also involving vulval tissue instigated by candida, is conventionally defined as vulvovaginal candidiasis (VVC). Vaginal discharge (curdy white/cheesy discharge is peculiar) and itching are the prime manifestations of VVC.[2] Pregnancy, diabetes mellitus, use of systemic antibiotics, and poor intimate hygiene are some of its risk factors.[3,4]

The pursuit of starting empirical therapy in vulvovaginitis is arduous due to diagnostic challenge owing to intersecting symptoms of VVC, bacterial, and mixed vaginal infections. This situation is more complicated by escalating emergence of resistant strains of pathogens which has compelled the use of intricate therapy regimes for longer duration.[5] Mixed infections are difficult to treat with monotherapy,
and hence, they are treated with combination of antifungal, antibacterial, and corticosteroid. Quandary of resistance and increased incidence of local and systemic adverse effects have overshadowed the success of this tactic.

Imidazole antifungals are commonly used to combat fungal infections which act by inhibition of ergosterol synthesis through blocking of P450 isoyme. Ergosterol is building block of fungal cell membrane. Skin and vulvovaginal infections can be effectively treated with variety of azole antifungal drugs such as fluconazole, clotrimazole, and miconazole. Fenticonazole belongs to same class of antifungals, which is well endured and has extensive gamut of activity against fungi and some Gram-positive bacterial cocci. Especially in VVC, it has been found to be more efficacious as compared to other orthodox therapies. Findings of in vitro retrospective analysis prompt us to consider the active role of fenticonazole in treating mixed infections of vulvovaginal tissue with Gram-positive bacteria and fungi. Moreover, it has shown high efficacy against three major sources of dermatophytosis- epidermophyton, trichophyton, and microsporum. In vitro studies have also revealed that fenticonazole is active against most of the pathogens causing bacterial vaginosis such as mobiluncus, gardnerella, and bacteroides species.

There are many ways by which pattern of drug use can be studied, like Drug Utilization (DU) retrospective analysis and prescription analysis. Whenever a DU retrospective analysis is planned, it is preferably done using anatomic and therapeutic classification (ATC)/defined daily dose (DDD) system laid down by the World Health Organization (WHO) since it is universally accepted and allows for better comparison of retrospective analysis findings. Each drug is classified in ATC in four levels with highest level being the organ system involved by the drug and subsequent levels being the drug identifiers. DDD is assumed average dose per day for that drug for the given indication in adult. To the best of our knowledge, the present retrospective analysis is first of its kind to retrospective analysis prescriptions on fenticonazole in India and its analysis using the WHO - DU indicators; hence, it will have a value addition.

Aims and Objectives

Objectives of the present retrospective analysis were to describe DU patterns of fenticonazole using the WHO - DU indicators, to get an insight into etiologies of vaginitis. Furthermore, we aimed to review drug use and/prescribing patterns, effects of fenticonazole (both beneficial and adverse), promotion of appropriate drug use through patient counseling, and other interventions. Final and the most important objective of present retrospective analysis were to provide results for the clinicians, to aid them in selecting appropriate antifungal drug.

MATERIALS AND METHODS

A survey was conducted through pre-validated questionnaire. The questionnaire was designed to assess the efficacy and safety of fenticonazole 600 mg in the treatment of vulvovaginitis. 6-month survey was carried out from April 2017 to October 2017. “Scrip intelligence database” was used to recognize gynecologists engaged in the treatment of vulvovaginitis. Only those gynecologists were included for final analysis who maintained complete patient record and Sobel’s score. Of 95 gynecologists, 60 were selected from four directional zones of country by simple random sampling. Care was taken to select gynecologists uniformly over these four geographies. Pregnant patients were excluded from the retrospective analysis. “Patients suffering from vulvovaginitis treated with fenticonazole were analyzed in 3 groups viz., patients treated on day 1/D1, patients treated on day 1 and 3 (D1/3) and patient treated on day 1 and 7 (D1/D7”). Relevant data were entered in Excel sheet in predesigned format.

We used mean Sobel’s score to assess the efficacy of fenticonazole in vulvovaginitis, where each symptom was graded on a scale from 0 (absent) to maximum of 3 (severe). Higher the score more severe was the disease presentation. Optimal improvement was defined by reduction in mean Sobel’s score by 1.5–2.0 points. Safety evaluation was done by evaluating occurrence of adverse events. The methodology adopted for the present retrospective analysis is depicted in Figure 1.

RESULTS

Of 2567 prescriptions screened, 2037 were included for our analysis. Mean age of patients in this retrospective analysis was 31.95 years. Among all variants of vaginitis, the most common variant was bacterial vaginosis found in 860 patients (42.2%) followed by mixed vaginitis in 677 (33.2%), vulvovaginitis in 304 (14.9%) patients, and trichomonas vaginitis in 193 (9.4%) patients [Table 1]. Of 2037 prescriptions, 404 (19.8%) patients were prescribed single dose of fenticonazole, 1211 (59.4%) patients were given two doses, i.e., one ovule each, at day 1 and day 3 (D1/D3), and 419 (20.5%) patients were prescribed with two doses of fenticonazole on day 1 and day 7 (D1/D7) [Figure 2]. Prescribed daily dose (PDD) of fenticonazole was more than DDD [Table 2].

Figure 3 shows symptom-wise effect of fenticonazole on mean of Sobel’s score in patients of D1 group. Mean improvement in Sobel’s score was found to be 1.47 in all symptoms with highest improvement in erythema and least in excoriation. In D1/D3 group, overall improvement in mean Sobel score was by 1.76 with highest positive effect on vaginal discharge and least in case of excoriation [Figure 4].
In D1/D7 prescription group, overall reduction in mean Sobel’s score was 1.45 with highest improvement in vaginal discharge and least in excoriation [Figure 5]. On scrutiny, it was found that the most common adverse effect was vaginal burning sensation followed by itching/irritation, erythema, and desquamation. Incidence of these adverse effects was most in D1/D3 group (mean 1.6%) followed by D1/D7 group (mean 1.2%) and least in D1 group [Table 3].

**DISCUSSION**

The finding of mean age in the present study was slightly different from findings of other comparative studies of fenticonazole with other antifungal drugs which showed mean age of patients to be around 27 years. Bacterial vaginosis was the most common cause of vaginitis in the present study followed by mixed vaginitis. This in corroboration with findings of other study. However, some authors cited VVC as the 2nd most common cause of vaginitis. Maximum prescriptions were in D1/D3 group, i.e., two doses were given on day 1 and day 3. Mean Sobel’s score was highest in D1/D3 group followed by D1/D7 group and least in D1 group. In recent editorial research paper by Verma and Madhu, authors opine that drastically changed clinical pattern of fungal infections has enabled dermatologists to use antifungal drugs for a longer period than that specified in standard guidelines to obtain optimal benefit. The same is reflected in PDD and DDD findings wherein PDD was greater than DDD. PDD reflects average of per diem dose of drug which is actually prescribed. When there is discrepancy in findings of PDD and DDD for anti-infective the diagnosis, optimal duration of therapy and national therapeutic guidelines should also be taken into account.

As per our knowledge, the present retrospective analysis is first of its kind to analyze the prescription pattern of fenticonazole using DU indicators laid down by the WHO.

<table>
<thead>
<tr>
<th>Item</th>
<th>Sub item</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of prescriptions screened</td>
<td>2567</td>
<td></td>
</tr>
<tr>
<td>Prescriptions included for analysis</td>
<td>2037</td>
<td></td>
</tr>
<tr>
<td>Mean age</td>
<td>31.95</td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td>VVC</td>
<td>304</td>
</tr>
<tr>
<td></td>
<td>Bacterial vaginosis</td>
<td>860</td>
</tr>
<tr>
<td></td>
<td>Trichomonas vaginitis</td>
<td>193</td>
</tr>
<tr>
<td></td>
<td>Mixed vaginitis</td>
<td>677</td>
</tr>
</tbody>
</table>

VVC: Vulvovaginal candidiasis

**Table 1: Prescription details and diagnosis in patients of present study**

**Figure 1: Methodology adopted for current retrospective analysis**

**Figure 2: Number of prescriptions in day 1, day 1/3, and day 1/7 regimen**
In all the three groups, there was clinically significant improvement in vaginal discharge as indicated by changes in mean Sobel’s score. This finding is corroborated with findings of other such studies in western part of the world. Usually, if the symptoms persist, then patients are called up for the 2nd dose at 7th day. However, in the present study, maximum patients were given the 2nd dose on day 3. This may be because fenticonazole forms its “vaginal reservoir” for 72 h during which drug is released slowly. Hence, in light of this finding, 2nd dosing at day 3 is in complete corroboration. This is supported by findings of other studies wherein optimal improvement in Sobel’s score was obtained by giving fenticonazole on day 1 and day 3. Single dose efficacy was found to be less in some studies. The efficacy of fenticonazole given on day 1 and day 7 was more or less same as on day 1 and day 3 in other studies. The United Kingdom Guidelines recommend topical therapy of fenticonazole 600 mg stat or 200 mg for 3 days. Furthermore, it has been found that systemic absorption of fenticonazole is very minimal; therefore, repeated dosing poses no significant threat of exposing other tissues to the drug. It is well-known fact that successful treatment of mixed infections is a challenging issue, which may be endorsed to sundry comportment of pathogenic flora in vagina. Currently, vulvovaginitis is treated with combination of antifungal, steroid, and antibiotics, which augments the prospect of exterminating the culprit pathogens and provides expeditious relief of symptoms. However, it has been found that adverse events and resistant strains are more with use of such approach. One unique advantage of fenticonazole is that it is the only imidazole antifungal which inhibits Candida proteinase, which is responsible for its adherence to epithelial cells, even in single dose. From findings of the present study, we recommend that fenticonazole be used as the first-line drug in the treatment

**Table 2: ATC/DDD evaluation of DU of fenticonazole**

<table>
<thead>
<tr>
<th>Item</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATC code</td>
<td>G01AF12</td>
</tr>
<tr>
<td>DDD</td>
<td>0.1 g</td>
</tr>
<tr>
<td>PDD</td>
<td>0.6 mg</td>
</tr>
</tbody>
</table>

ATC: Anatomic and therapeutic classification, DDD: Defined daily dose, PDD: Prescribed daily dose, DU: Drug utilization

**Table 3: Adverse effects seen with fenticonazole**

<table>
<thead>
<tr>
<th>Adverse effect/s</th>
<th>Number of patients facing the AE n (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>D1 (n=404)</td>
<td>D1/D3 (n=1211)</td>
<td>D1/D7 (n=419)</td>
</tr>
<tr>
<td>Burning sensation</td>
<td>4 (0.9)</td>
<td>30 (2.4)</td>
</tr>
<tr>
<td>Vaginal itching</td>
<td>3 (0.7)</td>
<td>26 (2.1)</td>
</tr>
<tr>
<td>Erythema</td>
<td>4 (0.9)</td>
<td>24 (1.98)</td>
</tr>
<tr>
<td>Desquamation</td>
<td>2 (0.4)</td>
<td>7 (0.5)</td>
</tr>
</tbody>
</table>

Figure 3: Effect of fenticonazole (day 1) on various symptoms of vulvovaginitis

Figure 4: Effect of fenticonazole (given on day 1 and day 3) on various symptoms of vulvovaginitis

Figure 5: Effects of fenticonazole (given on day 1 and day 7) on various symptoms of vulvovaginitis
of VVC. This is in line with findings of other such study wherein authors concluded that fenticonazole is economically feasible, the first-line therapy for the treatment of VVC.[10,13] These efficacious effects of fenticonazole in VVC may be attributed to its multifaceted action such as inhibition of fungal secretory aspartate protease (SAP), blocking of cytochrome oxidase and peroxidase, and disruption of fungal cytoplasmic membrane by inhibiting fungal P450 isoenzyme which is usually required for fungal cell wall sterol synthesis.[35] Inhibition of SAP is unique to fenticonazole since it is the only imidazole antifungal to do so, even in single dose. Inhibition of SAP leads to following three effects:

1. Reduction in number of hyphae and pseudohyphae - prevents growth of fungus
2. Prevents adhesion to vaginal mucosa
3. Prevents penetration of candida into the vaginal mucosa.[35]

Moreover, efficacy of fenticonazole has been studied in various head-to-head trials with conventional antifungal therapies like clotrimazole where fenticonazole had shown a favorable response in VVC.[1,37] Emergence of resistant strains is the foremost quandary with conventional antifungal therapies. Currently, the concept of stewardship is globally inculcating into daily clinical practice to curb the menace of resistance.

The present analysis had certain limitations. Due to its analysis design, chances of selection bias cannot be ruled out. Treatment with other drugs was not considered for the present analysis, which would have impacted the final outcome. The findings of the present analysis should be compared with that of other such studies so that results can be generalized.

CONCLUSION
Most of the prescriptions in the real-world setting were in D1/D3 group implying that vulvovaginitis needs to be treated adequately with two-dose regime, in contrast to single dose recommendation of standard guidelines.

ACKNOWLEDGMENTS
We would like to acknowledge the contribution of the gynecologists across India who provided data for this analysis.

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How to cite this article: Dhoot D, Mahajan H, Barkate H. Fenticonazole in Vulvovaginal Infections: A Real-world Clinical Experience in India - Force India Study. Int J Sci Stud 2018;6(1):91-96.

Source of Support: Nil, Conflict of Interest: None declared.
Profile of Cerebrospinal Fluid Analysis in Acute Central Nervous System Infections

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Abstract

Background: Confirmatory diagnosis of acute central nervous system (CNS) infection is a concern. Most often, it is presumed and empirical antimicrobials given. CSF findings may overlap in various infections and partially treated meningitis further complicates the CSF analysis.

Materials and Methods: This study included 90 patients with acute CNS infection admitted between July 2009 and August 2011. Ninety cases of community-acquired CNS infection were included in the study. The diagnosis of CNS infection was made based on the clinical features. Laboratory investigations such as complete blood count, random blood sugar, urine analysis, renal and liver function tests, and serum electrolytes were done in all cases. Cerebrospinal fluid (CSF) samples were collected and sent for cell count, glucose, protein, chloride, Gram stain, bacterial culture, AFB smear, culture of AFB, and viral markers like herpes simplex virus (HSV).

Results: 15 patients (16.7%) had bacterial meningitis, 32 (35.5%) had tuberculous (TB) meningitis, 9 (10%) had aseptic meningitis, 30 (33.3%) had encephalitis, and 4 (4.5%) had cryptococcal meningitis. The CSF sugar-to-blood sugar ratio was found to be <0.5 in 71.1% of all CNS infections. 93.3% of bacterial meningitis, 100% of TB meningitis, and 100% of cryptococcal meningitis had a CSF-to-blood sugar ratio <0.5 while only 33.3% of aseptic meningitis and 40% of encephalitis had such a value. TB meningitis had the maximum mean CSF protein of 275 followed by cryptococcal meningitis - 169. The mean CSF total count was found to be 257 for all CNS infections together. It was found to be maximum 559 for bacterial meningitis. Gram-positive cocci were reported in five patients and Gram-negative coccobacilli were reported in one patient. Polymerase chain reaction (PCR) for TB was positive in 10 (31.2%) patients with TB meningitis. PCR for HSV was positive in 8 (20.5%) patients with aseptic meningitis or encephalitis. IgM HSV was positive in 16 (41%) patients with aseptic meningitis or encephalitis.

Conclusion: Routine CSF cell count and biochemical analysis are of prime importance in differentiating between CNS infections and identifying individual CNS infections. PCR was not found to be useful in the diagnosis.

Key words: Central nervous system infection, Cerebrospinal fluid protein, Cerebrospinal fluid sugar, Cerebrospinal fluid total count, Tuberculous meningitis

INTRODUCTION

Central nervous system (CNS) infections are an important cause of mortality and morbidity. Clinical diagnosis of CNS infections (meningitis and encephalitis) always present with difficulties due to overlapping clinical features such as fever, irritability, altered sensorium, and associated chronic history of fever further compounds the diagnosis, i.e., tuberculous (TB) meningitis and autoimmune diseases. Hence, diagnosing CNS infections is an area of concern. Acute CNS infections can be mistaken for a wide range of conditions including drug intoxications, metabolic derangements, various tropical infections, and sepsis related encephalopathy.[9] The present study focuses on the accurate laboratory diagnosis of CNS infections which predominantly include cerebrospinal fluid (CSF) analysis and help in identifying the CNS infection and aid in the early treatment of these infections. Other investigations like CNS imaging were done in most of the patients to improve diagnostic accuracy.
MATERIALS AND METHODS

The present study is a longitudinal study done between July 2009 and July 2011 at Sri Ramachandra Medical College and Hospital. All adult patients admitted with CNS infection are included in the study. Patients with age <18 years, recent neurosurgical procedure in <1 week, history of head trauma with CSF leak preceding the onset of symptoms, and patients with localized infection of CNS such as brain abscess/ space occupying lesion were excluded from the study. Ninety cases of community-acquired CNS infection were included in the study based on the criteria mentioned above. The diagnosis of CNS infection was made by the admitting physician or team based on the clinical features. Laboratory investigations such as complete blood count, random blood sugar, urine analysis, renal and liver function tests, and serum electrolytes were done in all cases. CSF samples were collected through lumbar puncture in all cases, after informed consent. Samples were examined for cell count, glucose, protein, chloride, Gram stain, bacterial culture, AFB smear, culture of AFB, and viral markers like herpes simplex virus (HSV). CSF for polymerase chain reaction (PCR) TB and HSV was done in suspected case of TB and viral etiology, respectively. Neuro imaging computerized tomography (CT) or magnetic resonance imaging (MRI) brain was done in selected patients based on the clinical features such as fundus changes. CNS infections were further divided into bacterial meningitis, tubercular meningitis, aseptic meningitis, encephalitis, and cryptococcal meningitis based on CSF findings. Each group was analyzed in detail. Patients were again reexamined at the time of discharge to look for any neurological sequelae. Results were expressed as mean for continuous variables. For categorical data, univariate analysis was performed using Pearson Chi-square test. A P value < 0.05 is considered to be statistically significant. Statistical analysis was done using SPSS windows version 17.0 Software.

RESULTS

The study included 90 patients, 73 males and 17 females. 15 patients (16.7%) had bacterial meningitis, 32 (35.5%) had TB meningitis, 9 (10%) had aseptic meningitis, 30 (33.3%) had encephalitis, and 4 (4.5%) had cryptococcal meningitis [Table 1].

The mean ESR value was found to the maximum for bacterial meningitis (66) followed by TB meningitis (64). Bacterial and aseptic meningitis had a mean ESR value of 24, while encephalitis had a mean ESR of 38.

The CSF sugar-to-blood sugar ratio was found to be <0.5 in 71.1% of all CNS infections. 93.3% of bacterial meningitis, 100% of TB meningitis, and 100% of cryptococcal meningitis had a CSF-to-blood sugar ratio <0.5 while only 33.3% of aseptic meningitis and 40% of encephalitis had such a value. More profound decrease in CSF-to-blood sugar ratio of <0.03 was seen in 75% of patients with TB meningitis and 60% of patients with bacterial meningitis [Table 2].

The mean CSF protein concentration was found to be 154 for all CNS infections together. Individually among CNS infections, TB meningitis had the maximum mean CSF protein of 275, followed by cryptococcal meningitis - 169, aseptic meningitis - 94, bacterial meningitis - 80, and encephalitis - 76 [Table 3].

The mean CSF total count was found to be 257 for all CNS infections together.

It was found to be maximum 559 for bacterial meningitis, followed by 325 for cryptococcal meningitis, 291 for TB meningitis, 188 for aseptic meningitis, and 80 for encephalitis [Table 4].

Table 5 analyzes the CSF differential count.

CSF Gram stain was done in 15 patients. Gram-positive cocci were reported in five patients and Gram-negative coccobacilli were reported in one patient. Out of

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Male (%)</th>
<th>Female (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial meningitis</td>
<td>10 (66.6)</td>
<td>5 (33.7)</td>
<td>15</td>
</tr>
<tr>
<td>TB meningitis</td>
<td>11 (34.3)</td>
<td>21 (65.7)</td>
<td>32</td>
</tr>
<tr>
<td>Aseptic meningitis</td>
<td>6 (66.7)</td>
<td>3 (33.3)</td>
<td>9</td>
</tr>
<tr>
<td>Encephalitis</td>
<td>25 (83.3)</td>
<td>5 (16.7)</td>
<td>30</td>
</tr>
<tr>
<td>Cryptococcal meningitis</td>
<td>3 (75)</td>
<td>1 (25)</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>55 (60.3)</td>
<td>35 (39.7)</td>
<td>90</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>&lt;0.3 (%)</th>
<th>0.3–0.5 (%)</th>
<th>&gt;0.5 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All CNS infections (n=90)</td>
<td>35 (38.9)</td>
<td>29 (32.2)</td>
<td>26 (28.9)</td>
</tr>
<tr>
<td>Bacterial meningitis (n=15)</td>
<td>9 (60)</td>
<td>5 (33.3)</td>
<td>1 (6.7)</td>
</tr>
<tr>
<td>TB meningitis (n=32)</td>
<td>24 (75)</td>
<td>8 (25)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Aseptic meningitis (n=9)</td>
<td>0 (0)</td>
<td>3 (33.3)</td>
<td>6 (66.7)</td>
</tr>
<tr>
<td>Encephalitis (n=30)</td>
<td>1 (3.3)</td>
<td>11 (36.7)</td>
<td>18 (60)</td>
</tr>
<tr>
<td>Cryptococcal meningitis (n=4)</td>
<td>1 (25)</td>
<td>3 (75)</td>
<td>0 (0)</td>
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<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Mean CSF protein (mg/dL)</th>
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</thead>
<tbody>
<tr>
<td>All CNS infection</td>
<td>154</td>
</tr>
<tr>
<td>Bacterial meningitis</td>
<td>80</td>
</tr>
<tr>
<td>TB meningitis</td>
<td>275</td>
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<tr>
<td>Aseptic meningitis</td>
<td>94</td>
</tr>
<tr>
<td>Encephalitis</td>
<td>76</td>
</tr>
<tr>
<td>Cryptococcal meningitis</td>
<td>169</td>
</tr>
</tbody>
</table>

CSF: Cerebrospinal fluid, CNS: Central nervous system, TB: Tuberculous
In our study, of 15 patients with bacterial meningitis, 10 (66.6%) were male and 5 (33.3%) were female. The sex distribution in bacterial meningitis reported by other studies is as follows: Mani et al.\(^{(5)}\) found 76.1% of males and 23.9% of females; Van de Beek et al.\(^{(7)}\) found 49.6% of males and 51.4% of females; Thwaites et al.\(^{(9)}\) found 78% of males and 22% of females; and Moghtaderi et al.\(^{(4)}\) found 71.5% of males and 28.5% of females. Studies done in the Indian subcontinent by Wani et al.\(^{(7)}\) show TB meningitis to be more prevalent among females as observed in our study in contrast to studies done in the west. Sex distribution in TB meningitis by other studies as follows: Thwaites et al.\(^{(9)}\) found 64% of males and 36% of females and Moghtaderi et al.\(^{(4)}\) found 56.9% of males and 43.1% of females. In our study, of 30 patients diagnosed to have encephalitis, 25 (83.3%) were male and 5 (16.7%) were female. The sex distribution in encephalitis reported by other studies is as follows: Glaser et al.\(^{(6)}\) found 53% of males and 47% of females and Mailes and Stahl\(^{(1)}\) found 61% of males and 39% of females. In our study, of 4 patients diagnosed to have cryptococcal meningitis, 3 (75%) were males and 1 (25%) were females. The sex distribution in cryptococcal meningitis reported by other studies is as follows: Baradkar et al.\(^{(10)}\) found 52.6% of males and 47.4% of females, and in a study by Prasad et al.\(^{(11)}\) found 73.3% of males and 26.7% females.

Among CNS infections, the mean ESR value was found to the maximum for cryptococcal meningitis (66 mm/h) followed by TB meningitis (64 mm/h). Bacterial and aseptic meningitis had a mean ESR value of 24 mm/h, while encephalitis had a mean ESR of 38 mm/h. Wani et al.\(^{(3)}\) reported elevated ESR in 81% of patients with TB meningitis. Van de Beek et al.\(^{(4)}\) reported a mean ESR of 46 in patients with bacterial meningitis. The higher ESR value observed for cryptococcal meningitis in our study was probably due to low hemoglobin percentage as all four patients of cryptococcal meningitis were severely anemic. Among CNS infections, hyponatremia was present in 46.7% of cases of bacterial meningitis, 75% of cases of TB meningitis, 33.3% of cases of aseptic meningitis, 36.7% of cases of encephalitis, and 75% of cases of cryptococcal meningitis.

The CSF sugar-to-blood sugar ratio was found to be <0.5 in 71.1% of all CNS infections, 93.3% of bacterial meningitis, 100% of TB meningitis, and 100% of cryptococcal meningitis had a CSF-to-blood sugar ratio <0.5 while only 33.3% of aseptic meningitis and 40% of encephalitis had such a value. More profound decrease in CSF-to-blood sugar ratio of <0.03 was seen on 75% of patients with TB meningitis and 60% of patients with bacterial meningitis. Thwaites et al.\(^{(9)}\) reported a median CSF/blood glucose ratio of 0.28 for TB and 0.20 for bacterial meningitis. Wani et al.\(^{(3)}\) reported a CSF/blood glucose ratio of <0.6 for 80%...
and <0.4 for 28.6% of TB meningitis. Van de Beek et al.[4] reported a mean ratio of 0.2 for bacterial meningitis. Glaser et al.[5] reported a ratio <0.4 for only 4% of encephalitis. Both bacterial and TB meningitis had a low CSF/blood sugar ratio in our study as found in other studies. Our study showed a lower ratio for TB meningitis compared to bacterial.

In our study, TB meningitis had the maximum mean CSF protein of 275, followed by cryptococcal meningitis −169 mg/dL, aseptic meningitis −94 mg/dL, bacterial meningitis −80 mg/dL, and encephalitis −76 mg/dL. Thwaites et al.[3] reported a median CSF protein level of 191 for TB and 270 for bacterial meningitis. Moghtaderi et al.[6] reported a median CSF protein level of 113 for TB and 120 for bacterial meningitis. Van de Beek et al.[4] reported a mean CSF protein of 490 mg for bacterial meningitis. Wani et al.[7] reported an elevated CSF protein levels of more than 50 mg/dL for 73.7% and more than 150 mg/dL for 14.3% of TB meningitis. MAILLES and Stahl[8] reported elevated CSF protein levels of 110 for patients who survived and 290 for patients who expired among cases of encephalitis. Nowak et al.[12] reported an elevated protein levels of 138 mg/dL for patients with aseptic meningitis due to HSV. The mean CSF protein was found to be elevated in all forms of CNS infections in our study with maximum being TB meningitis. Other studies show a more elevated CSF protein for bacterial meningitis compared to TB meningitis.

In our study, the mean CSF total count was found to be 257 for all CNS infections together. It was found to be maximum 559 for bacterial meningitis, followed by 325 for cryptococcal meningitis, 291 for TB meningitis, 188 for aseptic meningitis, and 80 for encephalitis. Thwaites et al.[3] reported a median CSF total count of 300 for TB and 2583 for bacterial meningitis.


For cryptococcal meningitis, Baradkar et al.[9] reported the CSF total counts as non-specific. All studies including ours report the maximum elevation of CSF total count for bacterial meningitis; however, the mean CSF total count found in our study for bacterial meningitis was lower compared to other studies.

In our study, 100% of bacterial meningitis showed a polymorphic predominance. Lymphocytic predominance was showed by 90.6% of TB meningitis, 70% of encephalitis, and all cases of aseptic and cryptococcal meningitis. Thwaites et al.[3] reported a polymorphic predominance of 90% for bacterial meningitis and lymphocytic predominance of 64% for TB meningitis.


Of 15 patients diagnosed as bacterial meningitis, 5 (33.3%) had a positive Gram stain. 4 showed Gram-positive cocci and 1 showed Gram-negative coccobacilli. Van de Beek et al.[4] reported a positive Gram stain in 80% of cases with bacterial meningitis. Mani et al.[13] reported positive Gram stain in 65.7% of bacterial meningitis.

Of 15 patients diagnosed as bacterial meningitis, 4 (20%) had a growth of S. pneumonia and 1 (6.7%) had a growth of S. aureus in CSF culture. Mani et al.[3] reported a positive CSF culture in 40.8% of cases of bacterial meningitis. The most common organism isolated was S. pneumoniae, followed by Haemophilus influenza and S. aureus. Van de Beek et al.[4] reported the most common organism isolated as S. pneumoniae, followed by Neisseria meningitidis, Listeria monocytogenes, and S. aureus. The percentage of positive Gram stain and CSF culture in our study was lower compared to others probably due to early treatment with antibiotics before CSF analysis or delay in processing the CSF sample.

In our study, PCR was positive for 10 (31.2%) of 32 cases of TB meningitis and 8 (20.5%) of encephalitis and aseptic meningitis.

The sensitivity of PCR in detecting CNS infection was found to be low in this study.

**CONCLUSION**

The laboratory diagnosis of CNS infections still remains as a dilemma due to considerable overlap in findings. CSF findings of moderate lymphocytic predominant leukocytosis with low CSF-to-plasma glucose ratio and an increased protein concentration in a patient with longer duration of symptoms are suggestive of TB meningitis. The yield of CSF AFB stain was found to be poor. None of our patients had a positive AFB stain. The yield of Gram staining and culture of CSF was found be less probably due to early treatment with antibiotics. S. pneumoniae is found to be the most common etiological agent associated with
bacterial meningitis. PCR was found to be not of much use in the diagnosis since it was found to be positive only in less than one-third of the patients. Neuroimaging is not mandatory before LP unless there is a definite indication, since in most of our patients, imaging was found to be normal. Routine CSF cell count and biochemical analysis are of prime importance in differentiating between CNS infections and identifying individual CNS infections.

REFERENCES


Effect of Internet Use on Health College Students at King Saud University

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Abstract

Background and Objective: This study aims to evaluate the effect of Internet use on undergraduate medical and health science students living in the student residential compound at King Saud University (KSU) in Riyadh. Three dimensions are used to identify the positive and negative effects of Internet use: Academic (educational) performance, health (psychological) status, and social status.

Methodology: This study adopts a cross-sectional design. We included all the students of the health colleges at KSU who lived in the university dormitory in 2015, a total of 250 students. A structured self-administered questionnaire was used to gather data from the respondents.

Results: We found that 89.5% of the students who were able to increase their cumulative grades were using the Internet for less time per day, indicating that spending an excessive amount of time on the Internet has a negative impact on students’ academic performances. 156 students (78.7%) had no changes regarding their social relations relative to their Internet usage. 78.3% of the respondents claimed to use the Internet to escape from the stress of studying; however, excessive Internet use may, in fact, increase overall pressure on students.

Conclusion: Moderate use of the Internet helps health college students to improve their cumulative grade point averages, and there was no significant relationship found between Internet use and changes in the students’ social lives or moods.

Key words: Internet, Students, Academic performance, King Saud University, Saudi Arabia

INTRODUCTION

There is no doubt that the Internet has become the most popular consumer communicating technology and also an increasingly popular medium for accessing educational material.

Internet usage is expanding rapidly, with an estimated 900.4% growth rate worldwide between 2000 and 2016. The Middle East has the second highest usage growth rate in the world, a recorded 3936.5% increase. In Saudi Arabia, there were approximately 200,000 Internet users in the year 2000, a number that has dramatically increased in subsequent years, reaching more than 18 million users in November 2015 (65.9% of the region’s population).[1]

Nowadays, the Internet is widely and readily available in educational institutes and public libraries, and web use is becoming mandatory in academic studies, for both students and teaching staff. The Internet is a practical tool for students to access and research new information, and they now rely on the web for their study more than ever before. With such widespread accessibility, it can be said that the Internet has become an integral part of our lives.[2-9]

University students are at a higher risk of developing a dependence on the Internet than others because they depend on the web as a primary source of necessary educational information. In Taiwan, for example, most students leave their homes and move toward independent lives when they enter college. Many reside in school dormitories and have convenient and free Internet access through school network systems. They find the Internet to be an important window through which they can...
communicate and interact with the world, and their free and easily accessed connections, mean that Internet use is both implicitly and explicitly encouraged by a recognized, institutional authority. Given this influence, psychologists and educators should give more attention to the issue of student dependence on the Internet.\[^{[6,8]}\]

Communication through the Internet can reduce depression, especially among socially isolated populations, such as college students, who depend on social technology for social support. However, increases in the time of Internet have also been shown to correspond to a high level of emotional loneliness.\[^{[9,10]}\]

Many previous studies have shown that multiple factors including the age of exposure to the Internet, the age of student, living in city, homesickness, isolation, loneliness, bad social skills, poor social support, being a freshman, and being male are all risk factors for Internet addiction among students. All of these factors could significantly contribute to developing compulsive Internet use, thus resulting in adverse performance in other activities such as work, school, or relationships.\[^{[11-13]}\]

Most studies of Internet use focus mainly on the negative and problematic effects of the Internet use for individuals, and there has been no study on students in university dorms in Kingdom of Saudi Arabia, whom, as mentioned earlier, are more susceptible to isolation. It would therefore be useful to establish research on this group. Because the medical and health science fields are rapidly changing and require students to maintain a high standard of knowledge and independent learning, our study concentrated on students in the King Saud University’s (KSU’s) medical and health sciences departments.

Hypothesis

We hypothesize that average levels of Internet use enhance the understanding of scientific curriculum topics and contribute to the improvement of the cumulative grade point average (CGPA), while excessive Internet use is associated with mood changes and the impairment of social life.

Objectives

This work aims to evaluate the effect of Internet use on undergraduate medical and health sciences students living in the student residential compound at KSU. Three dimensions are used to identify the positive and negative effects of Internet use: Academic (educational) performance, health (psychological) status, and social status.

METHODOLOGY

We adopted a cross-sectional design in this study. The subjects included in this study are students of KSU’s health colleges (medicine, dentistry, pharmacy, and applied medical sciences) who lived in the dormitory in the 2015–2016 academic year. The study included students at different levels of education (1\(^{st}\), 2\(^{nd}\), 3\(^{rd}\), 4\(^{th}\), 5\(^{th}\), and internship years). The Institutional Review Board at KSU approved this survey by No.15/0262/IRB.

Sample Size

We included all the students of KSU’s health colleges who lived in the dormitory, for a total of 250 students.

Data Collection Tool

We developed a self-administered English language questionnaire, which contained an introduction, instructions, demographic information, and 21 closed questions (general questions about using the Internet, effects of Internet using on academic performance, social life, and health). Questions included the presence or absence (yes or no questions), bipolar (Likert scale), and a number of multiple-choice responses. We developed this questionnaire from related research studies. The questionnaire was reviewed by two professors for face validation, after which a pilot study was conducted on 15 students. The pilot study confirmed that the questions were clear, and the number of questions and time required to answer the questions were reasonable (3 min in average). No changes were made based on the pilot study.

Procedure

This study was conducted from May 2015 to August 2016, and the actual time devoted to data collection was 4 weeks (over the month of December 2015). We gained consent from the administration of student housing to distribute the questionnaire. A self-administered questionnaire was used to collect data from the male students only because we faced difficulties in delivering questionnaires to the female students. We distributed the questionnaire by going to the rooms where the students resided and giving them the questionnaire. After handing them the questionnaire and the consent to participate in this study is taken, we waited till the students finished answering the questions and then took the survey back. Every day of those weeks, we went several times a day to check the availability of students in their rooms and give them the questionnaire.

We used the Statistical Package for the Social Sciences version 20 for Windows for statistical analyses. A Chi-square test was used to find out the statistical significance of the differences in the proportions. \(P < 0.05\) was considered to be statistically significant.
RESULTS

Of the 250 students eligible for the survey, 198 (79.2%) responded.

According to Table 1, most of the students (87.9%) use the Internet on a daily basis; 54% of this group were able to increase their CGPA (based on the responses of the participants). Only 12.1% of students did not use the Internet daily, and of this group, 79.1% did not have their CGPA affected. 145 students (73.2%) used the Internet <4 h/day, 59.3% of students who were able to increase their CGPA. 45 students (22.7%) used the Internet between 4 and <8 h/day, 21 students (34.4%) of them did not experience any CGPA changes. Of the only 4% of students who used the Internet more than 8 h/day, 62.5% reported a CGPA decrease.

Figure 1 shows that the Internet was a primary source for more than half of the medical students (53.03%) to get their educational information, while 46.97% relied on the Internet as a secondary source.

Table 2 summarized that most of the students (69.2%) did not have their class attendance affected, 75.1% of this unaffected group were using the Internet for <4 h/day. The remaining students were evenly split between those who increased and those who decreased their attendance. 86.6% of the students who were able to increase their presence were used the Internet <4 h/day, and 51.6% of students whose attendance decreased were using the Internet <4 h/day. Exactly 63 students had CGPAs between 4.49 and 3.75, 80.9% of them were using the Internet <4 h/day. Of the only three students with CGPAs <2.49, two of them (66.6%) used the Internet more than 8 h/day.

Table 3 summarized that most of the students (34.5%) who were using the Internet <4 h, their main purpose to use the Internet was for visiting sites related to study, general knowledge, and entertainment. As for users exceeding 8 h, 37.5% of them were using the Internet for general knowledge and entertainment only.

Table 4 summarizes that 156 students reported that their social relations had not decreased because of their using the Internet. 74.3% of these 156 students were using the Internet <4 h/day. Only 42 students reported a decline in their social relations. In total, 144 students (72.7%) reported not having any mood changes; most of them (73.6%) were using the Internet <4 h/day. 54 students suffered from mood change due to the use of the Internet.

Table 5 summarizes how studying hours are affected using the Internet as a chance to escape learning stress. We found that of the 155 students who use the Internet to decrease their stress, 79 students (50.9%) decreased their studying hours due to their using the Internet as a means of stress relief. Further, 60 students (38.7%) said their studying hours have not been affected.

DISCUSSION

Most of the students in the survey were using the Internet, and majority of them (73.2%) were using the Internet <4 h/day, despite the fact that the Internet is free

<table>
<thead>
<tr>
<th>Variables</th>
<th>Impact on CGPA</th>
<th>Total</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Increased n (%)</td>
<td>Decreased n (%)</td>
<td>Did not change n (%)</td>
</tr>
<tr>
<td>Internet use per week</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily</td>
<td>94 (97.9)</td>
<td>38 (92.7)</td>
<td>42 (68.9)</td>
</tr>
<tr>
<td>Less than daily</td>
<td>2 (2.1)</td>
<td>3 (7.3)</td>
<td>19 (31.1)</td>
</tr>
<tr>
<td>Hours of Internet use per day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;4 h</td>
<td>86 (89.6)</td>
<td>22 (53.7)</td>
<td>37 (60.7)</td>
</tr>
<tr>
<td>4–&lt;8 h</td>
<td>10 (10.4)</td>
<td>14 (34.1)</td>
<td>21 (34.4)</td>
</tr>
<tr>
<td>8 h and more</td>
<td>0 (0)</td>
<td>5 (12.2)</td>
<td>3 (4.9)</td>
</tr>
</tbody>
</table>

CGPA: Cumulative grade point average
of charge and available 24 h a day. We compared these finding with those from another survey done by Albouq et al. at Taibah University, which reported that 100% of medical students were using the Internet and that most of them (53.4%) spent 2–4 h/day online.[14] Internet use among medical students in both studies was similar, likely because they are well educated and aware of the adverse effects of prolonged Internet use.

We found that 53% of students use the Internet as the primary source for their educational information, while 47% of students use the Internet as a secondary source. This percentage will likely increase over time because students increasingly seek scholarship materials and recent medical information through the web. This finding is consistent with those of a survey by Tsai and Lin, which found that approximately 90% of students rely on the Internet as their primary source for educational information.[3] We also noticed that most of the students who were able to increase their CGPA (89.6%) and class attendance (86.6%) used the Internet for <4 h/day, while only 10.4% of those who used the Internet for more than 4 h/day increased their CGPA. Amount of time of Internet use has a significant correlation with CGPA improvement and class attendance ($P < 0.0001$). A similar report in the study conducted by Khan et al. revealed that students who spent excessive time on the Internet had significantly higher academic impairment than those that did not.[15] This result suggests that spending excessive time using the Internet negatively impacts students’ academic performance. For the plurality of students (34.5%) who were using the Internet <4 h, their main purpose for using the Internet was to visit sites related to major, general knowledge, or entertainment ($P = 0.041$) this might have helped them to improve their CGPA. Moreover, based on the obtained results, it seems that excessive Internet use (exceeding 8 h) is coupled with reduced interest to utilize it for studying purposes as the majority of them (37.5%) used it only for general knowledge and entertainment.

In total, 156 students among the sample (78.7%) had no changes regarding their social relations, and there was no statistically significant relationship between the time of Internet use and quality of social life ($P = 0.524$). This result was contrary to what we expected and to the findings of the study by Asdaque et al., which reported that excessive use of Internet reduces the rate of building social relations.[9] However, our study applied to the students who came from outside Riyadh mainly; it is reasonable to expect that their social relations are much more powerfully affected by this larger contextual factor.

Most of the students (72.7%) reported not suffering from mood changes due to Internet use. This result differs from one by Clark and Everhart, which revealed that students who used the Internet for more time are significantly less likely to have mood changes because their use depends on their coping skills rather than on how much time they spend online.[16] It was

### Table 2: Relationship between Internet use per day and class attendance and CGPA

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hours of use per day</th>
<th>Total n (%)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;4h n (%)</td>
<td>4–&lt;8h n (%)</td>
<td>≥8h n (%)</td>
</tr>
<tr>
<td>Class attendance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased</td>
<td>0 (0)</td>
<td>4 (8.9)</td>
<td>26 (17.9)</td>
</tr>
<tr>
<td>Decreased</td>
<td>8 (100)</td>
<td>7 (15.6)</td>
<td>16 (11)</td>
</tr>
<tr>
<td>Not affected</td>
<td>0 (0)</td>
<td>34 (75.6)</td>
<td>103 (71)</td>
</tr>
<tr>
<td>CGPA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5–4.5</td>
<td>0 (0)</td>
<td>6 (13.3)</td>
<td>15 (10.3)</td>
</tr>
<tr>
<td>4.49–3.75</td>
<td>1 (12.5)</td>
<td>11 (24.4)</td>
<td>31 (35.2)</td>
</tr>
<tr>
<td>3.74–3.25</td>
<td>3 (7.5)</td>
<td>15 (33.3)</td>
<td>48 (33.1)</td>
</tr>
<tr>
<td>3.24–2.5</td>
<td>2 (25)</td>
<td>13 (28.9)</td>
<td>30 (20.7)</td>
</tr>
<tr>
<td>&lt;2.49</td>
<td>2 (25)</td>
<td>0 (0)</td>
<td>1 (7)</td>
</tr>
</tbody>
</table>

**CGPA:** Cumulative grade point average

### Table 3: Relationship between the duration of Internet use and the purpose of usage

<table>
<thead>
<tr>
<th>What sort of websites/pages you usually visit (you can choose more than one):</th>
<th>How many hours do you spend using the Internet a day</th>
<th>Total n (%)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;4h n (%)</td>
<td>4–&lt;8h n (%)</td>
<td>8 h and more n (%)</td>
</tr>
<tr>
<td>Sites related to studied major</td>
<td>12 (8.3)</td>
<td>5 (11.1)</td>
<td>1 (12)</td>
</tr>
<tr>
<td>General knowledge</td>
<td>16 (11)</td>
<td>4 (8.9)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td>Entertainment</td>
<td>9 (6.2)</td>
<td>4 (8.9)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>News</td>
<td>1 (0.7)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Sites related to studied major, general knowledge</td>
<td>16 (11)</td>
<td>2 (4.4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Sites related to studied major, entertainment</td>
<td>21 (14.5)</td>
<td>9 (20)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td>General knowledge, entertainment</td>
<td>15 (10.3)</td>
<td>6 (13.3)</td>
<td>3 (37.5)</td>
</tr>
<tr>
<td>Sites related to studied major, general knowledge, entertainment</td>
<td>50 (34.5)</td>
<td>13 (28.9)</td>
<td>1 (12)</td>
</tr>
<tr>
<td>Sites related to studied major, general knowledge, news</td>
<td>0 (0)</td>
<td>1 (2.2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Sites related to studied major, entertainment, news</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td>General knowledge, entertainment, news</td>
<td>1 (0.7)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Sites related to studied major, general knowledge, entertainment, news</td>
<td>4 (2.8)</td>
<td>1 (2.2)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>
Further discovered that 155 students (78.3%) use the Internet to escape from the pressures of studying and that using it negatively affects studying for 50.9% of them, a statistically significant relationship ($P=0.023$). Hence, in the end, the students who were using the Internet as a means of relieving stress were actually causing themselves stress by limiting their time for studying. These results reinforce Nastizaei's finding that people who use the Internet for long durations of time have considerable anxiety. The biggest limitation on gaining comprehensive results was the unavailability of students in their rooms. We also depended on participants’ subjective evaluations of their moods and changes in social life, which may have varied depending on their individual understandings and expectations of moods and social life.

### CONCLUSION

This survey found that Internet helps medical students to improve their CGPA if they use it for an average time and for educational purposes. The results did not indicate a statistically significant relationship between the students’ social life and their Internet use ($P=0.524$). Many of the students in this study used the Internet to escape from the pressures of studying.

### Recommendations

Students should be encouraged to use the Internet to promote and increase their knowledge, but they should be guided through the manners and procedures for its proper use, especially now that the Internet became a necessary tool for learning. To deepen our understanding of this phenomena, we suggest further studies on non-medical and female medical students who live in student dormitories and to conduct studies that involve multiple institutions.

### REFERENCES


**How to cite this article:** Saif AM. Effect of Internet Use on Health College Students at King Saud University. Int J Sci Stud 2018;6(1):102-106.

**Source of Support:** Nil, **Conflict of Interest:** None declared.
Right Ventricular Functional Assessment in Acute Myocardial Infarction Using Strain Imaging Parameters and Its Angiographic Correlation

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INTRODUCTION

Acute myocardial infarction (AMI) is characterized by a loss of contractile tissue and a change in ventricle geometry that causes a substantial impairment of the right ventricle (RV) and left ventricle (LV) systolic and diastolic functions. Echocardiographic RV functional parameters

Abstract

Introduction: Echocardiographic right ventricle (RV) functional parameters have independent and additive prognostic value in patients with left ventricle (LV) dysfunction following acute myocardial infarction (AMI) strain echocardiography is known to be a reliable method for the quantification of regional contractile dysfunction with the ability to detect subclinical cardiac dysfunction, and it is a feasible tool to evaluate RV global and regional myocardial function. It can measure RV systolic function in a non geometric manner like its evaluation of LV systolic function. Strain imaging has been proposed as an objective and quantitative measurement of wall motion abnormalities.

The Aim of Our Study: To correlate RV strain parameters with clinical, echocardiographic, and angiographic parameters.

Materials and Methods: Echocardiography was performed immediately after thrombolysis in patients with AMI using GE VIVID T8 machine, 3 Sc-Rs transducer adult probe equipped with tissue Doppler and speckle-tracking technology. RV strain assessment was done by speckle-tracking method. Coronary angiogram was performed in all patients included in the study.

Results: A total of 102 consecutive patients admitted in our Integrated Critical Care Unit with the first episode of AMI were included in our study. Among 102 patients, 80 (78%) were male and 22 (22%) were female. Anterior wall MI (AWMI) was more common (58%), inferior wall MI (IWMI) (40%), left ventricular mass index (LWMI) (2%). 40 patients out of the total 102 patients had single-vessel disease, 36 patients had double-vessel disease, and 8 patients had triple-vessel disease. A total of 14 patients had left main coronary artery involvement along with other vessel disease. In the study population, AWMI group had a mean mitral E/e’ of 9.742 ± 3.421, IWMI group had a mean mitral E/e’ of 10.556 ± 2.593, and LWMI group had a mean mitral E/e’ of 9.57 ± 0.707. AWMI group had a mean RV mid-velocity of 3.986 ± 0.933. IWMI group had a mean RV mid-velocity of 3.385 ± 0.465. LWMI group has mean RV mid-velocity of 5.15 ± 1.626. AWMI group had a global RV mean velocity of 4.231 ± 1.281. IWMI group had a global RV mean velocity of 3.712 ± 0.591. LWMI group had a global RV mean velocity of 5.2 ± 0.849.

Conclusion: Patients with IWMI had much lower segmental and global longitudinal strain RV values compared to AMWI patients and the difference was statistically significant. RV dysfunction has also been related to poor prognosis; therefore, the function of both ventricles after AMI should be considered. Quantitative assessment of RV function with RV strain may improve the risk stratification of patients after AMI.

Key words: Quantitative right ventricular assessment, Right ventricular longitudinal strain, Speckle tracking

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Month of Peer Review : 00-0000
Month of Acceptance : 00-0000
Month of Publishing : 00-0000

DOI: 10.17354/ijss/2018/123
have independent and additive prognostic value in patients with LV dysfunction.\textsuperscript{[1]}

RV dysfunction may be primarily attributed to an abnormality of RV myocardium or secondary to LV dysfunction, as a consequence of “ventricular interdependence” between the two ventricles.\textsuperscript{[4]} Hence, earliest recognition of RV dysfunction is warranted, but till today, it remains a challenging task because of complex structure and asymmetric shape of RV.\textsuperscript{[2]} Subclinical RV dysfunction is known in patients with right coronary territory ischemia. Right ventricular functions in LV anterior infarction have been the subject of several studies but with significant discrepancies in results.\textsuperscript{[3-8]} RV function is an important prognostic factor for clinical outcomes in patients with acute MI of LV. Moreover, RV involvement occurs in a percentage of patients suffering an inferior wall MI (IWMI) and increases in-hospital death rates.

Currently, strain and strain rate (S/SR) imaging is the most popular echocardiographic technique for use in AMI. Tissue Doppler imaging (TDI) and S/SR imaging are the most important modalities for revealing subclinical myocardial damage.\textsuperscript{[9]}

Strain echocardiography is known to be a reliable method for the quantification of regional contractile dysfunction with the ability to detect subclinical cardiac dysfunction, and it is a feasible tool to evaluate RV global and regional myocardial function.\textsuperscript{[10]} It can measure RV systolic function in a non-geometric manner like its evaluation of LV systolic function.\textsuperscript{[11]} Strain imaging has been proposed as an objective and quantitative measurement of wall motion abnormalities. Regional myocardial strain can be measured by velocity gradient from TDI. However, TDI is Doppler angle-dependent, which makes the acquisition and correct interpretation of the data more difficult.

The aim of our study was to evaluate RV regional functions using speckle tracking, diffusion tensor imaging (DTI)-derived S/SR imaging method in patients who experienced their first successfully treated AMI.

**Aim of the Study**

- To evaluate right ventricular regional functions using a derived strain and strain rate imaging by speckle-tracking/tissue Doppler method in patients who were successfully treated for their first AMI
- To correlate RV strain parameters with clinical and echocardiographic parameters.

To analyze angiographic results of the same patients in the study group.

**MATERIALS AND METHODS**

**Study Population**

One hundred and two patients who had suffered their first acute MI attack had been hospitalized within 1–12 h of the onset of symptoms and had undergone thrombolysis were enrolled in the study at Intensive Cardiac Care Unit, Government Rajaji Hospital.

**Inclusion Criteria**

One hundred and two patients suffering from first AMI who had been hospitalized within 1–12 h of the onset of symptoms and had undergone thrombolysis were enrolled in the study.

**Exclusion Criteria**

The exclusion criteria were as follows:

- Patients with:
  - Bundle branch block
  - A prior history of MI
  - Prior percutaneous transluminal coronary angioplasty or undergone recurrent percutaneous intervention
  - Acute stent thrombosis.
- Patients with pulmonary hypertension due to:
  - Valvular heart disease
  - Lung disease
  - Cardiomyopathy
  - Renal, hepatic, hematological disorders
  - Malignancy.

**Data Collection**

A detailed medical history, clinical examination, and relevant laboratory investigations were done as indicated in each patient.

**Study Protocol**

*Design of study*

The study was a prospective analytical study.

*Period of study*

This study was conducted from August 2015 to February 2016.

*Collaborating departments*

Department of Cardiology.

**Ethical clearance**

The ethical clearance was obtained.

**Consent**

Individual written and informed consent was obtained.

**Analysis: Statistical Analysis**

Data analysis was done with the help of computer using SPSS 16 software and Sigma Stat 3.5 version (2012). Using
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...this software, mean, standard deviation, and “P” value were calculated through Student’s t-test, One-way ANOVA, Chi-square test, and correlation coefficient from Pearson correlation and P < 0.05 was considered as statistically significant.

Echocardiogram
Echocardiography was performed immediately after thrombolysis in patients with AMI using GE VIVID T8 machine, 3 Sc-Rs transducer adult probe equipped with tissue Doppler and speckle-tracking technology.

LV systolic function was assessed by modified Simpson’s method. Pulse Doppler was used to assess mitral E/A, tricuspid E/A. Mitral E/e' was assessed by TDI.

RV strain assessment was done by speckle-tracking method. The image acquisitions are based on detecting speckles from the myocardium with two-dimensional echocardiography analyzing motion in different directions, longitudinal, radial, and circumferential. Strain measurements of the RV are best performed from the apical four-chamber view, assessing the RV free wall from the base to the apical level.

RV myocardial velocity, strain, and strain rate was assessed by TDI method. One-dimensional strain echocardiography is a dimensionless measurement that represents the fractional or percentage change in myocardial fiber shortening. To calculate strain, high frame rates are required, ideally ≥150 frames/s. As such, a narrow imaging sector focusing on the RV free wall is desired. Care should be taken to align the segment in the center of the sector to avoid errors due to the angle dependence of Doppler. A maximum tolerance of 10–15° of the axis is recommended. Imaging is in color-coded tissue Doppler mode, and ≥3 beats are acquired with suspended respiration. Values for strain and SR are then derived offline on the system or workstation using equipment-specific algorithms by placing sample volume(s) or regions of interest of varying sizes in the mid-portion of the segment(s).

Coronary Angiogram
Coronary angiogram was performed in all patients included in the study after getting informal consent.

Standard accesses chosen were either femoral or radial approach. Standard views for coronary angiogram included AP, left anterior oblique, right anterior oblique caudal and cranial views.

RESULTS
A total of 102 consecutive patients admitted in our Integrated Critical Care Unit with the first episode of AMI were included in our study. Among 102 patients, 80 (78%) were male and 22 (22%) were female. Anterior wall MI (AWMI) was more common (58%), IWMI (40%), left ventricular mass index (LWMI) (2%). 39 patients were <50 years and 63 patients were >50 years. Among patients presenting with AMI, 69 (68%) were smokers and 33 (32%) were non-smokers. 45 (44.1%) were diabetics and 57 (55.9%) were non-diabetics. Similarly, 45 (44.1%) were hypertensives and 57 (55.9%) were non-hypertensives. 102 patients had single-vessel disease (SVD), 36 patients had double-vessel disease (DVP), and 8 patients had triple-vessel disease (TVD). A total of 14 patients had left main coronary artery (LMCA) involvement along with other vessel disease. A total of 3 patients with AWMI had recanalized left anterior descending (LAD).

A total of 37 patients with AWMI had underwent percutaneous coronary intervention (PCI), while 10, 12 patients opted for coronary artery bypass surgery (CABG), medical management respectively. Similarly, 20 patients with IWMI had underwent PCI, while 21, 0 patients opted for CABG, medical management, respectively. In the same manner, two patients with LWMI had underwent PCI. AWMI group had a mean left ventricular ejection fraction (LVEF) of 39.37 ± 4.881%. IWMI group had a mean LVEF of 41.43 ± 6.091%. LWMI group had a mean LVEF of 47 ± 11.31%. The difference between the groups was statistically significant. In the study population, AWMI group had a mean mitral E/A of 1.036 ± 0.369. IWMI group had a mean mitral E/A of 1.005 ± 0.249. LWMI group had a mean mitral E/A of 0.7 ± 0.283. The difference between the groups was statistically insignificant. In the study population, AWMI group had a mean mitral E/e' of 9.742 ± 3.421, IWMI group had a mean mitral E/e' of 10.55 ± 2.593, and LWMI group had a mean mitral E/e' of 9.57 ± 0.707. The difference between the groups was statistically insignificant. In the study population, AWMI group had a mean tricuspid E/A of 1.131 ± 0.317. IWMI group had a mean tricuspid E/A of 0.98 ± 0.299. LWMI group had a mean tricuspid E/A of 0.6 ± 0.283. The difference between the groups was statistically significant.

In the study population, AWMI group had a mean TAPSE of 16.763 ± 2.593. IWMI group had a mean TAPSE of 14.049 ± 1.923. LWMI group had a mean TAPSE of 14.49 ± 2.29. Similarly age group <50 years had a mean RV strain of −14.26 ± 2. Age group >50 years had a mean RV strain of −14.49 ± 2.29. Similarly age group <50 years had a mean RV strain rate of −14.25 ± 2.24 and females had a mean RV strain rate of −14.98 ± 2.05. Similarly, males had a mean RV strain rate of −1.47 ± 0.21 and females had a mean RV strain rate of −1.43 ± 0.16. Smokers group had a mean RV strain of...
−14.17 ± 2.04. Non-smokers group had a mean RV strain of −14.89 ± 2.51. Similarly, smokers group had a mean RV strain rate of −1.47 ± 0.21. Non-smokers group had a mean RV strain rate of −1.44 ± 0.17.

Diabetics group had a mean RV strain of −14.34 ± 2.46 and nondiabetics group had a mean RV strain of −14.46 ± 2.02. Similarly, diabetics group had a mean RV strain rate of −1.44 ± 0.18 and non-diabetics group had a mean RV strain rate of −1.47 ± 0.22. In the study population, hypertensive group had a mean RV strain of −13.81 ± 2.73 and non-hypertensive group had a mean RV strain of −14.87 ± 1.57. Similarly, hypertensive group had a mean RV strain rate of −1.45 ± 0.22 and non-hypertensive group had a mean RV strain rate of −1.46 ± 0.19. The difference between the groups was statistically insignificant. In the study population, AWMI group had a mean RV basal velocity of 6.536 ± 2.442. IWMI group had a mean RV basal velocity of 5.854 ± 0.686. LWMI group had a mean RV basal velocity of 7.55 ± 0.778. AWMI group had a mean RV mid-velocity of 3.986 ± 0.933. IWMI group had a mean RV mid-velocity of 3.385 ± 0.465. LWMI group has mean RV mid-velocity of 5.15 ± 1.626. Similarly, AWMI group had a global RV mean velocity of 4.231 ± 1.281. IWMI group had a global RV mean velocity of 3.712 ± 0.591. LWMI group had a global RV mean velocity of 5.2 ± 0.849.

AWMI group had a mean RV basal strain rate of −2.02 ± 0.3. IWMI group had a mean RV basal strain rate of −1.773 ± 0.118. LWMI group had a mean RV basal strain rate of −1.95 ± 0.354. Similarly, AWMI group had a mean RV mid-strain rate of −1.656 ± 0.237. IWMI group had a mean RV mid-strain rate of −1.359 ± 0.086. LWMI group had a mean RV mid-strain rate of −1.55 ± 0.354. AWMI group had a mean RV apex strain rate of −1.032 ± 0.245. IWMI group had a mean RV apex strain rate of −0.784 ± 0.096. LWMI group had a mean RV apex strain rate of −1.2 ± 0.424. Similarly, AWMI group had a global RV mean strain rate of −1.563 ± 0.194. IWMI group had a global RV mean strain rate of −1.302 ± 0.046. LWMI group had a global RV basal strain rate of −1.55 ± 0.354. Global RV strain showed high correlation with LV function assessed by LVEF in our study population. However, global RV strain rate showed low correlation with LVEF.

<table>
<thead>
<tr>
<th>Table 1: Results sex</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

DISCUSSION

**RV Strain, on Comparison with Various Clinical Characteristics**

**Age and RV strain (Table 12a)**

In this study, there was no significant association detected between age and RV strain values. In the review of literature, no independent association could be detected between age and RV strain.[12,13] In their study of 44 patients with acute AWMI, Sonmez et al.[14] found no independent association between age and RV strain.

**Gender and RV strain (Table 13a)**

In this study, there was no significant association detected between gender and RV strain values. In the review of
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<table>
<thead>
<tr>
<th>Table 3: Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
</tr>
<tr>
<td>AWMI</td>
</tr>
<tr>
<td>IWMI</td>
</tr>
<tr>
<td>LWMI</td>
</tr>
<tr>
<td>Total</td>
</tr>
<tr>
<td>AWMI: Anterior wall myocardial infarction, IWMI: inferior wall myocardial infarction, LWMI: Left ventricular mass index</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 5: Coronary angiogram</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impression</td>
</tr>
<tr>
<td>DVD</td>
</tr>
<tr>
<td>LMCA+DVD</td>
</tr>
<tr>
<td>Recanalized LAD</td>
</tr>
<tr>
<td>SVD</td>
</tr>
<tr>
<td>TVD</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

In our study, 59 anterior wall myocardial infarction patients included, and there is 41 inferior wall myocardial infarction patients and 2 lateral wall myocardial infarction are included [Table 3]

<table>
<thead>
<tr>
<th>Table 4: Risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk factors</td>
</tr>
<tr>
<td>Smokers</td>
</tr>
<tr>
<td>DM</td>
</tr>
<tr>
<td>SH</td>
</tr>
<tr>
<td>DM: Diabetes mellitus, SH: Systemic hypertension</td>
</tr>
</tbody>
</table>

In our study there were 69 smokers, 45 patients had Diabetes, and hypertension [Table 4]

In the literature, no independent association could be detected between gender and RV strain. In their study of 145 patients with STEMI, Huttin et al. stated no significant independent association between gender and RV strain.

Smoking and RV strain [Table 14a]
In this study, there was no significant association detected between smoking and RV strain values.

In the review of literature, no independent association could be detected between smoking and RV strain. In various studies done using RV strain in MI patients, no independent significant association could be detected between diabetes and RV strain [Table 4].

Diabetes and RV strain [Table 15a]
In this study, there was no significant association detected between smoking and RV strain values. In various studies done using RV strain in MI patients, no independent significant association could be detected between diabetes and RV strain [Table 4].

Hypertension and RV strain [Table 16a]
Hypertensive group had a mean RV strain of $-13.81 \pm 2.73$. Nonhypertensive group had a mean RV strain of $-14.87 \pm 1.57$. The difference between the groups was statistically significant. The patients with LV systolic and diastolic dysfunction had significant RV dysfunction detected by RV strain. Abatte et al. showed remarkable RV cardiomyocyte apoptosis in the setting of AMI of the left ventricular wall. This apoptosis could be due to myocardial edema. Grothoff and Jensen et al. revealed considerable edema in the RV of patients with anterior MI in their MRI studies.
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ECHO Characteristics

LVEF (Table 7)

In the study population, AWMI group had a mean LVEF of 39.37 ± 4.881%, IWMI group had a mean LVEF of 41.43 ± 6.091%, and LWMI group had a mean LVEF of 47 ± 11.31%.

<table>
<thead>
<tr>
<th>Treatment modalities</th>
<th>AWMI</th>
<th>IWMI</th>
<th>LWMI</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCI</td>
<td>37</td>
<td>20</td>
<td>2</td>
<td>59</td>
</tr>
<tr>
<td>CABG</td>
<td>10</td>
<td>21</td>
<td>0</td>
<td>31</td>
</tr>
<tr>
<td>Medical</td>
<td>12</td>
<td>0</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>59</td>
<td>41</td>
<td>2</td>
<td>102</td>
</tr>
</tbody>
</table>

LVEF: Left ventricular ejection fraction, AWMI: Anterior wall myocardial infarction, IWMI: Inferior wall myocardial infarction, LWMI: Left ventricular mass index, PCI: Percutaneous coronary intervention, CABG: Coronary artery bypass surgery

In our study 59 patients had undergone PCI, CABG was done for 31 patients and 12 patients received medical treatment. [Table 6]

<table>
<thead>
<tr>
<th>Mitral E/A (Table 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>In the study population, AWMI group had a mean mitral E/A of 1.036 ± 0.369, IWMI group had a mean mitral E/A of 1.005 ± 0.249, and LWMI group had a mean mitral E/A of 0.7 ± 0.283. The difference between the groups was statistically insignificant. In the review of literature, mitral E/A of patients with AMI was significantly lower than control population. [14]</td>
</tr>
</tbody>
</table>

Table 8: Mitral E/A

<table>
<thead>
<tr>
<th>Mitral E/A</th>
<th>Mean±SD</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>AWMI</td>
<td>1.036±0.369</td>
<td>0.050</td>
</tr>
<tr>
<td>IWMI</td>
<td>1.005±0.249</td>
<td>0.344</td>
</tr>
<tr>
<td>LWMI</td>
<td>0.7±0.283</td>
<td>0.512</td>
</tr>
</tbody>
</table>

AWMI: Anterior wall myocardial infarction, IWMI: Inferior wall myocardial infarction, LWMI: Left ventricular mass index, SD: Standard deviation

Table 9: Mitral E/e'

<table>
<thead>
<tr>
<th>Mitral E/e'</th>
<th>Mean±SD</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>AWMI</td>
<td>9.742±3.421</td>
<td>0.121</td>
</tr>
<tr>
<td>IWMI</td>
<td>10.556±2.593</td>
<td>0.422</td>
</tr>
<tr>
<td>LWMI</td>
<td>9.5±0.707</td>
<td>0.644</td>
</tr>
</tbody>
</table>

AWMI: Anterior wall myocardial infarction, IWMI: Inferior wall myocardial infarction, LWMI: Left ventricular mass index, SD: Standard deviation
In our study population, patients with AMI had high E/e’, AWMI group had a mean mitral E/e’ of 9.742 ± 3.421, and IWMI group had a mean mitral E/e’ of 10.556 ± 2.593. In their study of 44 patients with acute AWMI, Sonmez et al. stated that with regard to conventional echocardiographic parameters, the mitral E/E’ were significantly higher in the patient group.[14]

**Mitral E/e’ (Table 9)**

In our study population, patients with AMI had high E/e’, AWMI group had a mean mitral E/e’ of 9.742 ± 3.421, and IWMI group had a mean mitral E/e’ of 10.556 ± 2.593. In their study of 44 patients with acute AWMI, Sonmez et al. stated that with regard to conventional echocardiographic parameters, the mitral E/E’ were significantly higher in the patient group.[14]

**Tricuspid E/A (Table 10)**

In the study population, AWMI group had a mean tricuspid E/A of 1.131 ± 0.317. IWMI group had a mean tricuspid E/A of 0.98±0.299. In their study of 44 patients with acute AWMI, Sonmez et al.[14] stated that tricuspid E/A did not vary significantly between AWMI patients and control group. In this study, there was a significant difference between AWMI patients and IWMI patients.
In the study population, males had a mean right ventricle (RV) strain of $-14.25\pm2.24$ and females had a mean RV strain of $-14.98\pm2.05$. The difference between the groups was statistically significant. Similarly, males had a mean RV strain rate of $-1.47\pm0.21$ and females had a mean RV strain rate of $-1.43\pm0.16$. The difference between the groups was statistically insignificant.

## TAPSE [Table 11]

In the study population, AWMI group had a mean TAPSE of $16.763 \pm 2.68$. IWMI group had a mean TAPSE of $14.049 \pm 1.923$. The difference between the groups was statistically significant ($P < 0.001$).

In their study of 282 consecutive IWMI patients, Park et al. concluded that global longitudinal strain of the RV (GLSRV) showed significant correlations with conventional echocardiographic indicators of RV systolic function, including right ventricular fractional area change (RVFAC) and TAPSE.
In this study, IWMI patients had a mean TAPSE of 14.049 ± 1.923 indicating the presence of RV dysfunction in most of the patients.

**RV Strain Imaging**

**RV myocardial velocity [Tables 17a-c]**

In the study population, AWMI group had a mean RV basal velocity of 6.536 ± 2.442. IWMI group had a mean RV basal velocity of 5.854 ± 0.686.

In our study mean strain and strain rate in DM patients were −14.34±2.46,−1.44±0.18 and in non DM patients were −14.46±2.02 and -1.44±0.22 [Table 15,15a]

Similarly, AWMI group had a mean RV mid-velocity of 3.986 ± 0.933 and IWMI group had a mean RV mid-velocity of 3.385 ± 0.465. The difference between the groups was statistically significant ($P < 0.001$).

Similarly, AWMI group had a global RV mean velocity of 4.231 ± 1.281 and IWMI group had a global RV mean velocity of 3.712 ± 0.591. The difference between the groups was statistically significant.
In their study of 44 patients with AWMI by Sonmez et al.\textsuperscript{[14]} stated decrease in the mean RV velocities were common in the study AWMI patients.

**RV myocardial strain (Tables 18a-c)**

In the study population, AWMI group had a mean RV basal strain of $-20.475 \pm 2.406$ and IWMI group had a mean RV basal strain of $-17.829 \pm 2.936$. Similarly, AWMI group had a mean RV mid-strain of $-16.284 \pm 2.308$. AWMI group had a mean RV apex strain of $-10.425 \pm 1.501$. IWMI group had a mean RV apex strain of $-6.888 \pm 0.868$. The difference between the groups was statistically significant.
Similarly, AWMI group had a global RV mean strain of $-15.68 \pm 1.521$ and IWMI group had a global RV mean strain of $-12.644 \pm 1.811$. The difference between the groups was statistically significant.

Strain echocardiography gives us objective information on global and regional RV systolic function. Since RV muscle fibers run longitudinally, longitudinal shortening generates 80% of the stroke volume, which makes it a major portion of RV systolic function.\(^{[17,18]}\)

In their study of 145 patients with acute AMI, Huttin \(et \ al\). stated that global RV strain was lower in IWMI than in AWMI.\(^{[15]}\)

In their study of 64 patients with acute AWMI, Sonmez \(et \ al\). stated that RV mid, apex strain/strain rate was significantly lower compared to control population.\(^{[14]}\)

In their study of 82 consecutive patients with IWMI, Song \(et \ al\). stated that all RV regional longitudinal strains are categorized into apical, mid, and basal levels. RV apical, mid, and basal longitudinal strains were significantly less in patients with IWMI than in controls.\(^{[19]}\)

Local longitudinal parameters such as TAPSE and S’ velocity failed to show any significant differences related to the location of MI at the acute phase in our patients, with relatively preserved RV function.\(^{[20]}\) This is in accordance with other studies reporting a poor diagnostic power of conventional parameters for initial RV extension of MI.\(^{[21]}\) RV dysfunction can be observed irrespective of the localization of MI.\(^{[22]}\) Indeed, RV dysfunction has been observed in over 40% of inferior MI patients and in up to 33% of anterior MI. Huttin \(et \ al\). showed a decrease of RV strain values in all MI locations albeit more substantial in inferior comparatively to anterior MI. In contrast, septal strain was similar in patients with inferior and anterior AMI. Huttin \(et \ al\). demonstrated that our study indicated that RV strain is likely more efficient than other conventional parameters in detecting RV dysfunction in the acute phase of small and non-complicated MI.

**RV myocardial strain rate (Tables 19a-c)**

In the study population, AWMI group had a mean RV basal strain rate of $-2.02 \pm 0.3$. IWMI group had a mean

---

**Table 19: RV strain rate and AMI**

<table>
<thead>
<tr>
<th>RV strain rate (basal)</th>
<th>Mean±SD</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>AWMI</td>
<td>$-2.02\pm0.3$</td>
<td>0.422</td>
</tr>
<tr>
<td>IWMI</td>
<td>$-1.773\pm0.118$</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LWMI</td>
<td>$-1.95\pm0.354$</td>
<td>0.644</td>
</tr>
</tbody>
</table>

**Table 19a: RV strain rate and AMI**

<table>
<thead>
<tr>
<th>RV strain rate (mid)</th>
<th>Mean±SD</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>AWMI</td>
<td>$-1.656\pm0.237$</td>
<td>0.244</td>
</tr>
<tr>
<td>IWMI</td>
<td>$-1.359\pm0.0865$</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LWMI</td>
<td>$-1.55\pm0.354$</td>
<td>0.644</td>
</tr>
</tbody>
</table>

**Table 19b: RV strain rate and AMI**

<table>
<thead>
<tr>
<th>RV strain rate (apex)</th>
<th>Mean±SD</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>AWMI</td>
<td>$-1.032\pm0.245$</td>
<td>0.054</td>
</tr>
<tr>
<td>IWMI</td>
<td>$-0.764\pm0.0968$</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LWMI</td>
<td>$-1.2\pm0.424$</td>
<td>0.022</td>
</tr>
</tbody>
</table>

**Table 19c: RV strain rate and AMI**

<table>
<thead>
<tr>
<th>RV strain rate (global)</th>
<th>Mean±SD</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>AWMI</td>
<td>$-1.563\pm0.194$</td>
<td>0.242</td>
</tr>
<tr>
<td>IWMI</td>
<td>$-1.302\pm0.0464$</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LWMI</td>
<td>$-1.55\pm0.354$</td>
<td>0.422</td>
</tr>
</tbody>
</table>

**Table 20: RV strain and LVEF**

<table>
<thead>
<tr>
<th>Correlation</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF versus global RV strain</td>
<td>0.659</td>
</tr>
<tr>
<td>LVEF versus global RV strain rate</td>
<td>0.083</td>
</tr>
</tbody>
</table>

**Table 20a: RV strain and LVEF**

<table>
<thead>
<tr>
<th>RV strain and TAPSE: Correlation</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAPSE versus global RV strain</td>
<td>0.535</td>
</tr>
<tr>
<td>TAPSE versus global RV strain rate</td>
<td>0.329</td>
</tr>
</tbody>
</table>
RV basal strain rate of $-1.773 \pm 0.118$. Similarly, AWMI group had a mean RV mid-strain rate of $-1.636 \pm 0.237$. IWMI group had a mean RV mid-strain rate of $-1.359 \pm 0.086$. AWMI group had a mean RV apex strain rate of $-1.032 \pm 0.245$. IWMI group had a mean RV apex strain rate of $-0.784 \pm 0.096$. Similarly, AWMI group had a global RV mean strain rate of $-1.563 \pm 0.194$. IWMI group had a global RV mean strain rate of $-1.302 \pm 0.046$. The difference between the groups was statistically significant. S/SR imaging is currently the most popular echocardiographic modality for revealing subclinical myocardial damage. In the literature, postmortem studies mention RV involvement after left ventricular infarction.

**RV strain and LVEF, TAPSE**

Global RV strain showed high correlation with LV function assessed by LVEF in our study population. However, global RV strain rate showed low correlation with LVEF.

Global RV strain showed good correlation with TAPSE in our study population. However, global RV strain rate showed low correlation with LVEF.

In their study of 282 consecutive IWMI patients, Park et al. stated that GLSRV showed significant correlations with conventional echocardiographic indicators of RV systolic function, including RV FAC and TAPSE.

**Coronary Angiogram**

In the study population consisting of 59 patients with AWMI, 30 (50.8%) had SVD involving LAD, 3 (5%) had recanalized LAD, 17 (28.8%) had DVD, 8 (13.5%) had TVD, and 1 (1.6%) had significant LMCA involvement. Essentially, all patients with AWMI had LAD involvement.

Of the 41 patients with IWMI, 9 (21.9%) had SVD involving RCA, 18 (43.9%) had DVD, 1 (2.4%) had TVD, and 13 (31.7%) had LMCA involvement with or without other vessel involvement. Essentially, all patients with IWMI in our study group had RCA involvement. Of the two patients with LWM1, 1 had SVd and 1 had DVD. Huttin et al. in their study had similar observation.

**Study Limitations**

This study was a single-center study with small sample size.

Entry criterion for this study was AMI patients who have undergone thrombolysis. This may have introduced a selection bias. Doppler tissue imaging is dependent on the angle at which the region of interest is imaged, has increased signal-to-noise ratio. Overall, heart motion, cardiac rotation, and wall motion from tethering segments limit the use of DTI. RV strain is most reproducible in the apical four-chamber view, interrogating the basal, mid, and to a lesser degree, apical segments of the RV free wall. As a result, one is limited to mostly longitudinal strain. There is a lack of normative data regarding speckle-tracking technique, which also requires additional validation. Requiring additional software, it is dependent on adequate image quality. The global nature is derived only from a single view, making it not a truly global assessment of RV function. Prognosis of patients with RV dysfunction assessed by RV strain was not done in this study, but this study may open roads for further studies related to this area.

**CONCLUSION**

Global Longitudinal Strain of Right Ventricle showed significant correlations with conventional echocardiographic parameters of RV systolic function like TAPSE and also LV systolic function measured by LVEF. RV strain provides incremental value over clinical information, infarct characteristics, LV function, and TAPSE. There is significant RV dysfunction detected by RV strain imaging in patients presenting with AMI immediately after thrombolysis. In this study, AWMI patients had lowered segmental and GLSRV compared to reference normal values. Patients with IWMI had much lower segmental and GLSRV values compared to AMWI patients, and the difference was statistically significant.

RV dysfunction has also been related to poor prognosis; therefore, the function of both ventricles after AMI should be considered. RV assessment with these imaging modalities will have an increased value during treatment. Quantitative assessment of RV function with RV strain may improve the risk stratification of patients after AMI.

**ACKNOWLEDGMENT**

The authors would like to thank the Department of cardiology, Government Rajaji hospital, Madurai.

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Source of Support: Nil, Conflict of Interest: None declared.
Major Effects of Delayed Graft Function and Cold Ischemia Time on Renal Allograft Survival

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Abstract

Background: There is mounting evidence from experimental and clinical studies that the quality of organs from cadaver donors may be influenced by events occurring around the time of brain death, and that these may affect transplant outcome. The aim of this study is to investigate the influence of donor factors on renal allograft outcome in a homogeneous cohort of 518 patients transplanted in a single center over a 9-year period.

Methods: End points of the study were delayed graft function (DGF), acute rejection (AR), 1-year graft survival, and long-term survival of those grafts that reached 1 year. Multivariate analysis was performed to determine factors that may have influenced the graft outcome indicators.

Results: DGF was the major predictor of graft failure overall with cold ischemia time (CIT) as an important independent factor. The level of histocompatibility did not influence graft survival. DGF was the major factor affecting 1-year graft survival ($P < 0.0005$) with effects persisting beyond 1 year. DGF was significantly influenced by CIT, donor age, female kidney into male recipient, and donor creatinine ($P < 0.05$). Other donor factors and factors associated with donor management were not risk factors for DGF, rejection episodes, or graft survival. The risk factors for a number of AR episodes were HLA–DR mismatch and DGF ($P < 0.005$). When grafts surviving for 1 year were considered, only CIT, recipient age, and creatinine at 1 year ($P < 0.05$) were found to affect graft survival significantly.

Conclusions: The results of this analysis of well-matched transplant recipients show that CIT and DGF are the most important predictors of poor short and long-term graft survival. Therefore, to improve the long-term survival of renal allografts efforts should focus on limiting CIT and the damage that occurs during this period and on improving our understanding of DGF.

Key words: Cold ischemia time, Delayed graft function, Donor factors, Outcome, Renal transplantation

INTRODUCTION

There is mounting evidence from experimental and clinical studies that the level of injury to organs from cadaver donors may be influenced by events occurring in the Intensive Care Unit (ICU)[1] and around the time of brain death,[2] and that these may affect subsequent transplant outcome.

Despite evidence that the quality of organs from cadaver donors is inferior to organs from living donors, it remains controversial whether this is associated with events in the management of the donor in ICU. For example, recent data suggest that the use of inotropes reduces the incidence of acute rejection (AR) and leads to superior long-term survival of the graft. While, in contrast, other studies have found a significant increase in delayed graft function (DGF) and reduced 1-year survival and renal function if the donor had required inotropes before death.[1]

Having been exposed to factors related to the dying process other influences will be added to the donor organ which will impact on the final outcome of transplantation. These will be related to the retrieval process itself and the subsequent period of cold ischemia before reperfusion. Finally, recipient factors will become active on reperfusion and for the lifetime of the graft. It is this blending of multiple donor and recipient factors that generate the final outcome of the transplant process.
The aim of this study was to analyze a comprehensive database of a large, homogeneous cohort of patients transplanted in a single center over a 9-year period to investigate the influence of donor and recipient factors on renal allograft function and survival.

SUBJECTS AND METHODS

Patients
Between 2009 and 2017, 541 cadaveric renal transplants were performed at the Oxford Transplant Centre. Data relating to donors and the retrieval process were obtained from the UK Transplant National Database Core Donor Data Form (Form CDD1) and from information kept locally by the transplant coordination team. Full donor data were available for 518 patients, which formed the study population. 23 patients were excluded from the study due to the lack of donor data. All kidneys were retrieved from conventional heart-beating, cadaveric donors diagnosed as brain stem dead. The retrieval technique and preservation fluid were unchanged during the study period. A detailed list of the variables studied is given in Table 1. Donor details and recipient demographics are described in Table 2. Clinical and follow-up data were collected prospectively from the Oxford Transplant Centre Database.

Immunosuppression
The immunosuppressive protocol used during the period studied was uniform and consisted of a triple-therapy regimen of cyclosporine (8mg/kg/day divided in two doses), azathioprine (1.5mg/kg/day), and prednisolone (20mg/day if recipient weight 60kg or above; 15mg/day if weight was <60kg). Cyclosporine dose was adjusted to maintain serum trough levels between 150–300ng/mL in the first 6 months post-transplant and 75–150ng/mL thereafter. Prednisolone dose was reduced gradually after 2 months to 5mg/day at 1 year. Most patients discontinued prednisolone at 18-month post-transplantation. Induction therapy with antilymphocyte globulin (ATG) was used only in highly sensitized patients. There was no change to the immunosuppressive protocol in the presence of DGF. From July 1991, patients were started on aspirin 75mg pre-transplantation and continued until 1 month after the transplant to prevent renal vein thrombosis.

End points
The end points of the study were: DGF, AR, 1-year graft survival, and long-term survival of those grafts that reached 1 year.

DGF was defined as the requirement for dialysis within the 1st week after transplantation. Patients transplanted before needing dialysis (pre-emptive transplantation) were considered to have DGF if the creatinine failed to drop in the 1st week.

AR was diagnosed histologically on core renal biopsies according to the Banff classification. Before the introduction of the Banff classification, rejection was diagnosed by a histopathologist on a qualitative basis. Biopsies were scored using the ‘93 Banff classification from 1996 to 1999, and the revised ‘97 Banff classification from April 1999. All patients in our unit had protocol renal transplant biopsies at days 7 and 28 after the transplant irrespective of renal function. In addition, diagnostic biopsies were performed at any time when clinically indicated. Three 500mg doses

Table 1: List of variables studied

<table>
<thead>
<tr>
<th>Year of transplant</th>
<th>Donor cause of death</th>
<th>Recipient sex</th>
<th>DGF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor sex</td>
<td>Trauma Y/N</td>
<td>Recipient age</td>
<td>AR Y/N</td>
</tr>
<tr>
<td>Donor age</td>
<td>Cardiovascular disease Y/N</td>
<td>Recipient blood group</td>
<td>AR day-7 Y/N</td>
</tr>
<tr>
<td>Donor age ≥50 years</td>
<td>Donor ventilation time (h)</td>
<td>Recipient rhesus (±)</td>
<td>AR day-14 Y/N</td>
</tr>
<tr>
<td>Donor weight</td>
<td>Donor infection Y/N</td>
<td>Recipient blood transfusions Y/N</td>
<td>Methylprednisolone treatments</td>
</tr>
<tr>
<td>Donor height</td>
<td>Donor antibiotics</td>
<td>Recipient number of blood transfusions</td>
<td>Antithymoglobulin treatment</td>
</tr>
<tr>
<td>Donor SeCr ≥150µmol/L</td>
<td>DDAVP Y/N</td>
<td>Cause of ESRF</td>
<td>SeCr and CrCl day-7</td>
</tr>
<tr>
<td>Donor CrCl ≥260mL/min</td>
<td>Donor inotropes Y/N</td>
<td>First transplant/regraft</td>
<td>SeCr 3 and 6 months</td>
</tr>
<tr>
<td>Donor serum sodium</td>
<td>Dobutamine Y/N</td>
<td>Days on transplant waiting list</td>
<td>Weight 3 and 6 months</td>
</tr>
<tr>
<td>Donor serum potassium</td>
<td>Dopamine Y/N</td>
<td>Pre-transplant antibodies*</td>
<td>CrCl* 3 and 6 months</td>
</tr>
<tr>
<td>Donor rhesus (±)</td>
<td>Local/imported organ</td>
<td>Highly sensitized†</td>
<td>Survival 3 and 6 months</td>
</tr>
<tr>
<td>Donor CMV status (±)</td>
<td>Graft damage‡</td>
<td>HLA class I MM</td>
<td>SeCr 1–9 years</td>
</tr>
<tr>
<td>Hypotension Y/N‡</td>
<td>Type of damage</td>
<td>HLA class II MM</td>
<td>Weight 1–9 years</td>
</tr>
<tr>
<td>Cardiorespiratory arrest</td>
<td>CII‡</td>
<td>HLA A MM</td>
<td>CrCl* 1–9 years</td>
</tr>
<tr>
<td>Donor blood transfusion</td>
<td>Anastoimosis time</td>
<td>HLA B MM</td>
<td>Survival 1–9 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HLA DR MM</td>
<td>Death with functioning graft</td>
</tr>
</tbody>
</table>

*Calculated by the Cockcroft–Gault formula [(140−age) × (1.23 if male/1.04 if female) × weight (kg)/serum creatinine (SeCr) (µmol/l)]. †systolic blood pressures<80mmHg for>10 min, ‡any type of injury (vascular, ureteric, or capsular) reported to the national database by the retrieving surgeon or recorded at the recipient center, †time from cold perfusion to the time the kidney was taken out of ice to start the anastomosis, ‡HLA lymphocytotoxic antibodies reactive with≥10% of a random panel, *HLA lymphocytotoxic antibodies reactive with≥85% of a random panel. CIT: Cold ischemia time; AR: Acute rejection.
of methylprednisolone were administered on consecutive
days for the treatment of confirmed AR. A 10–14 days
course of ATG was used to treat steroid-resistant rejection.

Uncensored 1-year graft survival and long-term survival of
those grafts that reached 1 year include those recipients
who died with a functioning graft. Results from patients
dying with a functioning graft were excluded from analysis
as indicated. This was performed to maintain the focus of
the study on the donor factors rather than recipient factors
such as advanced cardiac disease, on graft survival.

Statistical Analysis
Multivariate statistical tests with the SPSS (v12 for
Windows) statistics program were used to analyze the data.
Logistic regression was used to calculate the odds ratio for
the analysis of DGF, AR, and 1-year graft survival. Models
were fitted on the basis of improved fit, as measured by
change in Chi-squared statistics. The statistical models were
validated by the “Hosmer–Lemeshow” goodness of fit test. The “Nagelkerke R²” was used to evaluate the overall
fit of the model.[3]

Cox proportional hazard regression, log-rank analysis,
and Kaplan–Meier curves were used for the analysis and
illustration of the survival of those grafts that reached
1 year and long-term graft survival.

Continuous variables, such as age and cold ischemia time
(CIT), were analyzed as such in Cox and logistic regression.
However, to permit the use of Kaplan–Meier curves plots
were converted to binary variables, by splitting variables
at the median.

The significance of results from logistic and proportional
hazards regression were confirmed by examining changes
in overall log-likelihood of the model.

Possible interactions were examined by comparing
coefficients for one factor across levels of the other and
calculating a “normal deviate.”[4]

Linear regression was used to study the factors affecting
the 1-year creatinine.

To show further the effect of donor age and CIT, these
variables were banded by quintiles.

RESULTS

Overall Study End Points
DGF occurred in 31.1% (161/518) of the patients studied
[Table 3]. 54% of recipients had at least one episode of
biopsy-proven AR. Of the patients with AR, 35.7% had
two or more episodes of rejection. Graft survival of 1 and
5 years after censoring for death with a functioning graft
was 90.6% and 79.5%, respectively. The full data relating
to the end points of the study are given in Table 3.

Of the total set, 23 patients were excluded from the study
due to the lack of donor data. However, the incidence of
DGF, AR, and 1-year graft survival in these 23 excluded
patients (35, 43.5, and 90.5%, respectively) was comparable
to the remainder.

Analysis of the Factors Affecting Overall Graft Survival
Survival analysis methods were used to investigate the
factors affecting the overall graft survival. DGF emerged as
the dominant predictor of subsequent survival. Figures 1
and 2 show the Kaplan–Meier plots of the effects of DGF
and CIT and associated log-rank statistics. For this analysis,
CIT was categorized as being either above or below the

Table 2: Donor and recipient demographics and
retrieval factors

<table>
<thead>
<tr>
<th>Donor factors</th>
<th>Donor factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, M: F</td>
<td>281:237</td>
</tr>
<tr>
<td>Age</td>
<td>42±15.5</td>
</tr>
<tr>
<td>Cause of death</td>
<td></td>
</tr>
<tr>
<td>Trauma Y/N</td>
<td>145/373</td>
</tr>
<tr>
<td>CVD Y/N</td>
<td>335/183</td>
</tr>
<tr>
<td>CMV ±</td>
<td>249/246 (N/A 23)*</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>107±60 µmol/L</td>
</tr>
<tr>
<td>Creatinine clearance</td>
<td>84.7±31.9 mL/min</td>
</tr>
<tr>
<td>ICU factors</td>
<td></td>
</tr>
<tr>
<td>Cardiorespiratory arrest Y/N</td>
<td>129/389</td>
</tr>
<tr>
<td>Hypotension Y/N</td>
<td>339/179</td>
</tr>
<tr>
<td>Ventilation time</td>
<td>55±47 (h)</td>
</tr>
<tr>
<td>Infection Y/N</td>
<td>130/380 (N/A 8)*</td>
</tr>
<tr>
<td>DDAVP Y/N</td>
<td>201/317</td>
</tr>
<tr>
<td>Inotropes Y/N</td>
<td>423/95</td>
</tr>
<tr>
<td>Noradrenaline Y/N</td>
<td>80/438</td>
</tr>
<tr>
<td>Dobutamine Y/N</td>
<td>130/388</td>
</tr>
<tr>
<td>Dopamine Y/N</td>
<td>299/219</td>
</tr>
<tr>
<td>Adrenaline Y/N</td>
<td>93/425</td>
</tr>
<tr>
<td>Retrieval factors</td>
<td></td>
</tr>
<tr>
<td>Local/imported</td>
<td>367/151</td>
</tr>
<tr>
<td>Damage</td>
<td>85/433</td>
</tr>
<tr>
<td>CIT</td>
<td>23.6±8.6 (median=21h)</td>
</tr>
<tr>
<td>Anastomosis time</td>
<td>44.7±2.1 (min)</td>
</tr>
<tr>
<td>Recipient factors</td>
<td></td>
</tr>
<tr>
<td>Sex, M: F</td>
<td>316:202</td>
</tr>
<tr>
<td>Age</td>
<td>46.4±12.7</td>
</tr>
<tr>
<td>Cause of ESRF</td>
<td></td>
</tr>
<tr>
<td>Diabetes Y/N</td>
<td>55/463</td>
</tr>
<tr>
<td>Pre-transplant antibodies Y/N</td>
<td>241/277</td>
</tr>
<tr>
<td>Highly sensitized Y/N</td>
<td>38/480</td>
</tr>
<tr>
<td>CMV ±</td>
<td>259/222 (N/A 37)*</td>
</tr>
<tr>
<td>Days on waiting list</td>
<td>338±480 (median=168) (days)</td>
</tr>
<tr>
<td>Number of transplant 1:2:3:4</td>
<td>444:64:8:3</td>
</tr>
<tr>
<td>HLA DR mismatches 0:1:2</td>
<td>269:219:30</td>
</tr>
</tbody>
</table>

*Data not available
median CIT of 21h. It can be seen that CIT influenced the long-term survival of the graft significantly.

Results of the proportional hazards regression are presented in Table 4.

A “time-dependent covariate” was used to test departure from the proportional hazards assumption. The effect was not significant but was consistent with a tendency to earlier graft failure in the DGF group. This was confirmed by carrying out separate analyses for 0–3 months, 3 months to 1 year, and after 1 year [Table 5] that also showed that the effect of DGF persisted. This post 1-year effect of DGF was not significant after the inclusion of 1-year creatinine, suggesting that this mediated the effect.

Diagnosis of rejection had no overall effect on failure; however, there was a significant interaction with DGF (z = 2.26, P = 0.024), with rejection significantly increasing failure in the absence of DGF [Table 4].

Factors Affecting 1-year Graft Survival

The 1-year graft survival was studied by logistic regression. In this analysis, survival is treated as the outcome (with ‘death with functioning graft’ being omitted from the analysis), hence reduction in graft survival is indicated by an OR <1.0. 1-year graft survival was influenced only by DGF and the year of transplant [Table 4]. There were no adverse effects of donor factors or ICU management on 1-year graft survival.

Renal transplants performed in the early years of the study period had a significantly worse 1-year graft survival than those carried out in later years.

Table 3: End points of the cohort studied

<table>
<thead>
<tr>
<th>Factors</th>
<th>No DGF (357)</th>
<th>DGF (161)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of episodes of AR</td>
<td>54.9%</td>
<td>54%</td>
</tr>
<tr>
<td>1-year graft survival</td>
<td>90.6%</td>
<td>90.6%</td>
</tr>
<tr>
<td>5-year graft survival</td>
<td>79.5%</td>
<td>79.5%</td>
</tr>
<tr>
<td>Mortality with functioning</td>
<td>5.2%</td>
<td>5.2%</td>
</tr>
<tr>
<td>graft in 1st year</td>
<td>11%</td>
<td>11%</td>
</tr>
<tr>
<td>Mortality with functioning</td>
<td>5.2%</td>
<td>5.2%</td>
</tr>
<tr>
<td>graft in first 5 years</td>
<td>11%</td>
<td>11%</td>
</tr>
</tbody>
</table>

Table 4: Risk factors affecting the end points analyzed in this study

<table>
<thead>
<tr>
<th>Factors</th>
<th>OR 95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall graft survival</td>
<td>2.92</td>
<td>1.84–4.63</td>
</tr>
<tr>
<td>DGF</td>
<td>1.027</td>
<td>1.004–1.049</td>
</tr>
<tr>
<td>AR</td>
<td>1.15</td>
<td>0.73–1.82</td>
</tr>
<tr>
<td>Overall graft survival (no DGF)</td>
<td>2.05</td>
<td>1.03–4.08</td>
</tr>
<tr>
<td>AR</td>
<td>1.029</td>
<td>1.004–1.053</td>
</tr>
<tr>
<td>SeCr 1 year</td>
<td>0.71</td>
<td>0.39–1.3</td>
</tr>
<tr>
<td>1-year graft survival (no DGF)</td>
<td>1.264</td>
<td>1.051–1.519</td>
</tr>
<tr>
<td>DGF</td>
<td>0.152</td>
<td>0.069–0.333</td>
</tr>
<tr>
<td>Long-term survival of kidneys</td>
<td>0.963</td>
<td>0.937–0.989</td>
</tr>
<tr>
<td>reaching 1 year</td>
<td>1.035</td>
<td>1.002–1.069</td>
</tr>
<tr>
<td>Recipient age</td>
<td>1.006</td>
<td>1.006–1.104</td>
</tr>
<tr>
<td>SeCr 1 year</td>
<td>1.004</td>
<td>1.004–1.008</td>
</tr>
<tr>
<td>CIT</td>
<td>1.066</td>
<td>1.041–1.092</td>
</tr>
<tr>
<td>FtoM</td>
<td>2.437</td>
<td>1.536–3.869</td>
</tr>
<tr>
<td>Trauma</td>
<td>0.328</td>
<td>0.154–0.699</td>
</tr>
<tr>
<td>Donor age</td>
<td>1.013</td>
<td>1.006–1.026</td>
</tr>
<tr>
<td>Donor SeCr</td>
<td>1.004</td>
<td>1.000–1.008</td>
</tr>
<tr>
<td>CIT</td>
<td>1.066</td>
<td>1.041–1.092</td>
</tr>
<tr>
<td>FtoM</td>
<td>2.437</td>
<td>1.536–3.869</td>
</tr>
</tbody>
</table>

Factors Affecting 1-year Graft Survival

The 1-year graft survival was studied by logistic regression. In this analysis, survival is treated as the outcome (with ‘death with functioning graft’ being omitted from the analysis), hence reduction in graft survival is indicated by an OR <1.0. 1-year graft survival was influenced only by DGF and the year of transplant [Table 4]. There were no adverse effects of donor factors or ICU management on 1-year graft survival.

Diagnosis of rejection had no overall effect on failure; however, there was a significant interaction with DGF (z = 2.26, P = 0.024), with rejection significantly increasing failure in the absence of DGF [Table 4].
Important, no other factors were significant, including AR, HLA matching, highly sensitized recipients, regrafts, and donor age. Again, contrasting effects of rejection were found according to the occurrence of DGF, with rejection reducing graft survival in the absence of DGF. Neither result was significant individually; the test for interaction was ($\chi^2 = 2.0, P = 0.046$).

**Factors Affecting Long-term Survival of the Grafts that Reached 1 year**

Proportional hazards regression analysis was used to investigate factors affecting failure of grafts that survived beyond the 1-year post-transplant. The most important factor identified was serum creatinine at 1 year. CIT was also significant, as were donor and recipient age; older recipients had reduced graft loss [Table 4].

Serum creatinine has stronger predictor value than creatinine. In this analysis, regrafts, highly sensitized recipients and other donor and ICU parameters did not have a significant effect on long-term graft survival after the 1st year.

**Risk Factors for DGF**

In view of the importance of DGF, possible predictors of this state were investigated.

DGF was found to be significantly influenced by CIT, donor age, and donor serum creatinine [Table 4]. CIT, donor age, and donor serum creatinine were entered into the statistical model as continuous variables. The statistical analysis indicated that an increase in each of these variables independently increased the risk of DGF. Hence, an increase in each unit of the variable, each hour of CIT, year of donor age, and micromoles per liter of donor serum creatinine increased the incidence of DGF.

The only other factor that increased significantly the risk of DGF was transplantation of a female kidney into a male recipient ($P < 0.005$), which independently conferred a higher risk of DGF than a female kidney into a female recipient or a male kidney into either sex [Table 4].

No evidence was found for departures from the logistic model. The “Hosmer–Lemeshow” goodness of fit statistic was not significant. Addition of quadratic terms in donor age and CIT did not improve the fit, nor did replacement of CIT by its logarithm. Banded results for donor age and CIT are shown in Table 6.

However, the overall explanatory power of the model was not great, the Nagelkerke $R^2$ was 0.196. In the “classification table,” most of the DGF occurred in those cases where it was not predicted (sensitivity 30%, specificity 93%).

Donor factors, such as death resulting from cardiovascular disease, prolonged donor ventilation time, requirement for inotropes, and other factors associated with ICU management (as in Table 1) were not risk factors for DGF. Recipients who received a kidney from a donor who suffered a traumatic death had a significantly decreased risk of DGF, but this was not significant after inclusion of the “female-to-male” variable.

**Risk Factors for AR**

The most important predictors of rejection were the number of DR mismatches and the occurrence of DGF. However, there was evidence of an interaction between them with an effect of mismatches only in the absence of DGF [Figure 3], a test for interaction was significant ($\chi^2 = 2.44, P = 0.014$). Donor age was also a significant factor; the relation appeared to be continuous.

**Effect of DGF and DR Mismatches on Rejection**

Recipients who received kidneys from donors requiring inotropes had a significantly higher risk of early rejection ($P < 0.05$). AR was not more prevalent in highly sensitized patients or patients with pre-transplant HLA antibodies. In addition, the analysis of early AR (within 14 days after the transplant) suggested that DGF and the degree of DR mismatching were still the most significant risk factors ($P < 0.05$ and $P < 0.005$). However, in this early period, unlike in the overall analysis, younger recipients did have an increased risk of developing early rejection ($P < 0.05$). In contrast, in this early time period, donor age was not a statistically significant variable ($P > 0.05$).
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CIT was the most significant risk factor with a slope of 0.89 [5,6] and a P value of 0.004. Table 1.83.

19.2

Table 7: Factors affecting 1-year creatinine

<table>
<thead>
<tr>
<th>Factor</th>
<th>Slope</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DGF</td>
<td>19.2</td>
<td>0.035</td>
</tr>
<tr>
<td>Donor age</td>
<td>1.83</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Recipient age</td>
<td>-0.89</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Factors Affecting 1-year Creatinine

As creatinine at 1 year was a highly significant predictor of late failure, factors that might predict this were also investigated. Significant predictors were donor and recipient ages and DGF [Table 7]. The overall R² was low (0.166), showing again that the model did not explain the variation fully.

DISCUSSION

We have used multivariate analysis to investigate the influence of a number of factors and the relations between them. A single-center study permits the use of more detailed data in a fairly homogeneous set and provides a useful complement to multicenter studies. We selected the decade of the 1990s for this study, because in our unit, this was a period of very uniform immunosuppression and clinical practice. These immunosuppression agents are still of great relevance today as the use of cyclosporine and azathioprine are still part of the UK National Guidelines as laid down by the National Institute of Clinical Excellence. Similar studies published previously have often come from multicenter registry data, where the level of HLA matching is variable, CITs are often longer, and there are large variations in induction and maintenance regimens between centers.[5,6] Very few patients were excluded from this study, only when there was a lack of donor information. The incidence of DGF, AR, and the 1-year graft survival in these patients showed that this group was no different to the study population, suggesting that loss of these patients was unlikely to have distorted the results of the study.

DGF

The most striking effects found in our study are the strong impact of DGF and CIT, reduced importance of rejection, and the lack of impact of matching. The importance of DGF and rejection for subsequent failure has been a matter of controversy for some time.[7,8]

The lack of effect of matching on graft survival was not surprising. Recently, Su et al.[9] have reported a declining effect of matching in the USA during the period covered by our study. It is possible that improved immunosuppression, together with diagnosis and treatment of rejection, mean that in a relatively well-matched population such as ours these factors do not lead to failure (the mean total number of mismatches was 2.7, as against 3.6 in a recent multicenter report[10]).

The incidence of DGF in our series at 31% was consistent with our previous data[10] and comparable to that of other centers. [5,7,8] CIT was the most significant risk factor for the development of DGF and its effect appears to be continuous. This observation is supported by other investigators.[7] Other studies have suggested that there are significant time points after which the risk of DGF accelerates.[8,12] The importance of the finding in this study needs to be stressed, as it is attractive to imagine a specific threshold CIT after which the risk of DGF is significantly increased. However, from our findings, it is clear that each hour even at short CIT adds additional risk.

Recent multicenter studies have confirmed the importance of CIT and donor age for graft survival. Su et al.[9] show the effect is significant for times over 37 h compared with baseline. However, they do not test for discontinuity, and overall, their data appear consistent with a continuous effect of CIT. The collaborative transplant study[6] suggests that there is “little effect below 25 h;” however, they do not present any analysis to confirm this, and it is not obvious from their figures. Roodnat et al.[13] previously reported effects on graft survival over a wide range of CIT. Our results differ from theirs in that Roodnat et al. found the effect to be limited to the short-term, whereas we find evidence of an effect of CIT on late failure.

Despite the large number of variables studied in relation to DGF, the fit of the statistical model is far from complete; indeed one advantage of the model is that it emphasizes this. The “Nagelkerke R²” is a generalization of the standard measure of fit of a multiple linear regression model, but caution should be exercised in interpreting it. However, taken together with the results of the classification table from the logistic regression, it suggests that other unknown factors are having an effect. It is possible that some organs are more sensitive (susceptible) to cold ischemia, reperfusion injury, and the vasoconstrictive effects of calcineurin inhibitors than others and the reason for this need further investigation. We have not examined the effect of time on dialysis, which has been reported as a predictor in several studies.[7] In view of the evidence that DGF is a major predictor of graft failure, efforts should be made to understand better what is involved and how it may be reduced.

AR

The incidence of AR at 54% in this study may be considered to be high by contemporary standards. However, our data correspond to therapy based on cyclosporine, azathioprine, and steroids without routine use of antibody therapy. In our unit, rejection episodes were confirmed by core biopsy and protocol biopsies were carried out at day 7 and 28
post-transplant. Furthermore, fine-needle aspirations were performed routinely to monitor the level of infiltration in the graft in recipients with DGF. We have found as reported by Rush et al., that subclinical rejection occurred but was not treated or included in the analysis as AR. The degrees of severity of rejection were not analyzed individually as the study crossed over periods of significant changes in classification. However, ATG was used when severe rejection occurred and the use of ATG is not significant in multifactorial analysis.

DGF is also a significant risk factor for AR. It has been suggested that AR may be masked during DGF, as renal function cannot be used to detect episodes of AR. Hence, treatable episodes of rejection may not be diagnosed, and it is the failure to treat this occult rejection rather than the DGF itself that leads to a reduced long-term outcome. In our study, we believe, this difficulty in analysis has been avoided as all allografts are biopsied routinely and AR is diagnosed irrespective of function.

In the present study, the risk of AR was neither increased in regrafts nor in sensitized patients. Preformed donor-reactive anti-HLA antibodies are detected by modern crossmatching techniques and antibody screening was done to determine if antibody specificity is performed before the transplant. The thorough immunological workup of transplant recipients has prevented the presence of antibodies from being a risk factor for rejection.

1-year Graft Survival

The main determinant of 1-year graft survival in this series, after censoring for death with a functioning graft, was DGF. There were no adverse effects of other donor factors including donor age or ICU management on 1-year graft survival. Importantly, no other factors were significant, including AR, HLA matching, highly sensitized recipients, and regrafts. The lack of an effect of AR on 1-year graft survival is surprising but not unexpected. This phenomenon has been mirrored in many recent publications comparing immunosuppressive regimens. It would suggest that AR in the first year is no longer a good end point for comparative studies. Furthermore, highly sensitized recipients were treated with ATG as induction therapy which could account partly for the good results obtained on these patients as reports suggest that antibody therapy helps to prevent graft loss in these high-risk patients. However, this is not the full story as the variable “ATG on induction” has no independent effect on survival.

The only other significant factor that influenced the 1-year graft survival was the year of transplantation. The immunosuppressive regimen and other factors over this period were unchanged which suggests that other factors not included in the statistical model had an impact on short-term graft survival (Sandimmune vs. Neoral). It is possible that there were medical and technical improvements made over the study period that increased survival. In an observational study, we cannot exclude the possibility of such confounding factors. However, changes over time do not explain the effect of DGF on survival because this is maintained in the proportional hazards analysis including “transplant year,” and in log-rank analysis stratified by “transplant year.”

Censoring for death is a well-known and common practice in the analysis of transplant outcome, but this might have an unexpected effect on the analysis as it may selectively exclude patients with high serum creatinine. In a recent publication, Meier-Kriesche et al. have reported a strong association between renal function at 1 year and the risk of cardiovascular disease and infectious mortality. According to this publication, a serum creatinine level of 1.9–2.1 mg/dL conferred a 50% increased risk of cardiovascular death compared with a serum creatinine level of >1.3mg/dL.

Long-term Graft Survival

The only factors affecting the long-term survival of those grafts that reached 1 year after censoring for death were recipient age and CIT and no apparent effect of AR or HLA matching. Crucially, we have found in our study that CIT affects long-term graft survival independently of the phenomenon of DGF. Other studies have found that DGF is one of the most important factors related to graft loss but have not identified CIT as having an impact in the long-term. In contrast, Ojo et al. in a study from American registry data found that prolonged CIT directly and independently of DGF and AR, compromised the long-term graft survival. In this study, we have shown that the effect of CIT on long-term graft survival is linear, and hence, there is no threshold below which CIT is acceptable or a threshold beyond which the deleterious affect of CIT accelerates.

We have not shown an influence of AR on graft survival after 1 year. Even though AR was common (54%), the incidence of severe rejections and steroid-resistant rejections were low. In contrast, it has been demonstrated in less well-matched populations using large retrospective databases that there is an impact of HLA-matching and the more severe forms of rejection on long-term graft survival.

Finally, the serum creatinine at 1 year, rather than the serum creatinine at 3 or 6 months, was found from this analysis to be an excellent predictor of the long-term survival of the graft as was reported by Hariharan et al. It was also found to be an important factor in a recent report by He and Johnston.
CONCLUSION

In conclusion, the factors involved in the short-term and long-term outcome and function of the renal transplant graft are multiple and interrelated. Older donors with pre-existing medical conditions and more fragile donor organs will need to be used to bridge the gap between supply and demand for cadaveric organs. Even though this study has not shown a significant impact of donor management, it would still seem appropriate to study ways of minimizing harm to the donor organ during this period. Minimization of the injury during the period of preservation will have increased importance. At a local level, our study lends weight to the need for sympathetic treatment of kidneys at multiorgan retrievals and access to theaters at the earliest possible opportunity. Our study has stimulated research into the cost–benefit ratios of increased use of the more expensive cold preservation solutions. Furthermore, the use of organ perfusion by machine at both cold and warm temperatures is now being revisited.

CIT is clearly identified as an important factor and one that can be controlled. Efforts should, therefore, be made to reduce CIT as much as possible; indeed, it was reduced during the period of this study. It would be unwise to place emphasis on ‘cutoff values’ that have not been rigorously demonstrated.

HLA matching has been the major focus of national and local sharing schemes to improve outcomes from transplantation. Although sharing could result in an increased in CIT, this has usually been seen as a price worth paying for improved matching. Recent national data show that the CIT of shared kidneys is only slightly longer than that of local kidneys (UK Transplant, Bristol). We do not propose that attention to HLA matching should be reduced but that practices could be reviewed with the objective of reducing CIT while maintaining matching.

REFERENCES

Study of Frequency of Psychiatric Illnesses in the Family Members of the Patients Suffering from Schizophrenia

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²Postgraduate Student, Department of Psychiatry, Dr. Panjabrao Deshmukh Memorial Medical College, Amravati, Maharashtra, India

Hence, schizophrenia has been the focus of intense research with earlier work focusing on incidence and prevalence to the recent spotlight on identifying the risk factors, environmental, genetic and the complex interaction between them.

One of the first instruments used to study schizophrenia was the family studies.

According to Gottesman and Shields 1982 calculated that the morbid risk in first-degree relatives was 5.6% in the parents of schizophrenics, 12.8% in the children of one schizophrenic parent, and 46.3% in the children of two schizophrenic parents. In dizygotic twins and siblings, the rate is about 15%, and in monozygotic twins reared together or apart; the rate is over 50%. Kendler[11] concluded that in family studies using blind diagnoses, control groups,
personal interviews, and operationalized diagnostic criteria, the risk for schizophrenia in close relatives of patients with schizophrenia is 5–15 times greater than in the general population. Given the accumulated evidence from genetic epidemiologic research, overall heritability estimate for the liability to schizophrenia of 60–70% (Kendler, 1988; Jones and Cannon, 1998).

At present, there are many studies with analyze the disease pattern with respect to the presence of positive family history, but not many of them examine the presence of any congruity between disease profile and pattern of the index patient and affected family members. Hence, the current study was undertaken with an objective to study psychiatric morbidity in the family members of the patients suffering from schizophrenia and in addition to compare the phenomenology of illness between the family members and the index patient.

**Aims and Objectives**

A. To study the frequency of psychiatric disorders in family members of the patients suffering from schizophrenia.

B. To compare the phenomenology of illness (age of onset, course of illness, and overall outcome) between the patient and the affected family members.

**MATERIALS AND METHODS**

A. Study design: This was a cross-sectional study.

B. Sample size: A total of 100 consecutive patients attending the psychiatric Outpatient Department of Medical College and General Hospital were recruited for the study.

C. Definition of the subject:

1. Inclusion criteria
   a. All the patients are suffering from schizophrenia according to DSM V.
   b. All the patients between the ages of 12 and –65 years.
   c. All the patients and the family members willing to give the informed consent and participate in the study.

2. Exclusion criteria
   d. All the patients are lacking the adequate data.

D. Place of study: Psychiatric outpatient department of general hospital.

E. Duration of study: 6 months.

F. Parameters to be studied:

1. Demographic profile of the patient.
2. Details of the phenomenology of illness.
3. Information about first- and second-degree family members.
4. If present details about the phenomenology of the psychiatric illness in the family members.

G. Operational criteria: The operational criteria were devised to judge the overall outcome of the illness in the patient and affected family member.

   - Good: Lasting remission of active symptoms and engagement in occupational activity for more than 75% of duration since the onset of symptoms.
   - Poor: Lack of lasting remission of active symptoms and engagement in occupational activity for <75% of duration since the onset of symptoms.

**Method**

Patients attending psychiatric outpatient department fulfilling the above selection criterion were in the first interview were informed about the nature, and the purpose of the study and those willing to participate in the study after giving the informed consent were included in the study. The recruited patients were interviewed in detail using the special pro forma prepared for the study, and all the required data were collected from the patient and their relatives. Those patients having the presence of psychiatric illness in the family members were encouraged to bring the family members for a direct interview and for asked for the previous medical records if available. All the collected data were tabulated and analyzed using appropriate statistical methods.

**RESULTS AND DISCUSSION**

Table 1 shows majority (72%) of the patients had onset of schizophrenia between 15 and 45 years. Mean age of onset for schizophrenia in patients was 34.43 years. (S.D.- 13).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>&lt;15</td>
<td>04 (04)</td>
</tr>
<tr>
<td>Mean – 34.43 years</td>
<td>72 (72)</td>
</tr>
<tr>
<td>15–45</td>
<td></td>
</tr>
<tr>
<td>S.D. - 13</td>
<td>24 (24)</td>
</tr>
<tr>
<td>&gt;45</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>57 (57)</td>
</tr>
<tr>
<td>Female</td>
<td>43 (43)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
</tr>
<tr>
<td>Unmarried</td>
<td>48 (48)</td>
</tr>
<tr>
<td>Married</td>
<td>48 (48)</td>
</tr>
<tr>
<td>Widow/divorced</td>
<td>04 (04)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Psychiatric illness in family members</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>40</td>
</tr>
<tr>
<td>Absent</td>
<td>60</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
</tr>
</tbody>
</table>
Table 2 highlights the fact that psychiatric morbidity was observed in about 40% of the family members of the patients suffering from schizophrenia.

Table 3 shows that around 19% of family members (first- and second-degree relatives) suffered from schizophrenia and related disorders (schizotypal personality disorder, psychosis NOS, and paranoid personality disorder). Among the patients, 14% of patients had a first-degree family member, and around 4% of the patients had a second-degree family member suffering from schizophrenia. 4% patients had first-degree family members and 2% the patients had a second-degree family member suffering from other psychotic disorders related to schizophrenia.

Kendler et al. (1985) reported a value of 3.7% for the morbid risk for schizophrenia among relatives of schizophrenic patients who were diagnosed according to the DSM-III criteria.

Table 4 depicts the comparison of phenomenology between the patients and the family members affected with schizophrenia under four domains. Mean age of onset for patients was 34.43 years whereas for family members it was 30.50 years. 83% of the patients had a gradual onset of symptoms compared with 90% of the family members [Table 5].

As it can be seen, the age of onset for schizophrenia went on decreasing with each generation, maximum (42.33 years) for parents, and minimum for the offspring (14.66 years).

Kendler et al. found in systematically ascertained pairs of affected siblings, the age at onset of schizophrenia is modestly correlated, whereas the correlation in age atonset in concordant monozygotic twin pairs is much higher.

Summary

Schizophrenia affects around 1% of world population. Due to its chronic nature and associated occupational impairment, it puts an enormous financial and psychological burden on the family members of the affected patients. Given the enormity of the problem, schizophrenia has been the focus of substantial research.

Major facts that were highlighted from the family studies were that the risk for schizophrenia was higher in the relatives of schizophrenic probands than in relatives of control probands. Across these studies, the risk of schizophrenia was, on average, 11 times greater in relatives of schizophrenic probands than in relatives of matched control probands. The difference in risk for schizophrenia in the relatives of schizophrenic and control probands was quite unlikely to occur by chance (i.e., $P < 0.05$). According to Gottesman (1991), the risk of developing schizophrenia in family members increases with the degree of biological relatedness to the patient - greater risks are associated with higher levels of shared genes. Most first-degree relatives (e.g., siblings and dizygotic [DZ] twins) share about 50% of their genes and show a risk of about 9%. Monozygotic (MZ) twins share 100% of their genes and show risks near 50%.

Although there has been extensive research on the illness, little is known about its etiology. The current study uses the family history method, one of the earliest epidemiological tools to study the presence of any familial aggregation of illness and if schizophrenia is present in the family

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**Table 3: Type of psychiatric disorders in family members in first-degree and second-degree family members of the patients suffering from schizophrenia**

<table>
<thead>
<tr>
<th>Type of disorder</th>
<th>First degree</th>
<th>Second degree</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schizophrenia and related disorders</td>
<td>16 (16)</td>
<td>03 (03)</td>
<td>19 (19)</td>
</tr>
<tr>
<td>Schizophrenia*</td>
<td>14 (14)</td>
<td>02 (02)</td>
<td>15 (15)</td>
</tr>
<tr>
<td>Schizophrenia relatedb disorders</td>
<td>04 (04)</td>
<td>02 (02)</td>
<td>05 (05)</td>
</tr>
<tr>
<td>Bipolar mood disorder</td>
<td>01 (01)</td>
<td>-</td>
<td>01 (01)</td>
</tr>
<tr>
<td>Major depressive disorder</td>
<td>05 (05)</td>
<td>-</td>
<td>05 (05)</td>
</tr>
<tr>
<td>Substance use disorders</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Alcohol dependencec</td>
<td>07 (07)</td>
<td>06 (06)</td>
<td>11 (11)</td>
</tr>
<tr>
<td>Opioid dependence</td>
<td>01 (01)</td>
<td>-</td>
<td>01 (01)</td>
</tr>
<tr>
<td>Other disorders</td>
<td>05 (05)</td>
<td>02 (02)</td>
<td>07 (07)</td>
</tr>
</tbody>
</table>

*aOne patient had both first- and second-degree family member suffering from schiz..; hence, the overall percentage is 15%.
*bOne patient had both first- and second-degree family member suffering from schizophrenia-related disorder; hence, the overall percentage is 0.5%.
*cTwo patients had both first- and second-degree family member suffering from alcohol dependence; hence, the overall percentage is 13%.

**Table 4: Comparing phenomenology of schizophrenia between the patients and affected family members**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean age of onset (years)</th>
<th>Type of onset</th>
<th>Course of illness</th>
<th>Overall outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Acute (%)</td>
<td>Gradual (%)</td>
<td></td>
</tr>
<tr>
<td>Patients (n=100)</td>
<td>34.43 (S.D.- 13)</td>
<td>17 (17)</td>
<td>83 (83)</td>
<td>53 (53)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(P&lt;0.05)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Affected family members (n=20)</td>
<td>30.50 (S.D.-14.9)</td>
<td>02 (10)</td>
<td>18 (90)</td>
<td>12 (60)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(P&gt;0.05)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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members, to compare the phenomenology of illness between the patient and the affected family member.

In the present study, 100 patients suffering from schizophrenia were recruited, and details of first- and the second-degree relatives were obtained for the presence of any psychiatric illness.

Final analysis of the data revealed that 40% of the patients had a family member suffering from psychiatric illness. Psychiatric morbidity of 30% was found in the first-degree relatives, while among second-degree family members it was 12%. These results are in congruence with the previous studies. In terms of specific psychiatric disorders, it was found that 19% of family members (first- and second-degree relatives) suffered from schizophrenia and related disorders (schizotypal personality disorder, psychosis NOS, and paranoid personality disorder). Earlier family studies have shown the risk of developing schizophrenia in the family members anywhere between 2% and 16%. Among our patients, 14% of patients had first-degree family members, and around 4% of the patients had a second-degree family member suffering from schizophrenia. 4% patients had first-degree family members and 2% the patients had a second-degree family member suffering from other psychotic disorders related to schizophrenia. Among schizophrenia-related disorders, 3 patients had personality disorders, 2 having schizotypal, and 1 having paranoid personality disorder. Only one patient was found to have family member suffering from bipolar mood disorder (1%), and 5 (5%) patients had family members suffering from major depressive disorder. The overall prevalence of substance dependence in the family members of schizophrenia patients was found to be around 11%. All the affected family members were found to have alcohol dependence with one family member having both alcohol and opioid dependence. Mean age of onset for patients was 34.43 years whereas for family members it was 30.50 years. Although the mean age of onset between the patients and the family members was similar, surprisingly a low level (20%) of concordance was seen between the groups.

Hence, the age of onset was compared with respect to the relations between the affected family members. It was seen that the age of onset for schizophrenia went on decreasing with each generation, maximum (42.33 years) for parents and minimum for the offsprings (14.66 years) However, a high level of concordance was seen with respect to the type of onset, the course of illness and overall outcome between the patients and the family members suffering from schizophrenia. There was an equal propensity for developing schizophrenia between the family members of male and female schizophrenia patients in our sample population in contrast to the previous studies, which have shown a more preponderance of psychiatric illness of female schizophrenic patients.

CONCLUSION

Given study confirms the important findings of the study are the presence of significant psychiatric morbidity in family members of patients suffering from schizophrenia.

Hence, we should be proactive in eliciting about family history of psychiatric illness as it will help as giving better patient care.

REFERENCES

Dysphonia Causative Diagnosis Linked to Voice Handicap Index of the Patients with Dysphonia

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²AISSR, Department of Anthropology, University of Amsterdam

Abstract

Background: Dysphonia has a negative impact not only on communication but also on the patients’ social and professional life. Detection of the underlying causes and the role of the predisposing factors in various conditions leading to dysphonia are important to establish definitive management of the patients.

Purpose: The purpose of the study is to determine the relationship between dysphonia causative diagnosis and the voice handicap index (VHI) score.

Materials and Methods: This study is an analytical study involving 47 patients with dysphonia. History taking, otorhinolaryngology examination, VHI questionnaire, and optic laryngoscopy examination with endoscopy were conducted to establish the primary diagnosis.

Result: Most of the patients are male and above 40-year-old. Based on the diagnosis, the most common underlying causes were laryngeal cancer which was found in 22 patients (47%). The overall score of the VHI was mostly in severe level (68%), and a significant relationship between the causative diagnosis of dysphonia and the VHI score was revealed ($P < 0.05$).

Conclusion: Based on VHI calculation, dysphonia affects the majority of patient’s quality of life, and a relationship was found between the diagnosis and the VHI score itself.

Key words: Dysphonia, Quality of life, Voice handicap index

INTRODUCTION

Every voice disturbance caused by a disorder of the phonation organs, particularly larynx, is known as dysphonia. Dysphonia is not a disease, yet a symptom of diseases or disorders which affects larynx that can lead to impairment of social and professional communication.[¹,²]

Dysphonia has a negative impact not only on communication but also on the social and professional life of the patients. Patients with dysphonia tend to encounter social isolation, depression, impairment of the quality of life, and increased working absent rate. Therefore, voice disturbance affects not only on the individuals but also creates a social burden.[³]

It has been reported that patients with voice disturbance had a significantly worse quality of life, regardless of the underlying causes. Measuring quality of life has been considered a tool to assess treatment effectiveness.[⁴,⁵]

One of the instruments to evaluate voice problem in patients with dysphonia is voice handicap index (VHI). VHI is a widely accepted questionnaire and is used in various researches and clinical applications. In 2002, VHI has been accepted by the European Board of Medical Research and Quality as a valid and reliable diagnostic tool.[⁶,⁷] This study is aimed to determine etiologies, predisposing factors, and quality of life of the patients presented to the Adam Malik General Hospital Otorhinolaryngology outpatient care with dysphonia. Detection various etiologies, role of the predisposing factors, and patients’ quality of life presented with dysphonia are very important to establish accurate treatment for the patients.
MATERIALS AND METHODS

The study is an analytical cross-sectional study in 47 subjects presented with dysphonia to the Otorhinolaryngology Outpatient Care of Adam Malik General Hospital from the period of June 2017 to August 2017. Patients that are not cooperative to undergo optic laryngoscopy examination are excluded.

The patients were undergone history taking and routine otorhinolaryngology examination than were asked to fill up demographic data which involves age, gender, job, and predisposing factors which include the history of cigarette smoking, alcohol abuse, vocal abuse, septic focus, and inhaler application. Patients were asked to fill up VHI questionnaire and underwent optic laryngoscopy examination with endoscopy to establish the diagnosis. In patients with tumor, micro larynx surgery was performed to determine the histopathology.

Quality of life was measured using the VHI data. It consists of 30 statements, each statement must be read carefully and the patients must be able to determine the frequency of these statements in their actual life, starting from 0 (never), 1 (seldom), 2 (once in a certain period of time), 3 (frequent), to 4 (always). Therefore, the VHI score range is between 0 and 120. The statements represent three subgroups, which reflects functional aspect, physic and emotional aspect, and voice flaw aspect. VHI can be interpreted as mild voice flaw (VHI score 0–30), moderate voice flaw (31–60), and severe voice flaw (61–120).

Statistic test was performed to determine the relationship between diagnosis and VHI score. To assure that the VHI score is based on the main variable; therefore, two most common predisposing factors were chosen to be tested with the VHI score. The test was done with the application of mean difference test (ANOVA) at α = 0.05. This study involved a human being as subjects. Hence, regulation was strictly followed and was proved by the Ethical Committee on health research.

RESULTS

Out of 47 patients studied, 36 patients (76%) were male, and 11 were female (24%), with a range of age of 18–71 years old and the majority age group was >60-year-old (12%). Most of the patients have a predisposing factor of smoking (54%). Other predisposing factors were alcohol (26%), vocal abuse, septic focus, and inhaler use [Table 1].

However, Table 2 shows that there was no significant relationship between the VHI score to smoking and alcohol (P > 0.05).

In this study, the most diagnosis which leading to dysphonia was malignant laryngeal tumour (laryngeal carcinoma), as much as 47%, followed by other causes including laryngopharyngeal reflux (LPR), tuberculosis laryngitis, paralysis of vocal cord, laryngitis, polyp and nodule of vocal cord, and laryngeal papilloma, and the least amount was intubation granuloma, only 2% [Table 3].

According to the VHI category, most patients have the VHI score with the severe VHI degree (71%). Moderate degree 29%, and none had a mild VHI score, as shown in Table 4.

In Table 1, the most diagnosis which leading to dysphonia was malignant laryngeal tumour (laryngeal carcinoma), as much as 47%, followed by other causes including laryngopharyngeal reflux (LPR), tuberculosis laryngitis, paralysis of vocal cord, laryngitis, polyp and nodule of vocal cord, and laryngeal papilloma, and the least amount was intubation granuloma, only 2% [Table 3].

According to the VHI category, most patients have the VHI score with the severe VHI degree (71%). Moderate degree 29%, and none had a mild VHI score, as shown in Table 4.

Table 1: Frequency distribution of subjects based on predisposing factors

<table>
<thead>
<tr>
<th>Predisposing factors</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septic focus</td>
<td>3 (5)</td>
</tr>
<tr>
<td>Smoking</td>
<td>31 (54)</td>
</tr>
<tr>
<td>Alcohol</td>
<td>15 (26)</td>
</tr>
<tr>
<td>Vocal abuse</td>
<td>7 (13)</td>
</tr>
<tr>
<td>Inhaler use</td>
<td>1 (2)</td>
</tr>
</tbody>
</table>

Table 2: Result of ANOVA test

<table>
<thead>
<tr>
<th>VHI</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>To smoking</td>
<td>0.063</td>
<td>0.803</td>
</tr>
<tr>
<td>To alcohol</td>
<td>0.005</td>
<td>0.944</td>
</tr>
</tbody>
</table>

Table 3: Frequency distribution of subjects based on diagnosis criteria (n=47)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laryngitis</td>
<td>3 (6)</td>
</tr>
<tr>
<td>LPR</td>
<td>6 (13)</td>
</tr>
<tr>
<td>Tuberculosis laryngitis</td>
<td>5 (11)</td>
</tr>
<tr>
<td>Malignant tumors</td>
<td>22 (47)</td>
</tr>
<tr>
<td>Polyp of vocal cord</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Nodule of vocal cord</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Papilloma</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Intubation granuloma</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Paralysis of vocal cord</td>
<td>4 (9)</td>
</tr>
</tbody>
</table>

Table 4: Frequency distribution of subjects based on the VHI degree

<table>
<thead>
<tr>
<th>Degree of VHI</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>0</td>
</tr>
<tr>
<td>Moderate</td>
<td>14</td>
</tr>
<tr>
<td>Severe</td>
<td>33</td>
</tr>
</tbody>
</table>

VHI: Voice Handicap Index
malignant tumors, nodule of vocal cord, polyp of vocal cord, laryngeal tuberculosis, laryngeal paralysis, LPR, and laryngitis with the lowest score. Statistical tests used ANOVA to diagnosis categories above to see the difference of VHI values to show significant results ($P < 0.05$).

Table 5 shows that a significant relationship between the causative diagnosis of dysphonia and the VHI score was revealed ($P < 0.05$).

Table 5: Result of ANOVA test

<table>
<thead>
<tr>
<th>VHI</th>
<th>F</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>To diagnosis</td>
<td>5.516</td>
<td>0.000</td>
</tr>
</tbody>
</table>

VHI: Voice handicap index

DISCUSSION

Dysphonia is one of many disorders that give negative impacts to the quality of life mainly in the elderly group, which the amount increases rapidly. Early identification of elderly patients with voice impairment and then give an optimal treatment, important to improve their quality of life.[1]

In this study, most dysphonia patients were in the age group >60-year-old male. The study carried out by Haryana in 2005 which was performed in the Department of ENT-HN subdivision of endoscopy H. Adam Malik Central General Hospital Medan reported that the highest percentage was in the age group >60-year-old (32 patients) comprising 27 men (38.6%) and 5 women (13.5%).[8] Golub et al., in 2006, reported that the prevalence of dysphonia mostly found in patients above 65-year-old, dominated by men.[9] This seemed to occur because the majority of the case found in this study were malignant laryngeal tumors. Meanwhile, the malignant laryngeal tumors usually encountered more frequent in the elderly male group. It was assumed that some manly habits may relate to a higher incidence of dysphonia in the male group, such as cigarette smoking, alcohol consumption, and poor oral hygiene.

In Table 1, we obtained that the most predisposing factors of the occurrence of dysphonia were smoking and alcohol. The similar matter was reported by Shinde and dan Hashmi, year 2015 in the study performed in Loni, India in 100 patients with dysphonia reported the most predisposing factor was smoking (68%), followed by alcohol (42%) and vocal abuse (2%).[10] Smoking is the main predisposing factor that gives bad to the vocal health. The relationship between smoking to the disorder of larynx and vocal distortion has been empowered by various studies. A number of studies have reported that smoking is the main cause of the histologic change and laryngeal characteristic. However, in this study, there was no relationship found between smoking and the VHI score ($P > 0.05$). Also with alcohol consumption, which had no relationship with VHI score ($P > 0.05$), seen in Table 2. Since all the patients that were involved in this study had laryngeal disorder (dysphonia), thus no difference on VHI score between smokers and non smokers, alcoholics and non-alcoholics, which was caused by preexisting voice handicap among all patients that were involved in this study. As we knew, dysphonia can be triggered by several predisposing factors such as smoking, drinking excessive amount of alcohol, vocal abuse, focus septic and several more predisposing factors, and each patient is likely to be affected by more than one of these predisposing factors. The same matter also occurred for alcohol consumption.

Table 3 shows that the disease that mostly caused dysphonia was laryngeal malignant tumor, as many as 22 patients (47%). This differs from the study carried out by Cohen et al. (2012), reported that laryngitis was the most diagnosis causing dysphonia.[3] Parajuli reported that the majority cause of dysphonia was vocal nodule (34.21%), whereas laryngeal malignant tumor was in the second rank (15.78%), and followed by laryngitis, polyp of vocal cord, Reinke's edema, laryngeal papilloma, and intubation granuloma, respectively, until the least.[11] This is because the polyclinic of ENT-HN Haji Adam Malik General Hospital Medan is a central refer Rak Hospital In Sumatera Utara, so patients that came were dominated by patients with more severe types of disease (malignancy). Meanwhile, patients with types of disease that was caused by infection or inflammatory process mostly came to tertiary hospitals.

Several studies showed that laryngeal diseases may harm the patient's quality of life. As a consequence, patients may lose time for working, stated disable, worsen economic difficulties of the community and reduced productivity.[12] Table 4 shows that most patients have voice distortion and severe voice disability, experienced by 32 patients (68%), moderate voice distortion in 15 patients (32%), and no patients felt mild degree of voice distortion. Each patient examined was asked to report subjectively the voice problem experienced. Individual variation was present and how the individuals felt the progression of health occurring to them would give different perceptions which were an effect of voice distortion that may be affected by job, education, marital, psychological and mental status, requirement of voice condition, and other unknown factors.

The diagnosis of disease as the cause of dysphonia also participated in affecting the VHI score in all patients. Figure 1 explains that laryngeal papilloma
had a high recurrence rate, so patients with laryngeal papilloma tend to experience repeated dysphonia, although treatment has been given. The causal factor in voice distortion was quite complicated, and patients with dysphonia had various difficulties that may affect their quality of life, reflected by the severity of VHI. It is visible that the determinant of VHI score was the diagnosis of disease.

As seen in Table 5, a significant distinction was revealed among the VHI score based on the causative diagnosis of dysphonia ($P < 0.005$). A similar finding was reported by Cohen et al. in their study in San Francisco; a significant difference was also revealed among the VHI score based on the diagnosis of various larynx disorders.[12]

In this study, the quality of life included voice distortion of a patient with tumor was worse than voice distortion due to infection or inflammation. Aaby and Heimdel(2012) in Norway reported that quality of life of the patients with malignancy was worse than those with no malignancy.[13] It can be caused by the difficulties related to many factors, such as psychological, emotional, and professional, and also their impact to the patients’ social life. Besides, voice handicap of those with larynx malignancy will last longer than those with other milder larynx disorders.

**CONCLUSION**

The measurement of quality of life has been a more important matter as a tool to assess the effectiveness of treatment and management plan. In patients with dysphonia, the quality of life not only depends on the etiology or predisposing factor underlying it but also other various factors. In this study, the authors revealed that there was a significant relationship between various dysphonia causative diagnosis and the VHI score. Based on the calculation of VHI score, found that the voice disability degree in the majority of patients with dysphonia was severe, which means that the majority of patients with complaints of dysphonia experienced the quality of life disturbance.

**REFERENCES**

Efficacy of Ropivacaine in Wound Instillation through Surgical Drains for Post-operative Analgesia in Modified Radical Mastectomy

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Abstract

Background: “Pain” is an unpleasant sensory and emotional experience associated with actual or potential tissue damage after any surgery so as in breast surgery. Successful pain management should be a central component of patient care and it holds true for patients undergoing breast surgery.

Aim: The aim of this study is to assess the efficacy of ropivacaine in wound instillation through surgical drains for post-operative analgesia in patients undergoing modified radical mastectomy.

Study Design: This was a prospective, randomized, double-blind study

Materials and Methods: Our study included 50 patients aged between 15 and 70 years of ASA Grades I and II scheduled for elective breast cancer surgeries. Group R received ropivacaine 0.2% (0.5 mL/kg) through axillary and chest drains, Group C received normal saline 0.9% (0.5 mL/kg) through axillary and chest drains.

Results: The result of our study demonstrated that instillation of local anesthetic through axillary and chest drains placed post surgically provided better analgesia and less incidence of post-operative nausea and vomiting.

Conclusion: It was concluded that patients receiving local anesthetic (ropivacaine) through surgical drain required less cumulative analgesic dose along with better post-operative analgesia and less incidence of post-operative complications such as nausea and vomiting.

Key words: Local anesthetic, Modified radical mastectomy, Post-operative pain, Surgical drains, Visual analog scale

INTRODUCTION

Modified radical mastectomy remains the mainstay for operable breast malignancies. In contrast to other breast surgeries, modified radical mastectomy involves more extensive tissue dissection.¹⁻³ Pain is a predictable consequence of surgery that can often last for several days; if left untreated, it is associated with significant adverse consequences for the patient. The relief of pain should be a central component of patient care, as it is the right of the patient. Poorly managed pain can slow recovery, creates burden for patients and their families, and also increases the cost to the health-care system.⁴⁻⁵ Conventionally, various strategies such as nonsteroidal anti-inflammatory drugs, opioids, peripheral nerve blocks, and wound infiltration with local anesthetics were used but reported limited success in providing effective post-operative pain control and moreover were associated with adverse effects such as nausea, vomiting, and dyspepsia.⁶ Due to the fear of needle track seedings and cutaneous spread of malignancy, infiltration along the line of surgical incision is not recommended in malignant lesions.⁷⁻⁹
Recent advancements have led to the development of a local anesthetic with an extended duration of action and a novel delivery platform, thereby broadening its potential role as a component of some post-operative pain management regimens. Wound instillation with local anesthetic through surgically placed drains in axilla and chest is nowadays widely used as a part of multimodal approach to provide effective analgesia postoperatively. Until today, many local anesthetics drugs are in use for local wound instillation, for example, lidocaine, bupivacaine, levobupivacaine, and ropivacaine. Local anesthetic drugs are becoming increasingly popular because of their analgesic properties and lack of opioid-induced adverse effects for treating post-operative surgical pain. Extensive animal toxicological studies have shown a lower propensity for cardiotoxicity with ropivacaine than with bupivacaine. With its lower toxicity, especially cardiovascular toxicity and less intense motor blockade, ropivacaine has advantage over bupivacaine in pain relief. The administration of local anesthetic via instillation through the surgical drain is one component of multimodal approach that allows for minimal invasive exposure and also results in immediate pain relief, which has been proven to increase patient satisfaction and early mobilization.

The aim of the present study was to assess the efficacy of ropivacaine in wound instillation through surgical drains in alleviating early post-operative pain after MRM. The efficacy of ropivacaine in wound instillation through surgical placed drains was assessed by duration of analgesia, number of analgesic demands, and cumulative analgesic requirement for pain relief.

**MATERIALS AND METHODS**

In this clinical randomized prospective study, 50 patients, the ASA physical status I and II, 15–70 years scheduled for unilateral modified radical mastectomy were enrolled randomly in two groups after obtaining the institutional ethics committee approval. Patients with a history of allergy to local anesthetic, history of any chronic analgesic drug usage, pre-existing respiratory diseases such as obstructive pulmonary disease, coexisting cardiovascular diseases, pregnant and breastfeeding females, history of any musculoskeletal disorders, and bleeding diathesis were excluded from the study.

Patients undergoing modified radical mastectomy were randomly allocated into two groups, each group containing 25 patients for the assessment of post-operative analgesia following wound instillation through surgical drainage tubes with local anesthetic and normal saline as control.

- **Group R**: Group R received ropivacaine 0.2% (0.5 mL/kg) through axillary and chest drains.

- **Group C**: Group C received normal saline 0.9% (0.5 mL/kg) through axillary and chest drains.

During the pre-operative day, patients were thoroughly educated about the procedures to be undertaken and were made well conversant with the visual analog scale (VAS) for post-operative pain assessment and their consent was taken. In the operation theater, I/V access was established and standard monitors were attached. Baseline hemodynamic parameters such as pulse rate, non-invasive blood pressure, respiratory rate, peripheral arterial oxygen saturation (SpO₂), and electrocardiography were recorded. After premedication, all the patients were induced with injection propofol at the dose of 2 mg/kg and injection succinylcholine at the dose of 1.5 mg/kg to facilitate tracheal intubation, and the patient was maintained with isoflurane and nitrous oxide plus oxygen (60:40). Neuromuscular blockade was achieved using vecuronium 0.04 mg/kg. At the end of the surgical procedure, the surgical drains, one in the axilla near the axillary vessels and the second in the chest wall below the skin flap (over the pectoral muscles), were placed by the surgeon before closing the surgical incision [Figure 1]. After proper oral and tracheal suctioning, the patient was reversed with neostigmine and glycopyrrolate, and extubation was performed on meeting the criteria.

Patients were allocated randomly into two groups of 25 each by computer-generated numbers. The study drug was given through each drain as per randomization after the incision was closed. Group C patients received normal saline 0.9% (0.5 mL/kg). Total volume was divided into equal amount and given through each drain. Group R patients received ropivacaine 0.2% (0.5 mL/kg). The study drug being prepared by a separate anesthesiologist outside operation theater according to randomization number and

![Figure 1: Showing instillation of drug through surgical drain placed in the chest wall](image-url)
was labeled as “study drug.” Total volume (0.5ml/kg of 0.2% ropivacaine) was divided in equal amount and given through each drain. After instillation of the study drug, the drains were clamped for 10 min. After a dwell time of 10 min, the clamp was released to allow the test solution into the negative pressure suction drain.

Background analgesia was given to every surgical patient immediately after extubation in the form of intramuscular injection of diclofenac sodium (1.25 mg/kg) every 8 h in buttocks.

Patients were transferred to the post-anesthesia care unit for further monitoring. Pain score at “0” h was noted after extubation and subsequently every 4th h for 24 h, by the person who does not have knowledge regarding the solution which the patient had received. Post-operative pain was assessed by VAS using a 10 cm VAS (0 - no pain and 10 - worst imaginable pain). If the VAS exceeded “4” at any point of time, rescue analgesia with injection tramadol 1 mg/kg intramuscular was administered and the study terminated at that time.

The duration of analgesia was defined from the time of instillation of the study drug to the time for the first demand of analgesia. The number of demands and the total cumulative analgesic requirement was noted for 24 h. Surgical site related untoward effects such as hematoma, infection, and wound dehiscence were observed clinically till the patient was discharged. Adverse effects such as nausea and vomiting were noted as all patients received prophylactic antiemetic ondansetron.

**Statistical Analysis**

Descriptive statistics was used to describe the baseline characteristics. Numerical data were expressed as mean and standard deviation. Qualitative data were expressed as frequency and percentage. Chi-square test was used to examine the relation between qualitative variables. For quantitative data, comparison between the groups was done using independent sample t-test. For descriptive purposes, P value differences <0.05 were noted in the tables. All analysis was conducted using SPSS version.

**OBSERVATION AND RESULTS**

Median VAS score value was <4 up to 3rd h of the study. Its value was 4 at 12th h of the study in Group R and 4th h of the study in Group C, which decided the time of rescue analgesia and duration of analgesia [Table 1].

There was statistically significant difference between Group R and Group C, in terms of total tramadol consumption (P < 0.0001) [Table 2 and Graph 1].

There was statistically significant difference between the study Groups R and C, in terms of duration of analgesia (P < 0.0001) [Table 3 and Graph 2].

Incidence of post-operative nausea and vomiting (PONV) in Group R is 8% and in the Group C is 28% [Table 4 and Graph 3].

**DISCUSSION**

Pain is a predictable consequence of surgery, if not treated; it is associated with undesirable clinical consequences. The relief of pain should be a central component of patient care and it holds true for patients undergoing breast surgery. Providing post-operative analgesia to the patient gives subjective comfort and helps in restoring the altered physiology and immunological response. Appropriate acute pain management, however, remains the common goal in all the studies of pain after breast surgery, with the aim of achieving patient satisfaction and accelerated recovery and rehabilitation, and the potential later benefit of a reduction in chronic post-mastectomy pain. Conventionally, various strategies such as nonsteroidal anti-inflammatory drugs, opioids, peripheral nerve blocks, and wound infiltration with local anesthetics were used but reported limited success in providing effective post-operative pain control.

<table>
<thead>
<tr>
<th>VAS (in hours)</th>
<th>Group R</th>
<th>Group C</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>VAS1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>VAS2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>VAS3</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>VAS4</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>VAS8</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>VAS12</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>VAS16</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>VAS24</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

VAS: Visual analog score
and moreover were associated with adverse effects such as nausea, vomiting, and dyspepsia. Sidiropoulou et al. did their study comparing continuous wound infiltration with ropivacaine versus single-injection paravertebral block in patients undergoing modified radical mastectomy. They concluded that both the techniques were similar in respect to morphine consumption and reduction in post-operative pain. Paravertebral block needs expertise, sufficient time to perform the block, and necessary guidance, and it has a serious complication like pneumothorax. Due to the fear of needle track seedings and cutaneous spread of malignancy, infiltration along the line of surgical incision is not recommended in malignant lesions. All these problems play a key role to search a newer mode of analgesia. Till today, many local anesthetic drugs are in use for local wound instillation, for example, lidocaine, bupivacaine, levobupivacaine, and ropivacaine. Local anesthetic drugs are becoming increasingly popular because of their analgesic properties and lack of opioid-induced adverse effects for treating postoperative surgical pain. Extensive animal toxicological studies have shown a lower propensity for cardiotoxicity with ropivacaine than with bupivacaine. With its lower toxicity, especially cardiovascular toxicity and less intense motor blockade, ropivacaine has advantage over bupivacaine in pain relief. The administration of local anesthetic via instillation through the surgical drain is one component of multimodal approach that allows for minimal invasive exposure and also results in immediate pain relief, which has been proven to increase patient satisfaction and early mobilization.

In this prospective, randomized control study, the results showed that patients, who received instillation with 0.2% ropivacaine through surgical drains following MRM, experienced a better post-operative analgesia as compared with patients of control group who had received saline. Cumulative rescue analgesic consumption and number of demands for analgesia in the first 24 h were significantly lower in ropivacaine group compared with the saline group so as the use of injection tramadol is also less in ropivacaine group and their satisfaction scores were significantly higher as compared to the patients who received saline. Assessment of pain was done using VAS score. Our study showed that VAS score rises significantly early in Group C than Group R. When VAS score reached >4, rescue analgesia in the form of intramuscular tramadol (1 mg/kg) was administered. This finding is in concordance with the study of Jonnavithula.
et al. who studied the analgesic effect of instillation of 0.25% of bupivacaine versus 0.9% normal saline and control group with no instillation, in cases of modified radical mastectomy through surgical drains.\[3\] Fayman et al. conducted a comparative study between analgesic effect of bupivacaine and ropivacaine infiltration in a bilaterally symmetrical breast surgery model. They found that overall analgesia achieved with bupivacaine and ropivacaine infiltrations was not statistically different except for the risk of cardiotoxicity with bupivacaine.\[16\]

Our study was in contrast to the study of Talbot et al., who in their study determined the effect of irrigation of axillary drains with local anesthetic on post-operative pain following modified Patey mastectomy. They felt that it did not appear to offer any contribution for post-operative analgesia in some of their patients nor were there any differences in antiemetic or supplemental analgesic consumption. They opined that this could be because of malpositioned drain, blockade of some holes of the drain, or unequal distribution of the local anesthetic due to gravity and concluded that further refinement in the technique was needed.\[17\] Hence, to overcome this limitation, we have instilled through both the chest wall and axillary drains. This could have resulted in more uniform distribution of the drug, thereby improving the efficacy of the technique, and the patients were pain free in the post-operative period.

In our study, there was no case of local anesthetic toxicity observed which was in concordance with the study of Jonnavithula et al.\[3\] and Talbot et al.\[17\]

**CONCLUSION**

Post-operative analgesia is a key component of perioperative nursing care and the pain management paradigm has shifted to an increasing use of multimodal analgesia. Wound instillation with local anesthetics through surgical drains with an extended duration of action and a novel delivery platform has broadened its potential role as a component of post-operative pain management following MRM procedure.

**REFERENCES**

Morphometric Estimation of Cranial Index in Mahakaushal Region of Madhya Pradesh: Craniometrics Study

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Abstract

Background: Craniometrics is an important tool for an anthropologist and forensic experts for identification of the racial and sexual differences, offsprings and siblings towards their genetic transmission of inherited characteristics and also to a great extent for the facial reconstruction of disputed identity.

Aim: The purpose of this study was to establish specific standard data for sex determination from the cranium in Mahakaushal region of Madhya Pradesh.

Material and Methodology: The present study was carried out with 140 (90 male & 50 female) dry human skull procured from Department of Anatomy, N.S.C.B. medical college, Jabalpur, Madhya Pradesh. Cranial measurements were taken; data was tabulated and statistically analyzed

Results: The study showed that the mean cranial index was 77.89±3.55. The mean cranial index for male was 77.65 ±3.34 and for female was 78.13 ±3.76. The difference between male and female cranial index was statistically significant (p< 0.001). The result of present study shows that majority of Mahakaushal population are Mesocephalic followed by Dolichocephalic.

Conclusion: This study will serve as basis for comparison with future studies on other geographical region population and to achieve a more objective racial and sex assessment.

Key words: Cranial index, Maximum Cranium length, Maximum Cranium breadth, Dolicocephalic, Mesocephalic, Head shape

INTRODUCTION

Identification of human remains is an essential element in medico-legal investigations. One of the key tasks for the forensic anthropologist is the identification of dismembered, mutilated, and fragmentary remains. It is important here that accurate sexing of the human remains has the potential to primarily narrow down the search to a particular sex thereby giving a sense of direction to the ongoing forensic investigation. There is a need for regional studies in the process of identification of human remains as the human species inhabit diverse environments all over the earth and exhibit a lot of racial and ethnic variation. Human cranium is regarded as the best indicator of sex second to the pelvis. Many cephalic indices are widely used for racial and sex differences and they provide a recording of sizes and proportions of cranial features. These recordings yield a numerical expression which is important in evaluating population by comparison of head form. Human skulls have been studied both metrically and non-metrically earlier and these studies have thrown light on the functional and morphological aspect of skull. Craniometrics is an important tool for an anthropologist and forensic experts for identification of the racial differences, sexual differences, offsprings, and siblings toward their genetic transmission of inherited characteristics and also to a great extent for the facial reconstruction of disputed identity. The craniometric results can also be of great assistance
while evaluating patients in various fields of medicine such as medical imaging, pediatrics, and craniofacial surgery and also for studying growth trends in various castes/races within a defined geographic zone. Anthropometric study of the head is useful in designing various equipment of head and face such as helmets, headphones, and goggles by formulating standard sizes. The cranial index (CI) is one of the important craniometric indices. The cephalic index was defined by Swedish professor of Anatomy Anders Retzius (1796–1860) and first used in physical anthropology to classify ancient human remains found in Europe. Retzius described as gentes dolichocephaly to those individuals who had an elongated skull shape, and gentes brachycephaly to those whose skulls were short but he never, at that time, assigned numerical values to distinguish one category from the other. Retzius when applied to living individuals are known as a cephalic index, and when referring to dry skulls, CI. The cranial indices were calculated by multiplying the head breadth with 100 and dividing it with the head length. Cephalometry pertains to be the most versatile technique in the investigation of the craniofacial skeleton, because of its simplicity, acceptability, and practicality.

Variation between and within the population is attributed to the complex interaction between genetic and environmental factors. It is also used to analyze the evolution of human species in archeology. It is especially important in forensic practice where cranial remains are compared with existing photograph and radiologic records.

MATERIALS AND METHODS

The present study was carried out with 140 (90 male and 50 female) dry human skull procured from the Department of Anatomy, N.S.C.B. Medical College, Jabalpur, Madhya Pradesh. All the skulls were normal, fully mature, devoid of any fractures or damages. Instruments used for the measurement were spreading caliper, scale, and marker. All parameters were measured independently by two different observers, with a predetermined methodology to prevent interobserver and intraobserver error. The method used for assessing the CI was Hrdlicka’s method. The anatomical landmarks, Glabella (g), Inion (I), and Euryon (eu) were marked.

The anatomical landmarks were defined as follows:
• Glabella: A point above the nasal root between the eyebrows and intersected by mid sagittal plane.
• Inion: The distal-most point placed on the external occipital protuberance in the mid sagittal plane.
• Euryon: The lateral-most point placed on the side of the head.

The head length was measured with a spreading caliper from Glabella to Inion. Head breadth was measured as the maximum transverse diameter between the two Euryon using a spreading caliper.

All measurements were taken in centimeters and to an accuracy of 0.10. The cranial indices were calculated by multiplying the head breadth with 100 and dividing it with the head length.

Depending on these indices the types of head shapes were classified as given by William et al., 1995 [Table 1].

Statistical Analysis
The data were analyzed by Microsoft Excel, and all the statistical tests and calculations were performed using the software GraphPad Prism Version 5.

OBSERVATION AND RESULTS

From the collected data, the mean values and standard deviation (SD) were calculated for maximum head length, maximum head breadth, and CI. From the observations of the present study, the parametric data were analyzed using independent sample t-test.

Males’ cranial length ranged from 16.2 cm to 19.7 cm with

<table>
<thead>
<tr>
<th>Table 1: Types of head shapes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of skull</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Dolichocephalic</td>
</tr>
<tr>
<td>Mesocephalic</td>
</tr>
<tr>
<td>Brachycephalic</td>
</tr>
<tr>
<td>Hyper brachycephalic</td>
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<table>
<thead>
<tr>
<th>Table 2: Descriptive statistic showing various parameters of the present study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variables</td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td>CI (male)</td>
</tr>
<tr>
<td>CI (female)</td>
</tr>
<tr>
<td>CI (both)</td>
</tr>
<tr>
<td>Cranial length (male)</td>
</tr>
<tr>
<td>Cranial length (female)</td>
</tr>
<tr>
<td>Cranial length (both)</td>
</tr>
<tr>
<td>Cranial breadth (male)</td>
</tr>
<tr>
<td>Cranial breadth (female)</td>
</tr>
<tr>
<td>Cranial breadth (both)</td>
</tr>
</tbody>
</table>

CI: Cranial index
The mean CI was higher in females compared to males in the present study. Among the male skulls, the mean CI recorded to be 77.65 ± 3.34 whereas in females it was 78.13 ± 3.76. There was a statistically significant difference in the mean of the cranial indices in male and female skulls [Table 1]. Head shape was classified by cephalic index in which dominant type was mesocephalic (66.66%) and dolichocephalic (31.11%), followed by 1.11% each of brachycephalic and hyper brachycephalic in male skulls. The mean CI in female was 78.13 ± 3.76 which showed that majority were mesocephalic (68%), 28% of dolichocephalic, and 4% of brachycephalic and no hyper brachycephalic skulls were noted in females [Table 3].

**DISCUSSION**

Human species inhabit diverse environments all over the earth and exhibit a lot of racial and ethnic variation.\[^{2,3}\] Therefore, there is a need for regional studies in the process of identification of human remains pertaining to cranium. Variation between and within the population is attributed to the complex interaction between genetic and environmental factors.\[^{14}\] The most popular and widely anthropometric measurement used in the differentiation of race and ethnicity is cephalometry through which cranial dimensions can be determined. The most important of cephalometric dimensions are length and breadths of head that are used in cephalic index determination.\[^{17}\] Cranio-metry can be used to classify people according to race, intelligence, and capacity for moral behavior. Variations of the shape and size of the human skull have gained much attention, and continuous efforts are been made to associate these variations to characterize different races.\[^{18}\] Several studies have been conducted on the measurement of cephalic index in different geographical zones and have classified head shapes into four internationally accepted categories that include dolichocephalic (<74.9), mesocephalic (75–75.9), brachycephalic (80–84.9), and hyper brachycephalic (85–89.9). Kondo _et al._ showed that head breadth reaches to maximum at the age of 14 and head length will increase even after the age of 14. They also showed that in Japanese population, brachycephalization and secular changes in head length occur. Australian aborigines and native South Africans are dolichocephalic, Europeans and Chinese skull are Mesocephalic, and Mongolians and the Andaman islanders have brachycephalic skull.\[^{19}\] The comparative study of the present cranial measurements with the other workers studies is shown in Table 4. In our study, mean cephalic index of male skull was found to be 77.65 ± 3.34 and that of female skull was 78.13 ± 3.76.
so, according to Siewerts classification this population belongs to mesocephalic variety. The results of our study were similar to the study on Andhra males and females by Gujaria and Salve, 2012 in which the mean cephalic index in males was 76.28 and in females was 78.16. The dominant head type in males and female was Mesoscheplac followed by dolichocephalic and then by brachycephalic and ultra-brachycephalic.[20] The findings of our study were also similar to that on Srilankan males and females by Ilayperuma in 2011 in which mesocephalic was the dominant head shape in both males and females.[21] Bhargava and Kher in 1960 found mean cephalic index as 76.9 in Bhils population.[22] Further, Bhargava and Kher in 1961 found it to be 79.80 in Barelas population in central India.[23] As previously reported, genetic and environmental factors are largely responsible for variation in head shapes. We postulate based on our observations that the head type observed in the population of Mahakaushal region in comparison with other population is a true reflection of their location. The knowledge obtained from this study can be of great importance to a plastic surgeon when reconstructive surgery is essential.

CONCLUSION

Cephalic morphometry marks its identity in anthropology for the study and comparison of crania of a different population of different ethnic, racial, dietary, geographical, and genetic backgrounds. The differences in metrical dimensions of the human head among the different population are greatly valuable, and this suggests the strength of cephalic morphometry in the assessment of sex and races. This helps in better understanding of frequency distribution of human morphologies and comparison of different races. The significance and practicality of CI were less studied in a population of Mahakaushal region, and thus a research design was framed to study, analyze and report the head shapes and cephalic index of this population.

REFERENCES

Anatomical Variations in Position of Vermiform Appendix an Anatomical Study of Aborted Fetuses

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Abstract

Background: The appendix is a vestigial organ, narrow tube-like structure lying in the right iliac fossa. It is part of the large intestine, and its base is attached to the posterolateral surface of the caecum just below ileocecal junction, the tip is free, and it may be present in retrocecal, subcecal, pre/post ileal, or pelvic positions. Knowing the exact anatomical position of vermiform appendix is important in view of surgeons for on time diagnosis and management of acute appendicitis.

Aim of the Study: The aim of the study was to determine the different characteristics of vermiform appendix in aborted fetuses.

Materials and Methods: A total of 138 aborted fetuses were subjected to dissection to identify the position of the vermiform appendix. Other parameters noted were the length of the appendix, formation of mesoappendix, and direction of the tip of the vermiform appendix.

Observations and Results: Among the 138 fetuses included in the study 89 (64.49%) were male and 49 were female fetuses (35.50%). Observing the position of the appendix, it was noted that among the male fetuses the pelvic position was seen in 52 fetuses (58.42%) followed by subcecal in 14 (15.73%), retroileal in 12 (13.48%), retrocecal in 4 (04.49%), ectopic in 4 (04.49%), and pre-ileal in 3 (03.37%). The tip of the appendix was at 2’ O clock position, being the most common in 59 (%) of the male fetuses. The mean length of the appendix in fetuses between 11 and 20 weeks was 14.98 mm, in fetuses between 21 and 30 weeks was 23.65 mm, and in fetuses of 31 to –40 weeks was 35.24 mm. Mesoappendix was completely formed in 79.5% of the bodies.

Conclusions: There was no clear-cut association between the sex of the fetuses and the position of the appendix. Anterior anatomical position was the most common position for vermiform appendix which was not correlating with other reports from western countries. Most probably factors such as race, geographical location, and dietary habits play some role in determining the position of the vermiform appendix.

Key words: Appendicectomy, Appendicitis, Mesoappendix, Vermiform appendix

INTRODUCTION

The vermiform appendix is located in the right lower quadrant of abdomen appearing as a narrow, worm-shaped tube, arising from the postero medial caecal wall, 2 cm or less below the end of the ileum.[1] Its opening is occasionally guarded by a semicircular fold of mucous membrane known the valve of Gerlach.[2] The appendix is usually located at the junction of the three taenia, found on the surface of the caecum.[1,3] The length of appendix varies from 7 to 9 cm.[1,4] The attachment of the base of the appendix to the caecum remains constant, whereas the tip can be found in a retrocecal, pelvic, subcecal, pre-ileal, and post-ileal positions.[1-3] The appendix is connected to the lower part of ileal mesentery by a triangular fold called as mesoappendix.[1,2] The mesoappendix has a free border which carries the blood supply to the organ, by the appendicular artery which is a branch from the ileocolic artery. Inflammation of appendix is known as appendicitis, and usually, it is an acute condition affecting the young adults, a common cause of acute abdomen. Since the appendicular artery is an end artery, and also it’s close
proximity with the appendicular makes it more susceptible to thrombosis during inflammation. This reduces the blood supply to the tip and the cause for gangrene and rupture. Appendicectomy is the treatment of choice for appendicitis. If the surgery is delayed, it leads to complications such as rupture, hemorrhage, perforation, and shock. During surgery sound knowledge of the origin of the appendicular artery, its variations, and accessory appendicular arteries is very important to avoid complications. The anatomical knowledge of position and direction of the tip are not only important to the surgeon but also to the radiologist as most of the clinical diagnoses of appendicitis are being confirmed by ultrasound or Magnetic resonance imaging scan of the abdomen nowadays. The diagnostic uncertainty by virtue of its inflamed tip not reaching up to the average length and delay can lead to early perforation and gangrene.

Knowing common position(s) of the appendix helps on time diagnosis of acute appendicitis. Variable positions of the appendix may mislead physicians to make a wrong decision or diagnosis of other diseases. Hence, accurate information about the anatomical location of the appendix can improve the prognosis of the disease.\[6\] In this context, the present study was conducted to study them anatomical variations in the position of the vermiform appendix and its morphology.

**Institute of Study**
This study was conducted at Kannur Medical College, Anjarakandy, Kannur, Kerala.

**Period of Study.**
The period of the study was from March 2014 to February 2018.

**Duration of Study**
The duration of the study was 4 years.

**Type of Study**
This was a cross-sectional, prospective study.

**MATERIALS AND METHODS**
A cross-sectional prospective study was conducted including 138 aborted fetuses which were dissected to study the morphology and position of the vermiform appendix. An Institutional Ethical Committee clearance certificate was obtained before starting the study.

**Inclusion Criteria**
1. Aborted fetuses belonging to the gestational ages of 11 and 40 weeks were included.
2. Aborted fetuses of both the gender were included.
3. Aborted fetuses belonging to urban, rural, and tribal areas were included.

**Exclusion Criteria**
1. Aborted fetuses not immediately transferred to the department of anatomy were excluded.
2. Aborted fetuses which are for any reason might change the anatomical position of the appendix were excluded from the study.

The fetuses were obtained from the labor room and operation theater of the department of obstetrics and gynecology of the institute. Keeping the ethical standards in view, all the fetuses were embalmed using 10% formalin. The gestational age was calculated by the available obstetric history and the ultrasonographic reports from the donor department. Determination of sex was done by observing the external genitalia. The dissection was done in situ within 24 h of obtaining the specimen. The abdomen of the fetuses was opened by a long midline incision, and all the layers of abdomen (skin, anterior abdominal wall, and peritoneum) were reflected for good view of the abdominal cavity along with its contents. The organs were separated from the right iliac fossa and the taenia coli were visualized; the anterior caecal taenia coli act as the best guide for the vermiform appendix. Although the relation of the base of the appendix to the caecum is constant, the position of the vermiform appendix was studied in relation to the caecum, the terminal parts of ileum and the direction of the tip of the appendix. Accordingly, the position of the vermiform appendices was noted. The length was measured using a standard metal scale in millimeters to include the distance between the tip and the base of the appendix. The direction of the tip of the appendix was noted by lifting the caecum without disturbing base of the appendix.

**OBSERVATIONS AND RESULTS**
Among the 138 fetuses included in the study 89 (64.49%) were male and 49 were female fetuses (35.50%). Among the male, the fetuses belonging to the gestational age of 11–20 weeks were 37 (41.57%), 21–30 weeks were 28 (31.46%), and 31–40 weeks were 24 (26.96%). Among the female, the fetuses belonging to the gestational age of 11–20 weeks were 12 (24.48%), 21–30 weeks were 21 (42.85%), and 31–40 weeks were 16 (32.65%), [Table 1].

Observing the position of the appendix, it was noted that among the male fetuses the pelvic position was seen in 52 fetuses (58.42%) followed by subcecal in 14 (15.73%), retroileal in 12 (13.48%), retrocecal in 4 (04.49%), ectopic in 4 (04.49%), and pre-ileal in 3 (03.37%). Among the female fetuses, the pelvic position was seen in 26 fetuses.
Shaikh and Gurukkal: Position of Vermiform Appendix in Aborted Fetuses

(53.06%) followed by subcecal in 7 (14.28%), retroileal in 5 (10.20%), retrocecal in 4 (08.16%), ectopic in 3 (06.12%), and pre-ileal in 4 (08.16%) [Table 2].

Table 3 shows the direction of the tip of the appendix in the present study, the 2'O clock position being the most common in 59 (%) of the male fetuses followed by 2'O clock in 15 (16.85%), 5'O clock in 6 (06.74%), 7'O clock in 5 (05.61%), and 11'O clock in 4 (08.16%) fetuses [Table 2].

The fully formed mesoappendix is shown in Figure 1. In 49/138 (35.50%) fetuses, the mesoappendix was found to be well-formed in this study.

The mean length of the appendix in fetuses between 11 and 20 weeks was 14.98 mm, in fetuses between 21 and 30 weeks was 23.65 mm, and in fetuses of 31–40 weeks was 35.24 mm.

DISCUSSION

In the present study the position of the appendix, it was noted that among the male fetuses the pelvic position was seen in 52 fetuses (58.42%) followed by subcecal in 14 (15.73%), retroileal in 12 (13.48%), retrocecal in 4 (04.49%), ectopic in 4 (04.49%), and pre-ileal in 3 (03.37%). Among the female fetuses, the pelvic position was seen in 26 fetuses (53.06%) followed by subcecal in 7 (14.28%), retroileal in 5 (10.20%), retrocecal in 4 (08.16%), ectopic in 3 (06.12%), and pre-ileal in 4 (08.16%). This finding was similar to studies of Katzarski et al.,[7] Ojeifo et al.,[8] Rahman et al.,[9] and Paul et al.[6] Similarly the pre-ileal position was observed in 07 (07.86%) fetuses, [Table 2], in this study similar to the reports observed in the references from 6 to 9.[6-9] However, the studies by L. Ajmani and Ajmani in India,[10] Ojeifo et al.[8] in Bosnia,[8] and Clegg-Lamptey et al. in Ghana[11] have reported that the most common position of the appendix is retrocecal and pelvic. The studies by Denjalić et al.[12] and Golalipour et al. conducted in Iran,[13] were evaluated in the patients undergoing appendicectomy. The study by Yabunaka et al.[14] was undertaken by evaluating the size of the appendix by ultrasonography. Whereas the study of Rahman et al.[9] was undertaken during surgery to measure the size of the appendix. All these studies even though were undertaken by different methods were substantially similar to the present study. If the position of the appendix was viewed in relation to the caecum, then it could be divided into anterior: (Pelvic and pre- and retro-ileal) or posterior: (Retrocecal and para-caecal) locations.[15] In such a situation, the anterior location of the appendix was observed in 107/138 (77.53%) fetuses. Hence, early diagnosis of appendicitis and shorter duration of surgery and hospitalization are expected among such patients. This can reduce the complications of appendicitis surgery.[15] In the present study, pelvic position is the most common location of the appendix in both 52 (58.42%) in males and 26 (53.06%) in females. The mean length of the appendix in fetuses between 11 and 20 weeks was 14.98 mm, in fetuses between 21 and 30 weeks was 23.65 mm, and in fetuses of 31–40 weeks was 35.24 mm.

Table 1: The gender incidence of the fetuses included in the study (n=138)

<table>
<thead>
<tr>
<th>Gestational age (weeks)</th>
<th>Male - 89 (64.49%)</th>
<th>Female - 49 (35.50%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11-20</td>
<td>37 (41.57)</td>
<td>12 (24.48)</td>
</tr>
<tr>
<td>21-30</td>
<td>28 (31.46)</td>
<td>21 (42.85)</td>
</tr>
<tr>
<td>31-40</td>
<td>24 (26.96)</td>
<td>16 (32.65)</td>
</tr>
</tbody>
</table>

Table 2: The position of the appendix in males and females (n=138)

<table>
<thead>
<tr>
<th>Position of appendix (%)</th>
<th>Male- 89 (%)</th>
<th>Female-49 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pelvic - 78 (56.52)</td>
<td>52 (58.42)</td>
<td>26 (53.06)</td>
</tr>
<tr>
<td>Subcecal - 21 (15.21)</td>
<td>14 (15.73)</td>
<td>07 (14.28)</td>
</tr>
<tr>
<td>Retro-ileal- 17 (12.31)</td>
<td>12 (13.48)</td>
<td>05 (10.20)</td>
</tr>
<tr>
<td>Retrocecal - 8 (05.79)</td>
<td>04 (04.49)</td>
<td>04 (08.16)</td>
</tr>
<tr>
<td>Ectopic - 7 (05.07)</td>
<td>04 (04.49)</td>
<td>03 (06.12)</td>
</tr>
<tr>
<td>Pre ileal - 7 (05.07)</td>
<td>03 (03.37)</td>
<td>04 (08.16)</td>
</tr>
</tbody>
</table>

Table 3: The direction of the appendix in males and females (n=138)

<table>
<thead>
<tr>
<th>Direction of the tip of the appendix</th>
<th>Male - 89 (%)</th>
<th>Female - 49 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12'O clock</td>
<td>59 (66.29)</td>
<td>20 (40.81)</td>
</tr>
<tr>
<td>2'O clock</td>
<td>15 (16.85)</td>
<td>17 (34.69)</td>
</tr>
<tr>
<td>5'O clock</td>
<td>06 (06.74)</td>
<td>06 (06.74)</td>
</tr>
<tr>
<td>7'O clock</td>
<td>05 (05.61)</td>
<td>02 (04.08)</td>
</tr>
<tr>
<td>11'O clock</td>
<td>04 (08.16)</td>
<td>04 (08.16)</td>
</tr>
</tbody>
</table>

Figure 1: Photograph of appendix in ileocecal region with fully formed mesoappendix
2.35 ± 1.25 mm. In similar studies by Katzarski et al.,[7] Gholalipour et al.,[13] and Ajmani and Ajmani,[10] it was shown that the size of the appendix was longer in males when compared to females. However, the studies of Bakheit and Warille[16] and Rahman et al.[9] reported the length to be more in females. Searle et al. believe that after an initial growth period during early infancy up to about 3 years, the appendix achieves its adult proportions and does not continue to grow throughout childhood.[17,18] In 49/138 (35.50%) fetuses the mesoappendix was found to be well-formed in this study. It is recorded in literature that the frequency of incomplete mesoappendix is highest in the age group below 10 years. Incomplete mesoappendix may reduce blood supply to the tip of the appendix and make it prone to gangrene and perforation.

CONCLUSIONS

The incidence of the pelvic position of appendix (anterior position) was higher. Complete mesoappendix was observed in 35.50% of the fetuses. The mean length of the appendix was 24.62 mm.

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Source of Support: Nil, Conflict of Interest: None declared.
Comorbidities and their Management in Patients with Chronic Kidney Disease in a Tertiary Hospital of Kerala

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Abstract

Introduction: To manage patients with chronic kidney disease (CKD) optimally, it requires appropriate knowledge of markers and stages of CKD and early disease recognition. Replacing the terms such as chronic renal insufficiency, chronic renal disease, chronic renal failure the, the National kidney foundation kidney disease outcomes quality initiative, has defined the all encompassing term as CKD. An understanding of estimated glomerular filtration rate (eGFR) is required as it is still considered the best overall index of kidney function in stable, non-hospitalized patients. There are multiple risk factors and comorbid diseases which modify the natural course and progression of CKD and alter the necessity to change the management. The present study is conducted to study the comorbidities in patients with CKD.

Aim of the Study: The aim of the study was to study the comorbidities in patients with CKD.

Materials and Methods: This study was a retrospective observational study on consecutive new patients with CKD, who attended the dialysis unit of a tertiary teaching hospital in the northern part of Kerala. 89 consecutive new patients with CKD, who attended the dialysis unit of a tertiary teaching hospital, were included. Comorbid diseases, demographic data, and eGFR, were recorded.

Observations and Results: Out of 89 patients 63 were males and the remaining 26 were females. Patients belonged to the age group ranging from 35 to 80 years with a mean age of 54.42 ± 6.30. Among the various causes of primary kidney diseases diabetic nephropathy was found in 47/89 (52.80%) of the patients, chronic glomerulonephritis in 19/89 (21.34%), and hypertensive nephropathy in 8/89 (8.98%).

Conclusions: Among the various causes of primary kidney diseases diabetic nephropathy was found to be the most common followed by chronic glomerulonephritis in this study. Among the comorbid conditions, comorbid diabetes mellitus was observed the most common, hypertension presenting the form of myocardial infarction, Cerebro Vascular Accident (CVA), chronic pulmonary disease, congestive heart failure, and peripheral vascular disease.

Key words: Chronic kidney disease, Dialysis and comorbidities, End-stage renal disease, Glomerular filtration rate

INTRODUCTION

There is an increase in the chronic kidney disease (CKD) all over the world; clinical data from the USA show an increase in the trend of CKD and end-stage renal disease (ESRD). The prevalence rate of CKD and ESRD grew most quickly among the patients aged above 65 years.[1] The definition of CKD according to the kidney disease improving global outcomes is either damage to kidneys or a glomerular filtration rate (GFR) of <60 mL/min per 1.73 m² for a period of ≥3 mo, with implications for health. Kidney damage can be defined by structural (detected by imaging) or functional abnormalities of the kidneys with or without a decrease in GFR. These may be apparent as either pathological irregularities or as indicators of kidney damage which include albuminuria >30 mg/d, urine sediment abnormalities and electrolyte,
and other abnormalities secondary to tubular disorders. A significant number of them have comorbidities such as diabetes mellitus and cardiovascular diseases, and patient survival is poor in spite of dialysis due to poor functional abilities at the commencement of dialysis. It has also been observed in the literature that patients with extensive comorbidities do not live longer even dialysis as compared to patients treated conservatively. Moreover, these patients require frequent admissions to stabilize their hemodynamics and die during such admissions. The age of the patient in addition to comorbidities also plays a significant role in improving the functional status of kidney which declines as reported in recent studies. Although it is possible to slow the progression of CKD during its early stages, CKD-related risk factors (e.g., hyperglycemia and hypertension) and comorbidities become less manageable as CKD inevitably progresses, resulting in a life expectancy that decreases in parallel with decreasing kidney function. The present study was conducted to observe the various comorbidities of CKD and their management in a tertiary hospital of Kerala.

Aim of the Study

The aim of the study was to study the comorbidities in patients with CKD and their management.

MATERIALS AND METHODS

The present study was a retrospective observational study on consecutive new patients with CKD who attended the dialysis unit of a tertiary teaching hospital in the northern part of Kerala. The study period is between June 2011 and May 2013.

Inclusion Criteria
1. Patients with GFR <15 mL/min/1.73 m² for patients with diabetes mellitus, or <10 mL/min/1.73 m² for patients without diabetes mellitus.
2. Patients with all types of comorbidities were included.

Exclusion Criteria
1. Patients with premature referral for renal replacement therapy (RRT) assessment due to higher GFR (non-diabetic patient with GFR >10 mL/min/1.73 m² or diabetic patient with GFR >15 mL/min/1.73 m²).
2. Patients with acute renal disease; there was no age limitation in selection of patients.

Demographic data, primary renal condition, coexisting medical diseases, laboratory data, and calculated GFR were recorded. Symptomatology of the patients was also recorded. Standard statistical methods were used to analyze the data.

OBSERATIONS AND RESULTS

There were 105 new CKD Stage 4 and 5 patients (GFR 15 to 20 mL/min/1.73 m², <15 mL/min/1.73 m², respectively) referred to the nephrologists of the institute for renal assessment and if possible for dialysis/RRT. 11 were found to have been prematurely referred for assessment. 6 patients were found to have acute on chronic renal disease with failure; they were excluded from analysis. The remaining 89 patients were included in the study. Out of 89 patients, 63 were males and the remaining 26 were females. Patients belonged to the age group ranging from 35 to 80 years with a mean age of 54.42 ± 6.30. Among the various causes of primary kidney diseases diabetic nephropathy was found in 47/89 (52.80%) of the patients, chronic glomerulonephritis in 19/89 (21.34%), hypertensive nephropathy in 8/89 (8.98%), rapidly progressive glomerulonephritis in 5/89 (5.61%), systemic lupus in 4 (4.49%), obstructive uropathy in 4 (4.49%), and renal malignancy in 2/89 (2.24%) patients [Table 1].

The age range in the study was 35–80 years with a mean age of 54.42 ± 6.30. Diabetic nephropathy was observed in almost equally in all the age groups that are 17.97% in 35–50 years age group, 21.34% in 51–65 years age group, and 13.48% in the 66–80 years age group [Table 2]. The age wise distribution of primary renal cause of CKD in the study is shown in Table 2.

Among the 89 patients evaluated by the nephrologists of the dialysis unit 50 patients were managed by dialysis due to their GFR and the remaining 39 patients were given supportive therapy to manage the CKD. Among the comorbid conditions, comorbid diabetes mellitus was observed in 47 patients and that being the primary cause of CKD also. Myocardial infarction was found in 5 patients, CVA in 6 patients, chronic pulmonary disease in 6 patients, congestive heart failure in 3 patients, anemia in 5 patients, and peripheral vascular disease in 9 patients [Table 3]. 23 patients (25.84%) were found to have a hypertensive etiology in the form of comorbid diseases.

<table>
<thead>
<tr>
<th>Primary disease of the kidney</th>
<th>Male - 63</th>
<th>Female - 26</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic nephropathy - 47</td>
<td>31</td>
<td>16</td>
</tr>
<tr>
<td>Chronic</td>
<td>16</td>
<td>3</td>
</tr>
<tr>
<td>Glomerulonephritis - 19</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Hypertensive nephropathy - 8</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Rapidly progressive</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Glomerulonephritis - 5</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Systemic lupus - 4</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Obstructive uropathy - 4</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Renal malignancy - 2</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>
such as myocardial infarction, CVA, peripheral vascular disease, and congestive heart failure [3] [Table 3]. Among the 89 patients, 50 patients were undergoing dialysis during the period of this study and the remaining 39 patients were given supportive management [Table 3].

**DISCUSSION**

Even though life-prolonging treatments such as dialysis are available for patients with CKD with renal failure, it may be difficult to predict as to who will benefit and survive from dialysis. Prediction of prognosis is difficult especially in the presence of comorbid conditions making it hard to decide for both patient’s attendants and the doctors to proceed with the dialysis. In few of them, the quality of life may not improve with dialysis due to comorbid conditions. Before starting dialysis or supportive treatment without dialysis, a hard decision has to be made among patients, family members, renal physicians, and supportive nursing staff. The available dialysis types (continuous ambulatory peritoneal dialysis, automated peritoneal dialysis, and hemodialysis) and non-dialysis supportive management with end-of-life care should always be discussed in detail during counseling. The prevalence of CKD among individuals older than 65 years ranged from 5.8 to 51% in different international studies. There is an exponential increase in the incidence of CKD with age. Among the comorbid conditions in the present study, comorbid diabetes mellitus was observed in 47 patients and that being the primary cause of CKD also. The presence of diabetes mellitus was significantly higher among patients with CKD with a wide range starting from 25.3% to 5.05%. In fact, the prevalence of diabetes among chronic kidney patients has been higher than that of individuals without CKD. 23 patients (25.84%) were found to have a hypertensive etiology in the form of comorbid diseases such as myocardial infarction 5 patients, CVA 6 patients, peripheral vascular disease 9 patients, and congestive heart failure 3 patients [Table 3]. High blood pressure was considered as a ubiquitous disease in CKD; because, besides being itself the most important cause for the CKD, its onset and development, high blood pressure is a result of CKD also. Congestive heart failure was found in 3 patients in this study as a comorbid disease. Although the decrease in cardiac output brought about by the disease itself or its treatment can participate in the genesis of progressive kidney damage, it should be noted that the main causes of congestive heart failure are hypertension and ischemia, both closely associated with arterial hypertension. In the present study stage, 4 to 5 of CKD were included. Stratification of CKD into 5 stages focuses the clinician on CKD management aspects. The metabolic abnormalities of CKD evolve in a fairly well-established pattern. Anemia of CKD and CKD-mineral and bone disorder often begin during Stage 3. Hypertension is aggravated in CKD Stages 3–5 and acid-base balance, dyslipidemia, and glucose homeostasis become deranged later. During Stages 3–5, reductions in medication dosages may be required because of a lower estimated GFR (eGFR). The disease domains of HTN, proteinuria, and hyperlipidemia may appear at any stage and therapy must be targeted to specific levels. Finally, screening for metabolic complications of CKD is typically not recommended in persons with eGFR >60 mL/min/1.73 m² and no albuminuria, unless a genetic disorder with a high degree of penetrance is present (autosomal dominant polycystic kidney disease). Anemia was found in 5/89 patients in this study. Anemia of CKD usually begins during CKD Stage 3, i.e., GFRs <60 mL/min/1.73m². Anemia occurs in 42%, 54%, and 62% of Stage 2, 3, and 4 disease of CKD and is more severe in diabetes mellitus.

**CONCLUSIONS**

Among the various causes of primary kidney diseases diabetic nephropathy was found to be the most common
followed by chronic glomerulonephritis in this study. Among the comorbid conditions, comorbid diabetes mellitus was observed the most common, hypertension presenting the form of myocardial infarction, CVA, chronic pulmonary disease, congestive heart failure, and peripheral vascular disease.

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How to cite this article: Gurukkal CHMK, Bithun BK. Comorbidities and their Management in Patients with Chronic Kidney Disease in a Tertiary Hospital of Kerala. Int J Sci Stud 2018;6(1):149-152.

Source of Support: Nil, Conflict of Interest: None declared.
Evaluation of Liver Space-occupying Lesion

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Abstract

Introduction: Space-occupying lesion (SOL) on the liver can be caused by various diseases that may or may not be manifested with symptoms. Mass lesions of the liver occur quite frequently; thus, clinicians interested in liver diseases should have a thorough understanding of their presentations, diagnosis, and treatment.

Aim: This study aims to evaluate the different causes of SOL of the liver and find out etiology of liver tumor among patients of SOL of the liver.

Materials and Methods: This observational study was conducted among the liver SOL patients who were above 20 years of age. The inclusion criteria were patients having clinically and radiologically confirmed hepatic SOL with consent.

Results: Maximum numbers of cases were seen in the 5–6th decade of life. The most common etiology for SOLs of the liver in this study was metastatic liver disease. The most common primary for secondary liver was from carcinoma stomach. The second most common etiology for SOLs of the liver observed in this study was amebic liver abscess.

Conclusion: Metastatic liver diseases were mostly managed conservatively. For 5 cases having single secondary lesion is treated with lobectomy which gives better prognosis than conservative management. 1-year survival rate is >50% for single metastatic lesion surgically treated compared to <30% for multiple secondaries conservatively managed.

Key words: Adenocarcinoma, Liver abscess, Liver, Space-occupying lesion

INTRODUCTION

Space-occupying lesion (SOL) on the liver can be caused by various diseases that may or may not be manifested with symptoms. Mass lesions of the liver occur quite frequently; thus, clinicians interested in liver diseases should have a thorough understanding of their presentations, diagnosis, and treatment. Hepatic mass lesions include tumors, tumor-like lesions, abscesses, cysts, hamartomas, and confluent granulomas. The frequency with which each is seen varies in different geographic regions and different populations. Focal nodular hyperplasia is more common than hepatocellular adenoma. Focal nodular hyperplasia occurs at all ages, but most patients present in the third and fourth decades of life.¹ The cause of focal nodular hyperplasia is unknown. Some evidence suggests that focal nodular hyperplasia may be hormone dependent.²,³ The liver is the most common destination of hydatid cyst (70%), followed by the lungs (20%), kidney, spleen, brain, and bone. The sensitivity and specificity of both ultrasonography and computed tomographic (CT) in confirming the diagnosis are high.⁴ In adults, in most part of the world, hepatic metastasis is more common than primary malignant tumors of the liver, whereas in children, primary tumors outnumber both metastases and benign tumors of the liver. Hepatic metastases occur in 40–50% of adult patients with extrahepatic primary malignancies.⁵ Most cases of pyogenic liver abscess are cryptogenic or occur in older men with underlying biliary tract disease.⁶ Different liver SOL has different etiology and risk factor, so it is important to find out etiology and risk factor in Indian subcontinent, which would help us to treat different kinds of SOL of the liver.

Aim

This study aims to evaluate the different causes of SOL of the liver and find out etiology of liver tumor among patients of SOL of the liver.

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MATERIALS AND METHODS

This observational study was conducted among the liver SOL patients who attended Government Head Quarters Hospital, Pudukkottai. The study participants were above 20 years of age. The study was conducted for about 1 year. The inclusion criteria were patients having clinically and radiologically confirmed hepatic SOL with consent. The sample size of 100 was included who were satisfying inclusion criteria. The data were collected to study demographic profile and assessment of comorbid condition and risk factors. All patients were undergone detailed clinical examination and routine as well as specific blood and imaging study. Ethical committee approval was obtained.

RESULTS

Mostly, the liver was enlarged to about 3 cm below the costal margin in the downward direction, and the upward enlargement was common in amebic liver abscess cases. The right lobe of the liver was commonly involved due to the portal vein mainly drain into the right lobe. 25 cases were detected only by ultrasonography abdomen and CT abdomen. They have clinically no liver enlargement by they have other symptoms such as right upper quadrant abdominal pain, fever (commonly in abscess), anorexia, and weight loss (commonly in malignancy). The males were predominantly affected in this study. The male:female is about 64:36. Maximum numbers of cases were seen in the 5th–6th decade of life. Alcoholics are affected twice than non-alcoholics.

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondaries liver</td>
<td>58</td>
</tr>
<tr>
<td>Amebic liver abscess</td>
<td>22</td>
</tr>
<tr>
<td>Pyogenic liver abscess</td>
<td>8</td>
</tr>
<tr>
<td>Hydatid cyst of liver</td>
<td>5</td>
</tr>
<tr>
<td>HCC</td>
<td>3</td>
</tr>
<tr>
<td>Hemangioma</td>
<td>3</td>
</tr>
<tr>
<td>Non-parasitic solitary</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
</tr>
</tbody>
</table>

HCC: Hepatocellular carcinoma

The most common etiology for SOL of the liver in this study was metastatic liver disease. The most common primary for secondary liver was from carcinoma stomach. The second most common etiology for SOLs of the liver observed in this study was amebic liver abscess. 80% of the cases were resolved by conservative medical management alone. About 20% of the patients were required surgical management. Pyogenic liver abscess is less common cause of SOLs of the liver than amebic liver abscess. 70% of the patients responded with medical management. 30% of the patients were required surgical management like aspiration. Only 5 cases of hydatid cyst of the liver were observed in this study. All the cases were required surgical management.

DISCUSSION

Space-occupying liver lesions usually present with abdominal pain or abnormal physical findings such as a palpable abdominal mass or distention. Liver lesions identified in children include benign and malignant neoplasms, inflammatory masses, cysts, and metastatic lesions. Two-thirds of liver lesions in children are malignant. Hepatoblastoma accounts for two-thirds of malignant liver tumors in children. Benign lesions of the liver in children include vascular lesions, hamartomas, adenomas, and focal nodular hyperplasia. Although benign and malignant liver masses share some clinical manifestations, treatment and prognosis differ. Evaluation involves physical examination, imaging evaluation, and laboratory investigations such as serological markers [alpha-fetoprotein (AFP)] for malignant liver lesions. Ultrasound is the initial imaging modality of choice because it can detect, characterize, and provide the extent of liver lesions. However, CT or magnetic resonance imaging (MRI) is often subsequently performed for further characterization, assessment of precise extent, and detection of associated metastatic disease in cases of malignant hepatic neoplasm. Serological markers (such as AFP) can be useful in narrowing the differential diagnosis when they are markedly elevated, but a substantial number of patients, unfortunately, do not have high levels of these markers at the time of presentation or cautious interpretation is warranted as AFP level is frequently elevated in infants up to 6 months of age and may be slightly elevated with benign tumors and with hepatic insult or regeneration. Therefore, a tissue diagnosis is often required to guide subsequent management. The histology and anatomy of a pediatric liver tumor guide the treatment and prognosis.[7-9]

In a retrospective study of 84 patients who underwent MRI examination of the liver, the qualitative parameters margin, shape, internal structure, signal intensity, and the presence of a capsule were evaluated in 152 lesions comprising 48 hemangiomas, 54 secondary deposits, 23 hepatoma, 8 simple cysts, 17 hydatid cysts, 1 abscess, and 1 focal fatty infiltration. Our main objective was to differentiate hemangiomas from secondary deposits and hepatomas. In hemangiomas, the combination of smooth margin (98%), round or oval shape
(90%), homogeneity (96%), very high signal intensity on T2-weighted sequence (94%), and the complete absence of capsule helped to distinguish them from secondary deposits and hepatomas in the majority of cases. It is concluded that with MRI we can establish the diagnosis of focal lesions of the liver in about 95% of cases.\cite{10}

According to these two studies, the incidence of various SOLs in the liver is different for Pudukkottai, when compared to various parts of places in India like Delhi and Mumbai.

**CONCLUSION**

Metastatic liver disease was mostly managed conservatively. For 5 cases having secondary lesion is treated with lobectomy which gives better prognosis than conservative management. 1-year survival rate is >50% for single metastatic lesion surgically treated compared to <30% for multiple secondaries conservatively managed.

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**How to cite this article:** Raja M, Natesan M, Anandan H. Evaluation of Liver Space-occupying Lesion. Int J Sci Stud 2018;6(1):153-155.

**Source of Support:** Nil, **Conflict of Interest:** None declared.
A Study on Prescribing Trends of Drugs in the Management of Bronchial Asthma: A Hospital-Based Study

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Abstract

Background: Bronchial asthma is a common allergic condition with varied symptoms and necessitates the attention of the physician especially in acute attacks and poses a challenge to treat. Treatment to overcome the acute asthmatic episodes and control of chronic symptoms, nocturnal, and exercise-induced asthmatic symptoms leaves the physician in a dilemma. Pharmacologic management includes the use of control agents such as inhaled corticosteroids, long-acting bronchodilators (beta-agonists and anticholinergics), theophylline, and leukotriene modifiers. Relief medications include short-acting bronchodilators, systemic corticosteroids, and ipratropium.

Aim of the Study: The aim is to study the current prescribing trends of specialists in a tertiary teaching hospital who treat patients’ bronchial asthma as primary or secondary physicians.

Materials and Methods: A cross-sectional prospective study was conducted in the outpatient department (OPD) of a tertiary teaching hospital of Northern Kerala including the Departments of Medicine and Allied specialties over a period of 2 years. The specialties included were Medicine, Dermatology, Chest Diseases, and Psychiatry. 2,99,520 attended the OPD of the four specialty clinics of the hospital over a period of 2 years. 76,608 patients among these were positive history for different types of allergy. 31,194 patients (40.71%) among those patients with a history of various allergy disorders had a history of bronchial asthma. All the case records were accessed from the four specialty departments, and the demographic data were recorded for analysis including age, sex, occupation, history, family history, and drug prescription which includes the drugs prescribed dosage form and frequency. The percentage of all observed data was tabulated.

Observations and Results: Salbutamol (β-agonists) + ipratropium bromide (anticholinergic) + levocetirizine + montelukast was the most commonly used combination as bronchodilator in 10287 (32.98%) of the patients. Formoterol + budesonide + fexofenadine + diphenhydramine combination was used in 5893 patients (18.71%). Doxophylline + fexofenadine combination was used in 4134 (13.25%) patients. Budesonide + montelukast + fexofenadine combination was used in 3256 (10.44%) patients. Etophylline + theophylline + levocetirizine combination was used in 2048 (9.97%) patients. Hydrocortisone + theophylline combination was found in 1947 (6.24%) patients. Methyl prednisolone + doxophylline + levocetirizine combination was used in 1001 (3.21%) patients. Dexamethasone + theophylline combination was used in 833 (2.67%) patients. Montelucast + doxophylline combination was used in 1.13% of the patients. Fexofenadine + diphenhydramine combination was used in 1.01% of the patients. Levocetirizine + montelukast combination was used in 0.39% of the patients.

Conclusions: Combination therapy in the treatment of both acute and chronic types of bronchial asthma was found to be popular among the consultants of different specialties who treat the condition. The most common combination used in this study was salbutamol (β-agonists) + ipratropium bromide (anticholinergic) + levocetirizine + montelukast.

Key words: Allergy, Asthma, Bronchial asthma, Bronchodilator, Bronchospasm, Lung function tests

INTRODUCTION

Asthma is an allergic disorder characterized by immune-inflammatory response requiring prolonged treatment. There are many factors such as aeroallergens, chemicals, drugs, exercise, cold dry air, infections, and personal emotions which can aggravate the symptoms and precipitate attacks.[¹,²]
The incidence of asthma is increasing in view of increasing pollution in many cities, and the incidence is equally increasing in children as in adults all over the world.\[^{[8]}\] The fundamental principle of treatment of chronic disease should be based on establishing a working diagnosis and initial assessment of severity which provides as a guide to the intensity of therapy required. Regular follow-up thereafter monitors the control of the disease processes and their clinical manifestations.\[^{[9]}\] Bronchial asthma is characterized by narrowing of the smaller airways in the lungs. This narrowing is partially or completely reversible. Symptoms of asthma include wheezing, coughing, chest tightness, and shortness of breath. These symptoms tend to come and go and are related to the degree of airway narrowing in the lungs. In India, asthma is known to be one of the major causes of morbidity and mortality, comprising about 3–11% of adults and 3–5% of pediatric population.\[^{[8]}\] The target of asthma treatment is to achieve and maintain clinical control. Many bronchodilators are now available in the market which relieves the bronchospasm in asthma. Drug utilization reviews are important studies to understand the prescription patterns of physicians in various parts of the country. They play an important role in helping the health-care system to understand, interpret, and improve the prescribing administration and to maintain the rational use of drugs which assist the physician’s prescribing attitude in accordance with the predetermined standards.\[^{[8,9]}\] In this context, an institutional study was conducted over a period of 2 years to describe trends in the prescription and consumption of bronchodilators for managing acute exacerbation of bronchial asthma in adult population.

**Period of Study**
The study duration was from March 2013 to February 2015.

**Institution of Study**
This study was conducted at Kannur Medical College, Anjarakandy, Kannur, Kerala.

**Type of Study**
This was a cross-sectional prospective study.

**MATERIALS AND METHODS**
A cross-sectional prospective study was conducted in a tertiary teaching hospital of Northern Kerala. The study was conducted in the outpatient department (OPD) of Medicine and Allied specialties over a period of 2 years. An ethical committee clearance was obtained before the commencement of the study. The specialties included were Medicine, Dermatology, Chest Diseases, and Psychiatry.

**Inclusion Criteria**
1. All the patients with a history of allergy and bronchial asthma alone or in association with other specialty diseases were included.
2. Patients aged above 12 years and below 65 years were included.
3. Patients with acute or chronic bronchial asthma were included.
4. Patients already on treatment for bronchial asthma were included.
5. Patients who had suffered more than 3 acute attacks of bronchospasm were included in this study.

**Exclusion Criteria**
1. Patients aged below 12 and above 65 years were excluded.
2. Patients with acute infectious diseases were excluded.
3. Patients with fulminating diseases were excluded.
4. Patients with malignant hypertension and severe uncontrolled diabetes mellitus were excluded.
5. Patients who were having other respiratory problems such as chronic obstructive pulmonary disease (COPD) and cardiac problems were excluded from this study.

A total of 2,99,520 attended the OPD of the four specialty clinics of the hospital over a period of 2 years. 76,608 patients among these were positive history for different types of allergy. 31,194 patients (40.71%) among those patients with a history of various allergy disorders had a history of bronchial asthma. All the case records were accessed from the four specialty departments, and the demographic data were recorded for analysis including age, sex, occupation, past history, family history, and drug prescription which includes the drugs prescribed dosage form and frequency. The percentage of all observed data was tabulated.

**OBSERVATIONS AND RESULTS**

31,194 prescriptions of the patients attending the OPDs of Medicine, Psychiatry, Dermatology, and Chest Diseases were accessed and analyzed, and the data were tabulated. There were 18,058 males (57.88%) and 13,136 females (42.11%). The male-to-female ratio was 1.3:1. The demographic data are shown in Table 1.

The bronchodilators used in the present study are shown in Table 2. The bronchodilators were used alone or in combination with other drugs such as antihistamines, steroids, mast cell stabilizers, antibiotics, and mucolytic agents.

In this study, it was observed that patients received combination therapy in all the patients (100%). The bronchodilators and their combination drugs used are shown in Table 3.

Table 4 shows the drugs used in the combination therapy of the present study. The study showed salbutamol...
(β-agonists) + ipratropium bromide (anti cholinergic) + levocetirizine + montelukast was the most commonly used combination as bronchodilator in 10287 (32.98%) patients. Formoterol + budesonide + fexofenadine + diphenhydramine combination was used in 5893 patients (18.71%). Doxophylline + fexofenadine combination was used in 4134 (13.25%) patients. Budesonide + montelukast + fexofenadine combination was used in 3256 (10.44%) patients. Etophylline + theophylline + levocetirizine combination was used in 2048 (09.97%) patients. Hydrocortisone + theophylline combination was found in 1947 (06.24%) patients. Methyl prednisolone + doxophylline + levocetirizine combination was used in 1001 (3.21%) patients. Dexamethasone + theophylline combination was 02.67% patients. Montelukast + doxophylline combination was used in 01.13% of the patients. Fexofenadine + diphenhydramine combination was used in 01.01% of the patients. Levocetirizine + montelukast combination was used in 00.39% of the patients [Table 4].

**DISCUSSION**

The present study was conducted in a tertiary teaching hospital to know about the trends of prescription by various consultants of four specialties, namely, General Medicine, Psychiatry, Dermatology, and Chest diseases. Review of literature showed that many treatment guidelines[8,9] are available for bronchial asthma recommending bronchodilators, especially in the acute phase. They also recommend regular use of inhaled corticosteroids for
patients with mild persistent asthma. They also recommend regular use of inhaled corticosteroids for patients with mild persistent asthma, as this type of regimen provides control of asthma, suppresses airway inflammation, and may prevent the progression of asthma. Recommendations of various international bodies on asthma to improve the prescribing practices of the physicians and ultimately clinical standards are now available.[10,11] In the present study, the incidence of bronchial asthma was found to be more in males than in females with a male-to-female ratio of 1.3:1. In the present study, all the consultants used standard bronchodilators which are being used all over the world. In this study, majority of the prescriptions used nebulization as a preferred route of drug delivery to manage acute exacerbations of asthmatic episodes. Even though nebulizer delivered aerosol created by blowing air or oxygen through a solution to produce droplets requiring little coordination from the patient as drug is inhaled through a facemask or a mouthpiece using normal tidal breathing, the disadvantages include the longtime commitment maintenance treatments and lack of portability.[12] In the present study, salbutamol (β-agonists) + ipratropium bromide (anticholinergic) + levocetirizine + montelukast was the most commonly used combination as a bronchodilator in 10287 (32.98%) patients. These results are similar to the study done in Malaysia in which salbutamol was the most commonly prescribed[13] and also similar to the study done in Bareilly, which showed that inhaled salbutamol was received by 100% of the patients irrespective of the severity.[14] Formoterol + budesonide + fexofenadine + in another study conducted by Pinal et al[15] showed that 84% of patients and 76% of patients in Shimpi et al[16] were given combination therapy over monotherapy. In this study, in acute attacks of bronchial asthma, injection hydrocortisone was used. It actually prevents the side effect of inhaled medication which causes irritation on the respiratory tract. International guidelines recommend corticosteroids by oral route even for severe exacerbation, and it is reported to be as effective as intravenous route.[17] Anticholinergics were less prescribed as monotherapy but were given in combination with, as they are preferred medication for treating COPD instead of asthma. Diphenhydramine combination was used in 5893 patients (18.71%). Doxophylline + fexofenadine combination was used in 4134 (13.25%) patients. Budesonide + montelukast + fexofenadine combination was used in 3256 (10.44%) patients. Etophylline + theophylline + levocetirizine combination was used in 2048 (6.97%) patients. The reason for using short-acting β2 agonist, i.e., salbutamol is due to its rapid onset and its low cost according to the consultants of this hospital. Hydrocortisone + theophylline combination was found in 1947 (6.24%) patients. Methylprednisolone + doxophylline + levocetirizine combination was used in 1001 (3.21%) patients. Dexamethasone + theophylline combination was used in 833 (02.67%) patients. Montelukast + doxophylline combination was used in 1.13% of the patients. Fexofenadine + diphenhydramine combination was used in 1.01% of the patients. Levocetirizine + montelukast combination was used in 0.39% of the patients [Table 4]. Among the other injectable bronchodilators used in this study are doxophylline. It was the most commonly prescribed methylxanthines. Doxophylline is preferred over theophylline for it has less cardiotoxic effects than the former with preserved mucoregulatory and anti-inflammatory properties. Hence, doxophylline may constitute a safe and effective alternative treatment to aminophylline/theophylline in the treatment of acute exacerbation of bronchial asthma.[18] However, in a study by Faiz et al., they concluded that there was no significant difference in spirometric variables between doxophylline and theophylline.[19] Maragay et al.[19] added that doxophylline has better safety profile than theophylline. Montelukast a leukotriene receptor antagonist was seen in most of the prescription as add-on therapy. It was prescribed as a fixed dose combination with levocetirizine in a study done by Rajathilagam et al.[19] Limitations of our study were lack of follow-up and cost-effectiveness which should have been done. For higher authenticity, more number of prescriptions should have been included in our study.

CONCLUSION

Combination therapy in the treatment of both acute and chronic types of bronchial asthma was found to be popular among the consultants of different specialties who treat the condition. The most common combination used in this study was salbutamol (β-agonists) + ipratropium bromide (anticholinergic) + levocetirizine + montelukast. The most commonly prescribed bronchodilator in cases of emergency was intravenous doxophylline. Nebulization was preferred route to tackle the acute exacerbation of asthmatic symptoms.

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Source of Support: Nil, Conflict of Interest: None declared.
Outcome of Children with First Episode of Urinary Tract Infection

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Abstract

Background: Urinary tract infection (UTI) is one of the most common childhood infections. UTI occurs in 1–3% of girls and 1% of boys of the pediatric population. In the former, it occurs by the age of 5 years which peaks during infancy and toilet training and in the later during the 1st year of life. UTIs are much more common in uncircumcised boys, especially in the 1st year of life. The prevalence of UTI during the 1st year of life is more in males with a male:female ratio of 2.8–5.4:1. Beyond 1–2 years, female preponderance with a male:female ratio of 1:10 is observed.

Aim of the Study: The aim is to study the outcome of first episode of UTI in children in terms of treatment response, recurrence, need for surgical intervention, renal scarring, growth retardation, hypertension, and renal function abnormalities.

Materials and Methods: A total of 120 children between 1 month and 12 years of age with the first episode of confirmed diagnosis of UTI were included in this prospective cross-sectional study. All the children were thoroughly investigated after elicitation of history. Culture of urine, ultrasonogram, micturating cystourethrogram (MCU), and technetium 99m-labeled dimercaptosuccinic acid investigations were done in addition to routine investigations before and during follow-up of treatment. Children were treated standard UTI treatment protocols recommended by the International Pediatric Society. All the data were analyzed using standard statistical methods.

Observations and Results: A total of 120 children with the first episode culture positive UTI between the age group 1 month and 12 years were taken; 63.4% were male children and 36.6% were female children. Of 120 cases studied, 28 (23.3%) cases were below 1 year, 60 (50%) cases were between 1 and 5 years, and 32 (26.6%) cases were between 5 and 12 years. 88 (73.3%) Escherichia coli, 21 (17.5%) Klebsiella, 3 each of CONS, Enterobacter, and Staphylococcal aureus, and 2 Acinetobacter species were isolated. Most common organism isolated was E. coli followed by Klebsiella. MCU was done in 40 cases (31 males and 9 females) and was abnormal in 12 (30%) cases. 4 (10%) and 2 (5%) of 40 cases had grade 1–2 vesicoureteral reflux (VUR) and grade 3–4 VUR, respectively. 6 (7.9%) of 76 males studied had posterior urethral valve. All children with posterior urethral valves (PUV) had undergone cystoscopic fulguration, and 4 of these 6 children had undergone pyeloplasty after fulguration.

Conclusions: The recurrence chance of UTI is present in 7.5% of children within 6 months of first episode of UTI. Majority of children with recurrent UTI had their second episode within 6 months and that too, with the same organism suggesting an unresolved or persistent bacteriuria. The presence of VUR is a risk for recurrence of UTI and renal scarring. The relative risk of recurrence of UTI is 14 times in the presence of renal scarring than in children without renal scar formation, and thus, renal scarring is a good predictor of recurrence.

Key words: children, Urinary tract Infections, Bacteriuria, Cystourethrogram

INTRODUCTION

Urinary tract infection (UTI) is defined as growth of a significant number of organisms of a single species in urine culture with the presence of symptoms of UTI. According to IAP, the diagnosis of UTI should be made only in children with a positive urine culture. The incidence of UTI reported from various epidemiologic studies is 1.1–1.8% of boys and 3.3–7.8% of girls. UTI is 2–5 times more common in males than in females in the first few months of life; beyond this, male-female ratio is 1:10. Sobel et al. reported bacteria as the most common etiological agents of UTI and may occasionally be caused by viruses and fungi. Infection can reach the urinary tract in two ways: (1) The ascending route and (2) the hematogenous route; UTI in most of the cases...
results from an ascending infection; bacteria arise from the fecal flora, colonize the perineum, and enter the bladder through the urethra. In uncircumcised boys, the bacterial pathogens usually arise from the flora beneath the prepuce. These organisms ascend through the urethra to invade the urinary tract and cause asymptomatic bacteriuria, acute cystitis, or acute pyelonephritis in the host. Hematogenous spread of infection to the urinary tract accounts for <1% of UTIs. Escherichia coli adheres to uroepithelium with the help of adhesions or fimbriae which binds to specific receptors in the uroepithelium. The organism is then internalized into epithelial cells which lead to apoptosis, hyperinfection, and invasion of the surrounding epithelial cells or an establishment of bacterial focus which forms a base for recurrent UTI where drugs cannot reach the focus. UTI can be grouped into three clinically distinct presentations: (1) Cystitis, (2) acute pyelonephritis, and (3) asymptomatic bacteriuria. Cystitis occurs when infection is limited to the bladder and urethra, and it is mostly seen among girls who are more than 2 years old. Patients often present with localizing symptoms that include pain on urination (dysuria), frequency, urgency, cloudy urine, and lower abdominal discomfort. Acute pyelonephritis is an infection of the kidney and is the most severe form of UTI in children. Systemic features such as high fever, vomiting, abdominal pain or tenderness, malaise, poor feeding, or irritability in infants constitute the characteristic features of acute pyelonephritis. Diagnosis can be assisted by technetium 99m-labeled dimercaptosuccinic acid (DMSA) scan of the kidneys and inflammatory markers in the blood (e.g., C-reactive protein and erythrocyte sedimentation rate). Manifestations of UTI vary with age, site of infection within the urinary tract, and the severity of infection. From a clinical perspective, infection of the urinary tract may be discussed either as a non-febrile UTI (acute cystitis) or a febrile UTI (acute pyelonephritis). Urine analysis enables only a provisional diagnosis of UTI and so a specimen has to be taken for urine culture before therapy. Rapid tests include dipstick analysis for leukocyte esterase and nitrites which will be positive in infected urine although false negatives can occur in dilute urine. This test can be used as a screening for UTI. In a study of a cohort with 18% prevalence of UTI, a negative result on dipstick analysis had a negative predictive value of 96% which is more accurate than analysis of pyuria by microscopy in children. Significant pyuria is defined as >10 leukocytes/cu.mm in a fresh uncentrifuged sample or >5 leukocytes/hpf in a centrifuged sample. UTI can occur without pyuria, and pyuria can occur without infection of urinary tract. Sterile pyuria is defined as leukocytes in urine with a negative urine culture and can occur in partially treated UTI, viral infections, renal tuberculosis, and renal abscess, urinary infection with obstruction in urinary tract, interstitial nephritis, any fever, glomerulonephritis, renal stones, and foreign body in urinary tract. White blood cell casts may also be seen. The accuracy of positive findings in the above said tests are as follows. General measures include adequate fluid intake, frequent voiding, and treating constipation. Double voiding should be encouraged as it ensures adequate emptying of the bladder of post-void residual urine. “Drink plenty and don’t hold on” was propagated by the National Institute for Health and Clinical Excellence (NICE). Children are also advised to take sufficient fluids in frequent small amounts. Imaging studies are done in children to detect any anatomical abnormality, VUR, and renal parenchymal damage that is predisposing to urinary infection.

**MATERIALS AND METHODS**

**Study Design**
This was a cross-sectional prospective observational study.

**Institute of Study**
This study was conducted at the Department of Paediatrics, IMCH, Government Medical College, Kozhikode, Kerala, India

**Period of Study**
The study duration was from March 2014 to August 2015.

**Study Group**

**Inclusion criteria**
The following criteria were included in the study:
1. Children between 1 month and 12 years of age with the first episode of confirmed diagnosis of UTI during the study period.
2. Children who are followed up for a minimum period of 6 months after diagnosis and starting the treatment.

**Exclusion criteria**
The following criteria were excluded from the study:
1. Children with previously known urinary tract anomalies.
2. Children with comorbid medical renal diseases.

**Diagnostic criteria**
First episode of UTI: A diagnosis of first episode of UTI is considered in a child with a positive urine culture and symptoms of UTI with no previous history of UTI. All the children included in the study were with the first episode of UTI and evaluated on admission, and a semi-structured pro forma was used to record data regarding history, risk factors, clinical examination findings, investigations, treatment response, and any surgical procedures done. All children were started on empirical antibiotic guided by sensitivity pattern of prevailing organisms in our locality and then changed according to the culture sensitivity.
pattern of isolated organism in urine culture. Children who were toxic and who were not able to tolerate oral intake were given parenteral antibiotics. Advice regarding the need for further imaging studies as per guidelines of the Indian Society of Pediatric Nephrology was given. All children in the study group were screened by ultrasonography within 1–2 weeks. 40 children underwent micturating cystourethrogram (MCU) 2–3 weeks after treatment completion and 57 children underwent DMSA scan DMSA 2–3 months after treatment completion. Children were followed up regularly by clinical visits and telephone calls and assessed outcomes in terms of recurrence, renal scarring, growth retardation, hypertension, and renal function abnormalities at 3 months’ interval by necessary examination and investigations and recorded in pro forma. Antibiotic prophylaxis was given to children in the study population as and when indicated. The routine performance of urinalysis and urine culture was done during subsequent febrile illnesses in all children with the first episode UTI. Any second episode of UTI was considered as recurrent UTI. It is defined as recurrence of symptoms and signs of urinary infection with significant bacteriuria in patients who have recovered clinically following treatment of an episode of UTI. Blood pressure, weight, height, mid-arm circumference, serum creatinine, and blood urea levels were recorded at every 3 months’ interval during the follow-up period.

**Statistical Analysis**
The data obtained were coded and entered into Microsoft Excel spreadsheet and master chart was prepared. Categorical data were expressed in terms of rates, ratios, and percentages or graphically represented as pie diagrams or bar diagrams. The comparison for categorical data was done using Pearson’s Chi-square test to determine the association between continuous variables. A probability value (P value) of ≤0.050 at 95% confidence interval was considered as statistically significant. All the statistical operations were done through IBM SPSS for Windows (version 20).

**OBSERVATIONS AND RESULTS**

Observations and analysis of 120 children with UTI who met inclusion criteria were made. Children entered the study population at different times and had different lengths of follow-up.

Of these 120 cases with a minimum follow-up of 6 months, 13 cases were followed up to maximum 18 months, 21 cases were followed for maximum 15 months, 66 cases were followed for maximum 12 months, and 93 cases were followed for maximum 9 months [Figure 1].

### Age and Gender Distribution
Of 120 cases studied, 28 (23.3%) cases were below 1 year, 60 (50%) cases were between 1 and 5 years, and 32 (26.6%) cases were between 5 and 12 years [Figure 2].

### Gender Distribution
In the study population, 76 (63.4%) were males and 44 (36.6%) were females. Males outnumber females in children below 5 years (71.4% in children between 1 and 12 months and 73.3% in children between 12 and 59 months). Females (62.5%) outnumber males above 5 years [Figure 3].

### Spectrum of Isolated Organisms
88 (73.3%) *E. coli*, 21 (17.5%) *Klebsiella*, 3 each of CONS, Enterobacter, and Staphylococcal aureus, and 2 Acinetobacter species were isolated. Most common organism isolated was *E. coli* followed by *Klebsiella* [Figure 4].

### Ultrasonogram (USG)
USG was done in 120 cases and 14 (11.66%) cases had abnormal findings. Hydronephrosis is seen in 8 cases (7%), cystitis in 4 cases (3%), and pelviureteric junction obstruction in 2 cases (1.8%) [Figure 5]. All the hydronephrosis (8 cases) was detected in children below 5 years. Of 8 cases with hydronephrosis, 7 (87.5%) were males, and 5 (71.4%) of these 7 males with hydronephrosis had PUV [Figure 6].

### MCU
MCU was done in 40 cases (31 males and 9 females) and was abnormal in 12 (30%) cases. 4 (10%) and...
2 (5%) of 40 cases had grade 1–2 VUR and grade 3–4 VUR, respectively. 4 (13%) of 31 males and 2 (22%) of 9 females who underwent MCU had evidence of VUR; this female-to-male ratio of 1.7:1 found was not significant statistically ($P = 0.49$). In 31 males who underwent MCU, 6 (19.35%) had PUV. Of 6 PUV cases, 4 cases (66.7%) were detected before 12 months of age; 2 (33.3%) cases of PUV were detected after the age of 12 months [Figure 7].

**DMSA Renal Scan**
DMSA was done in 57 cases and detected abnormality in 21 cases (37%). All children with abnormal DMSA renal scan (21 cases) had renal scarring at 2–3 months after first episode UTI. None of the children had renal function impairment which was assessed by split renal function on DMSA renal scan [Figure 8].

**Treatment Outcome**
Of 120 cases, 48 (40%) cases responded (became non-toxic and devoid of urinary symptoms) within 5–7 days of antibiotics. 47 cases needed antibiotics for 7–10 days and 25 cases needed antibiotics for 10–14 days for complete clinical recovery [Figure 9].
Surgical interventions: 6 (7.9%) of 76 males studied had posterior urethral valve. All children with PUV had undergone cystoscopic fulguration and 4 of these 6 children had undergone pyeloplasty after fulguration [Figure 10].

Recurrence
9 (7.5%) of 120 cases had second episode of UTI (with the same organism) within 6 months. 2 (3%) cases had second episode UTI (with different organism) after 6 months of first episode \(n = 66\). None of 120 cases had more than one recurrence during the study period [Figure 11].

Recurrence of UTI in Relation to Age
3 (10.7%) of 28 cases under 12 months, 5 (8.3%) out of 60 cases in age group 12–59 months, and 1 (3.1%) of 32 cases above 5 years had recurrent UTI within 6 months of first episode UTI; this difference is not statistically significant: \(P\) value (0.54) [Table 1].

Recurrence of UTI in males and females under different age groups is observed as follows:

Overall 6 of 76 (7.9%) males and 3 of 44 (6.8%) females had recurrence within 6 months of first episode UTI; \(P\) value is 0.8) and hence not statistically significant [Table 2].

Recurrence in Children with VUR
3 (50%) of 6 cases with VUR had a recurrence of UTI.

Renal Scarring: Renal Scarring in Relation to Age Group
Renal scarring is detected in 28.6% of cases under 12 months and 35% of cases in the age group of 12–59 months who underwent DMSA renal scan, and the difference is not statistically significant (\(P = 0.66\)). Renal scarring is detected in all 3 cases in the age group of 5–12 years who underwent DMSA scanning for which it is indicated (abnormal USG finding) [Figure 12].

Renal Scarring in Relation to Gender
39% of males (16 out of 41) and 31.2% of females (5 out of 16) who underwent DMSA renal scan had renal scarring; this difference in renal scarring percentage in relation to gender is not statistically significant: \(P\) value (0.58) [Table 3].

Renal Scarring in Relation to Isolated Organism
17 (39.5%) cases of 43 \(E. coli\)-positive UTI and 6 (33.3%) of 9 cases of \(Klebsiella\)-positive UTI had renal scarring, \(P\) value (0.72) [Figure 13].

Renal Scarring and Recurrence
Renal scarring is found in 6 of 7 (85.7%) cases that had recurrence within 6 months of first episode UTI. Renal scarring is found in 15 of 50 (30%) cases that does not have recurrence within 6 months of first episode UTI. Relative

| Table 1: The incidence of recurrence according to the age groups \((n=120)\) |
|------------|------------------|
| Age group  | % of recurrence within 6 months |
| 1 month–<1 year | 3 (10.7) |
| 1 year–<5 years | 5 (8.3) |
| 5–12 years | 1 (3.1) |

- \(E. coli\) - Escherichia coli
- \(Klebsiella\) - Klebsiella pneumoniae
risk of recurrence was 14 times (95% confidence interval: 1.5–126) more in cases with renal scarring than cases without renal scarring; (85.7% vs. 30%; \( P \) value 0.04) [Figure 14].

**Renal Scarring in Cases with VUR**
Renal scarring is found in all 6 cases with VUR (4 cases of grade 3–4 VUR and 2 cases of grade 1–2 VUR) in the present study.

**Hypertension, Growth, and Altered Renal Function Tests**
Hypertension, growth retardation, or altered renal function tests due to UTI alone were not observed on follow-up of total of 120 cases for 6 months, and of these, 13 cases were followed up to maximum 18 months, 21 cases were followed for maximum 15 months, 66 cases were followed for maximum 12 months, and 93 cases were followed for maximum 9 months.

![Figure 11: The incidence of recurrence in the study (n = 120)](image1)

![Figure 12: The incidence of renal scarring according to the age (n = 120)](image2)

![Figure 13: The relation between renal scarring and type of organism (n = 120)](image3)

**Table 2: The recurrence of UTI according to the gender in the study (n=120)**

<table>
<thead>
<tr>
<th>Recurrence of UTI within 6 months</th>
<th>1 month–&lt;1 year</th>
<th>1 year–&lt;5 years</th>
<th>5–12 years</th>
<th>Overall %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>1 (5.3%)</td>
<td>4 (9%)</td>
<td>1 (8.3%)</td>
<td>6 (7.9%)</td>
</tr>
<tr>
<td>Females</td>
<td>2 (25%)</td>
<td>1 (6.2%)</td>
<td>0 (0%)</td>
<td>3 (6.8%)</td>
</tr>
<tr>
<td>( P ) value</td>
<td>0.12</td>
<td>0.72</td>
<td>0.21</td>
<td>0.88</td>
</tr>
</tbody>
</table>

UTI: Urinary tract infection
DISCUSSION

Age and Gender Distribution

In the observation study of 120 children with first episode culture positive UTI between the age group 1 month and 12 years, male children (63.4%) were more than female children (36.6%) which is not comparable with the literature as the total number of male and female children who came to our hospital during the study period is not known. In a similar hospital-based study conducted by Singh et al.[16,17] of 135 patients, 32.5% were males and 67.4% were females forming a ratio of 1:2. Males outnumber females in children below 5 years (71.4% in children between 1 and 12 months and 73.3% in children between 12 and 59 months) and females (62.5%) outnumber males above 5 years in the study. Age and sex distribution obtained in the current study was similar to other hospital based studies done by Ali et al.[18] in UAE, Raghubanshi et al.[19] in Lalitpur, Nepal, April Bay and Anacleto[20] in Philippines [Table 4].

In majority of these hospital-based studies including the current study, it is noted that males are more affected in infancy than females, and as age increases, the gender ratio is reversed.

Etiology

Most common causative organism isolated was *Escherichia coli* (73.3%) followed by *Klebsiella* (17.5%). This is comparable with the study by Sharma et al.[21] from Nepal and Akram et al.[22] from Aligarh, India [Table 5].

Bryan et al.[23] reported *E. coli* as the most common urinary pathogen accounting for 85% of community-acquired UTI. Bagga et al.[24] reported that about 90% of first symptomatic UTI and 70% recurrent infections were due to *E. coli*. The studies by Mantadakis et al.[25] and Islam et al.[26] showed *E. coli* as most common organism but with varying proportions. Gulati and Kher reported Gram-negative bacteria as the most common etiologic agents, among which *E. coli* was the most common.[27]

Imaging Studies

**USG**

Among imaging studies, 12% of children with UTI had abnormality in RUSG. This is similar to a study conducted by Hoberman et al.[16] in his prospective study involving 309 children with UTI. USG findings were abnormal in 12%. This is low when compared with the study by Singh et al.[17] from Nepal and Ali et al.[18] from Sudan in which abnormal USG findings were found in 25% and 32.6%, respectively. The lower number of abnormal USG finding in the present study may be due to the resolution of cystitis/pyelonephritis at 1–2 weeks after treatment. Doing an USG before or on the day of starting treatment may be more sensitive.

**Table 3: The incidence of scarring after UTI according to the gender in the study (n=120)**

<table>
<thead>
<tr>
<th>Renal scarring</th>
<th>1–11 months</th>
<th>1 year–&lt; 5 years</th>
<th>5–12 years</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>3</td>
<td>11</td>
<td>2</td>
<td>39%</td>
</tr>
<tr>
<td>Females</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>31.2%</td>
</tr>
<tr>
<td>P value</td>
<td>0.46</td>
<td>0.27</td>
<td>-</td>
<td>0.58</td>
</tr>
</tbody>
</table>

**Table 4: Age and sex distribution**

<table>
<thead>
<tr>
<th>Male to female ratio</th>
<th>Infancy</th>
<th>Older children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present study</td>
<td>2.5:1</td>
<td>1:1.5</td>
</tr>
<tr>
<td>Ali et al.[18]</td>
<td>2.1:1</td>
<td>1:1.2</td>
</tr>
<tr>
<td>Bay and Anacleto[20]</td>
<td>1.9:1</td>
<td>1:1.6</td>
</tr>
<tr>
<td>Raghubanshi et al.[19]</td>
<td>1.4:1</td>
<td>1:0.5:1</td>
</tr>
</tbody>
</table>

**Table 5: Comparison of common organisms isolated**

<table>
<thead>
<tr>
<th>Organism</th>
<th>Escherichia coli</th>
<th>Klebsiella</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present study</td>
<td>73.3%</td>
<td>17.5%</td>
</tr>
<tr>
<td>Sharma et al.[21]</td>
<td>67.5%</td>
<td>20%</td>
</tr>
<tr>
<td>Akram et al.[22]</td>
<td>61%</td>
<td>22%</td>
</tr>
<tr>
<td>Weisman et al.[23]</td>
<td>76%</td>
<td>6%</td>
</tr>
<tr>
<td>Zamir et al.[24]</td>
<td>85%</td>
<td>7.1%</td>
</tr>
</tbody>
</table>
**MCU**

MCU was normal in 70% of children who underwent this imaging and 15% of children had VUR. Grade 1–2 refluxes were shown by 10% of children who underwent this imaging and 5% showed Grade 3–4 reflux. In the study by Singh et al.[17] and Ali et al.,[18] VUR was found in 33.3% of children. Studies done by Pennressi et al.[31] and Ismaili et al.[32] also showed similar findings. Among children with VUR in the present study, female-to-male ratio of 1.7:1 found is not significant statistically. This can be explained by very low number of children with VUR. In a study by Tekgul et al., VUR was found to be more in boys than girls among children with UTI,[33] whereas in IAP guidelines on UTI 2011, VUR is found common in females than males.[34]

**Posterior urethral valve**

Of 6 PUV cases detected by MCU, 4 cases (66.7%) were detected before 12 months of age; 2 (33.3%) cases of PUV were detected after age of 12 months [Table 6].

7.9% of males studied here had posterior urethral valve. This observation was high compared to a similar study done by Gupta et al. in JIPMER, Puducherry (2013), where 3 (2.3%) of 129 males with culture-proven UTI had PUV.[38] There is a significant difference in male infant sample size (66 children) in the compared study, and as the age of presentation of PUV is mostly in infancy, this may be a insignificant finding because a number of PUV cases presented in infancy is not mentioned in the JIPMER study.

**DMSA**

DMSA renal scan done was normal in 63% of cases, and 37% of cases had renal scarring. In a similar study of 186 children with culture-proven UTI done by Gupta et al. in JIPMER puducherry (2013), renal scarring was noted in 33 (47.8%) of the 69 children who underwent DMSA scan.[38] Sheikh et al. (2010)[39] in their meta-analysis of similar studies found 15% chance of renal scarring.

**Outcome**

**Treatment response**

Of 120 children, 40% of cases responded to 5–7 days antibiotics. 39% needed 7–10 days of antibiotics and 21% needed 10–14 days of antibiotics. Michael et al. in a comparison study of short (2–4 days) course versus standard long course (7–14 days) concluded that there was no significant difference in the frequency of positive urine cultures at 0–7 days after treatment in children with UTI.[40] Schroeder et al. (2014) found that relapse was not associated with treatment duration.[41] Hoberman et al. in their control trial comparing oral and parenteral treatment in children with febrile UTI found that there was no difference and recommended oral cefixime for decreasing expenditure.[42] Neuhaus et al. (2008) concluded in their study of children aged 6 months–16 years with DMSA-documented acute pyelonephritis that once-daily oral cefixiben for 14 days yielded comparable results to sequential ceftriaxone/cefotaxime.[43] Bocquet et al. in 2012 found no significant difference between two treatment groups, who received either oral cefixime for 10 days or intravenous ceftriaxone for 4 days followed by oral cefixime for 6 days in relation to renal scarring and time to apyrexia.[44] In the present study, it was not able to compare the efficacy of oral versus intravenous antibiotics in the treatment of UTI in children as treatment was started with oral antibiotics for uncomplicated UTI and intravenous antibiotics for complicated UTI and non-responders to oral antibiotics. The study population should be randomized and given oral or intravenous antibiotics randomly to avoid selection bias.

**Surgical intervention**

All children with PUV had undergone cystoscopic fulguration followed by pyeloplasty for unresolved hydroureteronephrosis in 4 of these 6 children. The definitive treatment of PUV was cystoscopic fulguration of PUV which is supported by Warren et al.[45] Five male children underwent circumcision and 3 males underwent preputial dilatation. Shaikh et al.[46] in their study shown that circumcision was associated with a significantly reduced risk of UTI. Ginsberg et al. noted that 75% of boys with febrile UTI in the first 8 weeks of life were non-circumcised.[47] Studies suggest a 20–29-fold increase in febrile UTI in uncircumcised males in comparison to circumcised infants. The mechanism by which the intact prepuce predisposes to UTI is unclear. One of the possible explanations is that the prepuce allows the enteropathogenic bacteria to harbor and multiply in an uncircumcised male. However, the AAP taskforce on circumcision reports that the existing scientific evidence does not support a recommendation for routine neonatal circumcision.[48]

**Recurrence**

Recurrent UTI was present in 7.5% of children with first episode of UTI on a 6-month follow-up. This is supported by a meta-analysis of various studies under UTI done by Sheikh et al. 2010[39] in which recurrent UTI was found in 8% of cases. All nine children who had recurrence within 6 months had the same organism grown in their urine.

### Table 6: Age of presentation - posterior urethral valve

<table>
<thead>
<tr>
<th>Age of presentation of PUV</th>
<th>NICE[38]</th>
<th>Uthup et al.[39]</th>
<th>Parkhouse et al.[37]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between 0 and 1 month</td>
<td>9.5%</td>
<td>46.6%</td>
<td>33.3%</td>
</tr>
<tr>
<td>Between 1 month and 1 year</td>
<td>38%</td>
<td>36.6%</td>
<td></td>
</tr>
<tr>
<td>Between 1 and 6 years</td>
<td>33%</td>
<td>16.8%</td>
<td>33.3%</td>
</tr>
<tr>
<td>More than 5 years</td>
<td>19%</td>
<td></td>
<td>33.3%</td>
</tr>
</tbody>
</table>

NICE: National Institute for Health and Clinical Excellence
culture suggesting unresolved or persistent bacteriuria. This is in correlation with Pewit et al. stating unresolved bacteriuria as the most common type of recurrent UTI.\[48\] The most common cause for unresolved bacteriuria is inadequate antibiotic therapy, and other causes include noncompliance, malabsorption, and suboptimal drug metabolism and resistant organism.

**VUR and recurrence**

50% of the children with vesicoureteric reflux had recurrent UTI in the study. In a study by Keren et al. (2015), 25.4% of children with VUR had recurrent UTI compared with 17.3% of children with no VUR.\[59\]

**Recurrence in relation to age and gender**

Association of the incidence of recurrence of UTI following UTI in relation to age and gender was inconclusive (\(P > 0.05\)). The NICE: 2007\[52\] states that recurrence was not associated with gender.

**Renal scarring**

Renal scarring is found in all 6 cases with VUR (4 cases of grade 3–4 VUR and 2 cases of grade 1–2 VUR) in this study. Sheikh et al. (2010) in their study found that children with VUR were significantly more (2.6 times) likely to develop renal scarring compared with children with no VUR.\[39\] Children with VUR grades III or higher were 2.1 times likely to develop scarring than children with lower grades of VUR. However, in a recent study by Keren et al. (2015), no significance was found in children with VUR and children with any VUR in relation to renal scarring.\[49\]

**Renal scarring in relation to age and gender**

Association of renal scarring following UTI in relation to age and gender was inconclusive in the present study. Park et al. (2012), Blumenthal et al. (2006), Mingin et al. in 2004, and Najib et al. in 2009 concluded that the age of presentation of the first UTI was not predictive of scar formation.\[51-54\] Piepsz et al. in a 5-year study showed that children younger than 2 years were at greater risk (1.8 times) for renal scarring than older children regardless of treatment.\[55\] Benador et al. (1997) in a study observed that the rate of renal scarring after pyelonephritis was high between 1 and 5 years of age.\[56\]

**Renal scarring in relation to isolated organism**

Association between organism isolated in urine culture and renal scarring was inconclusive (\(P > 0.05\)). Ronald et al. and Zmyslowska et al. in their studies found *E. coli* as the common uropathogen and no difference between the scar forming and non-scar forming groups.\[57,58\] Orellana et al.\[59\] found a significant higher incidence of renal scarring in children with non-*E. coli* infection.

**Renal scarring and recurrence**

Relative risk of recurrence was 14 times (95% CI: 1.5–126) more in cases with renal scarring than cases without renal scarring (85.7% vs. 30%; \(P = 0.04\)). Renal scarring is a predictor of recurrence of UTI which is also supported by NICE (2007).\[50\]

**Growth retardation, renal function tests, and blood pressure**

Hypertension, growth retardation, or altered renal function tests due to UTI alone were not observed in this study. This may be due to the short period of follow-up compared to other studies which had a long-term follow-up to observe these parameters. Salo et al. (2011) observed that a child with normal kidneys is not at significant risk of developing CKD because of UTIs.\[60\] Jacobson et al. in a 27-year follow-up study found that children with focal renal scarring due to pyelonephritis are at high risk of serious long-term consequences.\[61,62\] Hannula et al. in a 6–17-year follow-up study of 193 patients with childhood UTI observed no significant difference in BP, renal function and somatic growth in different groups with or without renal scars and/or VUR; and the risk of long-term consequences from childhood UTI in their studies were very low.

**CONCLUSIONS**

The recurrence chance of UTI is present in 7.5% of children within 6 months of first episode of UTI. Majority of children with recurrent UTI had their second episode within 6 months and that too, with the same organism suggesting an unresolved or persistent bacteriuria. The presence of VUR is a risk for recurrence of UTI and renal scarring. The relative risk of recurrence of UTI is 14 times in the presence of renal scarring than in children without renal scar formation, and thus, renal scarring is a good predictor of recurrence. Hypertension, growth retardation, and renal function abnormalities were not found in children with an episode of UTI on a 6–18-month follow-up and may need a long-term follow-up to observe these complications.

**REFERENCES**


How to cite this article: Vinodkumar MS, Mohan MV. Outcome of Children with First Episode of Urinary Tract Infection. Int J Sci Stud 2018;6(1):161-171.

Source of Support: Nil, Conflict of Interest: None declared.
A Clinical Study on the Management of Chronic Mastoiditis and Mastoid Abscess - A Hospital-based Study

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Abstract

Background: In spite of the advent of antibiotics, the incidence of mastoiditis and mastoid abscess is not uncommon in the ENT practice. The pathogenesis is due to virulence of organism, insufficient antibiotics use, and ineffective antibiotics. Treatment consists of simple incision drainage to modified radical mastoidectomy. However, there seems to be no unanimous agreement on the best management strategy for this problem. The present study presents the outcome of patients undergoing treatment and also presents a protocol followed in a tertiary teaching hospital of North Kerala and its prognostic value.

Aim of the Study: The aim of this study is to review the available management protocols for treatment of mastoiditis and mastoid abscess and formulate our own hospital-based guidelines and protocol.

Materials and Methods: A study was conducted on 53 patients aged between 11 and 60 years, who presented with mastoiditis or mastoid abscess. All the patients were treated according to surgical protocols available. Demographic data, history, and otoscopy findings were recorded. Patients with mastoiditis were treated with mastoidectomy. Patients with mastoiditis were treated with mastoidecomy, and the patients with mastoid abscess were treated initially with incision and drainage and after 2 weeks with mastoidectomy. Laboratory investigations such as audiometry, culture, and sensitivity of pus from the ears were done. All the patients were followed for 6 months.

Observations and Results: A total of 53 patients were enrolled in this study. Mean age was 25.45 ± 2.35 in males and 23.76 ± 1.85 in females who presented with mastoiditis. Similarly, the mean age was 23.76 ± 1.85 and 20.46 ± 2.10 years for patients of mastoid abscess. There were 39/53 (73.58%) males and 14/53 (26.41%) females. Audiometry could be done in 32/37 (86.48%) patients with mastoiditis and 8/16 (50%) patients with mastoid abscess. These 40/56 (71.42%) patients had conductive deafness with a mean pure tone average of 32.45 dB. There were no post-operative complications reported during follow-up of 6 months.

Conclusions: A definitive management protocol is a must for every hospital to avoid delay and complications before and after surgical treatment in mastoiditis and mastoid abscess. Treatment guidelines should be followed meticulously in the diagnosis, laboratory investigations, and decision-making of definitive surgical procedure to be adopted in mastoiditis and mastoid abscess.

Key words: Chronic suppurative otitis media, Mastoid abscess, Mastoiditis, Otitis media

INTRODUCTION

Mastoiditis is an inflammatory process of the mastoid air cells in the temporal bone.[1] Chronic mastoiditis is generally a result of chronic suppurative otitis media (CSOM); it is rarely a result of failure of the treatment of acute mastoiditis.[2] CSOM is persistent inflammation of the middle ear or mastoid cavity with permanent changes in the tympanic membrane in the form of perforation. Synonyms include “chronic otitis media (without effusion),” chronic mastoiditis, and chronic tympanomastoiditis. CSOM is characterized by recurrent or persistent ear discharge (otorrhea) over 2–6 weeks through a perforation of the tympanic membrane.[3] Two types of mastoiditis are associated with bone destruction: Acute coalescent mastoiditis and chronic mastoiditis with osteitis. Acute coalescent mastoiditis generally follows a severe bout of acute suppurative otitis media (ASOM).[4]
Inadequate treatment of acute otitis media (AOM) may result in a clearing of the middle ear portion of the infection, with persistence of infection somewhere within the adjoining pneumatized spaces in the mastoid. This “masked mastoiditis” occurred in 15% of CSOM cases in the early antibiotic era[3] and, although uncommon, still occurs today.[4] The illness is common in resource-poor countries and those with poor socioeconomic status.[5] The effective control of AOM has reduced the number of cases of acute coalescent mastoiditis, but the incidence of chronic mastoiditis caused by cholesteatoma has not been decreased with antibiotic usage.[7] The occurrence rate of mastoiditis was found to be higher in countries with restricted antibiotic use.[8] Few cases of acute mastoiditis develop into chronic ones, whereas few cases of AOM results in CSOM. Acute mastoiditis may spread through the periosteum and induce periostitis, which may cause bone destruction (acute coalescence mastoiditis). The infection may progress through adjacent bones or through emissary veins beyond the mastoid air cells and may present as a subperiosteal abscess or an intracranial complication. Acute mastoiditis involves the formation of pus and only occurs in cellular mastoids. Chronic mastoiditis is a slow penetration of acellular bone by granulations accompanied by hyperemic decalcification of the bone. In most cases, otitis media is concurrent either acute or chronic. Some patients may present with a postauricular fistula which may be spontaneous or iatrogenic. It may persist to become a chronic fistula. With the advent of broad-spectrum antibiotics, the clinical course of middle ear disease has been altered. One result has been the occasional suppression of the presenting signs and symptoms of mastoiditis. The course may be so insidious that the first awareness of mastoiditis may be following the presentation of an intracranial complication such as meningitis, lateral sinus thrombosis, or brain abscess. Furthermore, mastoidectomy is rarely indicated for chronic mastoiditis as a treatment option, which was mandatory for included cases in the present work. There is a traditional view that chronic otitis media and chronic mastoiditis must exist in the presence of tympanic membrane perforation.[9] CSOM involves a cycle of inflammation, ulceration, granulation, and infection in the middle ear. There is conductive hearing loss and often inflammation of the mastoid cavity. Complications include hearing loss, mastoiditis, cholesteatoma, facial nerve paralysis, meningitis, brain abscess, and sigmoid sinus thrombosis.[10] Anaerobic bacteria are important pathogens in head and neck infections such as chronic otitis media, chronic sinusitis, chronic mastoiditis, head and neck abscesses, cervical adenitis, parotitis, and postoperative infection.[11]

**Type of Study**

This was a cross-sectional prospective study.

**Period of Study**

The study duration was from December 2016 to April 2018.

**Institute of Study**

This study was conducted at Kannur Medical College, Anjarakandy, Kannur, Kerala.

**MATERIALS AND METHODS**

The present study was conducted on 53 patients who presented with mastoiditis or mastoid abscess to the ENT Department of a tertiary teaching hospital of Northern Kerala. The Institutional Ethical Committee clearance was obtained for the study.

**Inclusion Criteria**

1. Patients aged above 11 years and below 60 years were included.
2. Patients with ASOM or CSOM complicating either with mastoiditis or mastoid abscess were included.
3. Patients with discharge from the ear were included.
4. Patients not responding to antibiotics were included for surgery.
5. Patients with cholesteatoma were included in this study.

**Exclusion Criteria**

1. Patients below 11 years and above 60 years were excluded.
2. Patients with prior surgery on the mastoid in the form of mastoidectomy were excluded from the study.
3. All the patients with ASOM or CSOM included in the study as per the inclusion criteria were thoroughly elicited of history, demographic data, and clinical examination including otoscopy. Examination under microscope was done to confirm the diagnosis. Radiological investigations like X-ray both mastoids, CT scan temporal bone were performed wherever required. Bacteriological examination of the pus was done. Audiological evaluation was done with the help of pure tone audiometry. For patients with acute or chronic mastoiditis, initially intravenous antibiotics, ceftriaxone 1 g twice daily was started for 1 week. Oral decongestants such as phenylpropanolamine were used in all patients. Ofloxacin ear drops were started after the admission. Patients with mastoiditis not responding to the treatment were subjected to cortical mastoidectomy or modified radical mastoidectomy depending on the intraoperative findings. Patients with mastoid abscess were subjected to incision drainage. Post-operatively, all the patients were given IV antibiotics, NSAIDs, and other supportive treatment. Post-operative evaluation was done at 1st, 3rd, and 6th month's intervals. For patients with mastoid abscess, medical treatment protocol was the same, but the patient was subjected to incision and drainage of the abscess and mastoidectomy was undertaken only after 2 weeks interval.
OBSERVATIONS AND RESULTS

There were 53 patients who were enrolled in this study. The mean age was 25.45 ± 2.35 in males and 23.76 ± 1.85 in females who presented with mastoiditis. Similarly, the mean age was 23.76 ± 1.85 and 20.46 ± 2.10 years in males and females who presented with mastoid abscess, respectively. There were 39/53 (73.58%) males and 14/53 (26.41%) females. There were 37/53 (69.81%) patients who presented with mastoiditis and 16/53 (30.18%) patients with mastoid abscess. The demographic data and type of inflammatory disease in the study are shown in Table 1.

The audiological evaluation was done by calculating the pure tone average (PTA) in the frequencies of 500, 1000, 1500, and 2000 KHZ by air conduction and bone conduction. Audiometry could be done in 32/37 (86.48%) of the patients with mastoiditis and 8/16 (50%) of the patients with mastoid abscess. These 40/56 (71.42%) patients had conductive deafness with a mean PTA of 32.45dB. The mean air-bone gap (a-b gap) calculated was 15dB. Staphylococci, Haemophilus influenza, Escherichia coli, Pseudomonas aeruginosa, and Enterobacteriaceae were the predominant isolates that were recovered from the pus sent for culture and sensitivity from patients with mastoiditis and mastoid abscess with CSOM. Streptococcus pneumoniae and Streptococcus pyogenes were the most common organisms recovered in mastoiditis and mastoid abscess with ASOM. The most sensitive antibiotic was cefotaxime, followed by ceftriaxone, kanamycin, and ciprofloxacin [Table 2].

Among the mastoiditis patients, 23/39 patients had tubotympanic type of CSOM and 16/39 had atticocanal type of CSOM. All these patients underwent definitive surgery; the former were subjected to cortical mastoidectomy with tympanoplasty and the latter modified radical mastoidectomy with tympanoplasty. All the patients were followed up for 6 months at an interval of 1st, 3rd, and 6th months. During follow-up, mastoid wound dressing was done and suction clearance of the external auditory canal done after 1 month under the operating microscope. The status of the graft, secondary infection, and hearing improvement were the parameters observed during this period. There was no post-operative complication in any of the patients undergoing definitive surgery. Among the 16 patients presenting with mastoid abscess, 9/16 presented with tubotympanic type of CSOM and 7/16 of them with atticocanal type of CSOM. All the patients with mastoid abscess were subjected to initial incision drainage, and after 2 weeks, definitive surgery was undertaken. There were no post-operative complications in this group either of this study. All the data were analyzed using standard statistical methods.

The incidence of acute mastoiditis in patients with AOM has dropped from 50% at the turn of the 20th century to 6% in 1955 and to 0.4% in 1959, and by 1993, only 0.24% of patients with AOM developed acute mastoiditis.[12] Petersen et al. reported a decline in the incidence of acute mastoiditis from 20% in 1938 to 2.5% in 1945.[13] The incidence of mastoiditis and mastoid abscess though rare nowadays it is, however, uncertain whether this is directly associated with the unscrupulous use of antibiotics or if an altered nature of the disease/microorganisms and/or the state of health is involve.[14] The increase in the incidence of these two complications may be due to the phenomenon of increasing antibiotic resistance of microorganisms like Streptococcus to penicillin.[14] S.

<table>
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<th>Observation</th>
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<th>Mastoid abscess (n=16)</th>
</tr>
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<td></td>
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PTA: Pure tone average

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<th>Mastoid abscess (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean PTA-dB</td>
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<td>28.64±2.08</td>
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<tr>
<td>a-b gap</td>
<td>17.40±1.50</td>
<td>14.60±2.10</td>
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<tr>
<td>Bacteriology</td>
<td>Staphylococci</td>
<td>Haemophilus influenza</td>
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<td>46.35%</td>
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<td>06.13%</td>
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<td>16.88%</td>
<td>03.40%</td>
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<td>01.71%</td>
<td>01.71%</td>
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</tbody>
</table>

ASOM: Acute suppurative otitis media, CSOM: Chronic suppurative otitis media

DISCUSSION

The observations and results of this study indicated that mastoid abscess occurred in 31% of patients with mastoiditis. The mean age of patients with mastoiditis was 25.45 ± 2.35 years, and the mean age of patients with mastoid abscess was 23.76 ± 1.85 years. The most sensitive antibiotic was cefotaxime, followed by ceftriaxone, kanamycin, and ciprofloxacin.

The audiological evaluation was done by calculating the pure tone average (PTA) in the frequencies of 500, 1000, 1500, and 2000 KHZ by air conduction and bone conduction. Audiometry could be done in 32/37 (86.48%) of the patients with mastoiditis and 8/16 (50%) of the patients with mastoid abscess. These 40/56 (71.42%) patients had conductive deafness with a mean PTA of 32.45dB. The mean air-bone gap (a-b gap) calculated was 15dB. Staphylococci, Haemophilus influenza, Escherichia coli, Pseudomonas aeruginosa, and Enterobacteriaceae were the predominant isolates that were recovered from the pus sent for culture and sensitivity from patients with mastoiditis and mastoid abscess with CSOM. Streptococcus pneumoniae and Streptococcus pyogenes were the most common organisms recovered in mastoiditis and mastoid abscess with ASOM. The most sensitive antibiotic was cefotaxime, followed by ceftriaxone, kanamycin, and ciprofloxacin.

Among the mastoiditis patients, 23/39 patients had tubotympanic type of CSOM and 16/39 had atticocanal type of CSOM. All these patients underwent definitive surgery; the former were subjected to cortical mastoidectomy with tympanoplasty and the latter modified radical mastoidectomy with tympanoplasty. All the patients were followed up for 6 months at an interval of 1st, 3rd, and 6th months. During follow-up, mastoid wound dressing was done and suction clearance of the external auditory canal done after 1 month under the operating microscope. The status of the graft, secondary infection, and hearing improvement were the parameters observed during this period. There was no post-operative complication in any of the patients undergoing definitive surgery. Among the 16 patients presenting with mastoid abscess, 9/16 presented with tubotympanic type of CSOM and 7/16 of them with atticocanal type of CSOM. All the patients with mastoid abscess were subjected to initial incision drainage, and after 2 weeks, definitive surgery was undertaken. There were no post-operative complications in this group either of this study. All the data were analyzed using standard statistical methods.

The incidence of acute mastoiditis in patients with AOM has dropped from 50% at the turn of the 20th century to 6% in 1955 and to 0.4% in 1959, and by 1993, only 0.24% of patients with AOM developed acute mastoiditis.[12] Petersen et al. reported a decline in the incidence of acute mastoiditis from 20% in 1938 to 2.5% in 1945.[13] The incidence of mastoiditis and mastoid abscess though rare nowadays it is, however, uncertain whether this is directly associated with the unscrupulous use of antibiotics or if an altered nature of the disease/microorganisms and/or the state of health is involve.[14] The increase in the incidence of these two complications may be due to the phenomenon of increasing antibiotic resistance of microorganisms like Streptococcus to penicillin.[14] S.
pneumoniae, S. pyogenes, Staphylococcus aureus, and H. influenza are the most common organisms recovered in acute mastoiditis. P. aeruginosa, Enterobacteriaceae, and S. aureus are the predominant isolates that have been recovered from chronically inflamed mastoids.[13] In the present study, the incidence of organism such as Staphylococci, H. influenza, E. coli, P. aeruginosa, Enterobacteriaceae, S. pneumoniae, and S. pyogenes in the pus for culture sensitivity test in the patients with mastoiditis was 46.35%, 17.48%, 14.50%, 10.43%, 6.13%, 03.40%, and 01.71%, respectively [Table 2]. In this study, all cases with mastoid abscess required some sort of surgical intervention, either by incision and drainage or by definitive surgery (cortical or radical mastoidectomy). Tarantino et al.[14] stressed the need for surgical drainage of a subperiosteal abscess to prevent the spread of suppuration to vital areas. Reported mastoidectomy rates in clinical studies have shown large variations, ranging from 12% to 98%.[7] The large variability suggests that the decision for or against mastoidectomy is not only a question of preferred conservative treatment or immediate surgical intervention but also to a large extent based on subjective surgical criteria.[16] Mastoidectomy (cortical or modified radical Mastoidectomy) is an effective surgical treatment for mastoiditis associated with one of the followings: Subperiostal abscess or exteriorization, cholesteatoma, intracranial complications, and otorrhea persisting for more than 2 weeks despite adequate antibiotic treatment or in children. No detectable recurrence of mastoiditis or mastoid abscess or any complication was recorded during follow-up of 6 months in this study. In this study, all patients with mastoid abscess were managed by incision and drainage.

CONCLUSIONS

A definitive management protocol is a must for every hospital to avoid delay and complications before and after surgical treatment in mastoiditis and mastoid abscess. Treatment guidelines should be followed meticulously in the diagnosis, laboratory investigations, and decision-making of definitive surgical procedure to be adopted in mastoiditis and mastoid abscess.

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How to cite this article: Kumar AS. A Clinical Study on the Management of Chronic Mastoiditis and Mastoid Abscess - A Hospital-based Study. Int J Sci Stud 2018;6(1):172-175.

Source of Support: Nil, Conflict of Interest: None declared.
A Clinico-pharmacological Study on Effect of Methylprednisolone in Acute Respiratory Distress Syndrome Patients

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Abstract

Background: Acute respiratory distress syndrome (ARDS) is an acute condition characterized by bilateral pulmonary infiltrates and severe hypoxemia in the absence of evidence for cardiogenic pulmonary edema. The diagnosis is based on the ratio of the partial pressure of oxygen in the patient’s arterial blood (PaO₂) to the fraction of oxygen in the inspired air (FiO₂); therefore, ARDS was defined by a PaO₂/FiO₂ ratio of <200, and in acute lung injury, it was <300. Late phase ARDS results due to inflammation and corticosteroids are considered as rescue therapy to improve oxygenation and hemodynamics in patients.

Aim of the Study: The aim of this study is to evaluate the effect of methylprednisolone in early ARDS in regard to outcome, incidence of infection, organ dysfunction, D-dimer, C-reactive protein (CRP), protein C, and protein S.

Materials and Methods: A total of 49 adult patients with ARDS were included. Group A patients (24) were administered methylprednisolone, and Group B patients (25) did not receive methylprednisolone. All the patients were diagnosed based on American-European Consensus Conference (AECC), Berlin and Kigali criteria for ARDS. History taking, clinical examination, radiological tests, blood investigations (CBC–LFT–RFT–electrolytes), arterial blood gas (ABG), serum lactate, international normalized ratio, fibrinogen, and aPTT, CRP, protein C, protein S, and D-dimer were undertaken before and after treatment with methylprednisolone.

Observations and Results: There were 49 patients with ARDS included in the study. The study group consisted of 24 (48.97%) patients, and the control group was 25 (51.02%) patients. 15 were males (62.32%) and 9 (37.50%) females in the study group. 16 were males (64%) and 9 females (36%) in the control group. The mean age in the study group was 44.12 ± 10.75, and the mean in the control group was 48.5 ± 11.26. Hospital-acquired Pneumonia (HAP), trauma, and community-acquired pneumonia (CAP) as the cause of ARDS were observed in 21.16%, 37.05%, and 33.33%, respectively, in the study group. The incidence of HAP, trauma, and CAP was 32%, 32%, and 36%, respectively, in the control group.

Conclusions: Including methylprednisolone in addition to regular ventilator support and treatment protocol of ARDS patients, when used on first 7 days, improves the LIS, decreases the systemic inflammation, allows earlier extubation from mechanical ventilation, and decreases the incidence of hospital-acquired infection.

Key words: Acute lung injury, Acute respiratory distress syndrome, Hypoxia, Methylprednisolone, Oxygen saturation

INTRODUCTION

Since its first description, the acute respiratory distress syndrome (ARDS) has been acknowledged to be a major clinical problem in respiratory medicine.[1] International multicenter studies quote that ARDS is underdiagnosed and requires potential for improvement in its management. Predisposing factors such as exposure to high ozone levels and low Vitamin D plasma concentrations were found to be predisposing circumstances. Not only curative but also preventive strategies remain a major challenge since the two trials on aspirin and statins failed to reduce the incidence in at-risk patients.[2] The 1st week of treatment of ARDS with mechanical ventilation determines its pathophysiologic progression and its late phase effect on inflammation and disease outcome.[2] Use of the lung

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injury score (LIS) quantifying the physiologic respiratory impairment calculated by a 4-point score based on the levels of positive end-expiratory pressure (PEEP), ratios of PaO2 to fraction of inspired oxygen (FIO2), the static lung compliance, and the degree of infiltration present on chest radiograph helps in decision making of treatment. In patients in whom these LIS do not improve by the end of the 1st week and have persistent elevation in circulating levels of inflammatory cytokines and chemokines, markers of alveolocapillary membrane permeability and fibrogenesis (dysregulated systemic inflammation) also have a higher mortality.

Glucocorticoids used in the 1st week of the treatment of ARDS help in downregulating the systemic inflammation which is associated with a significant clinical and oxygenation improvement with a reduced duration of mechanical ventilation and ICU length of stay. Methylprednisolone was used in high doses during the 1st week of ARDS in many trials of patients with persistent pulmonary infiltrates, fever, and high oxygen requirement despite resolution of pulmonary or extrapulmonary infection. Pulmonary infection is usually assessed with bronchoscopy and bilateral bronchoalveolar lavage (BAL) and quantitative culture. The present study was conducted with an aim to evaluate the effect of methylprednisolone when used in ARDS patients in regard to outcome, incidence of infection, organ dysfunction, D-dimer, C-reactive protein (CRP), protein C, and protein S.

Period of Study
The study duration was from August 2013 to July 2015.

Institution of Study
The study was conducted at Kannur Medical College, Anjarakandy, Kannur, Kerala.

Type of Study
This was a prospective, cross-sectional, and comparative study.

MATERILAS AND METHODS

A total of 49 adult patients with ARDS were included. Group A patients (24) were administered methylprednisolone and group B patients (25) did not receive methylprednisolone. All the patients were diagnosed based on the AECC, Berlin and Kigali criteria for acute respiratory distress syndrome (ARDS). History taking, clinical examination, radiological tests, blood investigations (CBC–LFT–RFT–electrolytes), ABG, serum lactate, international normalized ratio, fibrinogen, and aPTT, CRP, protein C, protein S, and D-dimer were undertaken before and after treatment with methylprednisolone.

Inclusion Criteria
(1) Patients with ARDS criteria of AECC, (2) patients who are on ventilator, (3) patients in whom methylprednisolone was started within 48 h, and (4) patients aged above 18 years were included in this study.

Exclusion Criteria
(1) Patients with PaO2/FIO2 ratio more than 200 and (2) patients who were not on ventilators were excluded from the study. Once the diagnosis is established, IV methylprednisolone was given as loading dose 1 mg/kg body weight followed by 1 mg/kg/day from day 2 to day 14. The steroid was mixed in 240 mL of normal saline solution, and the rate of infusion was adjusted to 10mL/h. Methylprednisolone was given from day 15th to 21st 0.5 mg/kg/day and from day 22nd to 25th 0.25 mg/kg/day and from day 26th to 28th the dose was reduced to 0.125 mg/kg/day. In addition to ventilator support measures, patients in this study received low-molecular-weight heparin (40 mg of enoxaparin or 5,000 units of dalteparin subcutaneously per day) or low-dose, unfractionated heparin (5000 units subcutaneously twice daily) to prevent venous thromboembolism. In the absence of contraindication, ARDS patients received stress ulcer prophylaxis with an agent such as sucralfate 1 g (orally or through nasogastric tube 4 times daily), ranitidine (orally or through nasogastric tube twice daily, 50 mg intravenously every 6–8 h, or a 6.25 mg/h continuous intravenous infusion), or omeprazole (orally, intravenously, or through nasogastric tube daily). Patients also received nutritional support (enteral) within 24–48 h of admission to the ICU. From the day of admission to the Intensive Care Unit till the discharge, all the parameters were observed and the data collected were analyzed using standard statistical methods.

OBSERVATIONS AND RESULTS

This was a prospective, cross-sectional comparative study conducted in a tertiary teaching hospital of Northern Kerala. 49 patients admitted in ICU diagnosed as ARDS based on the basis of AECC criteria, and laboratory investigations were included in the study. They were divided into two groups depending on the administration of IV methylprednisolone as mentioned in the materials and methods. The study group consisted of 24 (48.97%) patients and the control group was 25 (51.02%) patients. There were 15 males (62.52%) and 9 (37.48%) females in study group and 16 males (64%) and 9 females (36%) in the control group. The mean age in the study group was 44.12 ± 10.75, and the mean in the control group was 48.5 ± 11.26. Hospital-acquired pneumonia (HAP), trauma, and community-acquired pneumonia (CAP) as the cause of ARDS were observed in 21.16%, 37.05%, and 33.33%, respectively, in the study group. The incidence of HAP, trauma, and CAP was 32%, 32%, and 36%, respectively,
in the control group [Table 1]. The pre-treatment data are tabulated in Table 1 which shows no statistical significant difference between the methylprednisolone and control groups in all parameters except PEEP, protein S, PaO2 levels, and fibrinogen content. The values for these parameters were significantly higher in the methylprednisolone group when compared with the control group. The O2sat, PaO2, pCO2, HB, and creatinine were higher in the control group when compared with the methylprednisolone group before treatment [Table 1].

Post-treatment parameters after 1 week were compared with the pre-treatment parameters in both the study and control groups. It was observed that there were significant improvements of pulse, temperature, systolic blood pressure, PEEP, lactate, D-dimer, creatinine, and aspartate transaminase (AST) values in the methylprednisolone group. It was also observed that there was a significant increase of PaCO2 in the control group [Table 2].

**DISCUSSION**

ARDS is a rapidly progressive disorder that initially manifests as dyspnea, tachypnea, and hypoxemia and later quickly evolves into respiratory failure. The AECC has published diagnostic criteria for ARDS: Acute onset; ratio of partial pressure of arterial oxygen to fraction of inspired oxygen (PaO2/FiO2) of 200 or less, regardless of positive end-expiratory pressure; bilateral infiltrates seen on frontal chest radiograph; and pulmonary artery wedge pressure of 18 mm Hg or less when measured or no clinical evidence of left atrial hypertension.[8] Acute lung injury (ALI) is a slightly less severe syndrome characterized by less profound hypoxemia, but otherwise similar diagnostic criteria to ARDS[9,10] by the AECC defines ARDS as: (1) Acute onset of respiratory symptoms, (2) chest radiograph with bilateral infiltrates, (3) pulmonary artery wedge pressure (PAWP) of <18 mmHg (indicating no evidence of left heart failure), and (4) ARDS: PaO2/FiO2 ratio <200 mmHg. Treatment with drugs in ARDS is limited. Although Cochrane studies mention the use of surfactant therapy useful in children, its role in adults is controversial.[11] The use of corticosteroids in the management of ARDS is controversial. Few randomized controlled trials and cohort studies support early use of corticosteroids (with dosages of methylprednisolone ranging from 1 to 120 mg per kg per day) for decreasing the number of days on a ventilator; however, no consistent mortality benefit has been shown with this therapy.[12,13] In the present study, methylprednisolone was used in a regimen described in the materials and methods for 4 weeks. In ARDS, the evolution of systemic and pulmonary inflammation in the 1st week of mechanical ventilation determines the physiologic progression (resolving vs. unresolved) and outcome of the disease.[4] Glucocorticoid treatment-induced downregulation of systemic inflammation in ARDS is associated with a significant improvement in
Table 2: The clinical data, ventilator parameters, ABG, biochemical examination, and chest X-ray in methylprednisolone group and control group after 14th day of the study

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<th>Control (n=25)</th>
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<td>Pulse</td>
<td>93.50±14.86</td>
<td>113.11±4.26</td>
<td>0.015</td>
</tr>
<tr>
<td>Temperature</td>
<td>37.48±0.62</td>
<td>37.30±0.33</td>
<td>0.031</td>
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<tr>
<td>Systolic BP</td>
<td>146.47±14.99</td>
<td>125.13±13.02</td>
<td>0.041</td>
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<tr>
<td>Diastolic BP</td>
<td>71.00±13.38</td>
<td>65.56±6.82</td>
<td>0.174</td>
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<tr>
<td>FIO₂</td>
<td>65.90±10.40</td>
<td>63.64±15</td>
<td>0.916</td>
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<tr>
<td>PEEP</td>
<td>8.15±1.85</td>
<td>10.34±1.20</td>
<td>0.031</td>
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<tr>
<td>RR</td>
<td>13.99±1.65</td>
<td>15.88±1.67</td>
<td>0.029</td>
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<tr>
<td>PS</td>
<td>13.78±2.01</td>
<td>11.43±1.91</td>
<td>0.624</td>
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<tr>
<td>O₂ SAT</td>
<td>98.17±2.35</td>
<td>100.01±1.36</td>
<td>0.063</td>
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<tr>
<td>PaO₂</td>
<td>83.20±8.32</td>
<td>81.61±9.74</td>
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<tr>
<td>PaCO₂</td>
<td>26.11±14.99</td>
<td>47.09±5.70</td>
<td>0.001</td>
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<tr>
<td>PH</td>
<td>7.10±0.08</td>
<td>7.27±0.08</td>
<td>0.141</td>
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<tr>
<td>INR</td>
<td>1.17±0.11</td>
<td>1.29±0.31</td>
<td>0.074</td>
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<td>Lactate</td>
<td>1.58±0.60</td>
<td>2.38±0.19</td>
<td>0.003</td>
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<tr>
<td>APTT</td>
<td>31.87±1.72</td>
<td>36.95±4.14</td>
<td>0.001</td>
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<td>WBCs</td>
<td>12.00±1.93</td>
<td>12.89±1.64</td>
<td>0.717</td>
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<tr>
<td>HB</td>
<td>99.23±3.54</td>
<td>95.48±2.45</td>
<td>0.128</td>
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<td>Platelet</td>
<td>242.36±49.35</td>
<td>185.33±43.16</td>
<td>0.114</td>
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<td>D-dimer</td>
<td>240.39±45.47</td>
<td>489.61±215.09</td>
<td>0.004</td>
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<td>Na</td>
<td>140.50±4.78</td>
<td>140.56±0.53</td>
<td>0.761</td>
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<td>K</td>
<td>3.85±0.61</td>
<td>3.47±0.27</td>
<td>0.034</td>
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<td>Creatinine</td>
<td>72.17±19.80</td>
<td>121.59±13.38</td>
<td>0.011</td>
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<tr>
<td>Bilirubin</td>
<td>22.82±10.43</td>
<td>25.24±4.66</td>
<td>0.749</td>
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<td>AST</td>
<td>32.59±0.90</td>
<td>65.67±35.53</td>
<td>0.027</td>
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<tr>
<td>ALT</td>
<td>40.33±0.92</td>
<td>62.54±29.32</td>
<td>0.219</td>
</tr>
<tr>
<td>GGT</td>
<td>49.60±12.61</td>
<td>207.24±289.18</td>
<td>0.318</td>
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<tr>
<td>Albumin</td>
<td>24.00±1.99</td>
<td>27.61±2.84</td>
<td>0.652</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>6.07±1.46</td>
<td>7.94±1.92</td>
<td>0.157</td>
</tr>
<tr>
<td>CRP</td>
<td>106.33±75.04</td>
<td>138.11±49.90</td>
<td>0.315</td>
</tr>
</tbody>
</table>


In the present study, the aim was to evaluate the effect of methylprednisolone when used early in ARDS. There was no statistical significance between the methylprednisolone and control groups in relation to demographic data, etiology of ARDS, comorbidity, chest X-ray and most of clinical parameters, ventilator parameters, and biochemical investigations. It denotes that the both groups were comparable. After the 1st week of treatment, there were significant improvements of clinical parameters (pulse, temperature, and systolic blood pressure), peep (one parameter from lung injury score), lactate, D-dimer, and AST and highly significant improvement of creatinine in the methylprednisolone group when compared to the control group. In a similar study by Meduri, [4] who studied 91 patients with severe early ARDS (<72 h), 66% with sepsis, patients were randomized (2:1 fashion) to methylprednisolone infusion (1 mg/kg/d) versus placebo. Patients were randomized (2:1 fashion) to methylprednisolone infusion (1 mg/kg/d) versus placebo. The duration of treatment was up to 28 days and found patients with methylprednisolone achieving the primary endpoint of a 1-point reduction in LIS. In this study after 14 days from starting the treatment, there were significant improvements of clinical parameters (pulse and systolic blood pressure), ventilator parameters (FIO2, peep, and RR), systemic inflammation markers organ functions (O2sat, lactate, creatinine, WBCs, AST, and GGT), and CRP. Moreover, there was a significant improvement of CX-ray and earlier extubation from mechanical ventilation and improvement of mortality in the methylprednisolone group when compared with the control group. Improvement of mortality reflection to improvement of clinical status, oxygenation, inflammatory markers, and early extubation of this group. Moreover, there were significant decreases of protein C and protein S in the control group. This indicates worse clinical outcomes, including death, fewer ventilator-free days, and more nonpulmonary organ failures in this group. [7] Annane et al.[7] conducted a study with a long course of a low dose of corticosteroids in ARDS over a period of 28 days and observed a reduced all-cause mortality in Intensive Care Unit and hospital mortality and decreased incidence of infection. The findings of the study by Annane et al.[7] are similar to the present study with reduced mortality and improved oxygenation and parenchymal recovery of pulmonary infiltration at the end of 28 days period.

CONCLUSIONS

Including methylprednisolone in addition to regular ventilator support and treatment protocol of ARDS patients, when used on first 7 days, improves the LIS, decreases the systemic inflammation, allows earlier extubation from mechanical ventilation, and decreases the incidence of hospital-acquired infection.

REFERENCES


Source of Support: Nil, Conflict of Interest: None declared.
Cone-beam Computed Tomography - A Boon in Periodontology: A Review

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Abstract

Diagnosis of periodontal disease is firstly based on clinical signs and symptoms, however, when bone destruction is involved, radiographic examination is the most conclusive diagnostic method. Conventional radiographs including intraoral and panoramic imaging are used very frequently for this purpose. Cone-beam computed tomography (CBCT) is a new era in the field of oral radiology making the innovation provide high-quality, thin-slice accurate imaging. CBCT comes to complete help in providing new data to diagnose periodontal lesions. It is an imaging modality which would give an undistorted three-dimensional (3D) vision of a tooth and surrounding structures which is essential to improve the diagnostic potential. It has got the advantage of less exposure of radiation to the patient and reduced scan time. In the field of periodontology, it best enables the clinician to evaluate the crestal alveolar bone architecture and helps in treatment planning for implant placement, hence providing 3D images that facilitate the transition of dental imaging from initial diagnosis to image guidance throughout the treatment phase along with guided implant placement.

Key words: Cone-beam computed tomography, Periodontology, Three-dimensional imaging

INTRODUCTION

Periodontal disease is a chronic bacterial infection that affects the gingiva and bone supporting the teeth. Treatment of patients with advanced periodontal diseases requires not only extensive clinical recording but also radiological examination. Radiography provides key information on the amount and type of damage to the alveolar bone. The current diagnostic approaches including clinical probing and intraoral radiography have shown several limitations in their reliability.

Intraoral radiography is the most commonly used imaging technique for the diagnosis of periodontal bone defects. However, intraoral radiography provides only a two-dimensional (2D) view of three-dimensional (3D) structures which can lead to underestimation of bone loss and errors in identifying reliable anatomical reference points. 3D diagnostic imaging of the jaws has been of interest from the introduction of computerized tomography (CT) as a clinical tool. However, due to the factors such as high cost and high radiation dosage, use of this technology in dentistry has been limited.

Cone-beam CT (CBCT) is a relatively new imaging modality and with the introduction of dedicated dentomaxillofacial CBCT scanners in the late 1990s, there has been an explosion of interest in these devices in the field dentistry. It has the obvious advantage of relatively low cost and low-dose.

CBCT provides rapid volumetric image acquisition taken at different points in time that are similar in geometry and contrast, making it possible to evaluate differences occurring in the fourth dimension. In its various dental applications, images of jaws and teeth can be visualized accurately with excellent resolution, can be restructured three-dimensionally, and can be viewed from any angle. Most significantly, the patient radiation dose is 5 times lower than normal CT. Today, CBCT scanning has become a valuable imaging modality in periodontology as well as implantology. For the detection of smallest osseous defects,
CBCT can display the image in all its three dimensions by removing the disturbing anatomical structures and making it possible to evaluate each root and surrounding bone. In implant treatment, appropriate site or size can be chosen before placement, and osseointegration can be studied over a period of time.[3]

**PRINCIPLES AND IMAGE PROCESSING OF CBCT**

CBCT uses a single, relatively inexpensive, flat-panel, or image intensifier radiation detector. CBCT imaging is performed using a rotating platform to which the X-ray source and detector are fixed. As the X-ray source and detector rotates around the object, it produces multiple, sequential, and planar images that are mathematically reconstructed into a volumetric dataset. A single rotational sequence would capture enough data for volumetric image construction. The entire scanning of the target region is performed in a single rotation thereby significantly reducing the radiation exposure. Further, the exposure is reduced by 50% (0.0037 mGy) if a 180° scan is performed instead of 360°. In comparison, the radiation exposure in a digital panoramic radiograph is around 0.0063 mGy and around 0.0012 mGy in a periapical radiograph. It has been reported that for an intraoral status of the entire dentition an effective dose ranging from 33 to 84 Sv is required.[1]

**CBCT Image Production**

CBCT machines scan patients in the following three possible positions: Sitting, standing, or supine. Despite patient orientation within the equipment, the principles of image production remain the same. The four components of CBCT image production are as follows.

**Acquisition Configuration**

Continuous or pulsed X-ray beam and charged couple device detectors moving synchronously around the fixed fulcrum within the patient’s head.

**Image Detection**

It is determined by individual volume elements or voxels produced from the volumetric data set. CBCT units provide voxel resolutions that are isotropic (equal in all three dimensions).

**Image Reconstruction**

The processing of acquired projection frames to the volumetric dataset is done on the personal computer which is called as reconstruction.

**Image Display**

The compilation of all available voxels is presented to the clinician on the computer screen as secondary reconstructed images in three orthogonal planes.[2]

**INDICATIONS/ADVANTAGES/ DISADVANTAGES OF CBCT**

**Indications**

- 3D view of teeth position and structure
- Evaluation before the implant placement
- Endodontic evaluation
- Periodontal evaluation
- Evaluation of bone resorption
- Determination of anatomic bone sizes
- Study of the airways
- Positioning of temporary anchoring devices
- Cephalometric analyses
- 3D reconstructions
- Evaluation of jaw bones for
  - Pathology
  - Bony and soft tissue lesions
  - Recognition of fractures and structural maxillofacial deformities
  - Assessment of temporomandibular joint
  - Assessment of inferior alveolar nerve

In short, CBCT is ideally suited for high-quality and affordable CT scanning of the head and neck in dentomaxillofacial applications.[1,3]

**Advantages**

Following advantages are offered by CBCT,[2,3]

- It has a rapid scan time as compared with panoramic radiography.
- It gives complete 3D reconstruction and display from any angle.
- Its beam collimation enables limitation of X-radiation to the area of interest.
- Image accuracy produces images with submillimeter isotropic voxel resolution ranging from 0.4 mm to as low as 0.076 mm.
- Reduced patient radiation dose (29–477 μSv) as compared with conventional CT (approximately 2000 μSv). Patient radiation dose is 5 times lower than normal CT, as the exposure time is approximately 18 s, that is, one-seventh the amount compared with the conventional medical CT.
- CBCT units reconstruct the projection data to provide interrelational images in three orthogonal planes (axial, sagittal, and coronal).
- Multiplanar reformation is possible by sectioning volumetric datasets nonorthogonally.
- Multiplanar image can be “thickened” by increasing the number of adjacent voxels included in the display,
Thakkar, et al.: Cone-beam Computed Tomography

referred to as ray sum.

• 3D volume rendering is possible by direct or indirect technique.
• The three positioning beams make patient positioning easy. Scout images enable even more accurate positioning.
• Reduced image artifacts: CBCT projection geometry, together with fast acquisition time, results in a low level of metal artifact in primary and secondary reconstructions.

Disadvantages
1. The high cost compared to that of standard 2D radiographies.
2. It cannot offer a resolution with increased contrast, and also it is not indicated in the exploration of soft tissues but only in the exploration of bone tissue in the maxilla-facial sphere.
3. A significant disadvantage of CBCT is represented by the artifacts that may be present on the image - not due to the scan, but to the presence of implants, restorations from the amalgam, metallic prosthetic restorations, or endodontic treatments. These artifacts are characterized by hyperdense lines and dark images, which affect the quality of the desired image.\(^5\)

PERIODONTAL APPLICATIONS

CBCT in Assessment of Periodontal Ligament (PDL) Space
The earliest signs of periodontal disease in radiographs are fuzziness, break in the continuity of lamina dura, and a wedge-shaped radiolucent area at the mesial and distal aspect of the PDL space. In addition to this, the proper observation of PDL space may offer some potential regarding detection of occlusal trauma and the effects of systemic diseases on the periodontium.\(^2\) Therefore, only a sensitive imaging technique would be able to detect the earliest changes in the PDL space. The conventional intraoral radiographs have some significant disadvantages including the overlap of anatomical structures due to the positioning of the X-ray tube. Furthermore, there could be errors related to the chemical processing and patient positioning.\(^1,^4\)

CBCT for Periodontal Defect Measurements
The extent of periodontal marginal bone loss is not always easy to determine and certainly not the extent with which furcation areas are involved with the conventional radiographic methods.\(^2\) CBCT images provide better diagnostic and quantitative information on periodontal bone levels in 3D than conventional radiography.\(^3\)

The periodontal defects as seen in conventional radiography are short of accuracy in terms of 3D architecture of the bone morphology. In CBCT, the bony plates, buccal, and lingual can be visualized with accuracy and any discrepancy can be anticipated before surgical exposure. Furthermore, the defect morphology can be studied in all axial planes with the advent of CBCT modalities. Furthermore, the volumetric analysis of the defect depth preoperatively and postoperatively can lead to a better understanding of the functioning of bone graft eliminating the need of surgical reentry, which can also be useful for treatment planning.

Noujeim et al.\(^6\) created periodontal lesions of different depths in dried human mandibles and analyzed them using intraoral radiography and CBCT. They found that CBCT was more accurate in detecting the defects than the conventional radiograph.

Stavropoulos and Wenzel\(^7\) evaluated the accuracy of CBCT scanning with intraoral periapical radiography for the detection of periapical bone defects. CBCT was found to have better sensitivity compared to intraoral radiography.

Leung et al.\(^8\) evaluated the accuracy and reliability of CBCT in the diagnosis of naturally occurring bone defects by comparing the difference between the CBCT measurements and measurements made directly on the skulls. They reported that CBCT measurements were not as accurate as direct measurements on skulls. A certain discrepancy between direct measurements and estimated measurements on radiographs has to be considered as clinically acceptable.

Vandenberghe et al.\(^9\) studied 30 periodontal bone defects of two adult human skulls using intraoral digital radiography and CBCT. Periodontal bone levels and defects on both imaging modalities were assessed and compared to the gold standard. The study concluded that the intraoral radiography was significantly better for contrast, bone quality, and delineation of lamina dura, but CBCT was superior for assessing crater defects and furcation involvements.

CBCT in Measuring Periodontal Bone Levels
Sufficient alveolar bone volume and favorable architecture of the alveolar ridge are essential to obtain ideal functional and esthetic prosthetic reconstruction.\(^1\)

Persson et al.\(^11\) reported that conventional radiographic images provided a better resolution of the bone levels than what can be achieved from computer screen images.

Mol and Balasundaram\(^10\) compared the image quality between CBCT and conventional radiography in the
assessment of alveolar bone levels. They found that CBCT provided slightly better diagnostic and quantitative information on periodontal bone levels in three dimensions than conventional radiography.

Vandenberghe et al.\(^9\) reported that CBCT images demonstrated more potential in the morphological description of periodontal bone defects, while the digital radiography provided more bone details.

Soft tissue CBCT for the measurement of gingival tissue and the dimensions of the dentogingival unit.

This novel method is based on CBCT technology called soft tissue CBCT, to visualize and precisely measure distances corresponding to the hard and soft tissues of the periodontium and dentogingival attachment apparatus. With this simple and noninvasive technique, clinicians are able to determine the relationships between:

1. Gingival margin and the facial bone crest,
2. Gingival margin and the cementoenamel junction (CEJ),
3. CEJ and facial bone crest.

The width of the facial and palatal/lingual alveolar bone and the width of the facial and palatal/lingual gingival also could be measured.\(^3\)

**CBCT Precision in Alveolar Bone Density Measurement**

Radiographic follow-up of bone healing after grafting is challenging because of the overlapping of gaining and losing areas within the graft. The new volumetric imaging method, CBCT, offers an opportunity to see inside the bone and pinpoint and measure densities in small localized areas such as a vertical periodontal defect, or an alveolar bone graft. This precision would make it possible to reproducibly quantify the bone remodeling after bone grafting.\(^2\)

**CBCT for Diagnostic Imaging for the Implant Patient**

Cross-sectional imaging modalities that include conventional X-ray tomography, computed tomography, and CBCT are valuable imaging modalities. Of all the three, CBCT scanning is the most successful, useful, and valuable imaging modality for 3D and cross-sectional evaluation of the implant patient. It has similar advantages and disadvantages as CT scanning. The most significant difference is that CBCT imaging requires much less radiation exposure. Location is the most important factor while placing an implant. From 3D planning to CT-directed placement, to take the advantage of available bone and avoid anatomic structures, the science of implantology has been revolutionized by 3D imaging. Not only has it added safety and accuracy, it has also minimized or eliminated the need for supportive procedures like bone and tissue grafting in many situations. Software and technology development trends suggest that in the near future, CBCT scans will be used to develop a patient-specific 3D model that will be used for implant diagnosis, treatment planning, treatment simulation, implant placement (surgery), and tooth replacement (restoration of implant).\(^2\) Furthermore, the risk determination for osteoporotic patients can be predetermined by analyzing the density of bone. Clinicians have been diagnosing, treatment planning, placing, and restoring modern dental implants using periapical and panoramic imaging films to assess bone anatomy for several decades. Two-dimensional film images have been found to have limitations because of inherent distortion factors, and the noninteractive nature of film itself provides little information regarding bone density, bone width, or spatial proximity of key structures. Diagnostic imaging techniques must always be interpreted in conjunction with good clinical examination. Many factors influence the selection of radiographic techniques for a particular case, including cost, availability, radiation exposure, and case type. The decision is a balance between these factors and the desire to minimize risk of complications to the patient.

**CONCLUSIONS**

As CBCT scanning is finding more and more applications in dentomaxillofacial radiology, it stands as the privileged field of imaging in periodontics. Current methods of detecting alveolar bone level changes over time or determining 3D architecture of osseous defects are inadequate. This issue has been addressed by the recent low-cost CBCT machines, which has resulted in production of an affordable, low-radiation high-quality 3D data. CBCT is an essential diagnostic tool also for selection of implant design and its placement. CBCT provides high quality of diagnostic images that have an absorbed dose that is comparable with other dental surveys and less than a conventional CT and thus following the principles of radiation protection to reduce the radiations “as low as reasonably achievable” (ALARA). To conclude, CBCT with its high spatial resolution, affordability, smaller size, lower acquisition, and maintenance has made it as a natural fit in periodontal imaging.

**REFERENCES**


Source of Support: Nil, Conflict of Interest: None declared.