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Case Report

# A Fatty Spectacle – A Rare Case of Co-occurance of Tibialis Anterior Tendon Sheath Lipoma and Fibrolipomatous Hamartoma of Superficial Peroneal Nerve

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## Abstract

Fibrolipomatous hamartoma of nerve is a rare occurrence with only a few reported cases in literature, mostly described in the median nerve. Tendon sheath lipoma is an even rarer entity, mostly described in hands and wrist, with tibialis anterior tendon sheath lipoma being nearly unreported. In the following case report, we present a serendipitous concurrence of these two rare pathologies in one individual without any familial or syndromic association. To the best of our knowledge, such a presentation has not been reported so far.

**Key words:** Fibrolipomatous hamartoma, Musculoskeletal, Synovial lipoma, Tendon sheath lipoma

## CASE SUMMARY

A 28-year-old male presented with multiple long standing, painless, solid swellings in the left distal leg, ankle, and foot region, involving dorsum of foot, the lateral malleolus and anterolateral distal leg. There was no history of prior trauma to the region, no functional disability due to swellings, and no significant family history. On examination, no discoloration, prominent vessels, or pus points were seen. Elongated swelling on anterolateral aspect of leg only moved in direction perpendicular to shin of tibia. All the swellings were non-tender.

On ultrasound, elongated swelling on anterolateral aspect of leg and foot appeared hyperechoic with interspersed hypoechoic linear bands. Incidentally, hyperechoic lesion was seen within tibialis anterior tendon sheath, running along the tendon. Few well-defined homogeneous hyperechoic subcutaneous swellings showing reticulations, representing subcutaneous lipomas were also seen around the ankle joint [Figures 1 and 2].

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Magnetic resonance imaging (MRI) was performed which reinforced the ultrasound findings. Axial, coronal, and sagittal images showed fat signal intensity lesion within tibialis anterior tendon sheath – suggestive of tibialis anterior tendon sheath lipoma. The superficial peroneal nerve running lateral and superficial to tibialis anterior tendon was thickened and showed classical "coaxial cable" and "spaghetti appearance" which is suggestive of fibrolipomatous hamartoma. Few subcutaneous lipomas were also noted [Figures 3 and 4].

## DISCUSSION

Lipomas are proliferation of adipose tissue usually surrounded by a fibrous capsule and are the most common benign mesenchymal neoplasms. These are just the tip of the iceberg in a spectrum of lipomatous lesions. Benign lipomatous lesions of the soft tissue can be classified into nine distinct categories, which are lipoma, lipomatosis, fibrolipomatous hamartoma of the nerve, lipoblastoma or lipoblastomatosis, angiolipoma, myolipoma, chondroid lipoma, spindle cell lipoma or pleomorphic lipoma, and hibernoma.[1] Benign lipomatous lesions affecting the

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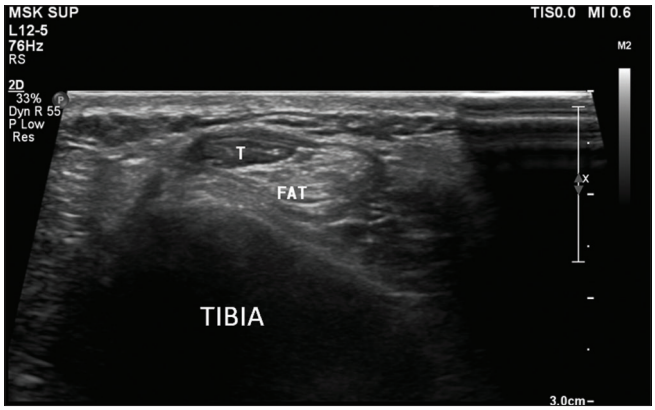


**Figure 1: Ultrasound image perpendicular to shin of tibia showing tibialis anterior tendon sheath with hypoechoic tendon and echogenic fat inside the tendon sheath**

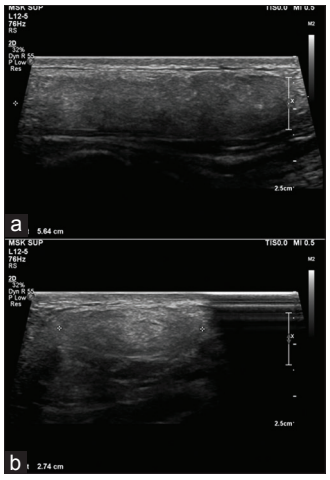


**Figure 2: Longitudinal (a) and transverse (b) ultrasound images of elongated chord-like hyperechoic lesion on anterolateral aspect of leg, ankle, and foot showing few hypoehoic linear areas**

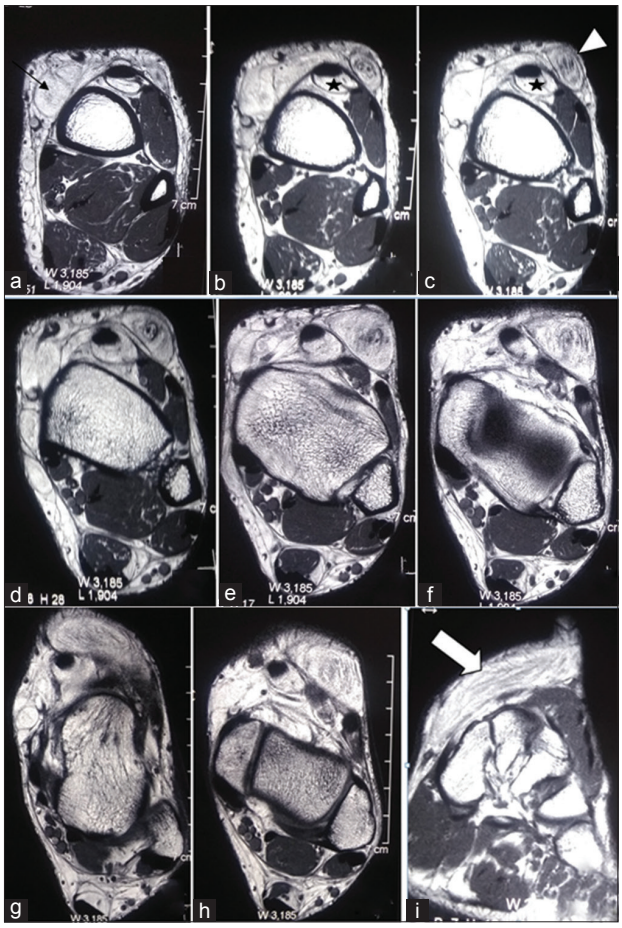


**Figure 3: (a-i): Axial (a-h) and coronal (i) T2-weighted magnetic resonance images of the left ankle joint showing hyperintense signal inside the tibialis anterior tendon sheath (star ★). Adjoining superficial peroneal nerve appears thickened and shows "coaxial cable" (arrowhead) and "spaghetti" appearance (white block arrow). Few subcutaneous lipomas are noted on medial aspect of ankle joint (black arrow)**

bone, joint, or tendon sheath are much rarer and include intraosseous lipoma, parosteal lipoma, liposclerosing myxofibrous tumor, synovial lipoma of the joint or tendon sheath, and lipoma arborescens.[2]

Subcutaneous lipomas are very frequently encountered as long-standing asymptomatic swellings on trunk and extremities. On the contrary, deeper soft-tissue lipomas are rare and depending on their location, can cause pressure symptoms – like carpal tunnel syndrome in median nerve fibrolipomatous hamartoma.[3] A case report of tendon sheath lipoma causing De Quervain's tenosynovitis has also been reported.[4]

Like most neoplasms, lipomas can be attributed to have genetic origin. Recent studies have shown a correlation between HMGA2 gene located on chromosome 12q14.3 and lipoma production. Another gene EHD-1, which interacts with insulin-like growth factors is purported to have a role in etiopathogenesis of tendon sheath lipomas.[5] Besides genetic link, another theory suggests that there is a direct positive correlation between trauma to an area and lipoma production. In addition to these, other possible risk factors that may lead to lipomas are obesity, alcohol abuse, liver disease, and diabetes mellitus.[6]

Lipomatous lesions are usually sporadic in occurrence. Multiple lipomatous lesions should prompt further evaluation of inherited conditions such as Proteus syndrome, familial hereditary lipomatosis, Decrum's disease, Madelung's disease, Cowden syndrome, and Gardner syndrome.[7]

## Synovial Lipoma

Synovial lipomas are a rare entity and can have two distinct presentations – a focal solid fatty mass in tendon sheath and diffuse proliferating fatty synovial thickening, called "lipoma arborescence" typically seen in knee joint.[8]

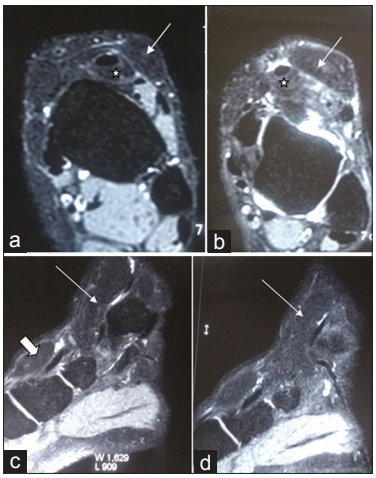


**Figure 4: Axial (a and b) and sagittal (c and d) fat-saturated magnetic resonance images of the left ankle joint showing suppression of signal in all the previously described lesions, suggesting fat component. The hyperintense lesion in tibialis anterior tendon sheath shows loss of signal on fat saturation which is suggestive of tendon sheath lipoma (star ☆). Loss of signal is also seen in thickened superficial peroneal nerve (arrow) suggesting fatty infiltration. Subcutaneous swelling also shows loss of signal on fat-saturated images verifying it's a lipoma (black arrow)**

Due to their asymptomatic nature and infrequent occurrence, lipomas of tendon sheath can go unreported. True discreet intra-articular lipoma is quite rare and reported more frequently in hand and wrist and infrequently in foot or ankle.[9] These are discrete lipomatous masses, with imaging features similar to those of a superficial or deep lipoma.

On ultrasound, these can be seen along superficial tendons as hyperechoic structures showing few reticulations similar to surrounding fat and no internal vascularity on color Doppler. On computed tomography images, these can be identified by their fat attenuation and appear hypodense to muscles and tendons. They follow fat signal intensity on all MRI sequences, appearing hyperintense on T1, T2, and PD sequences and hypointense on fat-saturated images. Rarely, they may show fluid-like signal intensity which has been attributed to mucoid degeneration.[10]

Lipoma arborescence is the other presentation of synovial lipoma. It is a benign collection of fat replacing the subsynovial layer, resulting in diffuse villonodular proliferation in the synovium that has a frond-like architecture. It affects joints more commonly rather than tendon sheath and is frequently associated with synovial effusion. Cases of extra-articular lipoma arborescens involving peroneal and flexor ankle tendon sheath, subdeltoid bursa, extensor tendon sheath of the hand, and biceps tendon sheath have been reported. Unlike tendon sheath lipoma which is well-defined lesion, lipoma arborescence involving tendon sheath has frond-like architecture.[11-15]

Asymptomatic tendon sheath lipoma can be managed conservatively. Treatment of symptomatic lipoma is surgical excision.[16]

### Fibrolipomatous Hamartoma

Fibrolipomatous hamartoma of nerve, as the name implies, is benign hamartomatous deposition of adipose tissue inside a peripheral nerve. The adipose tissue is deposited in between perineural fibers causing expansion of nerve and giving it classical "coaxial cable" appearance on axial sections and "spaghetti appearance" on coronal and sagittal sections.[17]

On MRI, the affected nerve appears thickened and shows discrete T1, T2 hypointense nerve fascicles surrounded by hyperintense adipose tissue. On fat suppression and inversion recovery sequences, the fat signal is suppressed. On ultrasound, the affected nerve appears echogenic and shows hypoechoic discrete fascicles corresponding to MRI appearance.[18]

Median nerve is the most common nerve to be affected. Two-thirds of affected nerves are associated with macrodystrophia lipomatosa.[19] Motor nerves are more frequently involved than sensory nerves. Depending on location, this lesion may be asymptomatic or cause compression neuropathies like carpal tunnel syndrome.[20]

Although mostly described as individual or isolated nerve involvements, rarely, fibrolipomatous hamartoma can be diffuse and involve nerve plexuses such as the brachial plexus or lumbosacral plexus and its branches. Such extensive fibrolipomatous hamartomas can be differentiated from plexiform neurofibromas by the relatively well-defined appearance of affected nerves which are encased in epineurium and maintain their shape as opposed to plexiform neurofibromas which are large irregular masses and do not show signal suppress on fat-saturated images. Association of plexiform neurofibroma with type 1 neurofibromatosis and fibrolipomatous hamartoma with macrodystrophia lipomatosa can also aid the differentiation. Signal loss on fat-saturated images also differentiates fibrolipomatous hamartoma from hereditary hypertrophic interstitial neuritis.[21]

Due to the fact that the lesion is interspersed within the nerve fibers, excision is rarely the treatment option and results in sensory and motor deficits. Management is focused on symptomatic treatment like nerve decompression.[22]

**Table 1: Multiple lipoma syndromes**

| Lipomatosis syndrome | Salient features |
|---|---|
| Proteus syndrome | Multiple lipomas, hemangiomas, epidermal naevi, scoliosis, hyperostosis of epiphysis and skull |
| Decrum's disease | Multiple painful lipomas of trunk and extremities, often with paresthesia of overlying skin |
| Familial multiple lipomatosis | Autosomal dominant inherited disorder. Typically presents in third decade with hundreds of non-infiltrating lipomas |
| Madelung's disease | Diffuse, infiltrative, symmetric, painless lipomas involving face, neck, and shoulder |
| Cowden syndrome | Multiple lipomas, oral papillomas, facial trichilemmomas, hamartomatous polyps of the gastrointestinal tract and breast, endometrial and thyroid carcinomas |
| Bannayan-Riley-Ruvalcaba syndrome | Multiple lipomas, intestinal hamartomas, genital lentigines, macrocephaly, and mental retardation |
| Gardner syndrome | Gastrointestinal polyposis, osteomas, multiple lipomas, epidermoid cysts, desmoids tumors |

### Lipomatosis Syndromes

Multiple lipomas can be a manifestation of various syndromes, salient features of some of these are tabulated in Table 1.[23-31]

## CONCLUSION

Although very common in subcutaneous plane, lipomas of deep soft-tissue structures such as tendon sheath and nerves are rare entities. Due to their asymptomatic nature and infrequent occurrence, lipomas of tendon sheath can go unreported. Fibrolipomatous hamartoma of nerve affects motor nerves more than sensory nerves and is associated with macrodystrophia lipomatosa in two-third of cases. As the lesion is interspersed within the nerve fibers, excision is rarely the treatment option and management is focused on symptomatic treatment like nerve decompression. Multiple lipomatous lesions should prompt further evaluation for inherited and syndromic conditions. The characteristic radiological appearance usually obviates the need for histopathological confirmation by biopsy. Although two rare forms of lipoma – tendon sheath lipoma and fibrolipomatous hamartoma, both were present in this case along with few subcutaneous lipomas, there was no familial or syndromic correlation. To the best of our knowledge, such a presentation has not yet been reported.

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Case Report

# A Free-floating Intravitreal Cyst in Adult Female: (A Ball in the Vitreous)

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## Abstract

A 49-year-old female presented with floaters in LE for 2 months. The uncorrected visual acuity was 6/6 in RE and 6/6p in LE. Ophthalmological examination of both eyes revealed a normal anterior segment. Fundus examination with slit-lamp biomicroscopy with a 90D lens was normal in the right eye, but in the left eye, a single oval cyst with pigmented walls was seen floating freely in the mid-vitreous. B-scan ultrasound showed a round uniloculated cyst with high-intensity echoes on its walls with no internal reflectivity, it was free from surrounding vitreous strands or retina and situated at the posterior vitreous. No evidence of scolex was noted. ELISA for *Echinococcus* and *Taenia solium* was negative. MRI brain was normal. Hence, a clinical diagnosis of an intravitreal cyst was made and the patient is coming on regular follow-up.

**Key words:** Intravitreal cyst, Pigment epithelial cyst, Vitreous opacity

## INTRODUCTION

Intravitreal cysts can be of two types congenital and acquired. Congenital cysts are remnants of the hyaloid vascular system such as Bergmeister's papilla and Mittendorf's dot and are sometimes present in normal eyes noticed incidentally on routine ocular examination.[1] Acquired cysts may occur in various conditions such as ocular trauma, inflammatory diseases such as toxoplasmosis or intermediate uveitis. They can also be associated with degenerative diseases of the retina and choroid, like high myopia with uveal coloboma and retinal detachment surgeries.[2] Here, we present a rare case of an intravitreal cyst (pigment epithelial cyst).

## CASE REPORT

A 49-year-old female presented with floaters in the left eye for 2 months. History of ocular trauma or inflammation was negative. The uncorrected visual acuity was 6/6 in the right eye and 6/6P in the left eye. Ophthalmological examination of both eyes showed a normal anterior segment. Fundus examination with slit lamp bio-microscopy with 90D lens was unremarkable in the right eye while in the left eye, a single oval cyst of size 8 DD with pigmented walls was identified floating freely in the mid-vitreous [Figure 1]. Red free Fundus photo showed Increased pigmentation of the cyst wall [Figure 2].

### Investigations

B-scan ultrasound showed round uniloculated cyst with high-intensity echoes on its walls with no internal reflectivity [Figure 3]. It was free from surrounding vitreous strands or retina and situated at the posterior vitreous. No evidence of scolex was noted.

TC, DC, and ESR were normal. ELISA for *Echinococcus* and *Taenia solium* was negative. MRI brain was normal and no evidence of cyst was present.

## DISCUSSION

Intraocular cysts are classified into three categories according to positions they are present – anterior chamber cyst, retrolental space cyst, and a vitreous cyst. Vitreous cysts are a sufficiently uncommon ocular disorder to be considered an

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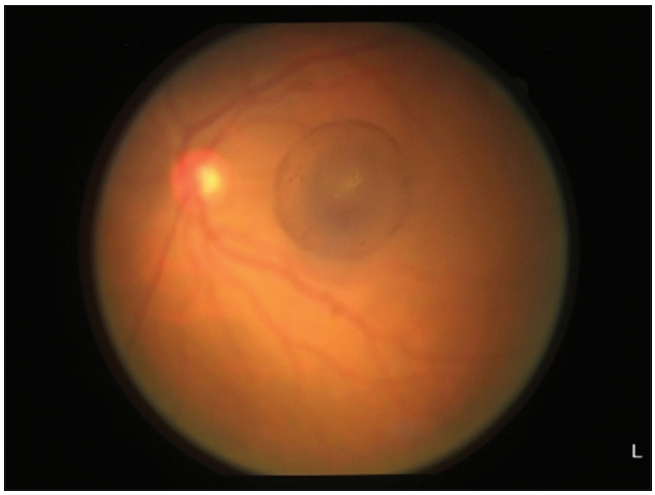

**Figure 1: LE shows a single cyst in the vitreous cavity with pigmented walls floating freely**

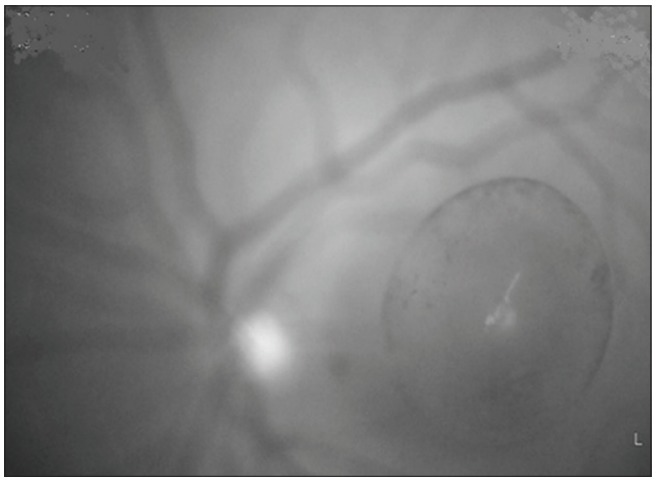

**Figure 2: Red free picture after 2 months follow-up**

"ocular curiosity." This condition has been seen to occur in younger patients of 6–8 years old[3-5] although it can be seen in any age group, common in 10–20 years of age. They can be single monolateral, single bilateral, and multiple monolateral. Cyst measurement ranges from 0.15 mm to 12 mm, and shapes may be from spherical, lobulated, or oval, and the cyst surface can be smooth or sharp. Cysts can be nonpigmented (yellow-gray) or pigmented (brown) appearance.

In our case, the cyst is unilateral, pigmented, and there is no evidence of progression except for increased pigmentation on a subsequent visit [Figures 4 and 5].

In symptomatic patients, laser photocystotomy or pars plana vitrectomy with cyst excision can be done as a treatment modality. As our case did not have any symptoms other than occasional floaters without affecting the vision, she was treated conservatively and is on regular follow-up.

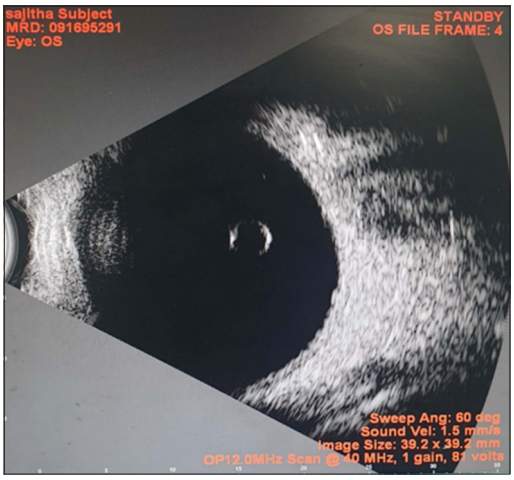


**Figure 3: B-scan shows free-floating cyst in mid-vitreous**

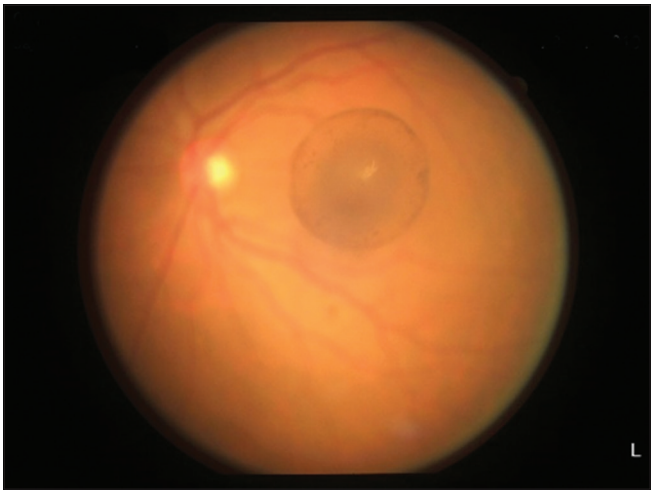

**Figure 4: Patient came for follow-up after 2 weeks. No change in shape and size noted**

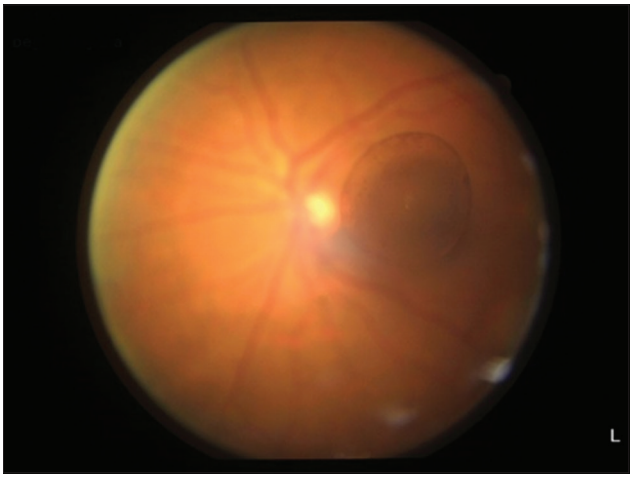

**Figure 5: Patient came for follow-up after 2 months. Increased pigmentation with no change in shape and size noted**

This case is presented for its rarity, as only a few approx.50 cases have been reported in the literature. And also, to stress the harmless nature of idiopathic vitreous cysts which do not require unnecessary aggressive surgical intervention.

## CONCLUSION

A middle-aged women who presented with complains of floaters in the left eye for 2 months was diagnosed with idiopathic intravitreal pigment epithelial cyst after ruling out infective causes by serological tests and neuroradiological investigations and history of trauma was absent. Presently, as the patient is not having any complaints except for occasional floaters with an unaided visual acuity of 6/6, she is kept under regular follow-up.

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Case Reports

# Ozone Oil: The Marvel Oil for Temporomandibular Joint Disorders

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## Abstract

Each day is an adventure in the medical and dental world. Every second an idea is spurred and within days an innovation takes birth. One such miracle is "Ozone Oil;" relatively new but containing immense potential in relieving pain in temporomandibular joint (TMJ) pain disorders. Ozone oil therapy is a non-pharmacological treatment protocol that has as anti-inflammatory and analgesic effects over the TMJ joint. These properties of ozone are attributed to its ability to oxidize the double bound compounds as arachidonic acid involved the inflammation process, thereby alleviating the pain. Here, we present two case reports of patients clinically diagnosed with the TMJ pain, (as per the research diagnostic criteria) and considered as transition-minimized differential signaling. After thorough investigations were done and later patient was subjected to the treatment with ozone oil therapy, as an innovative and non-invasive approach.The results showed as tremendous improvement in tenderness of masticatory muscles and on the pain (visual analog scale [VAS] scale) was found in both the patients. We concluded that ozone oil therapy because of it non-invasiveness, easy application and promising results could prove to be an innovative approach in treating the TMJ pain (musculoskeletal) disorders.

**Key words:** Orofacial pain, Ozone oil, Research diagnostic criteria, Temporomandibular joint disorder, Therapeutic ultrasound massage therapy, Transcutaneous electrical nerve stimulation, Visual analog scale

## INTRODUCTION

Orofacial pain is one of the most commonly attended chronic disorders in a dental set up. However, as common as it is, its diagnosis and treatment are equally daunting. Among diverse types of orofacial pain, one of the most common is the temporomandibular pain.

Temporomandibular pain disorder is impacted by multiple parameters such as stress, emotional disturbances, malocclusion, and hyperactivity of masticatory muscles, along with interplay of predisposing and perpetuating components.

Due to the complex nature of temporomandibular joint (TMJ) disorders, the diagnosis becomes challenging for the clinician. Therefore, a thorough knowledge and understanding of this disease process becomes essential to dispense appropriate treatment to the patient.

Over the years, wide range of treatment modalities has been utilized to render relief from the disturbing pain of TMJ, including pharmacological methods, behavioral corrections, orthodontontic corrections, and physical therapies as transcutaneous electrical nerve stimulation and therapeutic ultrasound massage therapy.[1]

Recently, a new entity is being acknowledged in the field of TMJ Disorders, that is, the ozone oil. Being a non-invasive modality, it could be a boon to the patients and clinicians dealing with the temporomandibular pain.

### Ozone Oil

The history of ozone therapy in medical literature dates back to the 19th century. Dutch physicist Martin van Marun in 1785, made its first mention. However, the formulation of ozone by the oxygen gas was first demonstrated by Christian Friedrich Schonbein in 1840, a Professor in University of Basel.[2] He also introduced

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the world to the Greek work, "OZEIN," meaning odor.[3,4]

Since years, ozone is being used in the form of gas, water, and oil in various fields of medical and dental science. The pharmacological benefits of ozone are attributed to its anti-inflammatory and analgesic effects.

Anti-inflammatory action is because of its potential to oxidize double bond compounds of arachidonic acid and other derivatives present at the inflammatory sites, thus resolving the pH. Plus, it oxidizes the product of albuminolysis produced at the nerve ending, therefore, manifesting its analgesic trait.[5,6]

In the history of its application in the field of dentistry, the ozone has been utilized only in the form of gas and water. Even in treating the TMJ disorder, the literature reveals its application mostly in the water form.[7,8] The administration of ozone oil has been limited to the dermatological and cosmetology purposes.[9] From the reviewed literature, it was found that there are only few mentions in regard to the application of ozone oil as a treatment modality for TMJ disorder (Musculoskeletal group).[10]

Therefore, as an innovative approach, an attempt was made to study the effectiveness of ozone oil as a treatment modality for TMJ disorders.

## CASE REPORTS

### Case Report 1

A 30–year-old male patient reported to the Department of Oral Medicine and Radiology, Teerthanker Mahaveer Dental College and Research Centre, with the chief complaint of pain on the left side of the face in the preauricular region since 5 years. The history of present illness was revealed as pain is of dull continuous nature that aggravated on chewing, especially hard food stuff and relieved by analgesics. The pain radiated to the temporal and facial region of left side involving the TMJ region. There was no contributory medical and dental histories were noncontributory.

However, personal history mentioned the habit of occasional tobacco chewing (3 packs/weeks, since 10 years). Extra-oral examination revealed tenderness over temporal muscle. No significant deviation on jaw opening or closing was present. On the intra-oral examination, oral hygiene was compromised with no mucosal changes were noted. However, on intra-oral palpation of the left lateral pterygoid is also tender on left side. The pain score was recorded according to the visual analog scale (VAS) scale. These measurements were tabulated and entered into the preformed given [Tables 1 and 2]. It was provisionally diagnosed as myofascial pain dysfunction syndrome (MPDS) of the left lateral pterygoid and left temporal muscle was given.

The diagnosis was made according to the Research Diagnostic Criteria, given by Leresche *et al.* 1992.[11]

### Case Report 2

A 42-year-old female reported to the Department of Oral Medicine and Radiology, Teerthanker Mahaveer Dental College and Research Centre, Moradabad, with the chief complaint of pain on right side of her face since 2 years. She also complained of difficulty in mouth opening since a year. On history of present illness, the patient had continuous dull ache that aggravated on talking and chewing.

She gave history of extraction in her lower right back tooth region 3 years back which was uneventful. No other contributory history was given. On extra-oral examination, her mouth opening was reduced along with tenderness over the right temporalis and masseter muscles. No deviation on mouth opening was noticed.

On intra-oral examination, her oral hygiene was seen to be compromised. 16, 22, 26, 46, and 47 were found to be missing and lateral pterygoid muscle is tender on palpation on right side. The tenderness was graded as mild, moderate, and severe. The pain score was recorded according to the VAS scale and entered the measurements in the pro forma given [Tables 1 and 2].

On the basis of the history given by the patient and clinical examination done, a diagnosis of MPDS of right temporalis and masseter was given.

### Treatment

Both the patients were advised to initiate the ozone oil therapy.

### Method of Application

Patient was asked to take the oil in pea-drop concentration and apply over the affected area, 3 times a day.

Patients were recalled after 5 days for five subsequent visits.

Massaging of oil was prohibited.

In addition to the ozone oil application:

First Patient: Habit counseling was done and he was referred to the department of periodontics for oral prophylaxis.

**Table 1: Tenderness table**

| Tenderness and pain chart | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Cases** | **Visits** | **Masseter** | | **Temporalis** | | **Lateral pterygoid** | | **Medial pterygoid** | |
| | | **Right** | **Left** | **Right** | **Left** | **Right** | **Left** | **Right** | **Left** |
| Case 1 | 1st visit | | | | Severe | | Severe | | |
| | 2nd visit | | | | Moderate | | Severe | | |
| | 3rd visit | | | | Moderate | | Moderate | | |
| | 4th visit | | | | Mild | | Mild | | |
| | 5th visit | | | | No pain | | No Pain | | |
| Case 2 | 1st visit | Moderate | | Severe | | | | | |
| | 2nd visit | Mild | | Moderate | | | | | |
| | 3rd visit | Mild | | Mild | | | | | |
| | 4th visit | Mild | | Mild | | | | | |
| | 5th visit | No Pain | | No Pain | | | | | |

**Table 2: Pain table**

| | 1st visit | 2nd visit | 3rd visit | 4th visit | 5th visit |
|---|---|---|---|---|---|
| Case 1 | 8 | 7 | 5 | 2 | 0 |
| Case 2 | 7 | 5 | 3 | 1 | 0 |

Second Patient: It was referred to the department of periodontics for oral prophylaxis and department of prosthodontics for replacement of missing teeth.

## DISCUSSION

Both these cases were clinically diagnosed as MPDS, which is musculoskeletal disorder in the broad spectrum of TMJ disorder. The diagnosis was based on the research diagnostic criteria.

Both the patients were referred for the oral prophylaxis and in the case of second patient; habit counseling was done in the first case and in the second case, patient was also referred for tooth replacement, as chronic tobacco chewing and missing teeth could be a contributing factor in history of chronic pain respectively.

As the main treatment protocol, both were advised to apply ozone oil in the instructed manner for a period of almost 1 month. In this duration, patient was recalled for visits, and tenderness and pain were recorded in the given chart.

It was observed that in the second visit itself, tenderness and pain were significantly reduced, except in the case of tenderness in left lateral pterygoid muscle in the first case. Subsequently, in the third and fourth visits, score on both the parameters were reported to be negligible and by the final visit, patients reported complete relief in pain.

Moreover, in both the cases, patients expressed the ease of the application of ozone oil. No side effects were reported. Although, it was advised to them not to massage the oil over a specific area for longer duration as it might increase the local temperature, which could manifest in the form of skin allergy. However, no such incidence of side effects was reported.

## CONCLUSION

Since time immemorial ozone is being used as a treatment modality for various medical and dental ailments. However, the use of ozone oil was limited apart from dermatological or cosmetic purposes. Therefore, an attempt was made to gauge the potential of the oil in field of temporomandibular pain disorder.

Because of its excruciating and disturbing nature, the TMJ pain disorder, often pose a dilemma before clinicians regarding the choice of appropriate and convenient treatment protocol.

Ozone oil, being a non-invasive modality and because of its relative ease of application, can prove to be a marvel modality. Nevertheless, wide range of studies is needed to be done to evaluate its true efficacy.

Therefore, on the one hand, the presented case reports display the immense capabilities of the ozone oil in relieving the temporomandibular pain disorder (musculoskeletal) and, on the other hand, it provokes an idea for future explorations.

### Ethical Clearance

Approved from the ethical committee.

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Original Article

# Epidemiology of Traumatic Dental Injury Patients Attending to the Department of Conservative Dentistry and Endodontics

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## Abstract

**Objective:** The aim of this study was to evaluate traumatic dental injuries (TDIs) and factors affecting the permanent dentition of patients with TDIs attending a dental department.

**Methods:** All patients with TDIs, who attended the Department of Conservative Dentistry and Endodontics, School of Dental Sciences, Chitwan Medical College, Bharatpur, Nepal, over a 5-year period from January 2014 to December 2018, were included in the study.

**Results:** A total of 274 TDIs patients in the age range of 14–70 years (mean 27.84 years) were included in this study. Evaluation of TDIs by age groups and gender found that the difference was not statistically significant $P = 0.243$. The most common etiology of TDIs was road traffic accidents (RTAs). The difference was not statistically significant ($P > 0.05$) on the assessment of the cause of trauma in terms of age distributions. Similarly, analysis of the frequency of the causes between the genders found no significant differences ($P > 0.05$). The most frequently observed TDIs were subluxation (18.91%) followed by uncomplicated crown fracture (18.43%). Injuries to the hard dental tissues and the pulp comprised 52.60% of injuries, whereas injuries to the periodontal tissues were seen in 47.39% of cases.

**Conclusion:** TDIs were found to most commonly affect the males of young age groups. RTA was the most common cause of TDIs. The maxillary central incisor was the most frequently injured teeth. Uncomplicated crown fracture was the most frequently observed TDIs. Injuries to the hard dental tissues and the pulp (fracture injuries) were more common than periodontal tissue injury. Therefore, restoration was the most frequently provided treatment.

**Key words:** Dental trauma, Epidemiology, Permanent teeth, Tooth injuries, Traumatic dental injuries

## BACKGROUND

Traumatic dental injuries (TDIs) include injuries to the tooth and its supporting structures. TDIs can range from enamel fractures to avulsion of teeth. Dental trauma comprises about 5% of all bodily injuries with oral injuries being the sixth most commonly injured body part.[1] TDIs may be at the fifth position if it is included in the list of most frequent diseases and injuries.[2]

The incidence of TDIs has risen during the past decades, according to a study by Glendor *et al.*[3] Different studies related to TDIs have shown significant variation in the incidence and prevalence rate of TDIs (6–59%) between studies and countries due to many factors.[4-7] Although TDIs have higher prevalence and incidence rates among children and adolescents compared to adults, different studies demonstrate that nearly one-third of adults experience trauma to the permanent dentition.[7] Due to its high prevalence among young patient, TDIs are considered as a public dental health problem.[3,7,8]

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Although TDIs are more common in young age groups (children and adolescents), it affects all age groups.[9] According to Lam, around 92% of TDIs occur before the age of 34.[10] Males experience TDIs more frequently than females, ratio (1.3–2.5:1).[7,8] TDIs can happen due to daily activities and events, which make it difficult to prevent.[3,11] The etiology of TDIs varies between and within a country.[12-14] TDIs are divided into seven fracture injury types and six luxation injury types.[3] Fracture injuries are frequently observed in permanent dentition, while luxation injuries are more common in the primary dentition.[3,10,15]

TDIs are dental emergencies because they frequently present as severe and complicated injuries. Hence, they require timely diagnosis and proper management to minimize complications and for better prognosis.[16,17] Treatment of TDIs is complicated, expensive, and difficult to predict; therefore, its consequences can impact the patient for a long time.[3,18-20] As a result, treatment of TDIs tends to be neglected and low rates of treatment are observed worldwide.[2]

Clinical studies related to TDIs in adults and permanent dentition is less and most countries lack sufficient data on the epidemiology of TDIs, particularly developing countries, according to the WHO.[21] Information about the epidemiology of TDIs in Nepal is also lacking. Few studies have been done in the field of dental trauma in Nepal, leading to inadequate data.

Therefore, the aim of this study was to evaluate TDIs and factors affecting the permanent dentition of patients with TDIs.

## METHODS

This cross-sectional observational study was conducted at Chitwan Medical College, School of Dental Sciences, Bharatpur, Nepal. All patients with TDIs, who were referred to or attended the Department of Conservative Dentistry and Endodontics over a 5-year period from January 2014 to December 2018, were included in the study. A total of 274 patients were included through convenience sampling with a total number of 810 traumatized permanent teeth (and total number of 1036 TDIs) were evaluated during the course of the study. The sample size was determined by considering an alpha of 0.05, a power 0.84, and effect size of 0.18. A detailed history of all the patients was taken followed by a thorough extraoral and intraoral clinical examination. All teeth were carefully evaluated for trauma. During the clinical examination, findings related to TDIs were recorded. Basic radiographic investigations were done as per the need to confirm the diagnosis and the information collected was documented. The patient's age and gender, etiology of trauma, type of trauma, type of traumatized tooth, number of traumatized teeth, and type of treatment provided were recorded from each patient. The type of TDIs was classified and recorded according to Andreasen's classification.[3] The study was carried out with the ethical approval of the Institutional Review Committee No. (Ethical Clearance No: CMC-IRC/F/075/076-117).

### Statistical Analysis

Data analysis was done using descriptive and comparative statistical methods. Chi-square tests were used to compare qualitative data ($P < 0.05$). Statistical analysis was done by Statistical Package for the Social Sciences version 20 (SPSS, IBM SPSS Inc., Chicago, IL).

## RESULTS

A total of 274 TDIs patients (199 males [72.62%] and 75 females [27.37%]) presenting with TDIs to the permanent teeth between January 2014 and December 2018, for a period of 5 years, were evaluated in this study. A total of 810 traumatized permanent teeth with 1036 injuries were assessed.

The age of the patients ranged from 14 to 70 years (mean 27.84 years). TDIs were most commonly observed in the 14–20: ($n$ = 84; 30%) year-old patients followed by the 21–25: ($n$ = 64; 23%) year-old patients. Distribution of TDIs, according to age group, did not show any significant differences ($P$ = 0.229) in Table 1. Males were more frequently affected than females. Male:female ratio was (2.65:1). TDIs were more frequent in the age group of 14–20 for both males as well as females. About 76.19% were male and 23.80% were female in this age group. Evaluation of TDIs by age groups and gender showed that the difference was not statistically significant ($P$ = 0.243).

The most common etiology was due to road traffic accidents (RTA) (68.97%) followed by fall (15.69%) in Table 1. Most of the RTA took place in the patient age group 14–20 years

**Table 1: Distribution of TDIs according to age groups and gender**

| Age distribution | *n* (%) | M:F (*n*) | *P* |
|---|---|---|---|
| 14–20 | 84 (30) | 64:20 | *P*=0.243 |
| 21–25 | 64 (23) | 45:19 | |
| 26–30 | 44 (16) | 31:13 | |
| 31–35 | 29 (10.5) | 19:10 | |
| 36–40 | 16 (5.8) | 14:2 | |
| 41–50 | 21 (7.6) | 14:7 | |
| 51–60 | 13 (4.7) | 8:5 | |
| 61–70 | 3 (1) | 3:0 | |
| Total | 274 | 199:75 | |

Chi-square test ($P$<0.05). TDIs: Traumatic dental injuries

(28.04%) followed by the 21–25 years old (24.86%). The difference was not statistically significant ($P > 0.05$) between the cause of trauma and age distributions in Table 2. Similarly, analysis of the frequency of the causes between the genders found no significant differences in Table 3. RTA and fall were equally seen more frequently in males.

The most frequently observed TDIs with respect to fracture injury (injuries to the hard dental tissues and the pulp) were uncomplicated crown fracture (18.43%), followed by complicated crown fracture: (14.18%) Irrespective of gender. The distribution of types of TDIs, according to Andreasen's classification, is presented in Table 4. Injuries to the hard dental tissues and the pulp comprised 52.60% of injuries, whereas injuries to the periodontal tissues were seen in 47.39% of cases. Subluxation was the most common injury to the periodontal tissues (18.91%) followed by concussion (14.96%). TDIs included injuries to the hard dental tissues and the pulp 1.109 times more frequently than periodontal tissues.

The most commonly affected tooth was maxillary central incisors. Both the maxillary central incisors were equally affected (23.45% each) followed by the maxillary left lateral incisor (13.58%). The most frequently traumatized tooth was the maxillary left central incisor in case of fracture injury, whereas in case of periodontal tissues injury, the most affected tooth was the maxillary right central incisor. The distribution of TDIs, according to affected tooth type, is presented in Table 5. The maxillary arch (81.97%) was more frequently involved than the mandibular arch (18.02%). The average number of traumatized teeth per patient was 2.95.

A single traumatic episode was found to have injured from one to ten teeth per patient. Most patients were found to have involved two teeth (28.10%) at the time of trauma. Only 58 patients (21.16%) had trauma to a single tooth, whereas 216 patients (78.84 %) suffered trauma to more than one tooth. Similarly, analysis of the type of injuries per patient found two types of injury (33.21%) more common than a single type of injury (28.10%).

The most common treatment provided was a restoration in 238 teeth (39.33%) followed by root canal treatment in 186 teeth (30.74%) in Table 6. No statistically significant differences ($P > 0.05$) were found between the treatments done on the traumatized teeth.

**Table 2: Distribution of TDIs according to age groups and etiology of trauma**

| Age distribution | *n* (%) | RTA:Fall:Assault:Impact:Sports | *P* |
|---|---|---|---|
| 14–20 | 84 (30) | 53:13:7:6:5 | *P*>0.05 |
| 21–25 | 64 (23) | 47:10:5:2:0 | |
| 26–30 | 44 (16) | 31:6:3:3:1 | |
| 31–35 | 29 (10.5) | 21:5:2:1:0 | |
| 36–40 | 16 (5.8) | 11:3:2:0:0 | |
| 41–50 | 21 (7.6) | 13:4:1:3:0 | |
| 51–60 | 13 (4.7) | 11:2:0:0:0 | |
| 61–70 | 3 (1) | 2:0:0:1:0 | |
| Total | 274 | 189:43:18:18:6 | |

RTA: Road traffic accidents, Chi-square test *P*<0.05. TDIs: Traumatic dental injuries

**Table 3:Distribution of TDIs according to gender and etiology of trauma**

| Gender distribution M:F (*n*) | *n* (%) | RTA:Fall:Assault: Impact:Sports | *P* |
|---|---|---|---|
| 64:20 | 84 (30) | 53:13:7:6:5 | *P*>0.05 |
| 45:19 | 64 (23) | 47:10:5:2:0 | |
| 31:13 | 44 (16) | 31:6:3:3:1 | |
| 19:10 | 29 (10.5) | 21:5:2:1:0 | |
| 14:2 | 16 (5.8) | 11:3:2:0:0 | |
| 14:7 | 21 (7.6) | 13:4:1:3:0 | |
| 8:5 | 13 (4.7) | 11:2:0:0:0 | |
| 3:0 | 3 (1) | 2:0:0:1:0 | |
| Total 199:75 | 274 | 189:43:18:18:6 | |

RTA: Road traffic accidents, Chi-square test *P*<0.05. TDIs: Traumatic dental injuries

## DISCUSSION

TDIs are a public dental health problem worldwide with many people having an experience of it. Despite this, TDIs are a neglected condition worldwide.[2,22] Although population-based studies provide more epidemiological evidence compared to clinic- and hospital-based studies, they lack in evidence of causes and effects, discussion about treatment procedures, and classification of TDIs.[11,23,24]

Although TDIs occur in all age groups, it is more frequently seen in children and teenagers, which supports age as a

**Table 4: Distribution of TDIs according to the type of injury**

| Type of TDIs | |
|---|---|
| **Injuries to the hard dental tissues and the pulp** | ***n*** |
| Enamel infarction | 51 |
| Enamel fracture | 61 |
| Enamel dentin fracture | 191 |
| Complicated crown fracture | 147 |
| Uncomplicated crown-root fracture | 6 |
| Complicated crown-root fracture | 38 |
| Root fracture | 51 |
| Total fracture injuries | 545 |
| **Injuries to the periodontal tissues** | ***n*** |
| Concussion | 155 |
| Subluxation | 196 |
| Extrusive luxation | 41 |
| Lateral luxation | 28 |
| Intrusive luxation | 9 |
| Avulsion | 65 |
| Total luxation injuries | 491 |
| Total no. of injuries | 1036 |

TDIs: Traumatic dental injuries

**Table 5: Distribution of TDIs according to affected tooth type**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Incisors: (693) | 11=190 | 12=90 | 21=190 | 22=110 | 31=31 | 32=25 | 41=32 | 42=25 |
| Canines: (57) | 13=19 | 23=28 | 33=4 | 43=6 | | | | |
| Premolars:(42) | 15=7 | 14=11 | 24=6 | 25=4 | 34=3 | 35= 4 | 44=4 | 45=3 |
| Molars: (18) | 17=1 | 16=3 | 26= 4 | 27=1 | 36=4 | 37=1 | 46=3 | 47=1 |

TDIs: Traumatic dental injuries

**Table 6: Distribution of type of treatments provided**

| Treatment provided: 605 teeth | | | |
|---|---|---|---|
| **Type of treatment** | **Patients (No)** | **Tooth (No)** | **(p)** |
| Root canal treatment | 109 | 186 | *P*=0.220 |
| Restoration | 137 | 238 | |
| Splinting | 47 | 76 | |
| Direct pulp capping | 42 | 47 | |
| Repositioning and splinting | 35 | 57 | |
| Reimplantation | 1 | 1 | |
| Follow-up and monitoring only | 20 | 84 | |

Chi-square test (*P*<0.05)

risk factor for TDIs.[6,9] Most of the TDIs happen before 30 years of age.[10,25,26] The mean age in our study was 27 years, which validates the same. This finding is in agreement with studies which state the third decade as the most frequent age group for TDIs.[10,25] The most commonly affected age group was 14–20 (30%) year-old patients followed by the 21–25: (23%) year-old patients. About 30% of patients belonged to the age group 14–20 years and 69% of patients were below age 30, which agree with studies showing a higher percentage of TDIs in the younger population. However, the difference observed in the distribution of TDI according to age group was not statistically significant. Analysis of the age group also found a decrease in the frequency of TDIs as age increased.

Higher rate of TDIs in adolescents and young adults could be due to their lifestyle and risk-taking behavior, making them more susceptible to TDIs. The most commonly affected age group in RTA in Nepal is 20–40 years.[27,28] Since RTA was found to be the main etiology of TDIs, the findings are expected.

Gender is also considered a risk factor for TDIs. Experience of TDIs among males has been found to be twice as often as females (male-to-female ratios ranging from 1.3 to 2.78:1) in permanent dentition.[8] This has been associated with the involvement of more males in sports and physical activities and also due to their way of living and tendency of taking risks. Nevertheless, these days gender differences in TDIs are decreasing and individual activities of the person are considered to have a more important part in TDIs than gender or age.[6]

Males (72.62%) experienced a significantly higher incidence of TDIs compared to females (27.62%). The male:female ratio was (2.65:1), which reveals that females were less affected and exposed to TDIs than males.

Males are also more exposed to TDIs risk factors due to outdoor activities such as RTA, risky work, and sports, which make them more prone to TDIs. The results approve that gender is still one of the predisposing and risk factor for TDIs. A higher incidence of RTA among males in Nepal also explains the findings.[27,28]

Etiologies of TDIs vary between and within countries among studies due to many factors.[5,12,13,14] However, the most common cause of TDIs in developed countries is sports or falls, whereas in developing and underdeveloped countries, RTA is more common.[5]

The etiologies of TDIs agree with other studies conducted in the region. The main causes of TDIs were RTA (68.97%) followed by fall (15.69%), which again may be due to the high rate of RTA, in Nepal.[27,28] Very few cases of TDIs were related to sports injury (2.18%), which correlates with the studies conducted in the region. Sports-related injuries are a common cause of TDIs in developed countries, where many young people participate in sports activities due to the availability of good sports facilities. Studies from developing countries have very few numbers of TDIs related to sports injury.

Etiology of TDIs is very much related to the age of the patient as it varies according to age group. RTA is the most common cause of TDIs in adults, whereas fall injury is more commonly observed in children.[5,12,29] However, RTA was found to be the main cause of TDIs in all the age groups analyzed, which disagrees that etiology of TDIs varies with the age group. Evaluation of age groups with respect to etiology did not find any variation. This could be due to the high rate of RTA in Nepal.[27,28] The results are similar to studies from underdeveloped countries where RTA is very common.

The classification of TDIs used is based on the criteria proposed by Glendor *et al.*[3] Uncomplicated crown fracture without pulp exposure is the most common type of TDIs found in permanent dentition.[30]

A total of 1036 injuries were seen in 274 patients. Uncomplicated crown fracture: (Fracture of enamel and

dentine, without the involvement of the pulpal chamber) (18.43%) was the most frequently seen type of fracture injury (injuries to the hard dental tissues and the pulp) followed by complicated crown fracture: (14.18%) (Fracture of enamel and dentine, with the involvement of the pulp), among both the genders. The ratio of the most common TDIs (uncomplicated crown fracture) in our study was (29.24%), which agrees with the international literature, where it is ranged between 20.2% and 51.6%.[9,10,29,31] Similarly, the percentage of complicated crown fracture (fracture of enamel and dentine, with the involvement of the pulp) was 26.97%, which is near to the rate described by Glendor *et al.* (26–76%).[3] Complicated cases of TDIs are generally seen more in studies done in a hospital set-up.

Luxation injuries are more common TDIs in primary dentition, whereas fracture injuries are frequently seen in permanent dentition.[32,33] Subluxation was the most frequent periodontal injury type (injuries to the periodontal tissues) (18.91%) followed by concussion (14.96%). However, some studies show a very low prevalence of concussions or subluxations.[29] Avulsion injury in permanent teeth is observed in 0.5–3% of all TDIs.[34,35] However, it was slightly higher (6.27%). This could be because the majority of TDIs cases were due to RTA and also due to the study being conducted in a hospital set-up. Intrusive luxation was the least common type of injury.

The range of luxation injuries varies between 15% and 61% in permanent dentition, according to Glendor *et al.*[3,10] The rate of luxation injuries in this study was 47.39%. Fracture injuries (injuries to the hard dental tissues and the pulp) were more common than luxation injuries (injuries to the periodontal tissues) (52.60% vs. 47.39%). Similarly, fracture injuries were involved 1.109 times more frequently than luxation injuries. Likewise, two types of injury (33.21%) per patient were more common than a single type of injury (28.10%).

Maxillary teeth are more commonly involved than mandibular teeth in TDIs.[11,12] Likewise, the maxillary central and lateral incisors are the most commonly injured teeth.[6,11] Maxillary central incisor was the most commonly traumatized tooth with both central incisors being equally affected (23.45%), followed by the maxillary left lateral incisor (13.58%) which is similar to other studies in the literature.[6,7,9,19,36,37] In cases of fracture injury, the most commonly injured tooth was the maxillary left central incisor (24.40%), whereas in cases of luxation injury, the maxillary right central incisor (27.12%) was the most affected tooth. The prominent and vulnerable positioning, inadequate lip coverage, exposed nature, and frequent protrusion of the maxillary teeth are responsible for their frequent involvement in TDIs.[38] The teeth on the left side were more frequently injured than the right side. Similarly, maxillary teeth were commonly traumatized than mandibular teeth.

More than one tooth was injured in a single episode of TDIs in the majority (78.84%) of patients, which agrees with studies demonstrating injury of multiple teeth more common than a single tooth.[39] About 21.16% of patients had an injury to a single tooth, whereas 28.10% of patients had an injury to two teeth. Two patients presented with involvement of ten teeth. The average number of traumatized teeth per patient was 2.95.

The number of injured teeth is determined by many factors and varies according to the etiology and extent of the injury. Most studies show that TDIs frequently involve multiple teeth, especially in cases of severe injury such as RTA and violence which increase the number of injured teeth.[3,5,11,29,36] Since RTA was the most common etiology of TDIs in the majority of the cases, injury to multiple teeth was frequently seen. Injuries to multiple teeth are also found more frequently in hospital-based studies.

There are different types of TDIs and each type has its own treatment protocols.[40] However, various studies support that treatment of TDI is often neglected and treatment needs of TDIs are not adequately met in both developing as well as developed countries.[2] Patients tend to come for treatment only when symptoms begin due to a lack of awareness of the treatment of TDIs and its long-term consequences.[11,19] Immediate treatment can provide a better prognosis for injured teeth. Even simple crown fractures can lead to pulp necrosis due to late treatment.[41,42] Therefore, it is essential to provide urgent and correct treatment to maximize the favorable outcome of TDIs.[16,17] Delayed treatment frequently results in unfavorable prognosis.[31,43]

The most frequent treatment provided was restoration (39.33%) which could be due to the fact that the majority of patients had uncomplicated crown fracture which required restorative treatment, followed by root canal treatment (30.74%). This may be due to many of the injuries being a complicated crown fracture. In addition, combination injuries (fracture injuries along with luxation injuries or vice versa) increase the chance of pulp necrosis.[44-46] Splinting was provided to the teeth with periodontal tissue injury with increased mobility. Repositioning and splinting were done in extrusion, intrusion, and lateral luxation injury. Direct pulp capping was performed in patients who reported early for treatment and in young patients. An avulsion is considered a serious injury and the prognosis depends on prompt management.[34,35] However, almost all patients with avulsion injury reported for treatment with already

lost avulsed tooth which may be due to lack of knowledge and awareness of treatment of avulsed tooth. Therefore, reimplantation could be done in a single case only. Follow-up and monitoring are very important in the management of TDIs. All teeth with TDIs must be kept on long-term follow-up according to the guidelines.[47] Therefore, patients with complicated injury and luxation injures were advised for regular follow-up visits and long-term monitoring.

TDIs related findings have significant differences due to variations in study methodology, experimental design, trauma classification, dentition studied, demographics, and geographical location.[4] Very few studies have similarities; therefore, a comparison between them is difficult and should be done judiciously.[48] Despite the lack of studies for comparison, the results of this study correlate with studies related to TDIs in the region.

This study is important due to the shortage of data on TDIs in the permanent dentition of the Nepalese population. One of the limitations of this study is the lack of follow-up of TDIs patients. However, it provides information about the frequency of TDIs in the area. Studies based on clinical outcomes, complications, efficacy of treatment protocols, and the long-time prognosis can be conducted with the help of follow-up of TDIs patients in future. Such prospective studies can significantly help to evaluate the effectiveness of treatment procedures and long-term complications. They can also facilitate a better understanding of the effects of TDIs, treatment plans, and prognosis.

TDIs are a well-known global public dental health problem.[8] An increase in the prevalence of TDIs has been predicted. TDIs happen in normal life situations, which make it basically inevitable. However, efforts for the prevention of TDIs and the benefits of early treatment cannot be ignored. Similarly, the role of correct and timely management of TDIs in the prevention and reduction of complications, costs, and time cannot be underestimated.[43]

## CONCLUSION

RTA was the most common cause of TDIs followed by fall. TDIs were found to most commonly affect the males of young age groups. This may be for the reason that RTA was the most common cause of TDIs seen in young age groups. The maxillary central incisor was the most frequently injured teeth. The uncomplicated crown fracture was the most frequently observed TDIs. Injuries to the hard dental tissues and the pulp (fracture injuries) were more common than periodontal tissue injury. Therefore, restoration was the most frequently provided treatment.

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Original Article

# Impact and Association of Sociodemographic and Socioeconomic Factors on Diabetic Foot Ulcer

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## Abstract

**Background:** Diabetic foot ulcer (DFU) has always been a complication among diabetics. DFU has many factors influencing it. Sociodemographic and socioeconomic factors play major roles. Age, occupation, income, and housing specifically have an influence on diabetic patients.

**Objectives:** The objectives of this study were to determine the sociodemographic and socioeconomic profile and assess its association and risk of diabetics developing DFU.

**Methodology:** A prospective study was conducted among 40 diabetics reporting to the department of general surgery with wound/s on foot. The study period was for a year. Details such as age, sex, education, occupation, income, and housing were noted using a questionnaire. The data were collected and analyzed.

**Results:** The total number of subjects was 40. The mean age among the subjects was 51.8 years. Eighteen subjects were male and 22 subjects were female. The majority of the subjects were Hindus and the remaining were Muslims and Christians. About 65% of subjects were uneducated. About 37.5% of subjects were housewives, 35% unemployed, and 27.5% were laborers. Subjects were divided based on economic status which showed to have an association. Housing was also considered and also seemed to have an association.

**Conclusion:** It can be concluded that sociodemographic and socioeconomic factors were associated with DFU.

**Key words:** Diabetic foot ulcer, Education, Income and housing, Occupation

## INTRODUCTION

India has the second-highest numeral cases of DM, approximately 69.1 million cases in the world, just behind China being the first.[1] This number is anticipated to jump up to 640 million cases by the end of 2040.[1] In India, the prevalence of DM ranges between 5% and 17%.[2-4] Neuropathy and foot ulcer are the most frequent complication of diabetes mellitus.[5] Foot ulcers are the most dreaded complication in India which causes impaired mobility, disability, and morbidity.[6] Among diabetic patients, foot complications are very common and also a costly complication to treat.[7] Among developed countries, one among every six diabetics, will have an ulcer in their lifetime, assuming the risk is higher among developing countries.[8] A patient's interactivity with the environment is a risk factor connected to a history of foot ulcer. Foot trauma, vascular diseases, and peripheral neuropathy also can cause foot ulcers.[9] The occurrence of a diabetic foot ulcer (DFU) is a long-term complication which can be prevented.[10] Multiple other factors such as age, education socioeconomic status, and foot care, play a key role among diabetics.[11,12] The present study is aimed at assessing the risk factors, leading to DFUs, as well as reducing the impact in that particular area.

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## METHODOLOGY

The present prospective study of 40 cases of diabetic foot disease was carried out in the Department of General Surgery, SVS Medical College and Teaching Hospital over a period of 1 year from July 2015 to June 2016. After

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obtaining the informed consent of the patients, data were collected using a pretested questionnaire. General assessment and systemic examination were done for all the patients which are done. A detailed collection of age, sex, education, occupation, income, and housing was noted. The socioeconomic status was done based on BG Prasad classification,[13] data were compiled and analyzed and presented as tables and percentages. Keeping the significance level at $P = 0.05$, the association was assessed and tabulated.

## RESULTS

The sociodemographic and socioeconomic data were collected from all the subjects. All 40 subjects are diabetic in this study as shown in Table 1. Age was noted, 50% of subjects were above the age of 60 years, and the remaining was between the age group 30 and 59 years. The mean age noted was 51.8 + 3.42 years. The current study shows female predominance of 55% subjects and 45% male subjects. The male and female ratio was 0.81:1.

**Table 1: Distribution of sociodemographic and socioeconomic characteristics among the subjects**

| Characteristics | Number (%) | Mean | *P*-value |
|---|---|---|---|
| Age | | | *P*<0.001 |
| 30–39 years | 6 (15) | 51.8+3.42 | |
| 40–49 years | 8 (20) | | |
| 50–59 years | 6 (15) | | |
| >60 years | 20 (50) | | |
| Sex | | Ratio | |
| Males | 18 (45) | 0.81:1 | |
| Females | 22 (55) | | |
| Religion | | | |
| Hindu | 31 (77.5) | | |
| Muslim | 8 (20) | | |
| Christian | 1 (2.5) | | |
| Education | | | *P*=0.03 |
| Educated | 14 (35) | | |
| Uneducated | 26 (65) | | |
| Occupation | | | *P*=0.11 |
| Manual laborer | 11 (27.5) | | |
| Housewife | 15 (37.5) | | |
| Unemployed | 14 (35) | | |
| Socioeconomic status | | | *P*<0.001 |
| Upper class | 0 | | |
| Upper middle | 0 | | |
| Middle | 6 (15) | | |
| Lower middle | 12 (30) | | |
| Lower class | 22 (55) | | |
| Housing | | | *P*<0.001 |
| Rural | 37 (92.5) | | |
| Urban | 3 (7.5) | | |
| Smoking | | | *P*=0.74 |
| Smoker | 9 (22.5) | | |
| Non-smoker | 31 (77.5) | | |
| Alcohol | | | *P*=0.86 |
| Alcoholic | 19 (47.5) | | |
| Non-alcoholic | 21 (52.5) | | |

The present study had 77.5% Hindus and 20% and 2.5% Muslims and Christians, respectively. Education, which is of high importance nowadays, was noted, where 65% of subjects were uneducated and 35% educated. The occupation of the subjects was taken so as to assess the risk of DFUs. About 37.5% of the subjects were housewives or homemakers, 35% unemployed, and 27.5% were daily wage workers. Based on the income, the subjects were classified accordingly using modified BG Prasad classification into which socioeconomic class they belong too. The majority of the subjects (55%) belonged to the lower class, 30% were in the lower-middle class bracket, and only 15% belonged to the middle class. The subjects were also classified based on place of living 92.5% of subjects reside in rural areas, and the remaining 7.5% were from an urban background. The habits of the subjects were also considered in the study. About 22.5% were smokers and 47.5% alcoholics.

## DISCUSSION

The mean age of study was 51.8 years, in which 50% of the subjects were above 60 years. With increasing age, the risk of developing DFU was higher and found significant ($P < 0.001$). A study done by Ashok *et al.*[14] had a mean age of 55.25 years. Females were higher than males. Risk factors such as age and sex are regarded as contributing factors in the study conducted by Lavery *et al.*[15] Among the 40 subjects, 65% were uneducated and showed to have an association ($P = 0.03$). Studies done earlier by Brancati *et al.*[16] and Lipton *et al.*[17] used education as a base for socioeconomic status. Using BG Prasad classification based on income, the subjects were divided and 55% of subjects belonged to the lower class and 45% belonged to the lower-middle and middle. Income had an influence on patients seeking health care for DFU ($P < 0.001$). Place of living 92.5% of subjects reside in rural areas and the remaining 7.5% were from an urban background. Hosing was a risk factor which was highly significant ($P < 0.001$). A cross-sectional study by Deribe *et al.*[10] in 2014 from South Ethiopia reported rural residence increases the possibility of having DFU by a factor of 4.1 when compared to urban residents. Ashok *et al.*,[14] in their results, concluded that diabetic patients belonging to rural areas were more prone to foot ulcers when compared to the urban background. This is due to farming, usage of heavy equipment, and also rodent bite causing injury which is a risk in turning into a chronic ulcer. A study by Jeffcoate and Harding[18] suggested that rural population, monks, devotees, and individuals who walk barefoot are highly prone to foot injuries. Smoking and alcohol were taken to check its association with DFU. There was no association in the study. Merza and Tesfaye.[19] reported that smoking and alcohol consumption did not appear to be a risk factor.

## CONCLUSION

It can be concluded from this study that age, education, occupation, income, and housing had an association with DFUs.

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Original Article

# Self-medication among Nursing Students of a Tertiary Care Hospital of Jammu and Kashmir: Knowledge, Practice, and Attitude

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## Abstract

**Background:** The practice of self-medication is common worldwide, and the irrational use of drugs is a cause of concern that may lead to drug resistance also. The prevalence rates are on the rise despite efforts to limit this problem.

**Aims and Objectives:** The objective of the study was to determine the prevalence, attitude, and knowledge of self-medication among nursing students.

**Methodology:** A cross-sectional study was carried out among nursing students of Government Medical College, Srinagar, from February 2020 to March 2020. The recorded data were collected through a self-administered questionnaire and compiled, entered in a spreadsheet (Microsoft Excel), and exported to data editor of SPSS v22.0 as Mean ± SD and categorical variables were summarized as frequencies and percentages. Graphically, the data were presented by bar diagrams.

**Results:** Out of 86 students enrolled, only 67 completed the questionnaire. The majority of the students self-medicate due to the fact that they believe self-medication provide quick relief (53.7%), followed by the availability of the previous prescriptions (50.7%) and ease and convenience. The main symptoms, leading to self-medication, were headache (67.2%) and cough (46.3%) followed by diarrhea, and the most common group of drugs used for self-medication was antibiotics (67.2%) followed by analgesics and antipyretics.

**Conclusion:** The self-medication practices are very common for treating clinical conditions that are simple or previously experienced. Awareness regarding the advantages and disadvantages of practicing self-medication must be done through proper education and conducting seminars.

**Key words:** Over the Counter drugs, Pattern, Prescription, Prevalence, Questionnaire, Self-medication

## INTRODUCTION

Self-medication is often considered as a component of self-care and is widely practiced worldwide.[1] The WHO defines self-medication as the use of medication by a patient on his own initiative or on the advice of a pharmacist or a layperson instead of consulting a medical practitioner.[2] Self-medication being practiced worldwide[3-7] often lead to misuse of drugs[8] and increasing chance of drug dependency and most of all masking the sign and symptoms of the underlying disease, complicating the existing problem creating drug resistance, and delaying diagnosis.[9-13]

Self-medication may lead to irrational drug use and delayed seeking medical advice and increased side effects and drug interactions.[14] Self-medication includes acquiring medicines without a prescription, resubmitting old prescriptions to purchase medicines, sharing medicines with relatives or members of one's social circle, or using leftover medicines stored at home.[15] In developing countries like India, not only Over the Counter (OTC) drugs, even prescription-only drugs are easily accessible without prescription in pharmacy outlets.[16]

The various studies have established that the practice of self-medication is on the rise among nursing students.[17]

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## METHODOLOGY

This cross-sectional study was carried out among nursing students to evaluate the knowledge, practice, and attitude toward self-medication in the Department of Pharmacology, Government Medical College, Srinagar from February 2020 to March 2020 after obtaining due approval from the Institutional Ethics Committee. Data were collected through structured, validated questionnaire which was adopted from various similar studies conducted previously[18-21] and after giving a brief description of the nature of the study and the procedure of completing the questionnaire was explained to them. The questionnaire included questions pertaining to demographic details, reasons for self-medication, symptomology, leading to self-medication, most common drugs used to self-medicate and frequency of self-medication during 1 year recall period, and sources of drug information.

### Statistical Methods

The recorded data were compiled and entered in a spreadsheet (Microsoft Excel) and then exported to the data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as mean ± SD and categorical variables were summarized as frequencies and percentages. Graphically, the data were presented by bar diagrams.

## RESULTS

A total of 67 students successfully completed the questionnaire, of which 58.2% were female and 41.8% were male. The mean age and standard deviation of the study population were 19.8 years and 1.14, respectively. The prevalence of self-medication was 89.6% with a high frequency of 32.8% resorting to self-medication 2–3 times in a year closely followed by every few months 29.9%. In our study, 80.6% of the students were from rural area and 13% were from urban areas. It was found that headache (67.2%), cough (46.3%) followed by fever (44.8%), and diarrhea (20.9%) were the predominant morbidity, for which the students practiced self-medication. Other causes of morbidity prompting the students to self-medicate included dysmenorrhea, allergy, and lack of sleep. The most common group of drugs used for self-medication included antibiotics (67.2%), analgesics (64.2%) followed by antipyretics (49.3%), cough suppressants (34.3%), antiemetics (22.4%) followed by sedatives, antiulcer drugs, and antihelminthics. The majority of the students self-medicate due to the simple ailment (61.2%) provide quick relief (53.7%), followed by availability of previous prescriptions (50.7%), ease and convenience, and crowd avoidance. The important sources of information for self-medication were old prescription (74.6%), Internet (52.2%), and pharmacists. Regarding practice toward self-medication, 64.2% of the students are of the opinion that it does not reduces the load on the medical services. About 97.1% of students are of the opinion that self-medication is not risk-free and 73.1% believe that it may lead to irrational drug use [Tables 1-3].

**Table 1: Socio-demographic characteristics of the study subjects**

| Variable | Category | Frequency | Percentage |
|---|---|---|---|
| Age (years) | ≤20 | 52 | 77.6 |
| | >20 | 15 | 22.4 |
| Gender | Male | 28 | 41.8 |
| | Female | 39 | 58.2 |
| Residence | Rural | 54 | 80.6 |
| | Urban | 13 | 19.4 |

Mean age: 19.8 years; SD: 1.14; Range: 18–23 years

**Table 2: Knowledge toward self-medication**

| Variable | Category | Frequency | Percentage |
|---|---|---|---|
| Define self-medication | Yes | 66 | 98.5 |
| | No | 1 | 1.5 |
| Medicine taken by self | Yes | 60 | 89.6 |
| | No | 6 | 9.0 |
| | Do not know | 1 | 1.5 |
| Reasons* | Simple ailment | 41 | 61.2 |
| | Quick-relief | 36 | 53.7 |
| | Availability of the previous prescription | 34 | 50.7 |
| | Ease and convenience | 20 | 29.9 |
| | Crowd avoidance | 12 | 17.9 |
| | Busy lifestyle | 11 | 16.4 |
| Symptomology leading to self-medication* | Headache | 45 | 67.2 |
| | Cough | 31 | 46.3 |
| | Fever | 30 | 44.8 |
| | Diarrhea | 14 | 20.9 |
| | Dysmenorrhea | 14 | 20.9 |
| | Allergy | 12 | 17.9 |
| | Lack of sleep | 10 | 14.9 |
| | Pain in the abdomen due to peptic ulcer | 8 | 11.9 |
| | Sore throat | 5 | 7.5 |
| | Common cold | 3 | 4.5 |
| Most common drugs used | Antibiotics | 45 | 67.2 |
| | Analgesics | 43 | 64.2 |
| | Antipyretics | 33 | 49.3 |
| | Cough suppressants | 23 | 34.3 |
| | Antiemetics | 15 | 22.4 |
| | Sedatives | 6 | 9.0 |
| | Antiulcer drugs | 5 | 7.5 |
| | Antihelminthics | 5 | 7.5 |
| | Antihistaminics | 3 | 4.5 |
| Frequency | 2–3 times in a year | 22 | 32.8 |
| | Every few months | 20 | 29.9 |
| | Every few weeks | 9 | 13.4 |
| | Once | 16 | 23.9 |
| Source of information* | Old prescription | 50 | 74.6 |
| | Internet | 35 | 52.2 |
| | Pharmacist | 16 | 23.9 |
| | Pharmacology knowledge | 13 | 19.4 |
| | Drug advertisement | 11 | 16.4 |
| | Friends | 7 | 10.4 |

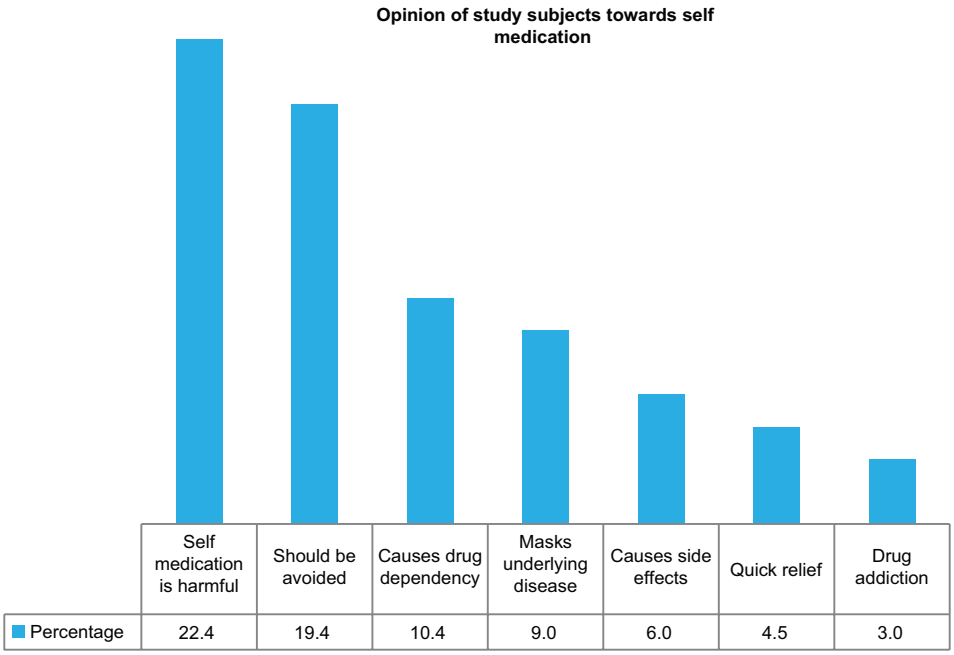


**Table 3: Practice toward self-medication**

| Question | Response | Frequency | Percentage |
|---|---|---|---|
| Do you think self-medication reduces the load on the medical services | Yes | 24 | 35.8 |
| | No | 43 | 64.2 |
| Is self-medication risk free? | Yes | 2 | 3.0 |
| | No | 65 | 97.0 |
| Do you think self-medication may lead to irrational drug use | Yes | 49 | 73.1 |
| | No | 18 | 26.9 |
| Do you think self-medication may lead to drug dependency and mask the sign and symptoms of underlying disease | Yes | 57 | 85.1 |
| | No | 10 | 14.9 |
| Have you given prescription to someone else | Yes | 12 | 17.9 |
| | No | 55 | 82.1 |

## DISCUSSION

The present study was conducted to evaluate the practices, attitude, and perception of self-medication among nursing students. The study showed that self-medication is widely practiced (89.6%) by the nursing students of this tertiary care hospital. The reason for the increased prevalence of self-medication may be contributed to the easy access to almost all types of medications, almost any drug available in the market can be purchased as an OTC medication. The majority of the patients in developing countries prefer to purchase medications from pharmacies directly as they are easily accessible, time-saving, and less expensive than going to doctors clinic first, and these practices are more common in village areas, where medical services are in adequate.

The present study revealed that self-medication practices are very common among nursing students. The majority of the students practiced self-medication of one or more drug with varied frequency over 1 year. In our study, the most common reason for self-medication reported by students was that self-medication provides quick-relief and availability of previous prescriptions. These findings were in contrast to the study from Ethiopia, Karachi, and Malaysia, where the most common reason being was the illness too trivial and previous experience of the same illness.[22-24] The findings were similar to the study from Punjab, where the most common cause of self-medication was the quick relief of symptoms.[25] Regarding the condition/symptoms which prompted the students to practice self-medication, headache and cough were most common, followed by fever and diarrhea. This finding was similar to the study conducted in Karachi, where headache was the most common condition that leads to self-medication.[26] Antibiotics were the most common (67.2%), followed by analgesics and antipyretics. This finding is in contrast to the study from Karachi and Bahrain were most frequently used drugs for self-medication were analgesics.[27] Although it is true that self-medication can treat minor ailments, thus reducing the load on medical services, but can also lead to several adverse effects, including the global emergence of multidrug-resistant pathogens, drug addiction, and masking the symptoms of underlying diseases. Another problem with self-medication is the risk of using expired drugs, sharing them with friends, or taking medicines that have been originally prescribed for some other problem that can result in accidental drug poisoning.

## CONCLUSION

The prevalence of self-medication is alarmingly high, so a holistic approach must be taken to prevent this problem from escalating which would involve awareness and education regarding the implications of self-medication and strategies to prevent the supply of medication without a prescription.

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# Prophylaxis for Post-operative Nausea and Vomiting: A Randomized Comparative Study between Granisetron versus Granistreon and Dexamethasone among Patients Undergoing Modified Radical Mastectomy

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## Abstract

**Introduction:** The patients undergoing modified radical mastectomy under general anesthesia has been associated with higher incidence of post-operative Nausea and Vomiting (PONV). The present study compares efficacy of Granisetron versus Granistreon and Dexamethasone for the incidence and severity of PONV in early (<6 h) and late (6–24 h) post-operative period in two groups and also to estimate the number of patients who required actual rescue antiemetics and showed complete response after 24 h.

**Materials and Methods:** This study was carried out on 110 female patients aged 25–60 years undergoing modified radical mastectomy under general anesthesia. They were randomly divided into Group G (Granisetron) and Group G+D (Granisetron + Dexamethasone). Tests drugs were given preoperatively and all followed up in post-operative period.

**Results:** Both the groups were comparable in terms of demographic variables, physical attributes, duration of surgery, and baseline vital parameters. It was observed that Granisetron+ Dexamethasone combination is better at controlling incidence and severity of PONV in both early and late post-operative period which is statistically significant. There was no need of rescue antiemetic in Group D patients. There is statistically significant difference noted between both groups regarding complete response, that is, after 24 h.

**Conclusions:** Granisetron + Dexamethasone combination is far more effective in controlling PONV among patients undergoing Modified radical mastectomy.

**Key words:** Antiemetics, Dexamehasone, Granisetron, Post-operative nausea and vomiting, Prophylaxis

## INTRODUCTION

Post-operative nausea and vomiting (PONV) is defined as nausea and/or vomiting experienced by patient within 24 h of a surgical procedure requiring anesthesia.[1] In the recent years, its incidence is ranging from 20% to 30% in general population to 30–40% among population who undergoing surgery under general anesthesia.[2] The female patients undergoing breast surgery with axillary dissection suffer a higher incidence of PONV (60%–80%),[3] due to risk factors associated such as obesity, female gender, and simultaneous chemotherapy. The etiology of PONV is complex and probably multifactorial. The causes can be attributed to various factors such as patient related, surgery related, and anesthetic factors. The impact of PONV and effectiveness of antiemetic therapy play an important role in the recovery of patients from anesthesia and surgery. Post-operative vomiting is frequently accompanied by rise in arterial blood pressure, intracranial pressure, and

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intraocular pressure. Persistence of PONV in a patient especially who is kept overnight fasting for general anesthesia can also result in dehydration, electrolyte imbalance. Persistent retching and vomiting can cause tension in suture lines, venous hypertension, bleeding under skin flaps, and increased risk of pulmonary aspiration of gastric contents, if airway reflexes are depressed from the residual effects of anesthetic and analgesic drugs. Over the years, there are various advances in PONV prophylaxis which include use of non-pharmacological measures that reduce baseline risk, a change to less emetogenic anesthetic techniques, or the use of new antiemetic drugs. However, the use of anti-emetics, either alone or in combination, remains the mainstay in PONV management.[4]

Most of the published trials and guidelines indicate that an improved antiemetic response when combinations of drugs acting which acts through different receptor sites are used as compared with monotherapy.

Receptors involved in PONV include dopamine, opioid, 5-$HT_3$ enkephalin, histaminic, muscarinic, and cholinergic receptors and the various drugs which act through these receptors were studied previously. It has been postulated that antiemetic and antinauseant effect of ondansetron is exerted by blockade of serotonin induced depolarization of vagal afferent nerves. It may also involve 5-$HT_3$ binding sites in the chemoreceptor trigger zone and nucleus tractus solitaire in the brain stem. Emetogenic action of chemotherapeutic agents and radiotherapy as well as PONV may involve activation of 5-$HT_3$ receptors in vagal afferents in the small intestine as well as central neurons in the area postrema near the fourth ventricles. These actions are effectively blocked by ondansetron which has a half-life of 3 h. Granisetron, new 5-$HT_3$ receptor antagonist more selective than ondansetron which has been shown to have a greater specificity and potency and longer duration of action. The half-life of Granisetron is 8-9 h which is longer duration of action than ondansetron. It is effective orally as well as intravenous (i.v.). It blocks the 5-$HT_3$ receptors at both the central and the peripheral sites. It acts on the vagal efferent nerves of the gut and produces blockade of 5-$HT_3$ receptors. The half-life of Granisetron is 8–9 h which is longer duration of action than ondansetron. Its role has been justified accurately and proven in preventing chemotherapy induced nausea and vomiting.[3] The role of dexamethasone in preventing PONV, decreasing pain and edema, enhance healing, and fasten overall post-operative recovery is very well known. It is also considered to be safe which does not affect patients hemodynamics and neurocognition.[5]

The present study was conducted to study the efficacy of Granisetron versus Granistreon and dexamethasone for PONV prophylaxis for reduction of incidence and severity of PONV in early (0–6 h) and late (6–24 h) post-operative periods. This study also aims to estimate the number of patients requiring rescue antiemetics and their complete response.

## MATERIALS AND METHODS

The present study was a prospective, randomized, open-label, and double-blind study. Prior approval of the Institutional Ethics Committee and scientific committee was taken. A total of 110 female patients, aged 25–60 years were included in to this study. All 110 patients were undergoing elective modified radical mastectomy under general anesthesia. Any patients who refusing to give consent, patients taken previous chemotherapy, history of PONV, pregnant and lactating women, morbidly obese patients, patients having any history of motion sickness, migraine, gastroesophageal reflux disease or allergy to the any drugs, or major systemic comorbidity were excluded from the study. Written informed consent was taken from all the patients.

All patients were assessed for preoperative fitness as per protocol. Preoperatively, all patients were kept nil by mouth by 8–10 h. All routine investigations, routine drugs of anesthesia on table and instruments were checked in the morning before general anesthesia.

The patients were, then, randomly divided into two groups into Group G and Group D. The study drug was prepared by a senior qualified anesthesiologist who was not a part of the study team and the same person administered the drug to patient. The study drug was administered just before the induction of anesthesia. Each of the test drugs was diluted to 10 ml of distilled water and administered intravenously slowly over 2 min preoperatively. The anesthesiologist who anesthetized the patient and all involved nurses were unaware of the content of the syringe. Hence, Group G received Inj. Granisetron 20 mcg/kg IV.[1,6] and Group D: received Inj. Granisetron 20 mcg/kg Inj. Dexamethasone 0.1 mg/ kg IV.[6,7]

All the patients were given general anesthesia as per routine standard protocol and their intraoperative course with vital hemodynamic parameters was monitored throughout the surgical procedure. The duration of surgery was noted. All the patients were extubated after surgery carefully and then patients were shifted to post anesthetic care units for monitoring.

The incidence and severity of PONV were assessed at early (less 6 h) and late (6–24 h) post-operative period in all patients. For severity of PONV was assessed, according to four-point verbal descriptive score (VDS).[8]

### VDS

- Severity of Nausea: No nausea, mild nausea, moderate nausea, and severe nausea.
- Severity of Vomiting: None = No episode of vomiting, mild = 1 episode of vomiting, Moderate = 2–3 episode of vomiting and Severe = more than 3 episode of vomiting.

Patients who experienced mild severity of nausea and vomiting were reassured and its underlying cause for PONV if any, such as pain, blood loss, hypotension, vasovagal response, hypoxia, dehydration, and hypoglycemia were addressed and treated accordingly.

For rescue treatment in the early post-operative period (0–6 h) the Inj. Metoclopramide 10 mg IV.[2] diluted until 10 ml with distilled water was given slowly over 5 min to those patients who had moderate degree of nausea and vomiting even after the contributing causative factor has been treated and metabolic, hemodynamic derangements if any have been corrected.

### Statistical Analysis

The analysis was performed by SPSS. Quantitative data were analyzed using Student's *t*-test, and qualitative data were analyzed using Fischer's test and Chi-square test. $P < 0.05$ was considered statistically significant.

## RESULTS

Both the groups were comparable in terms of their physical attributes such as age, weight, height, and BMI. Furthermore, as depicted in Table 1, they were comparable in terms of their American Anesthesia Society (ASA) grading, duration of surgery, and anesthesia. The difference between the both groups for their physical attributes, ASA grading, duration of surgery, and anesthesia was not found out to be significant ($P > 0.05$).

The incidence rate of nausea (5.5%, and 1.8%) and vomiting (3.6%, and 1.8%) was found out to be in Group D while in Group G the incidence of nausea (27.3%, and 20%) and vomiting was found out to be (21.8% and 14.5%) in both early and late post-operative period, respectively, and the difference between groups was also found out to be statistically significant ($P < 0.05$) [Table 2].

The comparison for the severity of nausea and vomiting in early and late period as per four-point verbal response indicated in Table 3. Very few (5.8% and 3.6%) of Group D patients has mild and moderate degree of nausea and vomiting in early period and this difference in both groups was found out to be statistically significant ($P < 0.05$). Similarly as shown in Table 4, in late post-operative period, only 1.8% of patients has complained of mild and moderate degree of both nausea and vomiting and this difference in both groups was also found out to be statistically significant ($P < 0.05$).

As far as, the rescue Antiemetic medication, that is, inj. Metoclopramide is concerned, only in 3.6% patient in early period and it was not required in late period in Group D while it was required in about 30.9% of patients belonging to Group G. This difference is found out to be statistically significant ($P < 0.05$) [Table 5].

**Table 1: Characteristics features of patients in Group G and Group D**

| Characteristics of patients | Group G | Group D | *P* value | Significance |
|---|---|---|---|---|
| | Mean±SD | Mean±SD | | |
| Age (years) | 46.09±6.42 | 45.84±7.04 | 0.8 | Not significant |
| Weight (kg) | 58.75±6.89 | 58.73±6.91 | 0.9 | Not significant |
| Height (cm) | 161.49±6.91 | 161.51±6.87 | 0.9 | Not significant |
| BMI (kg/m$^2$) | 22.52±2.08 | 22.51±2.08 | 0.9 | Not significant |
| Duration of Surgery (in minutes) | 73.91±16.82 | 73.45±17.90 | 0.9 | Not Significant |
| Duration of Anaesthesia (in minutes) | 84.91±16.43 | 86.00±18.27 | 0.7 | Not Significant |
| ASA I | 41 (74.5%) | 43 (78.2%) | 0.2 | Not significant |
| ASA II | 14 (25.5%) | 12 (21.8%) | | |

**Table 2: Comparison of incidence of Nausea and Vomiting in early and late period in Group G and Group D**

| Time period | Event | Status | Group G (*n*=55) (%) | Group D (*n*=55) (%) | *P* value | Significance |
|---|---|---|---|---|---|---|
| Early period | Nausea | Present | 15 (27.3) | 3 (5.5) | 0.0036 | Significant |
| | | Absent | 40 (72.7) | 52 (94.5) | | |
| | Vomiting | Present | 12 (21.8) | 2 (3.6) | 0.008 | Significant |
| | | Absent | 43 (78.2) | 53 (96.4) | | |
| Late Period | Nausea | Present | 11 (20.0) | 1 (1.8) | 0.004 | Significant |
| | | Absent | 44 (80.0) | 54 (98.2) | | |
| | Vomiting | Present | 8 (14.5) | 1 (1.8) | 0.03 | Significant |
| | | Absent | 47 (85.5) | 54 (98.2) | | |

**Table 3: Comparison of severity of nausea and vomiting in early period in Group G and Group D**

| Event | 4 point verbal descriptive score | Group G (%) | Group D (%) | Total (%) | *P* value | Significance |
|---|---|---|---|---|---|---|
| Nausea | None | 40 (72.7) | 52 (94.5) | 92 (83.6) | 0.02 | Significant |
| | Mild | 10 (18.1) | 2 (3.6) | 12 (10.9) | | |
| | Moderate | 5 (9.1) | 1 (1.8) | 6 (5.5) | | |
| | Severe | 0 (0.0) | 0 (0.0) | 0 (0.0) | | |
| Vomiting | None | 43 (78.1) | 53 (96.4) | 96 (87.3) | 0.04 | Significant |
| | Mild | 7 (12.7) | 1 (1.8) | 8 (2.7) | | |
| | Moderate | 5 (9.1) | 1 (1.8) | 6 (5.5) | | |
| | Severe | 0 (0.0) | 0 (0.0) | 0 (0.0) | | |

**Table 4: Comparison of Severity of Nausea and Vomiting in late period in Group G and Group D**

| Event | 4 point verbal descriptive score | Group G (%) | Group D (%) | Total (%) | *P* value | Significance |
|---|---|---|---|---|---|---|
| Nausea | None | 44 (80.0) | 54 (98.2) | 98 (89.1) | 0.006 | Significant |
| | Mild | 7 (12.7) | 1 (1.8) | 8 (7.3) | | |
| | Moderate | 4 (7.3) | 0 (0.0) | 4 (3.6) | | |
| | Severe | 0 (0.0) | 0 (0.0) | 0 (0.0) | | |
| Vomiting | None | 44 (80.0) | 54 (98.2) | 98 (89.1) | 0.02 | Significant |
| | Mild | 8 (14.5) | 1 (1.8) | 9 (8.2) | | |
| | Moderate | 3 (5.5) | 0 (0.0) | 3 (2.7) | | |
| | Severe | 0 (0.0) | 0 (0.0) | 0 (0.0) | | |

**Table 5: Comparison of requirement of rescue anti-emetics (Inj. Metoclopramide) in group G and Group D**

| Rescue Anti Emetic | | Group G (%) | Group D (%) | Total (%) | *P* value | Significance |
|---|---|---|---|---|---|---|
| Early period | No | 45 (81.8) | 53 (96.4) | 98 (89.1) | 0.03 | Significant |
| | Yes | 10 (18.2) | 2 (3.6) | 12 (10.9) | | |
| Late period | No | 48 (87.3) | 55 (100.0) | 110 (93.6) | 0.01 | Significant |
| | Yes | 7 (12.7) | 0 (0.0) | 7 (6.4) | | |

**Table 6: Comparison of total response (24 h) in Group G and Group D**

| Complete response | Group G (%) | Group D (%) | Total (%) | *P* value | Significance |
|---|---|---|---|---|---|
| No | 26 (47.3) | 4 (7.3) | 30 (27.3) | <0.0001 | Significant |
| Yes | 29 (52.7) | 51 (92.7) | 80 (72.7) | | |

In our study, 92.7% patients belonging to Group D while only 52.7% in Group G shown complete response and this difference between both groups also found out to be statistically significant ($P < 0.05$) [Table 6].

## DISCUSSION

The PONV is frequently the cause of great distress to patients and it is often the worst memory of their hospital stay.[2] The consequences of prolonged PONV (PONV) range from longer duration of stay in hospital for patients with its economic implications to physical, metabolic, and psychological effect[9] and on severe cases many the patients can landed up in aspiration of gastric contents and death.[1] Before 1990, various pharmacological agents belonging to antiemetic class such as phenothiazines, antihistamines, butyrophenones, prokinetics, and anticholinergics have been used alone but study done by Henzi had shown that combination antiemetic therapy was far more superior benefit than monotherapy.[9,10] Since then several studies have been conducted with combination of antiemetics for prophylaxis for PONV like Gan in 2002[11], Apfelbaum *et al.* in 2013[12] in which the anti-emetic efficacy of one drug is at the most a 50% only but when combination of serotonin antagonists with dexamethasone used then it has not only shown better efficacy of controlling PONV but also shown very good response with minimal adverse effects in patients with various risk factors.

The incidence of PONV in female patients undergoing modified radical mastectomy reported to be in range of 60–80% when they have not given any prophylaxis.[2] In our study, the overall incidence of nausea and vomiting found out to be 47.3% and 23.3%, respectively, among patients who received only Inj. Granisetron.

The study conducted by Fuji *et al*.[13] in Japan to evaluate the efficacy of Granisetron-dexamethasone combination for prevention of PONV among 135 female patients aged between 40 and 65 years under general anesthesia for breast carcinoma who received placebo (saline), Granisetron 40 mcg/kg i.v. or Granisetron 40 mcg/kg + dexamethasone 8 mg i.v. immediately before the induction of anesthesia. The corresponding incidence during 3–24 h after anesthesia was 56%, 84% and 96%, respectively. Similar incidences of PONV have been reported to be 40% by Gupta, Jain,[3] and 30% in a study conducted by Moussa *et al*.[14] among patients who received Inj. Granisetron for post-exposure prophylaxis.

In this study, the overall incidence of PONV in the patients who have received prophylaxis of Inj. Granisetron and inj. Dexamethasone has reported to be 6.3% and 5.4% for nausea and vomiting, respectively. This finding of patient receiving both Inj. Granisetron and Inj. Dexamethasone correlate well with study conducted by Islam *et al*.[15] and Gupta *et al*.[16] with 4% and 8%, respectively.

In this study, only 3.6% of patients in Group D had to receive Inj. Metoclopramide in the early post-operative period whereas there was not need of rescue antiemetic in the delayed post-operative in Group D.

Thomas and Jones[17] conducted a prospective randomized comparative study of dexamethasone, ondansetron, and ondansetron + dexamethasone as prophylactic antiemetic therapy in patients undergoing day case gynecological surgery. They found that failure of prophylaxis during 1st 3 h after surgery was recorded in 22%, 28.3%, and 8.6%. The overall incidences for the 24 h post-surgery were 42.4%, 48.3%, and 34.5%, respectively.

The over 24 h period complete response was noted in about 92.7% patients among patients who have received inj. Granisetron and inj. Dexamethasone for PONV. This finding has been coincident with the both studies conducted by Fuji *et al*.[13] and Gupta and Jain[2] in which the complete response was found out to be same, that is, 96% among patients who had received ini. Granisetron with Inj. Dexamethasone, respectively.

Bhattacharya and Banerjee[18] conducted a double-blind randomized placebo controlled trial to compare the efficacy of ondansetron and Granisetron for prevention of PONV after day care gynecological laparoscopy. They found that incidences of emetic episodes were 20% in ondansetron group and 7% in Granisetron group which is clinically significant ($P < 0.05$).

Hence, the results of our study are in concordance with the previous studies by different authors, with few differences, which are insignificant. Hence, it has been seen that combination prophylaxis of Inj. Granisetron and Inj. Dexamethasone has not only reduce the incidence of PONV in modified radical mastectomy among female patients but also reduced its severity in both early and late period.

## CONCLUSION

The combination prophylaxis of Granisetron and Dexamethasone is clearly more efficacious in preventing PONV than Granisetron alone in female patients undergoing modified radical mastectomy under general anesthesia.

### Limitation of Study

This study did not consider adverse effect of the concerned drugs; hence, we have not drawn any conclusion in this regard. There are some chances that even after thorough pre-operative assessment; certain unidentified or unreported pre-morbid conditions in breast carcinoma patents can affect the nausea and vomiting postoperatively. Furthermore, the present study has been restricted to only female patients undergoing modified radical mastectomy and, hence, the findings cannot be generalized to other variety of surgeries.

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Original Article

# Role of 128 Dual Source Computed Tomography Angiography Imaging for Detection of Cerebral Aneurysm – Retrospective Study

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## Abstract

**Background:** Multislice computed tomography (CT) has great potential for use in vascular studies. Multislice 128 slice CT angiography is an excellent non-invasive screening test in the assessment of intracranial aneurysms, both on a per-aneurysm and per-patient basis.

**Purpose:** The aim of the study was to evaluate non-invasive CT angiography (CTA) on 128 dual sources CT scan for detecting the aneurysm in spontaneous cases of subarachnoid bleed.

**Materials and Methods:** We evaluated 51 cases with spontaneous subarachnoid bleed by 128 slice dual-source CT in digital subtraction angiography (DSA) CT brain angiography protocol for the detection of aneurysms. The analysis of the scan for aneurysm detection was performed using 2D, multi-planar reconstructions, volume rendered techniques, and 3D maximum intensity projection. Aneurysms were evaluated for size, location, and other imaging characteristics. Patients with subarachnoid bleeds who were negative for aneurysm were further evaluated by the DSA.

**Result:** Fifty-one patients with age group of 23–85 (mean age 53.60 ± 13.76 years) were investigated. In 42 patients, aneurysms were identified in CT angiography, and their comprehensive evaluation such as location, size, and neck direction status were appropriately done, and information guided the neurosurgeons/interventionist for the proper management. Nine cases that were negative for aneurysm were also negative in DSA.

**Conclusion:** The faster high-resolution multislice 128 slice dual-source CT scan allows for non-invasive, safer, and accurate identification of cerebral aneurysms and accurately determines their size, morphology, and location. Specificity and sensitivity of 128 dual-source CT angiography in DSA protocol are near to the DSA which is the gold standard.

**Key words:** 128 Slice dual-source computed tomography, Cerebral aneurysm, Digital subtraction angiograph, Imaging, Subarachnoid bleed

## INTRODUCTION

Subarachnoid hemorrhage (SAH) is a devastating acute neurological disease with a 43.0% risk of death and a 57.0% mortality rate at 6 months.[1] The three most common causes of mortality were direct effects of the primary hemorrhage (55.0%), aneurysm rebleeding (17.0%), and medical complications (15.0%).[2] Aneurysms that have ruptured already have a greater risk of re-hemorrhage. Thus, it is essential to detect aneurysm, describes its morphology to guide treatment accurately. It makes neuro-imaging a critical element in assessing and curing patients with cerebral aneurysms.

Magnetic resonance angiography, CT angiography, and digital subtraction angiography (DSA) are used for detection of a cerebral aneurysm. Each neuro-imaging technique has its weaknesses, strengths, and current developments. In this article, we studied the accuracy of 128 dual source CT angiography and DSA protocol in detecting cerebral aneurysm and compared it with DSA imaging, where CT Angiography was negative to detect the aneurysm.

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The 128 dual-source CT performs the investigation in <1.9 s from base to the vertex and the special resolution of the machine is 0.5 mm with a high temporal resolution. DSA neuromode removes the bones in one click without causing any loss in image resolution. This gives us an easy, quick, and accurate analysis of the aneurysm.

This study's aim and objective was, does faster high resolution 128 slice dual-source CT scan allow accurate identification of cerebral aneurysms including tiny ones and can it be used as the first-line investigation to replace DSA which is the gold standard.

## MATERIALS AND METHODS

It is a retrospective study, and cases admitted in our 950-bedded hospital were included in the study. We collected 1½ year data for the analyses. All patients with spontaneous subarachnoid bleed on NCCT or strong clinical suspicion for SAH based on patients' symptoms even if NCCT was negative for subarachnoid bleed were included in the study. CT has the high sensitivity (91.0–98.0%) for detecting SAH, though the sensitivity of CT for SAH decreases with time.

### CT Protocols

All the scans of the studied patients were performed as per department protocols in DSA CT brain angiography protocols, a non-contrast sequence to subtract from post-contrast sequences obtained from base to top of the skull. Pre-monitoring ROI was placed in the air in a section taken just below the skull base. The post-contrast scan was planned from base to the top of the skull with a scan time of approximately 1.90 s and a delay of 02 s. 50–60 CC IV non-ionic contrast was given using a dual pressure injector at a rate of 5 ml/s followed by 30 cc saline chase with a similar rate. Post-contrast triggering was started manually by seeing the contrast in the internal carotid arteries in pre-mentioned section below the base of skull section, and a scan was taken.

The analysis of the scan for aneurysm detection was performed as per department protocol using 2D, multiplanar reconstructions, volume-rendered techniques, and 3D maximum intensity projection, on the syngovia platform. A comprehensive assessment of aneurysm location, size, and other characteristics of images were evaluated. Patients who were negative for aneurysm were further assessed by DSA.

### Inclusion Criteria

The following criteria were included in the study:

1. All patients referred with spontaneous subarachnoid bleed on NCCT.
2. The patient presenting late with a history of sudden severe headache and clinically with high suspicion of aneurysm.

### Exclusion Criteria

As such none

### Confounders

Present demonstration of cerebral aneurysm was done by spontaneous subarachnoid bleed on NCCT or strong clinical suspicion for SAH. A comprehensive assessment of aneurysm location, size, and other characteristics of images will be evaluated.

### Ethical Clearance

The research procedure followed was in accordance with the approved ethical standards of the Department of Radiodiagnosis, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh, India Ethics Committee (Human).

### Statistical Methods

All analyses were performed with Statistical Package for the Social Sciences version 23.0 statistical program. Quantitative variables were stated as mean ± SD and categorical variables as frequencies or percentages. For normally distributed data, a two sample student's *t*-test was used to examine the difference in the radiation dose between dual energy CTA and the digital subtraction CTA. To assess diagnostic performance of the dual energy CTA compared with the 3D DSA in detection of the intracranial aneurysms, data were examined on the basis of per-patient to differentiate patients with minimum one aneurysm and the patients with zero aneurysm. $P < 0.05$ was considered significant for all the tests.

## RESULTS/OBSERVATION

Of 51 patients, 42 were positive for the aneurysm, nine were negative for the aneurysm on CT angiography. All nine cases were negative for an aneurysm on CT underwent DSA [Chart 1].

The mean-age of the studied patients was 53.60 ± 13.76 years, and the majority of patients were of the age group of 50–59 years (33.33%), followed by the age 60–69 years (23.53%) and 40–49 years (17.65%) while only 5.88% were affected in age group of 20–29 years and 7.84% of the age group of 30–39 years and also the patients were equally divided, that is, out of the total 51 patients, 25 (49.02%) were males and 26 (50.98%) were females [Table 1].

In the present study in the majority of patients, the location was ACOM (33.33%) followed by MCA and ICA (13.73% each) [Table 2] and the mean aneurysm size was found to be 6.52 ± 5.46 mm with a majority of patients having size of aneurysm below 5 mm (48.7%), followed by 5-10 mm size (38.5%) and more than 10 mm (12.8%) [Chart 2].

### Images of CT Angiography

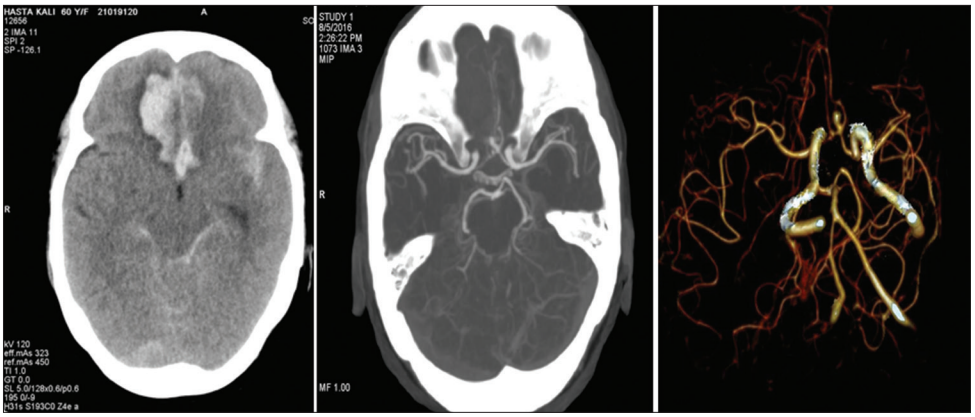

**Figure 1: 60 years/F, Small aneurysm from junction of left A1, A2 with A COMM**

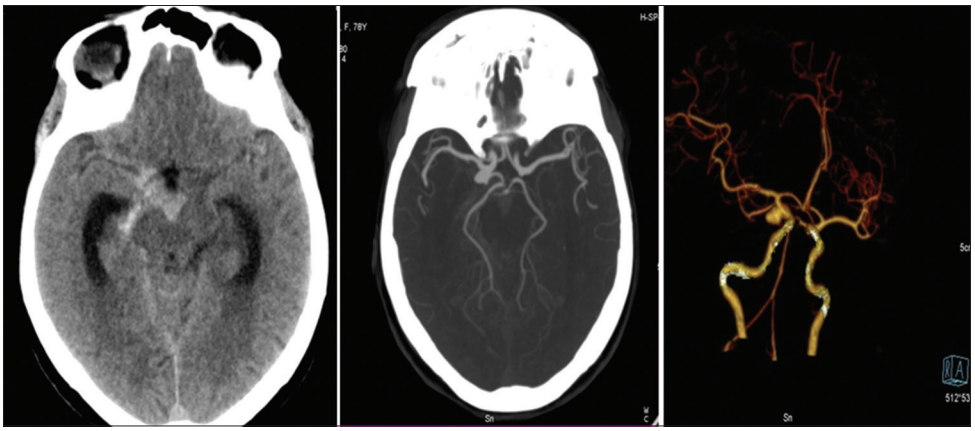

**Figure 2: 78 years/F, ANEURYSM FROM RT PCOM and ICA JUNCT**

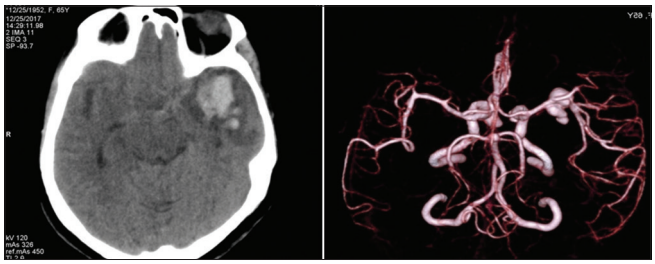

**Figure 3: 65 Y/F, Multiple aneurysms from right ICA, left MCA, and tip of basilar artery**

In the present study, the sensitivity of CT angiography was found to be 97.67%, specificity was 100.0%, PPV was 100.0%, NPV was 88.89%, and accuracy was 98.04% [Tables 3 and 4].

## DISCUSSION

The use of a non-invasive assessment method to diagnose cerebral aneurysms in subarachnoid bleeds is one of the medical centers' goals. From the beginning of modern imaging techniques, attempts have been made to find an alternative for DSA. Efforts are being made to replace it with non-invasive methods.

One of the most important causes of SAH is a ruptured cerebral aneurysm. Cerebral DSA has been used as the gold standard for aneurysm detection.[3,4] However, DSA is an invasive study. The risk of obtaining an enduring neurologic deficits with DSA cerebral angiography in the patients with the SAH is around 0.1%.[5,6] Computed tomographic cerebral angiography is the non-invasive imaging modality that is being increasingly used to evaluate suspected intracranial aneurysms. The introduction of 128 slice CT scanners has greatly advanced CT angiography's role in neurovascular imaging with further advantage of DSA mode.[7,8]

### Mean Age

In the present study, the average age of the studied patients was 53.60 ± 13.76 years and the majority of patients were of the age group of 50–59 years (33.33%), followed by the age 60–69 years (23.53%) and 40–49 years (17.65%) while only 5.88% were affected of the age group 20–29 years and 7.84% in the age group 30–39 years. Our findings are in accordance with Azhari *et al.*[9] who reported 48.3 years mean age of their patients, and in similar studies, the mean age was estimated between 49 and 55 years which makes our findings extensive.[10-13] This implies that aneurysms'

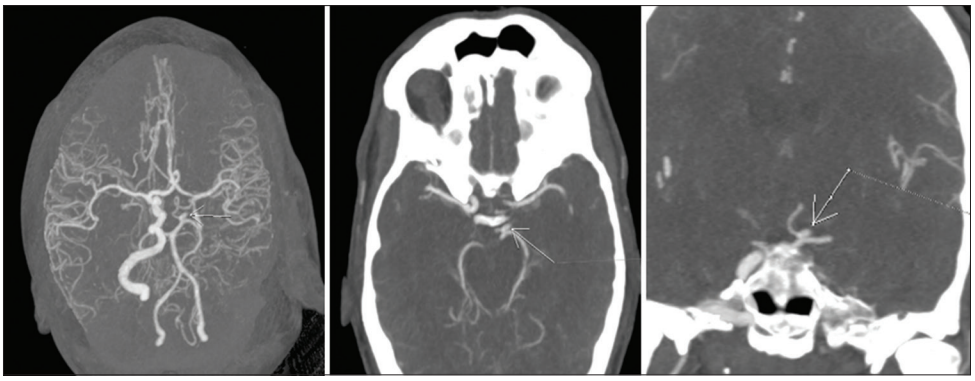

**Figure 4: 30 years/M, sudden headache, Small aneurysm from junction of left p COMM and P1**

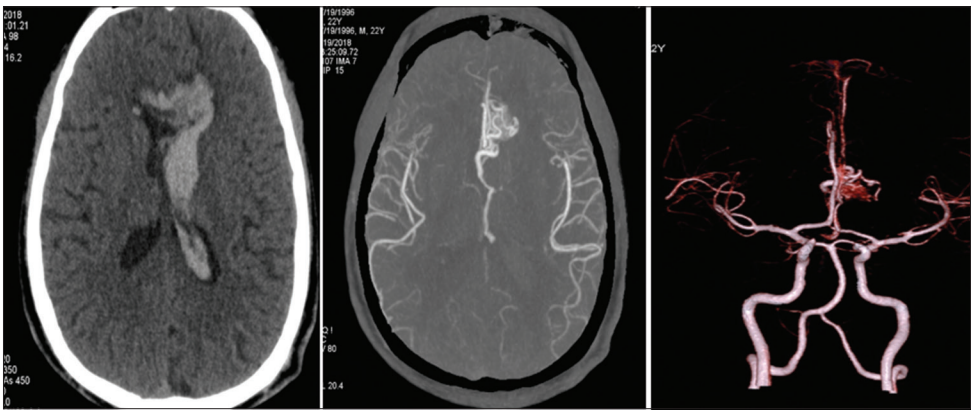

**Figure 5: 22 years/male with bleed left parafalcine and ventricle. SMALL av malformation in left parafalcine region**

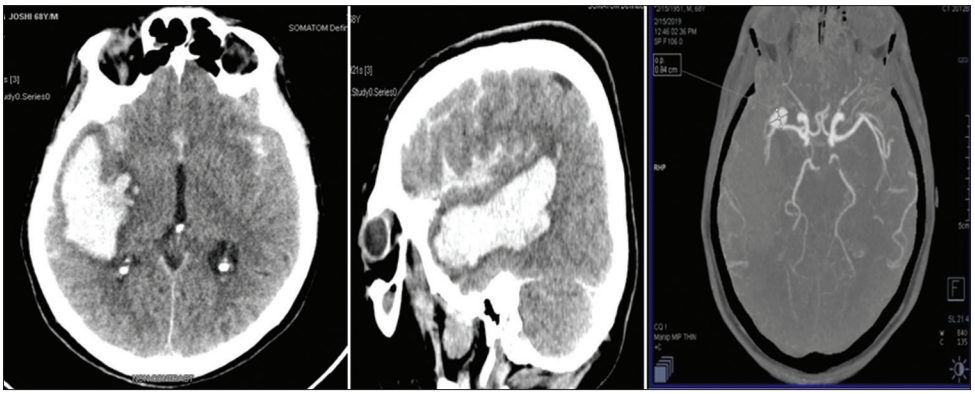

**Figure 6: 68 years/M, Large 13 × 8.5 mm aneurysm from right M1 and M2**

problem occurs majorly in the 6th and 7th decades of the human lifespan.

### Gender Distribution

In the present study, the patients were equally divided, out of the total 51 patients, 25 (49.02%) were males and 26 (50.98%) were females. Azhari *et al.*[9] reported similar findings as in the present study, that is, 21 (52.5%) patients were men and 19 (47.5%) were women. Takesam *et al.*[13] depicted that of 42 patients with the SAH and aneurysm shown by the DSA 26 (62.0%) were female and 16 (38%) were male patients.

### Location of Aneurysm

In the present study, in the majority of patients, the location was ACOM (33.33%), followed by MCA and ICA (13.73% each) [Figures 1-7]. Our findings were in accordance with Anderson *et al.*[14] who reported ACOM in 47.0% cases, followed by MCA (34.0%). Azhari *et al.*[9] quoted in terms of location of aneurysms; 15 were in the anterior communicating artery (ACOA), and 21 in the middle cerebral artery (MCA). This shows that the major locations for aneurysm were ACOM and MCA.

**Table 1: Demographic profile**

| Parameters | No. of patients (*n*=51) | Percentage |
|---|---|---|
| Gender | | |
| Male | 25 | 49.02 |
| Female | 26 | 50.98 |
| Age in years | | |
| 20–29 | 3 | 5.88 |
| 30–39 | 4 | 7.84 |
| 40–49 | 9 | 17.65 |
| 50–59 | 17 | 33.33 |
| 60–69 | 12 | 23.53 |
| 70–79 | 5 | 9.80 |
| ≥.8 | 1 | 1.96 |
| Mean age | 53.60±13.76 years | |

**Table 2: Location of an aneurysm**

| Location | No. of patients (*n*=51) | Percentage |
|---|---|---|
| ACA | 5 | 9.80 |
| ICA/PCA Junction | 1 | 1.96 |
| PCA P1 and POST COMM JUNCTION | 1 | 1.96 |
| ICA | 7 | 13.73 |
| MCA | 7 | 13.73 |
| ACOM | 17 | 33.33 |
| VBA | 3 | 5.88 |
| BA | 1 | 1.96 |

MCA: Middle cerebral artery

**Table 3: The diagnostic performance of dual-energy CTA compared with DSA in the detection of intracranial aneurysms**

| CTA | DSA | | Total (*n*=51) |
|---|---|---|---|
| | Positive | Negative | |
| Positive | 42 (82.3) | 0 (0.0) | 42 (82.3) |
| Negative | 1 (1.96) | 8 (15.7) | 9 (17.6) |
| Total | 43 (84.3) | 8 (16.9) | 51 (100.0) |

CTA: Computed tomography angiography

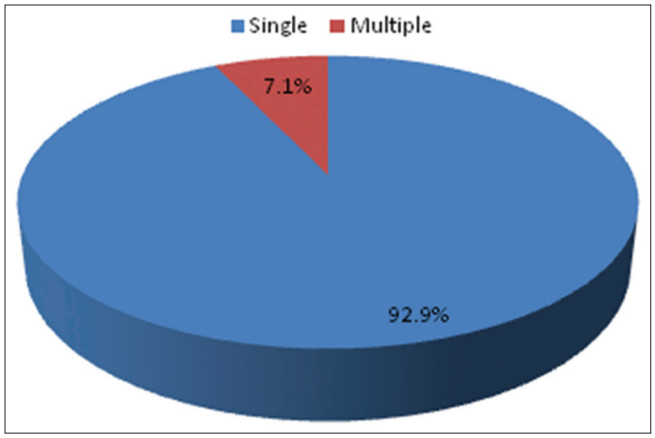


**Chart 1: Number of an aneurysm (*n* = 42) [Single 39 and Multiple 3]**

## Size of Aneurysm

In our study, the mean aneurysm size was found to be 6.52 ± 5.46 mm with the majority of patients having size

**Table 4: Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of dual-energy CTA**

| | |
|---|---|
| Sensitivity | 97.67% |
| Specificity | 100.0% |
| Positive predictive value | 100.0% |
| Negative predictive value | 88.89% |
| Accuracy | 98.04% |

CTA: Computed tomography angiography

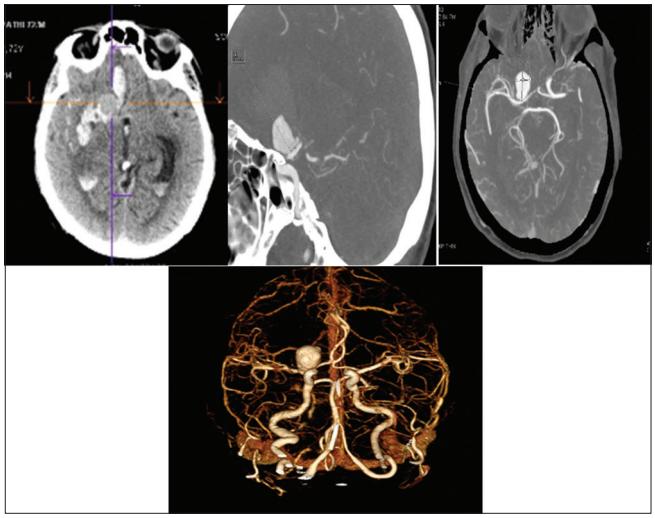

**Figure 7: 70 years male, h/o vomiting, and sudden unconsciousness 1 day, large aneurysm from junction of right ICA**

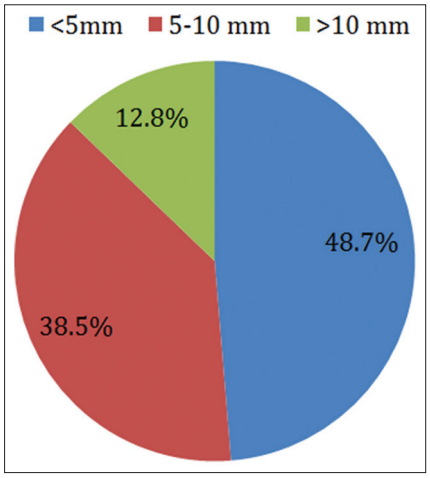


**Chart 2: Size of an aneurysm (single aneurysm only) with mean size 6.52±5.46 mm**

of aneurysm below 5 mm (48.7%), followed by 5–10 mm size (38.5%) and more than 10 mm (12.8%). Our findings were in accordance with Azhari *et al.*[9] who reported the mean size of the aneurysm as 6.3–2.1 mm. Furthermore, the mean size of aneurysms in a study performed by Luo *et al.*[15] was 6.4 mm and in a study performed by Chen *et al.*[16] was 5.5 mm.

### Diagnostic Performance of the Dual Energy CTA and 3D DSA

In the present study, the sensitivity, specificity, PPV, NPV, and accuracy of the CT angiography were 97.67%, 100.0%, 100.0%, 88.89%, and 98.04%, respectively, which was similar to the findings of Wintermark *et al*.[17] who reported that the overall performance of the spiral CT scanning technique was dramatically improved by the technological development of multidetector-row CT scanners, particularly in CT angiography. In this study, the sensitivity, specificity, and accuracy of MSCT angiography for detection of the intracranial aneurysms were 94.8%, 95.2%, and 94.90%, respectively, on per-aneurysm basis and 99.0%, 95.2%, and 99.0%, respectively, on a per-patient basis. The interobserver agreement was 98.0%.

In an analysis by Guo *et al*.,[18] a sensitivity of 97.0% and specificity of 91.0% were found for CT angiography. The sensitivity, specificity, and accuracy of CT angiography were 95.1%, 94.1%, and 95.0%, respectively, by Donmez *et al*.[19] study. Chen *et al*.[10] reported sensitivity, specificity, and accuracy of the CT angiography as 98.3%, 98.0%, and 97.9%, respectively. In a study performed by Teksam *et al*.,[13] accuracy, sensitivity, and specificity of detecting recurrent or residual aneurysms on the MSCTA were 0.80, 0.60, and 1.00, respectively, also negative and positive predictive values were 0.71 and1.00, respectively. The sensitivity, specificity, accuracy, PPV, and NPV for CT angiography were achieved as 99.0%, 99.0%, 90.0%, 96.0%, and 98.0% by Westerlaan *et al*.[19] Uysal *et al*.[20] reported the sensitivity and specificity of CT angiography in detecting aneurysm as 98.6 and 97.6, respectively. In all the previous quoted studies, the sensitivity and specificity were high and were consistent with our study. The differences may relate to the type of device, image quality, and neuroradiologists.

Recent studies observed overall higher detection rates of up to 97.0%, and few authors already exclusively rely on the results of CT angiography in patients with SAH.[21] Imaging after the surgical aneurysm clipping has conventionally been achieved with the conventional catheter based angiography, CT angiography may provide an adequate alternative in several cases.[22,23]

Pitfalls of the CT angiography consist of lack of the visibility of the small arteries, complexity in differentiating infundibular dilatation at origin of an artery from aneurysm, kissing vessel artifact, and demonstration of the venous structures which can imitate aneurysms, failure to identify the thrombosis and calcification on 3-dimensional images, and beam hardening objects produced by aneurysm clips.[24] Few of them are overcome by 128 slice dual sources CT.

## CONCLUSION

Multislice 128 slice CT angiography is an excellent non-invasive screening test in assessment of intracranial aneurysms, both on a per-aneurysm and per-patient basis. It provides a precise characterization of intracranial aneurysms, including size, structure, and orientation and can also depict the presence of thrombosis and rupture. Because of excellent image quality, high diagnostic accuracy, and lower radiation dose, dual energy CTA can be used regularly for the clinical purposes. CT angiography can be the preferred non-invasive modality for the measurement of intracranial aneurysms in the patients with the acute SAH and has the potential to substitute, in most cases, for DSA.

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Original Article

# Potentially Malignant Disorders of Oral Cavity – A Review of Etiology and Clinicopathological Correlation

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## Abstract

**Background:** Oral cancer is the most life threatening of all oral diseases and may be preceded by oral potentially malignant disorders (OPMD). Oral potentially malignant disorders show visible clinical changes in the oral mucosa in the form of white or red patch which may resemble each other clinically making biopsy mandatory for confirmation.

**Purpose:** This article is an attempt to classify oral potentially malignant disorders, correlate the clinical appearance and malignant transformation of these disorders for clinician's understanding of OPMD, which in turn can be helpful to take appropriate measures in patient management.

**Methodology:** In the systematic review process, 40 articles and 5 textbooks were reviewed. Literature search was done using Google search engine. Textbook references were done from institutional library.

**Conclusion:** Data from 5 textbooks and 27 articles were considered and it was concluded that clinical aspects of OPMD are of prime importance in predicting and preventing malignant transformation.

**Key words:** Etiology, Malignant transformation, Oral cancer, Potentially malignant

## INTRODUCTION

Oral cancer is the most life threatening of all oral diseases. It has a prolonged natural history with oral potentially malignant disorders (OPMD) which were earlier termed as precancerous lesions and precancerous conditions. The recognition and diagnosis of OPMD will help in early treatment, patient survival and in reducing morbidity related to treatment of oral cancer. The most common oral cancer which is squamous cell carcinoma is correlated to OPMD. It has been well established that oral cancers are preceded with visible clinical changes in the oral mucosa usually in the form of white or red patch. Sometimes these oral lesions resemble each other clinically hence making biopsy mandatory for confirmation.[1] The clinical characteristics of OPMDs can show remarkable variations within the same histopathologically defined lesions which may be critical in assessing malignant transformation potential and thus may serve as an important prognostic marker.[2] Surgical treatment of oral cancer and effects of radiation may produce difficulty in speech, mastication, swallowing, and reduced ability for social interaction along with economic burden.[3] Correct diagnosis and timely treatment of OPMDs will help in preventing it's malignant transformation.[4] This article is an attempt to correlate the etiology, clinical appearance, and malignant transformation of these disorders and help clinicians in better understanding of OPMD for its early diagnosis and management.

In the systematic review process, 40 articles and five textbooks were reviewed. Data from five textbooks and 27 articles were considered. Other articles were excluded

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because there was repetition of information. Literature search was done using Google search engine. Textbook references were done from institutional library.

## Concept of OPMD

Concept of malignant transformation in oral mucosa has been proposed for more than 100 years.[4] Clinical observation indicates that in a proportion of cases of squamous cell carcinoma in the mouth, they are preceded by or coexist with other distinctive oral mucosal lesion which are considered to be precancerous. It is suggested that these associated lesions occur more frequently than would be expected to arise and the implication is that these may be precursors of malignancies.[5]

Two stage mechanism hypothesis of carcinogenesis suggests that cells are first changed from normal to dormant tumor cells by some carcinogenic influence. At this phase of initiation tissue may be clinically and histologically normal. As there is subsequent exposure of initiated tissues to these carcinogenic agents, proliferation of dormant tumor cells results and a visible tumor is produced. Initiating agent causes carcinogenic alteration but not morphological change. Morphological alteration is caused by promoting action of same carcinogenic agent. It is unlikely that a single sudden event is responsible for malignant neoplasm. A progressive loss or diminished effectiveness of normal control mechanism on cell growth and division seems to be the more likely cause. It is reasonable that a stage would exist in which the epithelium was demonstrably abnormal, but had not invaded the underlying connective tissue. This stage is called as premalignancy or precancer.[5] Histological connotation to premalignancy is denoted by aberrant and uncoordinated cellular proliferation depicted basically at cellular level (atypia) and reflections of which could be seen at tissue level (dysplasia). Histopathological features of epithelial dysplasia as explained by Krammer in 1978 are as follows:[6]

- Loss of polarity of basal cells.
- Presence of more than one layer of cells having basaloid appearance.
- Increased nuclear to cytoplasmic ratio.
- Drop shaped rete processes.
- Irregular epithelial stratification.
- Increased number of mitotic figures.
- Presence of mitotic figures in superficial half of epithelium.
- Cellular pleomorphism.
- Nuclear hyperchromatism.
- Enlarged nucleoli.
- Reduction in cellular cohesion.
- Keratinization of single cells or cell groups in prickle cell layer.

Oral pathologists use this term epithelial dysplasia to describe the histopathological features of a tissue specimen which is associated with risk of malignant change and assign a grade of severity.[6] Dysplasia is graded as mild, moderate, severe, and carcinoma *in situ*. Mild epithelial dysplasia refers to alterations confined to basal and parabasal layers of epithelium. Moderate epithelial dysplasia shows involvement of basal layer and spinous layer up to its mid portion. Severe grade is given when epithelial dysplasia involves whole of basal and spinous layer. Carcinoma *in situ* refers to involvement of entire thickness of epithelium from basal to superficial most layer.[7]

Certain lesions denoted as premalignant are based on evidence that:

- In longitudinal studies areas of lesion identified as precancerous at first assessment have undergone malignant change during follow-up.
- Some of these alterations such as red and white mucosal changes are seen to coexist with squamous cell carcinoma at its margins.
- A proportion of these may share morphological and cytological changes observed in epithelial malignancies, but without frank invasion.
- Some of the molecular and genomic changes seen in oral cancers are detected in these precancerous or premalignant phases.[1]

## Evolution of Terminologies

The term precancer was first described by Victor Babes in 1875. However, the concept of precancer was present since 1805 as suggested by a European panel of scientists. They described precancer as certain benign lesion which will always develop into invasive malignancy. Sir James Paget described a lesion of oral mucosa termed leukokeratosis of palate and tongue in smokers with an increased risk of conversion into malignant tumor. Later on various terminologies such as premalignancy, preneoplastic, carcinoma prone, and intraepithelial neoplasia were evolved and used by many researchers. The World Health Organization (WHO) workshop in 1978 proposed the term precancer for such lesions and classified them into precancerous lesions and conditions. The WHO defined precancerous lesion as morphologically altered tissue in which cancer is more likely to occur than its apparently normal counterpart and precancerous condition as a generalized state associated with significantly increased risk of cancer. Recent workshop of the WHO in 2005 proposed the term OPMD instead of classifying them as precancerous lesions and conditions since all these lesions may not transform into oral cancer. They also used the terminology "epithelial precursor lesion" to describe the same.[1]

## Working Classification of OPMD

A comprehensive classification helps clinicians to develop a treatment algorithm. The working classifications

**Table 1: Classification of OPMD based on clinical presentation**

| Red lesions | White lesions | Mixed red and white lesions |
|---|---|---|
| Erythroplakia | Leukoplakia | Speckled leukoplakia |
| Erosive lichen planus | Proliferative verrucous leukoplakia (PVL) | Oral submucous fibrosis |
| | Candidal leukoplakia | |

OPMD: Oral potentially malignant disorders

**Table 2: Classification of OPMD based on etiology**

| | |
|---|---|
| i. OPMDs related to habits | |
| 1. Tobacco induced | Leukoplakia and its variants<br>Erythroplakia<br>Palatal lesion associated with reverse smoking |
| 2. Areca nut induced | Oral submucous fibrosis |
| ii. OPMDs with no related habits | |
| 1. Autoimmune diseases | Oral lichen planus<br>Discoid lupus erythematosus<br>Graft versus host disease |
| 2. Nutritional deficiencies | Plummer Vinson syndrome<br>Oral epithelial atrophy associated with Vitamin B deficiency |
| 3. Infections | Hyperplastic candidiasis<br>Syphilis |
| 4. UV radiation induced | Actinic cheilitis<br>Keratoacanthoma |
| 5. Immunodeficiency diseases | Blooms syndrome<br>Fanconi's anemia |
| 6. Genodermatosis | Epidermolysis bullosa<br>Dyskeratosis congenita<br>Xeroderma Pigmentosum |
| 7. Immunosuppressive states | Solid organ transplantation<br>AIDS |

OPMD: Oral potentially malignant disorders

formulated in this article is an attempt to categorize OPMD based on etiopathogenesis, clinical presentation, and risk of malignant transformation [Tables 1-3].

## Discussion of Various OPMD

A clinician comes across various OPMD in their routine practice. Clinical presentation and its correlation with risk of malignant transformation of these commonly encountered OPMD are discussed below:

1. Leukoplakia

It is a precancerous white lesion defined by the WHO as "white plaque of questionable risk having excluded other known diseases or disorders that carry no increased risk for cancer."[8] Use of the term "disorder" is preferred than "lesion" since malignant transformation does not always take place in leukoplakia areas. It has an increased prevalence among adult males and the most common etiologic factor is tobacco use. Leukoplakia may occur in non-users of tobacco as well.[9] Clinically, this disorder can be classified as homogenous and non-homogenous. The homogenous type is thin, flat, and uniform white plaque which is demarcated from surrounding normal appearing tissues.[8] Non-homogenous type is characterized by well demarcated raised white areas interspersed with erythematous areas.[7] Proliferative verrucous leukoplakia, considered as a form of non-homogenous leukoplakia, has a different clinical presentation. It is more common in elderly females; only < 40% of cases are associated with tobacco and has a significantly increased risk of malignant transformation than other forms of leukoplakia. Erythematous areas, areas of firmness, or induration and ulcerated areas should always be submitted for biopsy.[8] Leukoplakia is a clinical term and histologically it is reported with note on presence or absence of epithelial dysplasia. Dysplasia is graded based on the extent and degree of cytological atypia. The WHO 2005 grading of dysplasia based on architectural disturbances and cytological atypia is as follows:[10]

Grade 1: Squamous hyperplasia
Grade 2: Mild dysplasia
Grade 3: Moderate dysplasia
Grade 4: Severe dysplasia
Grade 5: Carcinoma in situ

Risk of malignant transformation in homogenous leukoplakia is only 0.6–5%, whereas in non-homogenous leukoplakia it is high as 20–25%.[2] Proliferative verrucous leukoplakia shows higher risk of malignant transformation between 70% and 100%.[8]

2. Erythroplakia

Erythroplakia refers to a red patch that cannot be categorized clinically or pathologically as any other condition. It is considered as the most severe form of OPMD because of its high malignant transformation potential.[11] Shear classified erythroplakia into three variants.

- Homogenous erythroplakia – flat, velvety lesion with uniform red appearance.
- Granular erythroplakia – red lesion with granular appearance.
- Speckled erythroplakia – predominantly red lesion speckled with white spots.[3]

**Table 3: Classification of OPMD based on risk of malignant transformation**

| High risk OPMD | Intermediate risk OPMD | Low risk OPMD |
|---|---|---|
| Erythroplakia | Non homogenous leukoplakia | Homogenous leukoplakia |
| Proliferative verrucous leukoplakia | Palatal lesion associated with reverse smoking | Erosive lichen planus |
| | Oral submucous fibrosis | Discoid lupus erythematosus |
| | Candidal leukoplakia | Oral epithelial atrophy associated with nutritional deficiency |

OPMD: Oral potentially malignant disorders

Erythroplakia possess a malignant transformation risk of 90%. According to Shafer and Waldron, 51% of erythroplakia at the time of diagnosis were squamous cell carcinoma histologically, 40% were carcinoma *in situ*, and 9% were mild-to-moderate dysplasias.

3. Oral submucous fibrosis

It is a chronic progressive potentially malignant disorder predominantly seen in people of Asian descent with areca nut chewing being the most important etiologic factor. Clinically, patient presents with trismus along with restricted movement of tongue, lips, and palate which can be attributed to presence of fibrosis histologically. Initial signs and symptoms include vesicle formation, blanching of mucosa and intolerance to spicy food stuffs. Arecoline is the most abundant alkaloid in areca nut and these alkaloids undergo nitrosation and give rise to N-nitrosamines, which might have a cytotoxic effect on cells. Arecoline has been demonstrated to promote collagen synthesis due to its effect on TGF-β. Arecoline activates TGF-β thus stimulating collagen synthesis.

Three main events that are modulated by TGF-β, which favors the collagen production are:

1. Activation of procollagen genes.
2. Elevation of procollagen proteinases levels: (a) Procollagen C-proteinase (PCP)/bone morphogenetic protein1 (BMP1) and (b) procollagen N-proteinase (PNP).
3. Upregulation of lysyl oxidase (LOX) activity.[12]

TGF-β activates the genes for Tissue Inhibitor of Matrix Metalloproteinases (TIMP), thereby more TIMP is formed. This inhibits the activated collagenase enzyme that is necessary for the degradation of collagen. Thus, TGF-β also causes fibrosis by its influence on collagen degradation pathway. Lysyl oxidase, the enzyme required for collagen cross linking is activated by copper. Arecanut is rich in copper, thus increasing the collagen crosslinking and organization of extracellular matrix. Malignant potential of OSF was first described by Paymaster in 1956. Risk of transformation into oral squamous cell carcinoma was found to be 7–13%.[13]

4. Palatal lesion associated with reverse smoking

In reverse smoking habit, cigarette is placed in reverse direction inside the mouth which leads to certain changes in palate which are considered to be potentially malignant. Clinically, it may present with keratosis, excrescence, patches, redness, ulcerations, and non-pigmented areas.[6] Histopathological findings include hyperorthokeratosis, dysplasia, and increased melanin containing cells in basal layer.[14] According to Alvarez Gomez, 12.5% cases showed squamous cell carcinoma histologically.[4]

5. Oral lichen planus

Lichen planus is a chronic, immune mediated mucocutaneous disorder. It involves skin and oral mucosa commonly and can also occasionally involve genital mucosa, nails, and scalp. The prevalence of oral lichen planus worldwide is 0.5–2.6%. The lesion carries a female predilection and is common after fifth decade of life. Clinically, oral lichen planus exhibits reticular, white plaques which are characteristically seen symmetrically on bilateral buccal mucosa. Reticular appearance is due to the presence of interlacing white lines termed as Wickham's striae. It may also show erosive or ulcerative lesions which may be symptomatic. Based on clinical appearance, different types of lichen planus are described which include reticular lichen planus, erosive lichen planus, bullous lichen planus, atrophic lichen planus, papular lichen planus, and plaque like lichen planus.[15]

Cell mediated immunity plays an important role in pathogenesis of lichen planus. Lichen planus antigen induces CD8+ T lymphocytes which are recruited and retained in the subepithelial connective tissue. These lymphocytes induce basal keratinocyte apoptosis by release of cytokines. Thus, histologically lichen planus shows basal cell degeneration producing civatte/hyaline/cytoid bodies and subepithelial band of lymphocytes.[16] Other histological features include hyperkeratosis, focal thickening of spinous layer of epithelium (responsible for Wickham's striae clinically), and saw toothed rete pegs.[15]

Malignant potential of lichen planus is much debated in recent years. The erosive lichen planus possess malignant transformation potential of 1–2%. Even though the etiology of malignant transformation is uncertain, it is thought to be due to the genetic alteration in epithelial cells as a result of persistent increase in levels of cytokines.[15]

6. Candidal leukoplakia (Chronic hyperplastic candidiasis)

Chronic hyperplastic candidiasis is the least common of all variants of candidiasis comprising only 5%.[17] Clinically, it appears as a white nonscrapable plaque on buccal mucosa, tongue, and oral commissures bilaterally and is classified under OPMD in recent WHO classification.[18] Carcinogenic nitrosamines and acetaldehyde which are released by candida albicans are the probabale explanation of malignant transformation in chronic hyperplastic candidiasis. A microenvironment of chronic inflammation will also favor carcinogenesis. Malignant transformation is described in 10% of reported cases.[19] Tobacco use along with candidiasis may increase this risk due to reduction of IgA levels in saliva and impaired neutrophil function.[17]

7. Actinic cheilitis

Actinic cheilitis appears clinically as an ulcerative crust forming lesion of vermilion border of lower lip and

histologically as hyperkeratosis with or without dysplasia.[7] Risk of the development of dysplasia and squamous cell carcinoma of lip in actinic cheilitis is found to be 6–10%.[4]

8. Discoid lupus erythematosus

Discoid lupus erythematosus (DLE) is an auto immune collagen vascular disease characterized by scaly patches which heal with atrophy, scarring, and pigmentation. DLE represents cutaneous form in which systemic symptoms are not seen whereas systemic lupus erythematosus shows systemic symptoms. Somatic mutations in genes coding for lymphocytic stem cells resulting in production autoantibodies are implicated in pathogenesis of DLE.[20]

Oral lesions of DLE are mostly identical to lichen planus characterized by ulcerated or atrophic central zone with radiating white striae on periphery. However, it is rarely seen in oral mucosa in the absence of skin lesions unlike lichen planus. Histopathologically, DLE shows hyperkeratosis, alternate atrophy, and thickening of spinous layer, basal cell degeneration, diffuse lymphocytic infiltrate, PAS positive material in basement membrane zone, and subepithelial edema.[7]

Carcinoma of skin from cutaneous DLE and its healed scar (both squamous cell carcinoma and basal cell carcinoma) is between 3.3 and 3.4%. Malignant transformation may be as late as 20 years after the occurrence of DLE. Neoplastic transformation of DLE to malignant fibrous histiocytoma and atypical fibroxanthoma is also reported.[20,21]

9. Plummer–Vinson syndrome

Plummer–Vinson syndrome is a severe form of iron deficiency anemia characterized by esophageal webs, koilonychia, and glossitis.[6] Deficiency of iron dependent enzymes and high turnover rate in epithelium of esophagus makes it vulnerable to DNA damage resulting in epithelial changes and malignant transformation especially in young individuals.[22] It possesses 3–15% risk of development of squamous cell carcinoma of the upper gastrointestinal tract.[23]

10. Syphilitic glossitis

Syphilis is bacterial infection caused by spirochete, *Treponema pallidum*. Lesion on tongue in secondary syphilis occurs as spirochetes have affinity to mobile tissues and these lesions possess increased risk malignant transformation. This risk may be attributed to vasculitis and obliterative endarteritis caused by *Treponema pallidum* resulting in circulatory deficiency of lingual papillae leading to its atrophy. Atrophic epithelium may predispose to the development of oral leukoplakia which, in turn, can transform into squamous cell carcinoma.[24] Arsenic agents used for the treatment of syphilis in the past were also thought to be an etiology for malignant transformation.[7]

11. Graft versus host disease (GVHD)

GVHD is a common complication of allogenic bone marrow transplant. Oral GVHD predisposes to oral cancer and is unrelated to tobacco exposure. The reason for malignant transformation into squamous cell carcinoma is attributed to immunological injury of chronically inflamed oral epithelium which may arise after many years of post-transplantation unlike secondary hematological malignancies which are immediate complications associated with GVHD.[25]

12. Epidermolysis bullosa

It is blistering genodermatosis which exhibit oral involvement in two of its types which are junctional and dystrophic epidermolysis bullosa. These types also exhibit malignant potential and in oral cavity epidermolysis bullosa affecting tongue possess an increased risk of malignant transformation.[4] Similar genodermatosis such as dyskeratosis congenita also predispose to oral leukoplakia and carcinoma.[26]

Various immunosuppressant states also predispose oral mucosa to squamous cell carcinoma. Immunosuppression due to use of immunosuppressant drugs following organ transplantation leads to DNA mutation in epithelial cells.[27] Even though HIV infection also causes immunosuppression, oral and laryngeal cancer in HIV patients is suggested to be due to their synergistic interaction with HPV and HSV viruses.[28]

Vitamin B deficiencies cause epithelial atrophy which in rare instances is prone to develop epithelial dysplasia.[5,29]

Apart from the lesions discussed above, other lesions like long standing tobacco pouch keratosis which does not regress even after tobacco habit cessation does show significant epithelial dysplasia with a risk for malignant transformation. Hence, these lesions should also be considered as OPMD and biopsy should be performed.[30]

## Risk Factors for Malignant Transformation

Risk of malignant transformation varies greatly between various above discussed OPMD. Clinical variables that may determine malignant transformation are summarized below:[31,32]

- Site – OPMD if present on ventral surface of tongue and floor of mouth may show greater malignant transformation potential when compared to other sites.
- Increasing age and female gender can contribute to increased risk of malignancy.
- OPMD that occurs in non-users of tobacco possess greater risk of oral cancer.
- Synergistic effects of tobacco and alcohol carry higher risk of cancerous changes when compared to use of tobacco alone.
- Changes such as erythema and ulceration may be indications to probable malignant transformation.

## CONCLUSION

Dental professionals play a key role in early identification of both habit related and non-habit related mucosal disorders. Development of OPMD and oral cancer is multistep process involving genetic changes due to exogenous and endogenous factors. Since there is currently no molecular and even histopathological pathognomonic hallmark that can predict malignant transformation of OPMD, the analysis of clinical aspect of these lesions remains the best way to control and prevents the development of oral squamous cell carcinoma.

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Original Article

# Observational Study of Interface Dermatitis with Clinicopathological Correlation

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## Abstract

**Introduction:** Interface dermatitis (ID) is a commonly encountered dermatopathological reaction pattern, which is seen in a wide variety of dermatoses. Since it is a distinctive entity, it's presence can be used to validate the diagnosis in numerous skin problems that can be clinically challenging.

**Purpose:** The present study aimed to evaluate the histopathological features of clinical conditions primarily presenting with ID and correlate histopathological features with clinical findings.

**Methods:** This 2-year prospective observational study included 50 patients with clinical conditions, which typically present with ID. Biopsy samples were subjected to conventional processing and stained using hematoxylin and eosin stain. Each biopsy specimen was systematically examined to assess epidermal and dermal changes. Eventually, correlation between clinical and histopathological parameters was analyzed.

**Results:** Lichen planus was the most common disease with ID, 31–50 years (48%) was the most common age group, and extremities were the most common site of infection. Twenty-nine (58%), 19 (38%), and two (4%) patients exhibited severe, moderate, and mild inflammation, respectively. Thirty (60%) patients exhibited melanin pigment incontinence. Basal cell vacuolation (82%) and hyperkeratosis (52%) were the most common epidermal changes seen. Forty-two (84%) patients were clinicopathologically concordant, with 100% concordance in lichenoid drug eruption, lichen striatus, lichen nitidus, discoid lupus erythematosus, and pityriasis lichenoides chronica.

**Conclusion:** Establishing a definitive diagnosis in a wide spectrum of clinical conditions becomes easier when ID is observed histopathologically. A clinicopathological correlation with direct communication between dermatologists and pathologists will improve diagnostic accuracy.

**Key words:** Dermatitis, Inflammation, Lichen planus, Lichenoid eruptions, Lichens, Melanin, Skin, Skin diseases

## INTRODUCTION

The skin is considered as the largest organ of the body, with a plethora of inflammatory diseases occurring at the dermoepidermal junction (DEJ).[1-3] Interface dermatitis (ID) is a subset of numerous inflammatory patterns commonly encountered in dermatopathology.[4] The widespread disease spectrum associated with ID presents a substantial overlap of clinicohistological characteristics.[1,3]

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Thus, knowledge of both clinical and histological features of skin diseases is of great help in establishing a diagnosis.[1,3] ID refers to dermatoses, in which inflammatory infiltrate envelops the DEJ.[4] Pathological alterations occur predominantly at the DEJ, and subsequent morphological alterations involve mainly the DEJ, basal cells, and papillary dermis.[5] The typical changes observed in ID involve basal cell layer vacuolar degeneration and keratinocyte necrosis with apoptotic eosinophilic anucleate structures in the upper dermis and dyskeratotic keratinocytes in the epidermis.[4] The third primary change is an inflammatory infiltrate in the upper dermis.[4] ID is categorized on the basis of the primary cell type of infiltrate – neutrophilic, lymphocytic, or lymphohistiocytic – or degree of interface inflammation.[5,6] Secondary changes could be seen in the epidermis ranging from epidermal flattening to

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hyperkeratosis, hypergranulosis, and acanthosis. Moreover, melanophages and melanin incontinence associated with ID can be observed within the papillary dermis.[5]

A remarkable challenge in dermatopathology is to obtain a specific diagnosis of inflammatory skin diseases.[1] Considering the heterogeneous nature of skin problems exhibiting ID, it is important to diagnose and categorize diseases into distinct clinical and histopathological entities.[4,7,8] Although histological evaluation is critical for diagnosing various dermatopathological diseases, it alone does not contribute to a dependable diagnosis.[2] Thus, implementation of an integrative dermatopathological approach using clinicopathological correlation is highly preferred.[4,7]

Thus, the present study aimed to evaluate the histopathological spectrum of conditions which could present with ID and correlate histopathological features with clinical findings.

## MATERIALS AND METHODS

This 2-year prospective observational study enrolled total of 50 patients with ID. Written informed consent was obtained from all the patients. The study was approved by the Institutional Ethics Committee and conducted in accordance with the Helsinki Declaration of 1975.

Inclusion criteria included patients with a clinical diagnosis of any dermatological disorder that exhibits ID as a primary change on histology, that is, lichen planus and its clinical variants, lichenoid drug eruptions, lichen striatus, lichen planus pemphigoides, lichen nitidus, lupus erythematosus, erythema multiforme, and pityriasis lichenoides chronica. Exclusion criteria included patients with a clinical diagnosis of dermatoses which could exhibit ID as a secondary histologic feature, such as secondary syphilis, mycosis fungoides, poikiloderma, lichenoid purpura, leprosy, and tumors – squamous and basal cell carcinomas and melanomas. Exclusion criteria also included patients who were on topical or systemic treatment within the past 4 weeks.

Based on standard cutaneous morphology, clinical conditions, which would typically exhibit ID on histopathology, were chosen by a trained dermatologist. A biopsy sample or resection specimen was obtained from each patient. In the case of multiple lesions, the most representative lesion was identified and sampled by a dermatologist. Based on punch biopsy, 4–5-mm-thick slices were obtained, immediately fixed in 10% formalin for 24 h, and conventionally processed using routine paraffin-sectioning techniques. Subsequently, 3-mm-thick paraffin sections of specimens were sliced and stained by hematoxylin and eosin stains. Histopathological diagnosis was made by reviewing the stained slides. Each biopsy specimen was systematically examined to assess any epidermal and dermal changes. Finally, any correlation between clinical and histopathological parameters was evaluated.

### Statistical Analysis

Data were analyzed using MS Excel, graphical analysis, and frequency distribution analysis.

## RESULTS

Of the 50 patients, 26 (52%) and 24 (48%) were male and female, respectively. Table 1 represents clinical and demographic characteristics of patients. Clinically, the diseases included in our study were classical lichen planus, hypertrophic lichen planus discoid lupus erythematosus, lichen planopilaris, lichenoid drug eruption, lichen striatus, lichen nitidus, erythema multiforme, and pityriasis lichenoid chronica. On histopathology, observed epidermal changes included hyperkeratosis, orthokeratosis, hypergranulosis, follicular plugging, acanthosis, atrophy and basal cell vacuolation, and colloid bodies. The classification of patients based on histopathological characteristics of the epidermal lesions is shown in Table 2.

**Table 1: Clinical and demographic characteristics of patients**

| Variables | No. of patients, *n*=50, *n* (%) |
|---|---|
| Age (years) | |
| <20 | 8 (16) |
| 20–30 | 6 (12) |
| 31–40 | 12 (24) |
| 41–50 | 12 (24) |
| 51–60 | 6 (12) |
| 61–70 | 5 (10) |
| >70 | 1 (2) |
| Duration of the disease | |
| <1 week | 1 (2) |
| 1 week to 1 month | 6 (12) |
| 1 month to 3 months | 19 (38) |
| 3 months to 1 year | 12 (24) |
| >1 year | 12 (24) |
| Symptoms | |
| None | 21 (42) |
| Pruritus | 28 (56) |
| Alopecia | 2 (4) |
| Photosensitivity | 4 (8) |
| Type of skin lesions | |
| Macule | 5 (10) |
| Papule | 22 (44) |
| Nodule | 0 |
| Vesicobullous | 2 (4) |
| Plaque | 38 (76) |

The dermal changes included apoptotic keratinocytes, variable expansion/fibrosis of the papillary dermis to accommodate the inflammatory cell infiltrate, subepidermal clefts, and melanin pigment incontinence. Twenty-nine (58%), 19 (38%), and two (4%) patients exhibited severe, moderate, and mild inflammation, respectively. Thirty (60%) patients exhibited melanin pigment incontinence.

Interface inflammation was seen in all the patients. The inflammatory infiltrate was lymphocytic and lymphohistiocytic in 38 (76%) and 9 (18%) patients, respectively. Mixed inflammation (lymphocytes, histiocytes, plasma cells, eosinophils, and polymorphs) was seen in three (6%) patients with lichenoid drug eruption. Histological sites of inflammation included the DEJ, perivascular, perifollicular, periappendageal, dermis, and rete ridges in 41 (82%), 17 (34%), 16 (32%), 14 (28%), four (8%), and three (6%) patients, respectively.

## Clinicopathological Concordance

### *Lichen planus*

Twenty-one out of 25 cases were histologically concordant. All these cases showed dense band-like lymphoplasmacytic infiltrate with basal cell vacuolation and tendency to invade the lower epidermal layers [Figure 1a-c].

### *Lichen nitidus*

In both cases of this entity, a well-circumscribed subepidermal inflammatory infiltrate was observed with lymphocytes and histiocytes with an overlying thinned epidermis and basal cell vacuolation. The inflammatory infiltrate was confined to the upper dermis within the dilated dermal papillae [Figure 2a and b].

### *Lichen striatus*

In two cases included, irregular acanthosis, focal spongiosis, and lichenoid reaction pattern were observed [Figure 3a and b]. The interface inflammation was mild-moderate.

### *Discoid lupus erythematosus*

There were five clinically diagnosed cases. Epidermal atrophy, follicular plugging, variable degeneration of basal cells, thickened basement membrane, and periappendageal, perivascular, and perifollicular mononuclear inflammatory lymphocytic infiltrate were observed in the dermis [Figure 4a and b]. Follicular plugging was noted in 37.5% of patients. Civatte bodies were shown in four patients.

### *Lichen planopilaris*

In four out of five concordant cases, there was dense lymphocytic infiltrate with hypergranulosis with dense inflammation around the perifollicular region in hair sparing the inter follicular epidermis [Figure 5]. Follicular plugging was not observed in 75% of patients.

### *Lichenoid drug eruptions*

Focal parakeratosis, necrotic keratinocytes in the basal and spinous layers, exocytosis of lymphocytes to the upper layers of the epidermis, and inflammatory infiltrate with

**Table 2: Spectrum of histological findings in epidermis in different entities causing interface dermatitis**

| Epidermal changes | Total, *n*=50, *n* (%) | Number of cases of each entity | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | LP | LS | LN | HLP | LPP[1] | LPP[2] | DLE | SLE | LAK | EM | LPP[3] | LDE | PLC |
| HK | 26 (52) | 15 | 0 | 0 | 2 | 0 | 1 | 4 | 1 | 0 | 0 | 1 | 1 | 1 |
| OK | 13 (26) | 8 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 0 |
| HG | 19 (38) | 11 | 0 | 0 | 2 | 1 | 4 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| FP | 9 (18) | 0 | 0 | 0 | 0 | 0 | 3 | 5 | 1 | 0 | 0 | 0 | 0 | 0 |
| Acanthosis | 24 (48) | 12 | 2 | 0 | 2 | 1 | 1 | 2 | 1 | 1 | 0 | 1 | 1 | 0 |
| Atrophy | 11 (22) | 0 | 0 | 2 | 0 | 0 | 2 | 6 | 1 | 0 | 0 | 0 | 0 | 0 |
| Basal cell vacuolation | 41 (82) | 20 | 1 | 2 | 1 | 2 | 1 | 5 | 1 | 1 | 2 | 1 | 3 | 1 |
| Colloid bodies | 19 (38) | 12 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 2 | 1 |

LP: Lichen planus, LS: Lichen striatus, LN: Lichen nitidus, HLP: Hypertrophic Lichen Planus, Lpp[1]: Lichen Planopilaris: Lpp[2]: Lichen Planus Pigmentosus, DLE: Discoid Lupus Erythematosus, SLE: Systemic Lupus erythematosus, LAK: Lichenoid actenic keratosis, EM: Erythema multiforme, LPP[3]: Lichen planus pemphigoides, LDE: Lichenoid drug eruption, PLC: Pityrisis lichenoid chronica, HK: Hyperkeratosis, OK: Orthokeratosis, HG: Hypergranulosis, FP: Follicular plugging

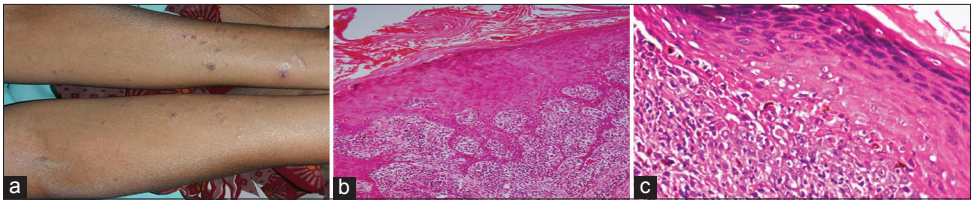


**Figure 1: (a) Patient with lichen planus showing erythematous–violaceous flat-topped polygonal papules and plaques with Wickham's striae. (b) Lichen planus showing hyperkeratosis, acanthosis, and dense lymphocytic infiltrate at the dermoepidermal junction (H&E, ×100). (c) Lichen planus showing hypergranulosis, civatte bodies (arrow), and pigment incontinence (H&E, ×400)**

numerous eosinophils were reported in all the three cases [Figure 6].

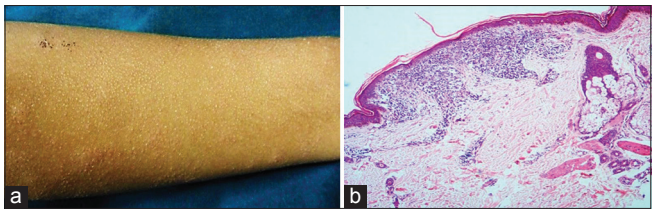

**Figure 2: (a) Patient with lichen nitidus showing monomorphic, minute, and skin-colored papules. (b) Lichen nitidus showing claw-clutch appearance of lymphocytic inflammation in the upper dermis (H&E, ×100)**

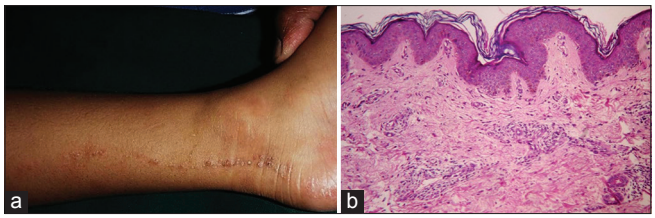

**Figure 3: (a) Patient with lichen striatus showing linear, discrete, pin-head-sized papules. (b) Lichen striatus showing perivascular peri-eccrine lymphocytic inflammation with sparse inflammation at the dermoepidermal junction (H&E, ×100)**

**Figure 4: (a) Patient with discoid lupus erythematosus showing multiple hyperpigmented plaques involving scalp. (b) Discoid lupus erythematosus showing atrophic epidermis, follicular plugging, and inflammation in perifollicular region and the dermoepidermal junction (H&E, ×400)**

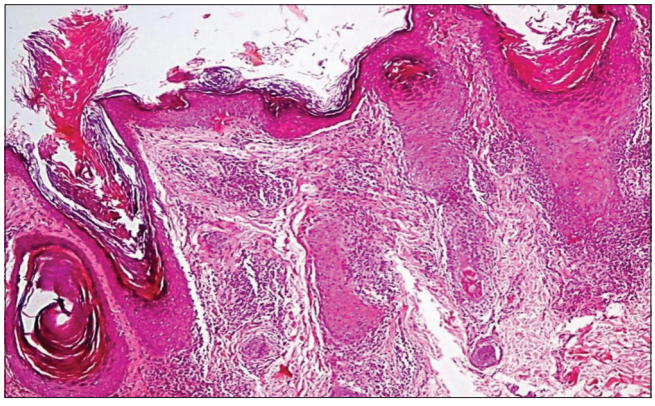

**Figure 5: Lichen planopilaris showing dense perifollicular inflammation with follicular plugging (H&E, ×100)**

### *Hypertrophic lichen planus*

In two out of three concordant cases, there was marked hyperplasia of the epidermis, hyperkeratosis, hypergranulosis, and dermal infiltrate near the tip of rete ridges which were reported [Figure 7a and b].

### *Erythema multiforme*

In two out of four concordant cases, hyperkeratosis, extensive basal cell vacuolation, and civatte bodies with mild-moderate inflammatory infiltrate in the dermis were observed [Figure 8a-c]. Subepidermal vesiculation was reported in one patient.

### *Pityriasis lichenoides chronica*

In the solitary case, hyperkeratosis, parakeratosis with focal areas of spongiosis, interface change of the DEJ, superficial perivascular lymphohistiocytic infiltrate, and extravasation of RBCs were reported.

## Clinicopathological Discordance

Forty-two (84.3%) patients were clinicopathologically concordant, whereas eight (15.7%) were not. Classification of patients based on clinical and histopathological diagnoses and clinicopathological correlation between each type of ID is shown in Tables 3 and 4.

Of the eight (15.7%) discordant cases, four were clinically diagnosed as lichen planus. Of these, two were diagnosed as

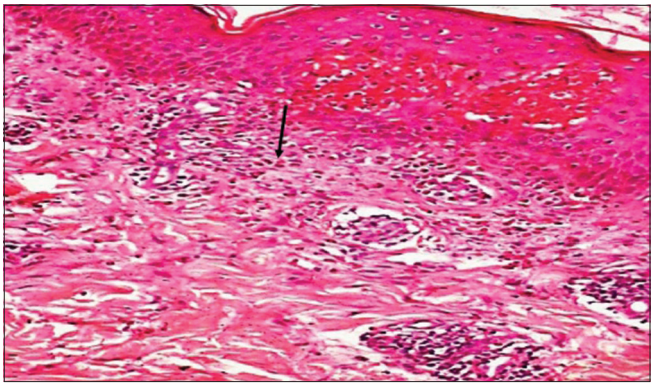

**Figure 6: Lichenoid drug eruption showing inflammation at the dermoepidermal junction and perivascular region composed predominantly of eosinophils (arrow) (H&E, ×400)**

**Figure 7: (a) Patient with hypertrophic lichen planus showing multiple pigmented plaques. (b) Hypertrophic lichen planus showing acanthosis and inflammation at base of rete ridges (H&E, ×100)**

**Table 3: Clinicopathological correlation of various forms of ID (based on concordance)**

| Type of ID | Clinical diagnosis, *n*=50, *n* (%) | Histopathological diagnosis, *n*=50, *n* (%) | Clinicopathological correlation/ concordance (%) |
|---|---|---|---|
| Classic lichen planus | 25 (50) | 21 (42) | 84 |
| Discoid lupus erythematosus | 5 (10) | 5 (10) | 100 |
| Lichen planopilaris | 5 (10) | 4 (8) | 80 |
| Lichenoid drug eruption | 3 (6) | 3 (6) | 100 |
| Lichen striatus | 2 (4) | 2 (4) | 100 |
| Lichen nitidus | 2 (4) | 2 (4) | 100 |
| Hypertrophic lichen planus | 3 (6) | 2 (4) | 66.67 |
| Erythema multiforme | 4 (8) | 2 (4) | 50 |
| Pityriasis lichenoid chronica | 1 (2) | 1 (2) | 100 |

ID: Interface dermatitis

**Table 4: Clinicopathological discordance observed in the study**

| Clinical diagnosis with number and percentage *n*=50 | Number and percentage of discordant cases, *n* (%) | Histopathological diagnosis | Clinicopathological discordance (%) |
|---|---|---|---|
| Lichen planus 25 (50) | 4 (8) | 2 cases of DLE<br>1 case of lichen planus pigmentosus<br>1 case of lichenoid actinic keratosis | 16 |
| Lichen planopilaris 5 (20) | 1 (2) | 1 case of discoid lupus erythematosus | 20 |
| Erythema multiforme 4 (16) | 2 (4) | 1 case of systemic lupus erythematosus<br>1 case of lichen planus pemphigoides | 50 |
| Hypertrophic lichen planus 3 (6) | 1 (2) | 1 case of lichen planus pigmentosus | 33.33 |

ID: Interface dermatitis

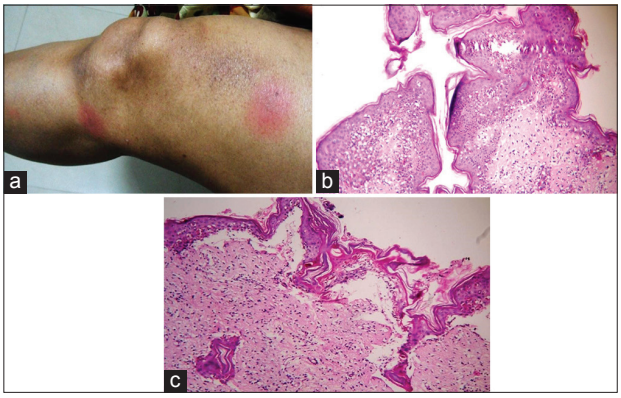


**Figure 8: (a) Patient with erythema multiforme showing erythematous patch. (b) Erythema multiforme showing extensive basal cell vacuolation with sparse inflammation at the dermoepidermal junction (H&E, ×100). (c) Erythema multiforme showing subepidermal bulla with basal cell vacuolation (H&E, ×100)**

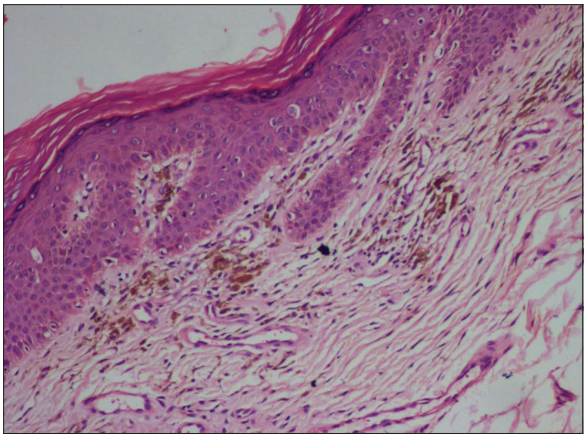

**Figure 9: Lichen planus pigmentosus showing epidermal atrophy, basal cell vacuolation, and marked melanin pigment incontinence in the dermis (H&E, ×100)**

discoid lupus erythematosus histologically, as the epidermis showed mild loss of rete ridges, follicular plugging, and perifollicular lymphocytic infiltrate in the dermis. Another was diagnosed as lichen planus pigmentosus due to mild epidermal atrophy, vacuolar degeneration of the basal cell layer, and marked melanin pigment incontinence [Figure 9].

The fourth case was diagnosed as lichenoid actinic keratosis on histology and showed hyper and parakeratosis, lymphoid cell exocytosis, and focal spongiosis.

Further, a clinically suspected case of lichen planopilaris was histologically confirmed as discoid lupus erythematosus, as it showed orthokeratotic hyperkeratosis, follicular plugging, thickened basement membrane, and lymphocytic infiltrate in the superficial dermis. A direct immunofluorescence test on the skin biopsy was positive for IgG and IgM.

Another case which was discordant was a clinically suspected case of erythema multiforme which exhibited atrophic epidermis with lymphocytic exocytosis, mild ID, and perivascular lymphocytic infiltrate. Serum ANA test was positive, and a final diagnosis of systemic lupus erythematosus was confirmed.

The seventh discordant case was clinically diagnosed as hypertrophic lichen planus, but on histology, it showed

mildly thinned out epidermis, marked basal cell vacuolation, and heavy melanin pigment incontinence. Hence, a diagnosis of lichen planus pigmentosus was made.

The last discordant case presented as a vesiculobullous lesion clinically diagnosed as erythema multiforme, but histopathology showed a subepidermal bulla and mild eosinophil rich infiltrate at the dermoepidermal junction. Further, a direct immunofluorescence test showed IgG deposit at the basement membrane. Thus, it was diagnosed as lichen planus pemphigoides.

## DISCUSSION

Considering varying clinical appearances of dermatoses manifesting with ID, clinicohistological correlation is crucial for optimum prognosis, treatment, and clinical management.[1,9] The present study aimed to study histopathological changes in conditions presenting primarily with ID and correlate them with clinical diagnosis.

In the present study, lichen planus was the most commonly observed disorder that showed features of ID.[1,9,10] Concurrent with the literature, in the present study, common epidermal changes included hyperkeratosis, orthokeratosis, hypergranulosis, follicular plugging, acanthosis, atrophy, basal cell vacuolation, and colloid bodies, wherein basal cell vacuolation ($n = 41$ [82%]) and hyperkeratosis ($n = 26$ [52%]) were predominantly observed.[2] The basal cell degeneration has been attributed to the presence of activated T cells that attach to and induce apoptosis in the basal epidermal cells.[2] Basal cell vacuolation is seen during the early stages of infection and may not be evident in fully-developed or resolving lesions.[5] The phenomenon is more commonly observed in drug- or ultraviolet light-induced dermatoses.[4] In dark-skinned population, pigment incontinence is prominent in nearly all skin-related diseases, commonly affecting epidermis.[11] Reportedly, the degree of incontinence is higher in disorders with ID than in other diseases.[11] This could be attributed to melanogenesis stimulation, keratinocyte annihilation, and flawed transfer of melanin in ID.[11] Concurrent with the literature, the present study suggests that melanin incontinence with melanophages in the upper dermis is the most consistent feature of ID.[12,13] The study further proposes that this feature could easily be observed in dark skin due to the involvement and characteristics of eumelanin, as the study comprised only dark-skinned individuals. Morphology of pigment incontinence in ID could be different in white-skinned individuals with pheomelanin.

### Clinicopathological Overtones

#### *Lichen planus*

Concurrent with the literature, the present study reported lichen planus to be the most common prototype that is identified by basal cell damage, colloid bodies, band-like infiltrate at the DEJ, wedge-like hypergranulosis, and saw-like rete ridges. However, other histopathological manifestations can be reported in various clinical types of lichen planus.[4] Of the four discordant cases, two were diagnosed as discoid lupus erythematosus; one, as lichen planus pigmentosus; and another as lichenoid actinic keratosis.

#### *Lichen nitidus, Lichenoid drug eruption, and lichen striatus*

These cases were all clinicohistologically concordant, with histological features as described in the literature.[4,14]

#### *Discoid lupus erythematosus*

The present study findings were similar to those of Fabbri *et al.* (2003).[15] This prototype comprises a follicular/peripilosebaceous deep and superficial lymphocytic inflammatory infiltrate. Hyperkeratosis, basal cell vacuolation, colloid bodies, and keratotic plugging are observed in a condensed manner.[4] However, one case of discoid lupus erythematosus was clinically diagnosed as lichen planopilaris because it appeared on the scalp, while another was clinically suspected to be erythema multiforme but showed features of lupus erythematous on histopathology and subsequently confirmed to be systemic lupus erythematosus. One case of clinically suspected lichen planus was found to have features of discoid lupus erythematosus histologically.

#### *Lichen planopilaris*

The present study findings were as described in the literature in all four cases. Lichen planopilaris involves hyperkeratosis, wedge-like hypergranulosis, colloid bodies, band-like infiltrate consisting of lymphocytes, and follicular plugging.[16-18] However, one case of discoid lupus erythematosus was clinically diagnosed as lichen planopilaris.

#### *Lichenoid drug eruption*

The observed cases were in concordance with the description in the literature. These resemble lichen planus, but present eczematous factors with residual pigmentation. Parakeratosis and mild basal cell vacuolation are reported. Melanin incontinence is relatively more predominant in lichen drug eruption than other subtypes, whereas dermal inflammatory infiltrate is comparatively less dense and shows eosinophil admixture.[4]

#### *Hypertrophic lichen planus*

In this study, the findings were similar to those of Weedon (2002).[14] The noteworthy feature of hypertrophic lichen planus is extensively raised hyperpigmented pruritic plaques. This prototype exhibits moderate-marked hyperkeratosis and basal cell degeneration in the epidermal layer with band-like infiltrate comprising lymphocytes and plasma cells at the DEJ. Although benign, hypertrophic lichen

planus can turn malignant when the disease prolongs.[3] It is therapeutically important to differentiate hypertrophic lichen planus from classic lichen planus because squamous cell carcinoma can develop in the lesions of long-standing hypertrophic lichen planus.[19] One case of hypertrophic lichen planus clinically showed features of lichen planus pigmentosus histologically, possibly due to incorrect choice of biopsy site, since clinically, they are distinctive entities.

### *Erythema multiforme*

This is a type of cutaneous eruption that is identified by mild-to-moderate infiltrate of lymphocytes and macrophages, along with epidermal cell death extending beyond basal cell layer. The infiltrate obscures the DEJ and surrounds peripheral blood vessels in dermis and mid-dermis.[4] In two cases, these features were seen, but one case showed features of systemic lupus erythematosus histologically while another turned out to be lichen planus pemphigoides, a relatively rare autoimmune disorder which exhibited a subepidermal bulla with a mixed cell inflammatory infiltrate with predominant eosinophils.

In the present study, 42 (84%) patients were clinicopathologically concordant. In the literature, concordance of 87.2%, 70.94%, and 78.50% has been reported.[2,9,19,20] In our study, the discordance was attributed to a variation in morphology and possibly the site of the biopsy. The present study suggests that reliable diagnosis can be obtained using histopathological evaluation; however, clinical parameters, such as site and nature of lesion, should be considered as they can induce clinicopathological discordance.[10] The present study is one of the few studies in the literature reporting about clinicopathological concordance in ID. The present study reported 100% concordance in discoid lupus erythematosus, lichenoid drug eruption, lichen striatus, lichen nitidus, and pityriasis lichenoid chronica, whereas some discordance was reported in lichen planus, lichen planopilaris, hypertrophic lichen planus, and erythema multiforme.

The present study is limited in terms of sample size, which is too small to extrapolate the findings to the general population. It highlights the importance of an integrative clinicopathological approach to diagnose the widespread disease spectrum of ID. The more comprehensive analysis could be achieved by cooperative consultation between dermatologists and pathologists. Future research can also include the evaluation of immunopathogenesis to gain in-depth knowledge of immune system-related alterations occurring in ID.

## CONCLUSION

Although there was a high level of clinicopathological concordance, it could be improved further by appropriate choice of biopsy site, to provide a definitive diagnostic chassis for the wide spectrum of dermatologic disorders presenting with ID.

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Original Article

# Clinicoepidemiological Profile of Acute Myocardial Infarction Patients Admitted in a Tertiary Care Hospital of Tripura

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## Abstract

**Introduction:** Acute myocardial infarction is one of the leading causes of morbidity and mortality throughout the world, which has raised considerable interest in recent years. It is a significantly raising problem, particularly in India, in young as well as in elderly patients. The current study was conducted to assess the role of various clinicoepidemiological determinants of myocardial infarction.

**Aim and Objectives:** The aim of this study was to estimate the clinicoepidemiological profile of acute myocardial infarction patients admitted to Agartala Government Medical College and GBP Hospital.

**Methodology:** A cross-sectional hospital-based study conducted in the Department of Medicine, Agartala Government Medical College and GBP Hospital, Agartala within a period of January 2020 to June 2020. Data were analyzed by SPSS software version 15 using appropriate statistical tests.

**Results:** Male preponderance was observed in this study. The male-to-female ratio was 5:1. The age distribution of these patients ranged from 35 years to 85 years with maximum number of patients in the age above 60 years. Hypertension was present in 46% of the patients. About 45% of the patients were alcoholics in this study. About 27% of the patients were diabetics in this study. About 24% of the patients had hypercholesterolemia. About 19% of the patients in this study were obese. Tobacco smoking was present in 9% of the patients. Seventeen patients had blood pressure more than 160/90 mmHg at presentation with breathing difficulty, along with fourth heart sound, bilateral basal crepitations suggesting left ventricular failure. Twenty-seven patients had bradycardia, seven patients had second-degree heart block six complete heart block, and three patients had first-degree heart block. Five patients had ventricular fibrillation and died. One hundred and seven patients had chest pain as a presenting symptom. ST-segment elevation myocardial infarction (STEMI) was found among 63% of patients. About 37% of patients had non-ST segment elevated myocardial infarction (NSTEMI). Inferior wall myocardial infarction consists of 34%, anteroseptal wall myocardial infarction 22%, anterolateral wall myocardial infarction 15%, lateral wall myocardial infarction 10%, posterior wall myocardial infarction 8%, anterior wall myocardial infarction 8%, and septal wall myocardial infarction 3% of patients. Trop I positivity was observed among 120 patients.

**Conclusion:** A total of 120 consecutive cases of acute myocardial infarction admitted to AGMC and GBP hospital were selected for the study. Several conventional risk factors for myocardial infarction were identified, which included hypertension, diabetes, alcohol consumption, dyslipidemia, smoking, obesity, and among them, hypertension (46%) and alcohol consumption (45%) seem to be the most common risk factor contributing to acute myocardial infarction in the study population. The age of the patients ranged from 35 years to 85 years with elderly patients most commonly affected. STEMI was found among 63% of patients. The predominant sites of infarction were an inferior wall, anteroseptal wall, and anterolateral wall. Probably, the left coronary artery was mostly affected, followed by right coronary artery. Large case–control studies are needed to stratify, in which conventional risk factor independently contributes the most in the occurrence of coronary artery disease.

**Key words:** Acute myocardial infarction, Non-ST elevated myocardial infarction, ST elevated myocardial infarction, Trop I: Cardiac troponin I

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## INTRODUCTION

Acute myocardial infarction is the most common diagnosis in hospitalized patients in industrialized countries. In the United States, approximately 660,000 patients experience a new AMI, and 305,000 experience a recurrent AMI each year.[1] Acute coronary syndrome is an important global

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cause of death and also the major cause of morbidity and mortality in India.[2] A meta-analysis of prevalence studies done in India reported a 300% rise in the incidence of myocardial infarction for the past 50 years.[3] A 111% rise in deaths due to cardiovascular diseases in India has been predicted by 2020.[4] Changing in risk factors was observed in the period of 1990 to 2010. In 1990, the leading risks were childhood underweight 7.9%, household air pollution from solid fuels 6.8% and tobacco smoking including second-hand smoke 6.1%. In 2010, the three leading risk factors for global disease burden were high blood pressure 7.0%, tobacco smoking including second-hand smoke 6.3% and household air pollution from solid fuels 4.3%.[5] In India, out of all deaths, nearly 24.8% of deaths are due to cardiovascular diseases as estimated by the global burden of disease study (2010). The average age-standardized death rate in India due to cardiovascular disease is 272 per 100,000 population which is much higher than the rate of global deaths, that is, 235 per 100,000 population.[6] Worldwide, the prevalence of coronary heart disease (CHD) is increasing, although there are regional variations due to the influence of economies, industrialization, and advancement in health-care systems.[7] In Urban India, CHD prevalence in adult has increased considerably and occurred at a much younger age as compared to North America and Western Europe.[2] Hospital mortality in various parts of the state has been reported to vary greatly, and it may be related to differences in the severity of the cases and differences in the quality of medical treatment. Myocardial infarction is a multifactorial non-communicable disease. Considering all that, this study aimed at analyzing the clinical and epidemiological profile of a representative sample of acute myocardial infarction treated at AGMC and GBP hospital.

### Aim and Objectives

The aim of this study was to estimate the clinicoepidemiological profile of acute myocardial infarction patients admitted to Agartala Government Medical College and GBP Hospital.

## METHODOLOGY

A cross-sectional hospital-based study (IPD) at the Department of Medicine, Agartala Government Medical College and GBP Hospital and study duration is of 6 months.

### Inclusion Criteria

Patients satisfying the WHO definition[8] for diagnosis of myocardial infarction patients were included in the study.

The diagnosis was based in the presence of at least two of the following-

1. A clinical history of ischemic type chest discomfort
2. Changes in serially obtained electrocardiographic tracings
3. A rise and fall of serum cardiac markers.

### Exclusion Criteria

Nil.

The first electrocardiogram (ECG) was recorded at the earliest after admission and subsequently at 8 hourly intervals on the 1st day, daily for the next 7 days and thereafter as per need. If thrombolytic therapy was given, 12 lead ECG was recorded before and after the thrombolytic therapy. Right ventricular leads were recorded whenever deemed necessary (in patients with inferior wall MI).

The other investigations to which the patients were subjected are as follows:

- Blood routine (hemoglobin percentage, total count, differential count, and erythrocyte sedimentation rate)
- Random blood sugar and fasting blood sugar/post-prandial blood sugar were done whenever necessary, blood urea and serum creatinine
- Lipid profile.

### Special Investigations

a. Echocardiography (2D) was done to confirm a myocardial infarction
b. Chest X-ray/screening (whenever required).

### Limitation of the Study

A coronary angiogram is not done due to a lack of facility.

Patients were classified on particular aspects as follow:
WHO Asian BMI classifications:

- Underweight - <18.5 kg/m$^2$
- Ideal - 18.5–23 kg/m$^2$
- Overweight - 23–27.5 kg/m$^2$
- Obese - >27.5 kg/m$^2$.

### Socio-economic Status

As per modified B.G Prasad's classification for 2013 socioeconomic status upper class was classified those who have income 5156 and above.
Middle class was classified in to three parts
Part II of income between Rs 2578-5155
Part III of income between Rs 1547-2577
Part IV of income between Rs 773-1546
Lower class have income below Rs 773.

### Study Population

Patient those will be diagnosed to have acute myocardial infarction admitted at Agartala Government Medical College and GBP Hospital during this study duration, will be included in the study.

| Modified B. G. Prasad's classification for 2013. Socioeconomic status | Class | Per capita income |
|---|---|---|
| Upper class | I | Rs 5156 and above |
| Middle class | II | Rs 2578–5155 |
| | III | Rs 1547–2577 |
| | IV | Rs 773–1546 |
| Lower class | V | Below Rs 773 |

### Sample Size

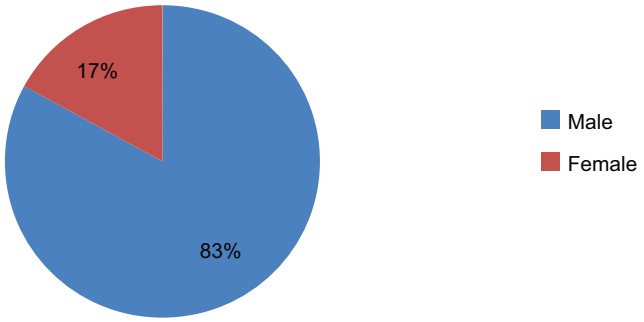
All the patients suffering from acute myocardial infarction admitted to Agartala Government Medical College and GBP Hospital following inclusion and exclusion criteria will be included in the study. From the previous records, it is found that in 1 year; approximately 240 patients were admitted at the medicine department. Hence, 120 patients were enrolled in this study.

### Sample Technique

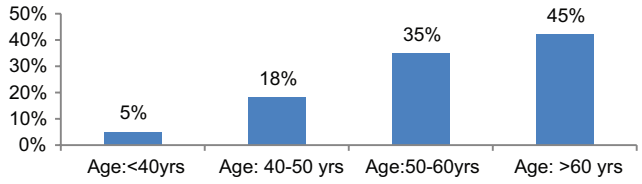
No sampling technique is required as approximately all the patients diagnosed with acute myocardial infarction have been included in the study.

## RESULTS

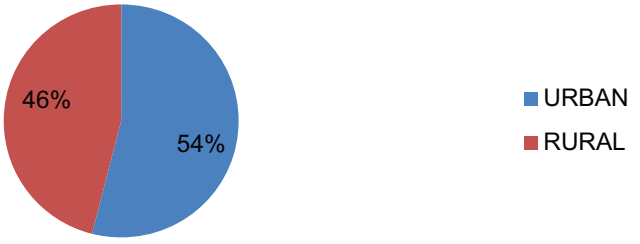
Sex-wise distribution



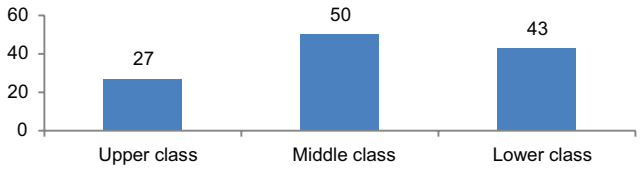

Age-wise distribution



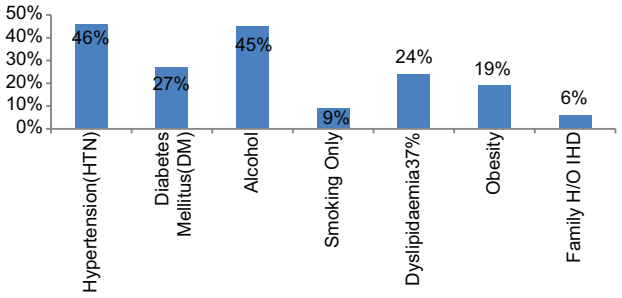

Urban versus rural



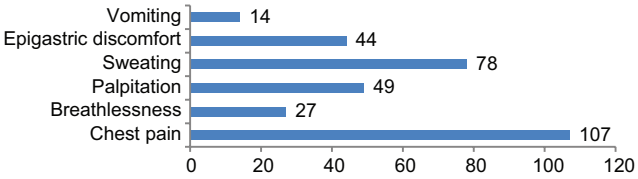

Socio-economic status



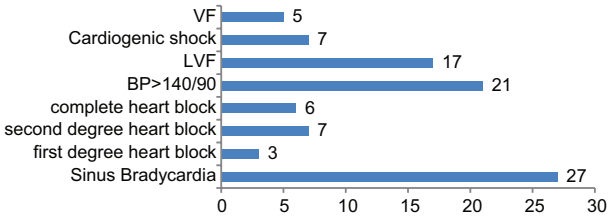

Risk factor associated with acute myocardial infarction



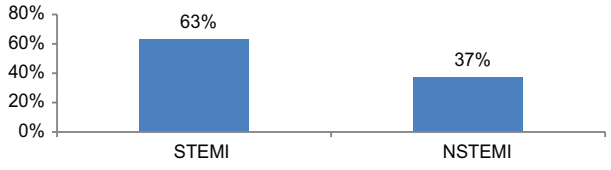

Clinical presentation of acute MI



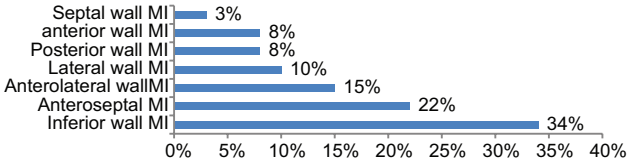

Clinical and ECG findings



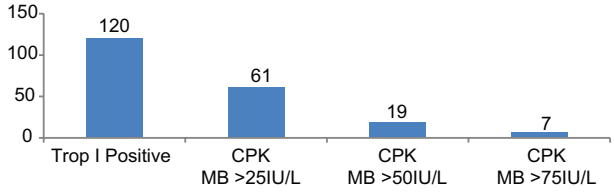

ST-segment elevation myocardial infarction (STEMI) versus non-ST segment elevated myocardial infarction




ECG findings



CPK MB and Trop I positivity




## DISCUSSION

One hundred and twenty cases of acute myocardial infarction were admitted in AGMC and GBP Hospital, Agartala, between January 2020 and June 2020, and the results have been compared with other studies.

The age distribution of these patients ranged from 35 years to 85 years with 42% of patients in the age above 60 years. Seetharama *et al.*[9] study reveals 22% in the above 60 years.

There were 100 males (83%) and 20 females (17%) in the present study. The male-to-female ratio was 5:1. This findings are consistent with that of Seetharama *et al.*[9] (2015) 4.5:1.

The current study shows that hypertension was present in 46% of the patients. This finding correlates with that of Walia *et al.*[10] who have reported hypertension as a risk factor in 43.6%.

About 45% of the patients were alcoholics in this study. Narang *et al.*[11] study revealed that 44% of patients were alcoholics.

About 27% of the patients were diabetics in this study. This is comparable with studies of Steyn *et al.*[12] who have reported diabetes as a risk factor in 23.6%.

About 24% of patients in the present study had hypercholesterolemia. This corelates with the study of Bhattacharya[13] who have reported it to be present in 21.43% of the patients.

About 19% of patients in this study were obese. According to Majeed *et al.*,[14] obesity is a risk factor in 15% factor.

Smoking was present in 9% of the patients. This finding corelates with that of Walia *et al.*[10] who have reported a risk factor in 7.5%.

Seventeen patients had blood pressure patients more than 160/100 mmHg at presentation with breathing difficulty, along with 4$^{th}$ heart sound, bilateral basal crepitations suggesting left ventricular failure.

Twenty-one patients had blood pressure more than 140/90 mmHg but <160/100 mmHg.

Seven patients were under inotropic support with low blood pressure.

Twenty-seven patients had bradycardia, seven patients had second-degree heart block six complete heart block, and three patients had first-degree heart block.

Five patients had ventricular fibrillation and died.

In the present study, 107 patients had chest pain as a presenting symptom. Kudenchuk *et al.*[15] have reported that 99 patients had chest pain.

Sweating was present in 78 patients. Palpitation was present in 49 patients. Forty-four patients had epigastric discomfort.

STEMI was founded among 63% of patients. About 37% of patients had non-ST segment elevated myocardial infarction (NSTEMI).

ECG findings shown that left coronary artery was commonly affected and ECG pattern revealed Inferior wall myocardial infarction among 34% patients, anteroseptal wall myocardial infarction among 22%, anterolateral wall myocardial infarction among 15%, lateral wall myocardial infarction among 10%, posterior wall myocardial infarction among 8%, anterior wall myocardial infarction among 8%, septal wall myocardial infarction among 3% patients..

Trop I positivity observed among 120 patients. CPK MB >25IU/L observed among 61 patients. CPK MB >50IU/L observed among 19 patients. CPK MB >75 IU/L observed among seven patients. CPK MB <25 IU/L observed among 37 patients.

## CONCLUSION

From the above study, several conventional risk factors for myocardial infarction were identified, which included hypertension, diabetes, alcohol consumption, dyslipidemia, smoking, obesity, and among them, hypertension (46%) and alcohol consumption (45%) seem to be the most common risk factor contributing to acute myocardial infarction in the study population. The age of the patients ranged from 35 years to 85 years with the elderly patients most commonly affected. There was a high male preponderance with male-to-female ratio being 5:1. There was no statistically significant difference in risk factors between rural and urban population. Chest pain (96%) was the most common presenting symptom. STEMI was

found among 63% of patients. The predominant sites of infarction were inferior wall, anteroseptal wall, and anterolateral wall. Probably, left coronary artery was mostly affected, followed by the right coronary artery, though coronary angiogram is required to locate the exact site of involvement. Large case–control studies are needed to stratify, in which conventional risk factor independently contributes the most in the occurrence of coronary artery disease. The present study highlights the immediate need to initiate measures for early detection of risk factors, to raise awareness of hypertension, diabetes, alcohol consumption, dyslipidaemia, tobacco smoking, and obesity among the general population and that the risk of myocardial infarction can be averted with dietary modification and a change in lifestyle.

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Original Article

# Randomized Open-Label Study to Compare the Safety and Efficacy of Paracetamol, Ibuprofen, and Mefenamic Acid in Febrile Children

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## Abstract

**Background:** Fever is the most common symptom presenting in the OPDs. Antipyresis is one of the most usual therapeutic interventions done. The present study compares the efficacy and tolerability of three antipyretics: Paracetamol, ibuprofen, and mefenamic acid.

**Methodology:** We performed a prospective study involving children with fever admitted in the general ward. Children were blocked randomized into three groups based on antipyretic treatment. Each of the children received either oral paracetamol/ibuprofen/mefenamic acid. The temperature was recorded at admission, hourly for the first 3 h and thereafter 6$^{th}$ hourly for 24 h.

**Results:** The fall in mean temperature from the baseline at different observation points for the study groups are evaluated and shown in Table 1. At the end of 2 h, the fall in mean temperature from the baseline for the mefenamic acid group is maximum (1.85°F) as compared to the other two groups and is statistically significant ($P$ = 0.028). Even at the end of 6 h, the fall in mean temperature for the mefenamic acid group is more (2.60°F) and is statistically significant (0.028).

**Conclusion:** Mefenamic acid has better efficacy and tolerability when compared to paracteamol and ibuprofen.

**Key words:** Ibuprofen, Mefenamic acid, Paracetamol

## INTRODUCTION

Fever is the most important and presenting symptom in pediatric clinics, OPDs, and Emergency. The normal body temperature is 36.5–37.5°C (97.7–99.5°F). Fever is defined as having a temperature above the normal range due to an increase in the body's temperature set-point.[1,2]

Hypothalamus is the body's thermoregulatory center that regulates the set-point at which the temperature of the body is maintained. Fever, however, is not the primary illness but is a physiological mechanism that has beneficial effects in fighting infection. A rise in body temperature by 1°C increases the neutrophil and macrophage activity almost double the normal. An increase in the temperature of the body puts the child under discomfort.

Administration of antipyretic is therefore one of the most common therapeutic measures. Non-steroidal anti-inflammatory drugs (NSAIDs) are the most frequently used antipyretics. Antipyretics are regularly prescribed for febrile kids by most pediatricians.

Antipyretics are of various classes, including acetylsalicylic acid acetaminophen (paracetamol) and other anti-inflammatory non-steroidal agents (NSAIDs) represented by indomethacin, mefenamic acid, and ibuprofen. "NSAIDs inhibit cyclooxygenase (COX) that catalyzes arachidonic acid transformation to prostaglandin E2. This decrease in prostaglandin E2 in the brain is thought to reduce the hypothalamic set-point to normal."[1,2]

At present, paracetamol, mefenamic acid, and ibuprofen are the preferred antipyretics used to treat fever in kids. Acetaminophen (paracetamol) has been in use for a long time. Paracetamol's antipyretic effect is thought

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**Table 1: Difference in fall of mean temperature between study groups**

| Difference in temp (h) | Paracetamol | | Ibuprofen | | Mefenamic acid | | ANOVA *P*-value |
|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | Mean | SD | |
| After 1 | 0.96 | 0.50 | 0.99 | 0.21 | 1.05 | 0.36 | 0.431 |
| After 2 | 1.62 | 0.65 | 1.67 | 0.30 | 1.85 | 0.36 | 0.028* |
| After 3 | 2.04 | 0.78 | 2.14 | 0.35 | 2.26 | 0.54 | 0.152 |
| After 6 | 2.28 | 0.79 | 2.44 | 0.51 | 2.60 | 0.57 | 0.028* |
| After 12 | 2.67 | 0.72 | 2.58 | 0.57 | 2.62 | 0.71 | 0.786 |
| After 18 | 2.65 | 0.77 | 2.49 | 0.50 | 2.68 | 0.75 | 0.301 |
| After 24 | 2.52 | 0.63 | 2.48 | 0.54 | 2.60 | 0.65 | 0.585 |

*Significant at 5% level of significance ($P<0.05$)

to be caused by its ability to diminish the synthesis of prostaglandin in the brain. Since paracetamol in the periphery does not inhibit prostaglandin synthesis, it has no anti-inflammatory action. Paracetamol has potential side effects in addition to its beneficial effects and may even cause severe hypersensitivity reactions.

Ibuprofen is a propionic acid derivative which inhibits prostaglandin biosynthesis. Gastrointestinal bleeding is its side effect.

Mefenamic acid is a powerful cyclooxygenase inhibitor. It has both central and peripheral actions of an analgesic. This medication is commonly used in patients with osteoarthritis, rheumatoid arthritis, and dysmenorrhea.

Finding a cause for fever and treating it is crucial and providing efficient contemporary therapy is also important. It is necessary to consider the judicious use of antipyretics and to give due consideration to the side effects of antipyretics. The choice of an antipyretic should be determined by efficacy, safety, tolerability, duration of action, and cost of the particular antipyretic.

Paracetamol has been the most preferred antipyretic with the advantage of being a cheaper drug and is relatively safer. However, there have been reports of hepatotoxicity and liver failure with its overdosage. Recently, there has been an increasing trend regarding the use of mefenamic acid as antipyretic. Since there are only a few studies comparing efficacy and tolerability of paracetamol, ibuprofen, and mefenamic acid, it was thought prudent to evaluate these three drugs for better efficacy, tolerability, and adverse events in pediatric patients with febrile illness.

### Aims and Objectives

The objectives of this study were as follows:

1. To compare the efficacy of paracetamol, ibuprofen, and mefenamic acid
2. To compare the tolerability and adverse effects of paracetamol, ibuprofen, and mefenamic acid.

## METHODOLOGY

### Study design

Prospective randomized open-label study

Study approval: The study was approved by the Institutional Ethics Committee of Shri B.M. Patil Medical College and Research Centre, Vijayapura

Study site: Pediatric general ward

Study period: 1 year (1-Jan-2018 to 1-Jan-2019).

### Source of Data

The sample for the study is febrile pediatric patients admitted in the general ward at Shri B. M. Patil Medical College, Hospital and Research Center, Vijayapura.

### Sample Size

With anticipated mean difference of percent reduction in temperature between paracetamol, ibuprofen, and mefenamic acid as 0.81% and anticipated SD as 1.22, the minimum sample size per group is 60 with 90% power and 5% level of significance.

Total 180

By using the formula:

$$n= (z\alpha+z\beta)^2 2\ SD^2$$

$MD^2$

Where Z=Z statistic at a level of significance

MD=Anticipated mean difference

SD=Anticipated standard deviation.

### Inclusion Criteria

The following criteria were included in the study:

1. All children presenting with fever at the time of admission

2. Patients/attenders ready to give informed consent
3. Patients in the age group of 1 month – 14 years.

### Exclusion Criteria

The following criteria were excluded from the study:

1. Uncooperative patients
2. Patients not following the protocol
3. Patients who were hypersensitive to drugs
4. Patients who received antipyretics within 6 h preceding study
5. Severely ill patients requiring ICU admission.

Children admitted in the general ward are block randomized into three groups based on the oral antipyretic given and were observed for 24 h.
Group A: Paracetamol at a dose of 15 mg/kg 6 hourly
Group B: Ibuprofen at a dose of 10 mg/kg 6 hourly
Group C: Mefenamic acid at a dose of 8 mg/kg 6 hourly.

The following parameters were recorded in all the groups:

1. Evaluation of efficacy

Axillary temperature was recorded using a Omron® MC 246 Digital.
Thermometer.

The temperature was measured at:

- At the time of admission
- At hourly intervals for first 3 h and then every 6$^{th}$ hourly.

2. Withdrawal of the patient from the study
   - The patient condition deteriorates or becomes severely ill
   - Withdrawal of consent of the parents/guardians.

3. Tolerability evaluation

Modified treatment tolerability evaluation score.[3,4]
Symptoms such as vomiting, dislikeness for meals (nausea), and daytime sleeping were assessed and scores were recorded from 0–3.

- Score 0: Absent–symptom is not present
- Score 1: Mild–symptom is present but is not troublesome
- Score 2: Moderate–symptom is frequently troublesome but would not interfere with daily activity
- Score 3: Severe–symptom is troublesome.

### Statistical Analysis

All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean ± SD were used. For categorical data, the number and percentage were used in the data summaries and diagrammatic presentation. Chi-square test was used for the association between two categorical variables. The difference of the means of analysis variables between 2-time points in the same group was tested by paired t-test. The difference of the means of analysis variables between more than two independent groups was tested by ANOVA and F-test of testing of equality of variance. If $P < 0.05$, then the results were considered to be statistically significant; otherwise, it was considered as not statistically significant. Data were analyzed using SPSS software v.23.0. and Microsoft Office 2007.

## RESULTS

In our study, we randomized 60 patients to each of the three study groups – oral paracetamol, oral ibuprofen, and oral mefenamic acid. However, a few patients had to be administered the antipyretics intravenously, as shown in Table 2, thereby reducing the actual sample size to that extent.

The number of patients experiencing adverse effects of vomiting, dislikeness for meals, and daytime sleeping among the three study groups is shown in Table 3. Vomiting was reported in the paracetamol group by 11.5% of patients, followed by 5.4% and 5.3% in the ibuprofen and mefenamic acid group, respectively. Dislikeness for meals was reported by 10.5% of patients in the mefenamic acid group, followed by 7.7% of patients in the paracetamol group and 5.4% patients in the ibuprofen group. Daytime sleeping was reported by 5.4% and 5.3 % patients in the ibuprofen and mefenamic acid groups, respectively. In the paracetamol group, none of the patients reported daytime sleeping.

**Table 2: Distribution of study groups**

| Antipyretic | Total sample | IV antipyretic given | Actual sample |
|---|---|---|---|
| Paracetamol | 60 | 8 | 52 |
| Ibuprofen | 60 | 4 | 56 |
| Mefenamic acid | 60 | 3 | 57 |

**Table 3: Distribution of adverse effects between study groups**

| Adverse effects | Paracetamol | | Ibuprofen | | Mefenamic acid | | *P*-value |
|---|---|---|---|---|---|---|---|
| | *n* | % | *N* | % | *n* | % | |
| Vomiting | 6 | 11.5% | 3 | 5.4% | 3 | 5.3% | 0.359 |
| Dislikeness for meals | 4 | 7.7% | 3 | 5.4% | 6 | 10.5% | 0.593 |
| Daytime sleeping | 0 | 0.0% | 3 | 5.4% | 3 | 5.3% | 0.239 |

The plot of the patient temperature at different time periods after admission for the three study groups is shown in Figure 1. At the end of 24 h, the maximum fall in temperature is observed in the mefenamic acid group, followed by ibuprofen group and then paracetamol group.

The fall in mean temperature from the baseline at different observation points for the study groups is shown in Table 1 and Figure 2. At the end of 2 h, the fall in mean temperature from the baseline for the mefenamic acid group is maximum (1.85°F) as compared to the other two groups and is statistically significant ($P = 0.028$). Even at the end of 6 h, the fall in mean temperature for mefenamic acid group is more (2.60°F) and is statistically significant (0.028).

## DISCUSSION

Fever is not a primary illness but it is a physiological 18 mechanism that has beneficial effects in fighting infection. The increase in body temperature causes discomfort for children. Hence, antipyresis is one of the most usual therapeutic interventions undertaken. Paracetamol and, more recently, ibuprofen are generally used over the counter drugs for antipyresis. However, of late, there is a trend of increased use of mefenamic acid as antipyretic. All three drugs belong to the class of NSAIDs. They inhibit COX-dependent production of prostaglandins which are involved in mediating inflammation, pain, fever, and swelling. We evaluated these three drugs for their antipyretic efficacy and adverse events in pediatric patients with febrile illness. In our study, all three drugs – paracetamol, ibuprofen, and mefenamic acid proved to be effective antipyretic drugs. In the paracetamol group, the mean body temperature decreased from 100.99°F at baseline to 99.28°F at 2 h, while, in the ibuprofen group, it decreased from 100.72 ± 0.47 at baseline to 99.14°F ± 0.48 at 2 h and in the mefenamic acid group from 100.91° F ±0.63 at baseline to 99.16 °F ± 0.54 at 2 h. This decrease in body temperature at 2 h from the mean baseline temperature at admission was statistically significant in the mefenamic acid group ($P = 0.028$). Similarly, at the end of 6 h, the mean body temperature decreased significantly ($P = 0.028$) in the mefenamic acid group. Thus, the onset of action is faster for mefenamic acid group. The efficacy after 6 h is maximum for mefenamic acid as compared to paracetamol and ibuprofen. At the end of 24 h, mefenamic acid group showed a maximum reduction in baseline mean temperature among the three study groups.

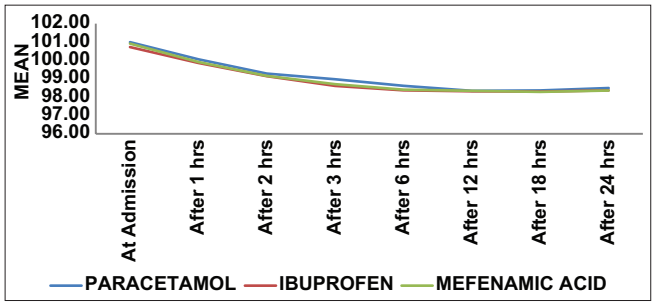


**Figure 1: Fall of mean temperature among the study groups**

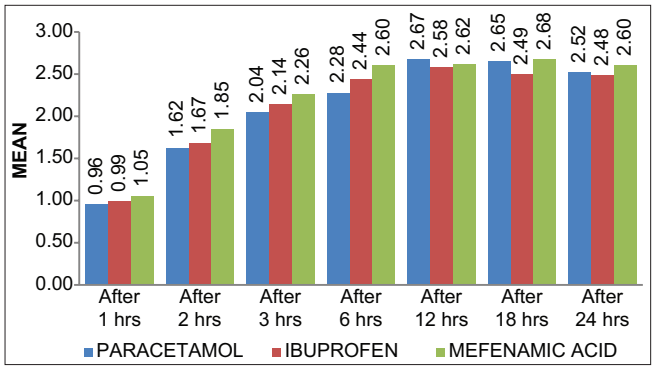


**Figure 2: Difference of mean temperature between study groups**

Very less data are available on comparative studies between the three drugs – paracetamol, ibuprofen, and mefenamic acid, as compared to data evaluating paracetamol and ibuprofen.

A comparative study between paracetamol suspension (15 mg/kg) and mefenamic acid suspension (4 mg/kg) by Kunkulol *et al.*[2] reported that the fall in temperature at 1 h was more in mefenamic acid group (102.12°F–99.5°F) compared with paracetamol group (101.81°F–100.32°F). At 6 h, the decrease was significantly more in mefenamic acid group as compared with paracetamol group (3.23% vs. 2.47%, $P < 0.01$). This is in line with our results. An Indian study by Khubchandani *et al.*[5] showed that mefenamic acid (6.5 mg/kg) demonstrated significantly better antipyretic activity compared to paracetamol (10 mg/kg) ($P < 0.05$) over the 4 h period of observation and ibuprofen (7 mg/kg) ($P < 0.05$) in the 2–4 h range. Mefenamic acid continued to show antipyretic activity at the end of 4 h in contrast to ibuprofen and paracetamol, but since the period of observation in the study was restricted to 4 h, the study was unable to quantify the precise duration of extended antipyretic efficacy of mefenamic acid. Our study corroborates the same result.

In our study, 11.5%, 5.4%, and 5.3% of patients reported vomiting in the paracetamol, ibuprofen, and mefenamic acid group, respectively. The occurrence of vomiting was not significantly associated with any particular study group ($P = 0.359$). In a study by Kunkulol *et al.*,[2] 6% and 4% of patients in the paracetamol and mefenamic acid group, respectively, reported vomiting, with no significant association with the study group ($P > 0.05$). Dislikeness for

meals was reported by 10.5% of patients in the mefenamic acid group, followed by 7.7% of patients in the paracetamol group and 5.4% of patients in the ibuprofen group in our study. Dislikeness for meals was not significantly associated with any of the study groups ($P = 0.593$). In the study by Kunkulol *et al*.,[2] dislikeness for meals was reported by 10% of patients in the paracetamol group and 14% of patients in the mefenamic acid group, but the association was not significant ($P > 0.05$). In both studies, the mefenamic acid group reported higher dislikeness for meals, though not significant. In our study, daytime sleeping was reported by 5.4% and 5.3% of patients in the ibuprofen and mefenamic acid groups, respectively, while none of the patients in the paracetamol group reported daytime sleeping. Daytime sleeping was not significantly associated with any particular study group ($P = 0.239$). In the study by Kunkulol *et al*.,[2] 4% of patients in the paracetamol and ibuprofen group each reported daytime sleeping, without any significant association ($P > 0.05$).

Thus, in our study, mefenamic acid is found to be a better antipyretic as compared to paracetamol and ibuprofen, providing a faster onset of action and prolonged effect.

## CONCLUSION

Mefenamic acid in the doses used in the study was shown to be more effective and well-tolerated than ibuprofen and paracetamol in the treatment of fever in young children. Although the treatment appeared safe, it will require continuing vigilance from those caring for children before mefenamic acid is given the confidence afforded by paracetamol or ibuprofen as antipyretics.

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Original Article

# Our Experience with Different Skin Closure Techniques in Meningomyeloceles

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## Abstract

**Introduction:** Myelomeningocele is a spinal dysraphism containing a placode of neural tissue attached to the surrounding skin. Although common and a serious malformation of the Central nervous system, it is compatible with life. Neurologic impairment corresponds to size and location of the malformation Closure of the defect is challenging as the tissue available is less, with high chances of wound dehiscence. Therefore, multispecialty treatment to close both the neural tube and provides a stable skin cover over the defect and avoid complications is necessary.

**Aim of the Study:** To study various reconstructive skin closure techniques for the defects of meningomyeloceles and their outcomes.

**Material and Methods:** Prospective study of 2 years between 2017 and 2019 included 27 children who were operated for meningomyelocele where there was a skin defect after closure of it. Different closure techniques were analyzed.

**Results:** Eighteen were male children and nine were female. Common location was lumbosacral region (17 of 27). The defect size varied from 10–40 $cm^2$. Common technique was primary closure at 40.7%. Various other flaps like bipedicled and transposition flaps were used in another 60%. Complications amounted to 24%. The mean hospital stay was 12 days.

**Discussion and Conclusions:** Although musculocutaneous flaps are around, we preferred fasciocutaneous flaps for their reliability, ease of dissection less operative time, and minimal blood loss. The disadvantage with these flaps is their random pattern of blood supply, and so careful planning and wide base are required.

**Key words:** Bipedicle flap, Cerebrospinal fluid, Closure, Defect, Fasciocutaneous flap, Limberg flap, Meningomyelocele, Musculocutaneous flap, Primary, Rotation flap, Transposition flap

## INTRODUCTION

Myelomeningocele (MMC) is a form of spinal dysraphism. The etiology of neural tube defects may include genetics, geography, low socioeconomic status, and folic acid deficiency.[1] At four weeks of gestation, the lateral edges of the neural plates elevate toward each other and fuse to form a tube known as the neural tube. Failure of this process results in a neural tube defect and represents a localized failure of primary neurulation. When the failure involves a posterior closure, it is called spinal dysraphism.[1]

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The resultant malformation contains a placode of neural tissue attached peripherally to the surrounding skin. The underlying cerebrospinal fluid (CSF) elevates the placode on a dome or sac. If the thin tissue on the dome tears, the CSF is allowed to escape and the malformation is flat. Whether domed or flat, there will always be a placode on the skin surface and, MMCs are, therefore, open malformations.[1] An MMC is the most common of the dysraphic malformations and is also the most serious CNS malformation compatible with life. Neurologic impairment and sensorimotor paralysis corresponds to size and location of the malformation.[1]

Global prevalence of MMCs ranges from 0.8 to 1.0 in 1000 live births.[2] MMCs cause chronic disability. Closure of such defects is a challenging task, as the amount of tissue available in an infant is less, and there are high chances of wound dehiscence. Therefore, treatment with multidisciplinary care involving both neurosurgeons and

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plastic surgeons to close the neural tube and provides a stable cover over the defect and avoid complications is necessary to improve the quality of life, and survival.

The aim of the study is to analyze the size of MMC defects, and various reconstructive skin closure techniques for those defects and the outcome of such closures.

## MATERIALS AND METHODS

This is a prospective study done over a period of 2 years from September 2017 to October 2019 at a tertiary care hospital. A total of 27 children were included in the study. They underwent surgery of closure for meningomyelocele and it was followed by plastic surgical intervention for closure of the skin defect. They were followed up. The data such as demography, site of the defect, site of the defect, closure technique, and post-operative complications were analyzed, results and conclusions drawn.

After explaining the complexity of the disease, all aspects of treatment, complications, and long-term problems associated with this disease, to the parents, the informed consent was taken, and the patients were operated.

### Surgical Techniques

The newborn is placed in mild Trendelenburg prone position on firm chest rolls to allow thoracic expansion and avoid CSF escape.

Although different methods are described, closure of large meningomyelocele defects remains a challenging problem. Several authors prefer musculocutaneous flaps for managing large Meningomyelocele defects, but it is recognized that musculocutaneous flap coverage of large lumbosacral MMC defects is associated with high complication rates.[3,4]

To avoid this some authors prefer using skin flaps such as advancement flaps, bipedicled flaps, local transposition flaps, bilobed flaps, double Z-plasty, rotation flaps, and Limberg flaps, which can be used successfully in the closure of large MMC defects.[5-8]

Large defects of more than half of the width of the child's back cannot be closed reliably by simple skin undermining. In addition to defect size, location and shape, the general status, associated kyphosis, and the condition of the surrounding tissues are other important parameters that can influence the technique of the reconstruction.

A perfect approximation of suture edges may be possible in cases of well-epithelized MMC with redundant skin. This may not be the case with large flat myeloceles with deficient cutaneous layers that will require a more complex plastic surgery reconstruction.

At our center, we managed to close the defects either through primary closure, or bipedicled flaps with primary closure of donor defect, bipedicled flap with skin grafting of the donor defect, transposition flap, triple rotation flap, and Limberg flap.

Although the correction of MMC should be performed as soon as possible, preferentially within the first 72 h of life, in some of the patients the correction was made at two years of age. Closure of MMC defect increases intracranial pressure, leading to CSF flow through the recently repaired dura, resulting in subcutaneous fluid collection, increase in tension on the fragile wound edges. A ventriculoperitoneal shunt for hydrocephalus was placed in 22 (81.05%) patients either preoperatively (19), intraoperatively (1), or postoperatively (2), and it reduced the risk of CNS infection.

The goals of closure are to preserve the function of the neural tissue, provide a stable skin cover over the repaired neural tissue in the form of flap and to prevent secondary infection.

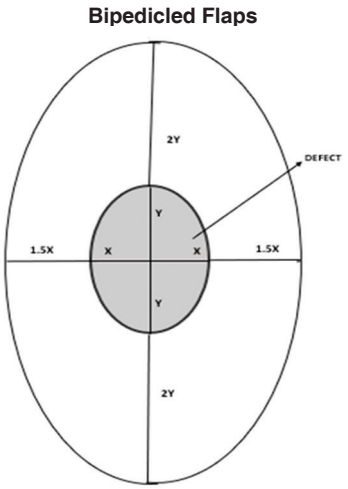
### Primary Closure with Advancement

MMC defects with sizes ranging from 10 $cm^2$ to 40 $cm^2$ underwent excision of the MMC sac and water tight dural closure, followed by immediate reconstruction of any residual skin defect. Ideal solution for covering the skin defect in MMC surgery is still lacking. There is no decision-making guide in the literature on whether to use a flap or primary closure for the reconstruction of all types of these skin defects. We did tension free primary closure in few cases after undermining up to posterior axillary lines where there was laxity of the skin.

### Bipedicled Flaps

In cases, where there was tension over the suture line, we adopted standard planning techniques for bipedicled flaps in our institution. Most of the defects were addressed with bipedicled flaps usually two, one from either side of the defect and in a few, other flaps also were used. The planning of the flaps was done for the defect after the excision of the MMC sac and dural closure. The defect size was measured in length "Y" and width "X." Both "X" and "Y" were divided into equal halves and the flaps were planned on both sides of the defect. The horizontal dimension of the flap is marked at 1.5"X" from the margin of the defect limiting at the posterior axillary line on either side. The vertical height of the flap was marked at 2"Y" both above and below the defect. These markings are joined on either side to draw

bipedicled flaps on both sides from the defect margin [Clinical picture 1].




## Transposition Flap

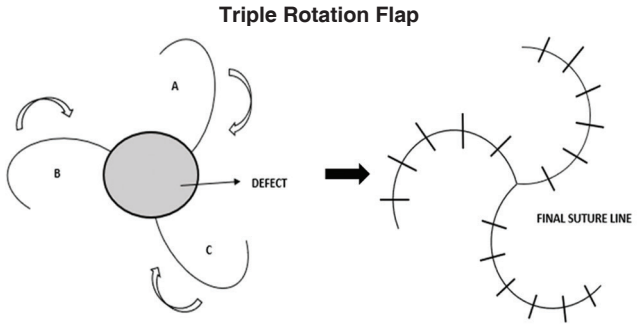
In one case, a classical transposition flap was used. In the planning of the local transposition flap, the defect was triangulated first. The transposition flap was designed as a rectangle in a ratio of not more than 2:1 immediately adjoining the defect and was moved to cover the defect. The base of the flap was alongside the apex of the triangle [Clinical picture 2]

## Limberg Flap

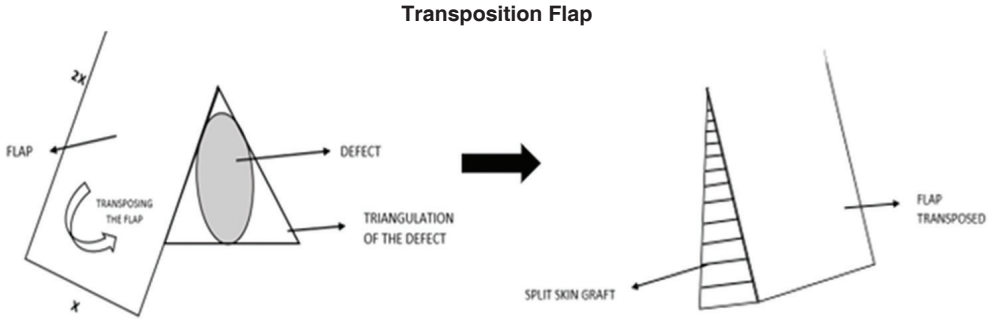
In one case, Limberg flap was planned keeping the angles at 60 and 120°. The margin of the defect was then trimmed into a parallelogram to act as the Limberg flap. A vertical line equal to the length of one side of the rhomboidal defect was determined, followed by a second line parallel to one side of the rhombus.

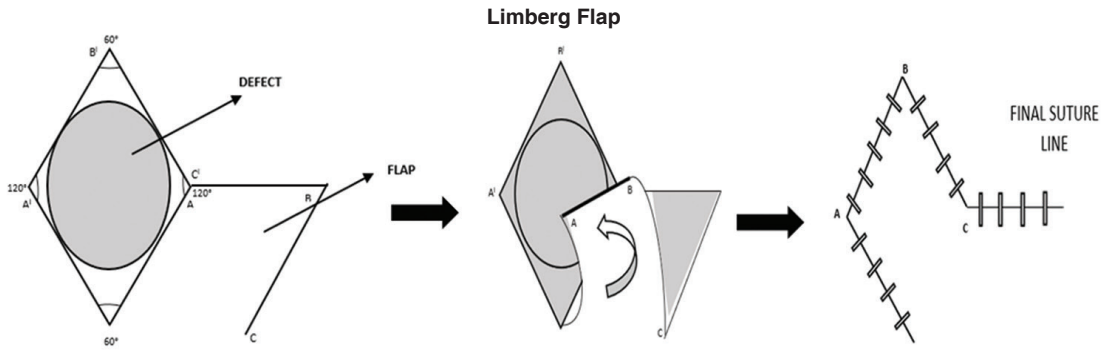
## Triple Rotation Flap

In one more case, a triple rotation flap was used [Clinical picture 3].




The first step of MMC repair is the development of the subcutaneous layer and flap elevation by digital dissection in the fascial plane all around the spinal defect. Excessive coagulation of perforator vessels to the skin that may compromise the blood supply of the cutaneous coverings is avoided. The subcutaneous layer is usually minimal at the border of the malformation. Suturing at the margins is done without excessive tension with absorbable 3-0 Rapid Vicryl in two layers. Care is taken to interpose adequate subcutaneous layer beneath the superficial skin layers to



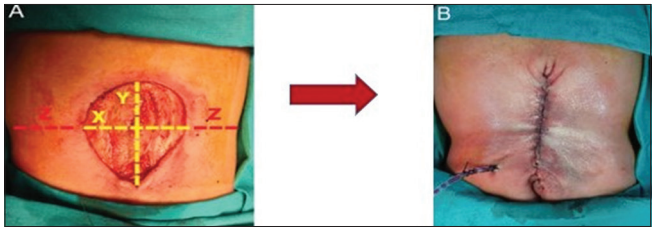



reduce the incidence of retracting scars. Initially, following closure, the skin may be blanched as a sign of tension due to edema. This usually improves as the edema subsides and wound dehiscence rarely occurs.

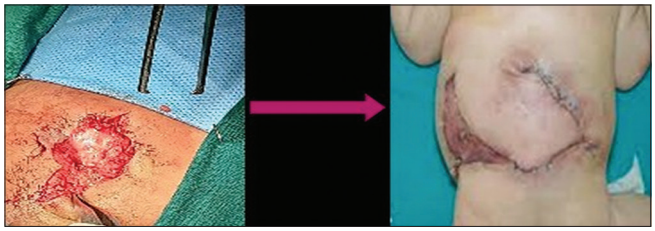
### Post-operative Care

After completing skin closure, the wound is cleaned and covered with sterile gauze. The perineal area and anus are kept separated from the wound dressing by a separate adhesive plastic drape to limit the contact of the wound with urine or fecal matter. The newborn is kept in the neonatal ICU for 1–2 post-operative days, for any signs of apnea or of brainstem dysfunction. The child is maintained prone with the lower back slightly elevated above the level of the head to reduce the risk of CSF leak from the wound.

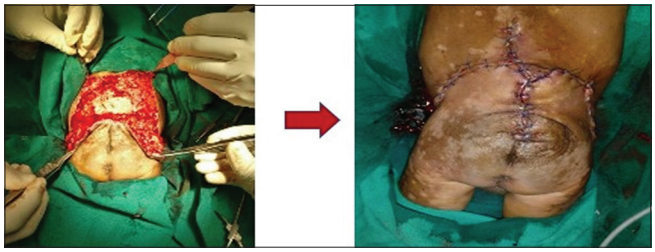
Intravenous antibiotics are given for 5 days or more if there is significant risk of infection. The wound dressing is changed every 48 hrs, or anytime if soiled. As we used absorbable sutures, there was no need of suture removal.




**Clinical picture 1: Left Picture showing planning of bipedicle flap. X and Y measured. Posterior axillary lines marked. Flap is planned as 1.5X (Z) in horizontal dimension from defect margin and 2Y in vertical dimension from defect margin. Markings joined to form bipedicle flap on both sides. The right picture showing final closure of the defect with bipedicle flap**



**Clinical picture 2: The left picture showing defect and its reconstruction with transposition flap in right picture**



**Clinical picture 3: The left picture shows triple rotation flaps elevated and final closure in right picture**

Complications and their management are described in the section below.

## RESULTS

A total of 27 patients were included in the study.

### Demography

About 18 (66.67%) were male children and nine (33.33%) were female [Figure 1]. 44.5% (12) were of age < 72 h. About 22.1% (6) were between 4 to 7 days old. About 25.9% (7) were of age from one week to 30 days. About 3.7% one patient was 10 months age. Another patient 3.7% was of 18 months age [Table 1].

### Location

The most common location of the MMC in this study was the lumbosacral region with 17 cases (62.9%). In 1.5% of the cases, it was in the lumbar region. There were three (11.1%) patients with thoracolumbar MMC. There were no cases of cervical MMC. And two (2.74%) patients presented with sacrococcygeal MMC [Figure 2].

### Size

The defect sizes varied from 10 to 40 $cm^2$. In 7.4% (2) cases, defect was about 10 $cm^2$, in 48.14 % (8) cases it was

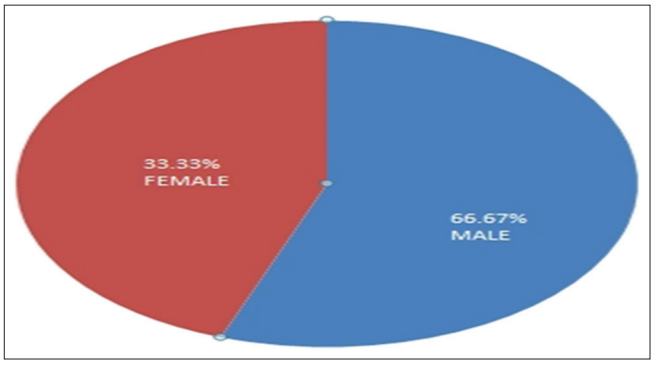



**Figure 1: Gender distribution (*n*=27)**

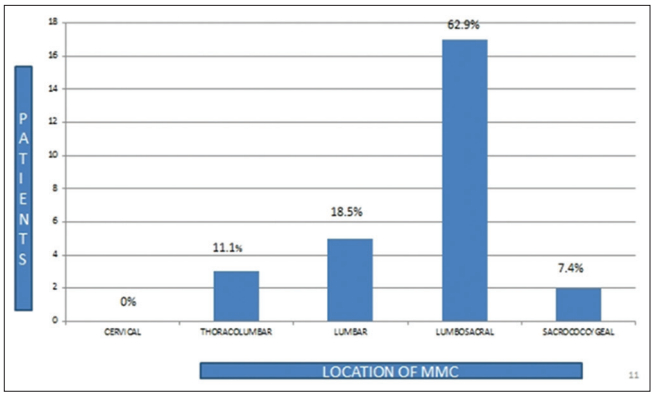



**Figure 2: Location of MMC and number of patients (*n*=27)**

10–20 $cm^2$, in 11.1% (3) cases it was 20–30 $cm^2$, and in one case (3.7%), the largest of the defect was 40 $cm^2$ [Table 2].

### Closure Technique

In most of the cases, 11 of 27 (40.7%) a tension free primary closure could be done with undermining of the surrounding skin in the subcutaneous plane. In 7 of 27 cases (25.9%), defect was closed using bipedicled flaps after giving relaxing incisions in the posterior axillary lines. These relaxing incisions were also closed with primary suturing. In four cases (14.8%), after the bipedicled flap was sutured, the relaxing incisions could not be approximated so skin grafting was done at the donor site. We used rotation flap in two cases (7.4%). Limberg flap in one case (3.7%), classic transposition flap in one case (3.7%), and triple rotation flap in one case (3.7%) [Figure 3].

### Relation of Defect Size to the Flap Planned

For primary closure of defect, the average size of the defect was 10.5 $cm^2$, the mean size of the defect for bipedicled flap and primary closure was 32.3 $cm^2$. While bipedicled flaps requiring closure and skin grafting, the size was around 36.4 $cm^2$. In case of the Limberg flap, the size was 39.4 $cm^2$. The size of defect for closure with classical transposition flap was 26.9 $cm^2$. The defect size was an average of 38.3 $cm^2$ for closure with rotation flaps. Moreover, the single triple rotation flap had a defect size of 40.1 $cm^2$ [Table 3].

### Complications (*n*=6)

We encountered complications in the form of wound infection in one cases (4%), wound dehiscence in four cases (16%), three cases of primary closure where the defect size was 16 $cm^2$, 18 $cm^2$, and 20 $cm^2$, one case of bipedicled flap. Marginal flap necrosis in one patient where triple rotation flap was done (4%) [Figure 4].

**Table 1: Relationship of age to number of patients (*n*=27)**

| Age | Number of patients | Percentage |
|---|---|---|
| 48–72 h | 12 | 44.5 |
| 4–7 days | 6 | 22.1 |
| <30 days | 7 | 25.9 |
| 1 month–1 year | 1 | 3.7 |
| 1–2 years | 1 | 3.7 |

**Table 2: The dimensions of defect (*n*=27)**

| Defect size in $cm^2$ | Number of patients | Percentage |
|---|---|---|
| <10 | 2 | 7.4 |
| 10–20 | 13 | 48.14 |
| 20–30 | 8 | 29.6 |
| 30–40 | 3 | 11.1 |
| >40 | 1 | 3.7 |

Wound infection was managed by altering the antibiotics as per culture sensitivity of wound swab and daily dressings. Other complications were managed by secondary procedures.

### Wound Dimensions Where Complications were Encountered

Wound dehiscence was noted in cases of primary closure of defect size 16 $cm^2$, 18 $cm^2$, and 20 $cm^2$, and in another case of bipedicle flap with dimension of 15 $cm^2$ [Table 4].

### Secondary Procedures (*n* = 6)

In four of six cases, (67%) wound complication was managed by debriding the skin margins and closure with flap advancement. In another two of the six (33%) cases, the complication was addressed by debridement of skin margins and skin grafting. luckily, the graft take was good even on exposed closed neural tube defect [Figure 5].

### Hospital Stay

In patients, where rotation and transposition flaps were used, the mean hospital stay was 8 days. In cases, where the defect was addressed with bipedicled flap and primary closure, the mean hospital stay was 10 days. In patients with bipedicled flap and skin grafting, the stay was for 12 days. Patients with

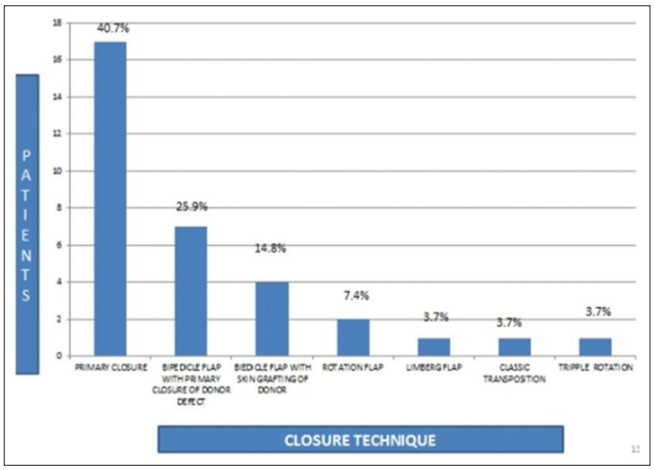



**Figure 3: Different closure techniques (*n*=27)**

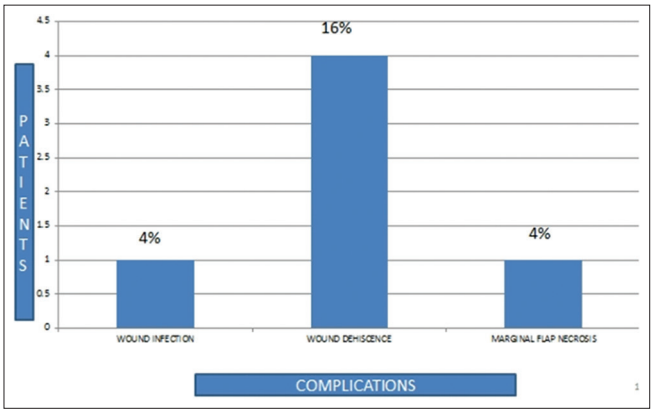



**Figure 4: Complications (*n*=6)**

**Table 3: Different closure techniques for various size of defects (*n*=27)**

| Closure technique | Number of patients | Average defect size |
|---|---|---|
| Primary closure | 17 | 10.5 $cm^2$ |
| Bipedicle flap with primary closure of donor defect | 7 | 32.3 $cm^2$ |
| Bipedicle flap with skin grafting of donor | 4 | 36.4 $cm^2$ |
| Rotation flap | 2 | 38.3 $cm^2$ |
| Limberg flap | 1 | 49.4 $cm^2$ |
| Classic transposition | 1 | 26.9 $cm^2$ |
| Triple roration | 1 | 40.1 $cm^2$ |

**Table 4: Complications for techniques and defect size**

| Technique of closure | Size of defect |
|---|---|
| Primary closure | 16 $cm^2$ |
| Primary closure | 18 $cm^2$ |
| Primary closure | 20 $cm^2$ |
| Bipedicle flap with primary closure of donor defect | 15 $cm^2$ |

primary closure after undermining the flaps, the mean stay was for 18 days due to complications encountered during healing. In one case where a triple rotation flap was used, the stay was for long period of 22 days as there was wound infection which healed slowly [Figure 6].

### Deaths

There were two deaths (7.4%). One baby operated within 48–72 h of birth died two days later to surgery. Another baby operated at one week of birth died five days after surgery. In both the cases, the cause of death was due to CSF leak and CNS infection.

### Follow-up

All the patients were followed up till the flaps healed well for a period of three months.

## DISCUSSION

There are many techniques available in the armamentarium of the plastic surgeon that can be useful for the closure of MMC defects. Regardless of the technique used, it should be tension free closure with good soft-tissue padding of the neural tube, prevent CSF leakage, and facilitate proper wound healing, especially for large defects. The techniques should lead to minimal morbidity. To achieve successful outcomes, reconstruction and planning should be done specifically for each patient.

Closure of the larger defects especially in children is always challenging. There is a range of options as per

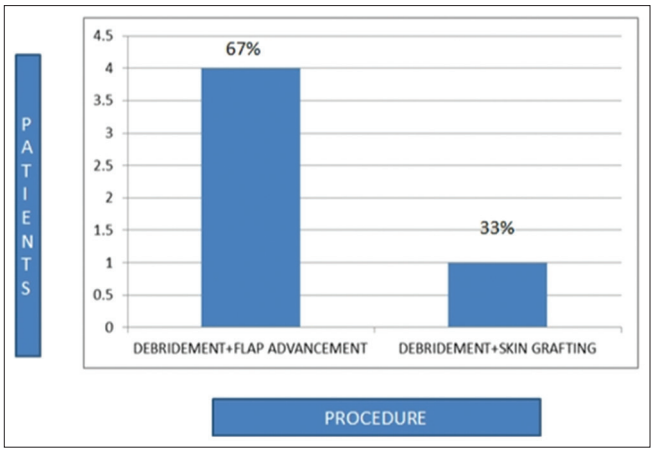



**Figure 5: Secondary procedures (*n*=5)**

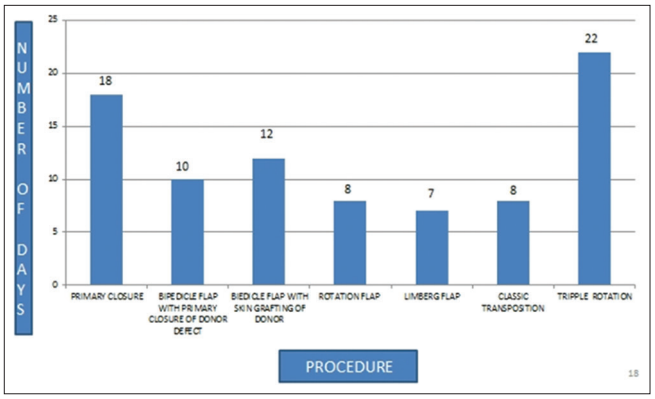



**Figure 6: Hospital stay (*n*=25)**

reconstructive ladder from a simple skin graft to the local flaps to various regional flaps, musculocutaneous flaps, and even the perforator flaps. Musculocutaneous flaps as an option for wide MMC defects was described by Mustarde in 1968. McCraw *et al.* in 1978 used bilateral latissimus dorsi musculocutaneous flaps for the closure of MMC. McDevitt *et al.* in 1982 had used bilateral latissimus dorsi musculocutaneous flaps with extended gluteal fasciocutaneous flaps for the closure of thoracic and lumbar defects. Use of these flaps was extended to sacral defects by Ramirez *et al.* in 1987. These musculocutaneous flaps did not gain much popularity due to extensive flap dissection, increased blood loss, and prolonged operative time, thereby limiting their use.

Perforator flaps were effectively used by El-Sabbagh in 2011[9] and Duffy *et al.* in 2004. The limitation of these perforator flaps is that these flaps require expertise with microsurgical instrumentation and the microscope.

More recently, in 2012, Patel *et al.*[10] had described the local turnover fascial flaps and the midline linear skin closure as methods of repair for the extradural MMC defects. Some

surgeons relied on single flap for MMC defects. Patterson[11] used only rotation flaps. Cemal Alper Kemaloğlu *et al.*[12] proposed some decision-making guidelines for closure of MMC defects. A similar type of guidelines was used in this study for planning bipedicled local flaps. Length and width are marked as "Y" and "X" from the centre of the defect on either side. Width of 1.5 times X on either side from centre point, and length of 2Y on each side for each of the bipedicled flaps are marked. This planning has enabled our bipedicled flaps to settle well without any major complications.

In this study, we also used other flaps such as advancement flaps, local transposition flaps, triple rotation flaps, and Limberg flaps, which were used successfully in various studies.[2,13,14] The dissection of local skin flaps is much easier to perform, requires less operative time, and results in less blood loss. Primary closure with advancement is possible by undermining of the wound margins in almost 40% of cases. However, in the remaining 60% of patients, we planned for flaps as our aim was to achieve a tension free closure and avoid wound dehiscence. The drawback of these commonly used techniques is the vascular compromise and seroma formation which can lead to wound dehiscence. The use of fasciocutaneous flaps has been described in plastic surgery literature. Flaps with primary midline closure heal well with a cosmetically pleasing scar as there is good vascular supply to both skin and fascial edges.

In the previous studies, approximately 75% of MMC defects were closed by direct repair, while the remaining 25% required other reconstructive options.[11] While in this study, 40% were primary closures and 60% of cases needed flaps.

The most frequent location of MMCs in this study (62.9%) was lumbosacral region which is also, a finding in study done by others.[2,14-16] Although this may be the reason for satisfactory post-operative ambulation in these patients, we had limited time to assess the follow-up because of the prevailing COVID situation. Patients with MMC at high level can also achieve community ambulation when they receive good care, as reported by Charney *et al.*[12]

Male to female ratio in this study is 1.25 almost similar to the findings as other studies[2,11,17] where there is preponderance of males over females. Complication rate is 24% of which wound dehiscence was noted in four (16%) patients, and one was a triple rotation flap and the same was seen in other studies.[2,15] Wound dehiscence arising more in primary closure cases than where flaps are planned states that wherever possible, closure with well planned and executed flaps gives better outcomes. This was the reason for relatively long hospital stay in cases of primary closure where discharge could have been planned early.

Types of flaps planned for the defect size in this study is correlating to those planned by Mukesh Kumar sharma.[2]

## CONCLUSIONS

In spite of many options for closure of MMC defects, flaps are more reliable in giving a good closure and support to the underlying cord structures. Although there are many flaps described in various studies, there is a lack of a standard road map to guide the young plastic surgeons. Fasciocutaneous flaps rather than musculocutaneous flaps are easy to practice and reliable as there is no muscle dissection which may compromise the physical quality of life later.

Furthermore, fasciocutaneous flaps take less operative time in a child already under general anesthesia and critical life. There is minimal intraoperative blood loss in case of fasciocutaneous flaps. Bipedicled flaps planned in the manner described with 1.5 X and 2Y had satisfactory results.

The disadvantage with these flaps is because of the random pattern of blood supply, careful planning and wide base are required.

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Original Article

# A Study of Clinical Profile, Etiology, and Management of Liver Abscess in a Tertiary Care Center in Jammu

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## Abstract

**Background:** The aim of this observational study of liver abscess is to determine the demographic profile, clinical presentation of the subjects, etiology, laboratory investigations, and different treatment modalities.

**Methods:** This observational study was carried out in the Department of General Surgery, Govt. Medical College, Jammu. A total of 50 cases with proven liver abscess were taken and a designed pro forma was used to collect all the data and different modalities of treatment were noted.

**Results:** Amebic liver abscess (58%) is more common than pyogenic liver abscess (42%). Liver abscess is more common in male subjects as compared to females. The right lobe of the liver is commonly involved with mostly solitary lesions. The right upper abdominal pain, fever, and abdominal tenderness are the most common complaints. Alcoholism is the most common risk factor documented in about 58% of the subjects. Most of the patients were managed medically (46%) followed by USG-guided percutaneous drainage (42%).

**Conclusion:** The modern radiological techniques had greatly helped in early diagnosis and management of liver abscess, thereby reducing the morbidity and morbidity related to disease. Medical management and percutaneous drainage (USG guided) has become the mainstay of the treatment of liver abscess.

**Key words:** Amebic, Liver abscess, Open drainage, Percutaneous drainage, Pyogenic

## INTRODUCTION

The first description of liver abscess is credited to Hippocrates in the year 4000 BC but it still poses great challenges for the treating doctor due to its wide variety of clinical presentation and difficulty in diagnosis (especially in tropical countries due to poor hygiene and illiteracy) with significant morbidity and mortality, though the introduction of the newer antibiotics and advancements in radiology has great impact on the outcome. India being a tropical country harbors around 400 million people with *Entamoeba histolytica* which is the cause for amebic liver abscess thus it is of immense importance.[1-3]

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Abscess formation within the liver occurs in variety of circumstances and in response to different agents. Abscess of the liver may be pyogenic or parasitic in origin. With introduction of antibiotics, the incidence of pyogenic abscess of the liver has decreased to a greater extent. Liver abscess is the most common extraintestinal manifestation of amebiasis. Hepatic amebiasis is reported in 3–10% of afflicted patients. The incidence is high in tropical countries and is attributed to lack of proper sanitation and personal hygiene due to low socioeconomic conditions.

Pyogenic and amebic liver abscess shares many clinical features. Clinically, the first diagnostic requirement is the demonstration of an abscess followed by demonstration of its nature. Until recently, the diagnosis of liver abscess was dependent on variable clinical criteria, characteristics of pus aspirated from abscess cavity or on a clinical response

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to appropriate chemotherapy. With the advent of imaging techniques such as ultrasound, CT scan, and serological tests, the diagnosis of liver abscess can be made early, rapidly, and accurately. The management of hepatic abscess has been greatly influenced by advances in diagnostic imaging and interventional radiology.[4-6]

Major cause for the pyogenic abscess is biliary tract diseases. In alcoholics, diabetics, and immunocompromised individual, there is increasing trend of the disease.

*Escherichia coli*, *Klebsiella* species, enterococci, and *Pseudomonas* species are the most common aerobic organisms cultured in recent series, whereas *Bacteroides* species, anaerobic streptococci, and *Fusobacterium* species are the most common anaerobes. *Klebsiella pneumoniae* is extremely prevalent in liver abscesses in Asian countries as well as in predominantly Asian population in the Western world for unclear reasons. *Mycobacterium tuberculosis* is a common infecting organism in the acquired immune deficiency syndrome. Confirmation of pyogenic liver abscess involves aspiration of the abscess as well as positive blood cultures. Amebic serology is both a highly sensitive and specific test in identifying patients with amebic infection, thus aiding in differentiation between pyogenic and amebic hepatic abscess.[7-9]

## METHODS

This observational study was carried out in the Department of General Surgery, Government Medical College, Jammu.

### Inclusion Criteria

The following criteria were included in the study:

- All the patients of both sexes of liver abscess diagnosed clinically and/or ultrasonographically
- All cases of bacterial and parasitic liver abscess
- All cases in evolving, liquefied and ruptured stage with or without peritonitis
- All cases of diagnosed liver abscess being referred to GMC Jammu.

### Exclusion Criteria

- Patients with liver abscess associated with trauma or malignancy were excluded from the study

Patients for the study will be taken from those attending surgical OPD and emergencies as a case of liver abscess. The patients will be evaluated as per following protocol.

- Demographic detail such as age, sex, residence, and comorbidities shall be noted for all patients
- A detailed history including presenting complaints, past history, and history of any immunocompromised state shall be noted
- Investigations such as complete hemogram, coagulation profile, and liver function tests will be done
- Radiological investigations such as USG and chest X-ray will be performed on the day of admission
- Patients will be started on intravenous antibiotics with monitoring of clinical status of the patient
- Follow-up USG abdomen to be done if there is no improvement in the symptoms of the patient
- CECT abdomen and pelvis will be performed if patient's condition worsens or does not improves
- Various modalities of the treatment of liver abscess used will depend on multiple factors such as site of abscess, size of abscess, single or multiple, and clinical examination
- Various modalities included are as follows:
  a. Conservative management
  b. USG-guided percutaneous aspiration/drainage
  c. Open drainage.

### Follow-up of Patients

Patients will followed up every 2 weekly for 1 month followed by monthly for 6 months. The patient will be evaluated for the residual cavity, efficacy of treatment, or recurrence.

## RESULTS

A total of 50 patients were taken having proven liver abscess. Amebic abscess was more common than pyogenic liver abscess. Out of 50 patients, 29 (58%) had amebic liver abscess and 21 (42%) had pyogenic liver abscess [Table 1].

Out of 50 patients, 46 were male and only 4 were female. It was observed that 28 out of 50 patients were alcoholics, 2 were diabetics, and 1 had a history of ATT intake [Table 2].

The incidence of liver abscess was found to be more common in 21–40 years age group followed by 41–60 years age group. Moreover, it was observed that pyogenic liver abscess is more common in elderly age group [Table 3].

**Table 1: Distribution of patients**

| Type | Frequency | Percentage |
|---|---|---|
| Amebic | 29 | 58 |
| Pyogenic | 21 | 42 |
| Total | 50 | 100 |

**Table 2: Sex distribution**

| Sex | Frequency | Percentage |
|---|---|---|
| Male | 46 | 92 |
| Female | 4 | 8 |
| Total | 50 | 100 |

The right lobe involvement was more common with 33 patients followed by involvement of the left lobe in 10 patients followed by involvement of both lobes in 7 patients [Table 4].

Thirty-nine patients had a solitary liver abscess while 11 patients had multiple liver abscesses. However, it was seen that frequency of multiple liver abscesses was more of bacterial origin [Table 5].

Pain was the most common symptom (92%) followed by fever (84%) and tenderness was the most common sign [Table 6].

Forty-four patients presented with abdominal tenderness more so in the right upper abdomen, 20 patients had hepatomegaly while 10 patients presented to emergency in sepsis.

About 46% of patients were treated conservatively while 42% of patients underwent USG-guided pigtail drainage and 12% of patients were subjected to open drainage [Table 7].

## DISCUSSION

Patients of liver abscess were studied for general parameters, etiological and predisposing factors, symptoms, signs, laboratory findings, radiological findings, and various treatment modalities. Liver abscesses are classified mainly into amebic and bacterial origin. Amebic liver abscess is mainly a disease of developing countries like India.[10,11]

**Table 3: Age distribution**

| Age group | Frequency | Percentage |
|---|---|---|
| <20 | 4 | 8 |
| 21–40 | 23 | 46 |
| 41–60 | 17 | 34 |
| >60 | 6 | 12 |

**Table 4: Anatomical distribution based on lobe involved**

| Lobes involved | Frequency | Percentage |
|---|---|---|
| Right | 33 | 66 |
| Left | S10 | 20 |
| Both | 7 | 14 |
| Total | 50 | 100 |

**Table 5: Anatomic distribution based on number of cavities**

| Anatomic distribution | Frequency | Percentage |
|---|---|---|
| Solitary | 39 | 78 |
| Multiple | 11 | 22 |

In the present study, 58% of the patients were of amebic liver abscess and rest were pyogenic. Anatomically right lobe of the liver is mainly involved with mostly solitary lesions. The findings of the study are consistent with the previous reports on liver abscess by Mukopadhyay *et al.* and Sharma *et al.* and various other studies. Rahimian *et al.* also reported the same findings in their study in which 70% of abscesses were seen in the right lobe, majority of them being solitary. Most of the patients were in the age group of 21–40 years of age. Pyogenic liver abscess was noted mostly in elderly age group which is consistent to the findings reported by Seeto *et al.* in their study.

About 58% of the patients had a history of alcohol intake, which came out to be major predisposing factor for liver abscess. Siroliya *et al.* reported that 68% of study subjects had history of alcoholism. Hai *et al.* in his study reported that 85% of his study subjects had history of alcoholism and concluded that there is a 5-fold incidence of ALA among alcoholics.

Pain upper abdomen is the most common presenting complaint followed by fever. In the study, 92% of patients presented with abdominal pain, 84% of patients with fever, and abdominal tenderness is present in about 88% of study subjects. Findings of the study are similar to findings reported in various other studies.

About 62% of patients had leukocytosis and 54% of patients were anemic which is consistent with the study conducted by Krishnanand *et al.*

In the present study, most of the patients were managed conservatively. About 50 % of the patients were managed conservatively while 38% of the patients have undergone USG-guided percutaneous drainage and 12% have undergone open surgical drainage. Similar findings were reported in various other studies.[9-15]

**Table 6: Clinical presentation**

| Symptoms | Frequency | Percentage |
|---|---|---|
| Pain | 46 | 92 |
| Fever | 42 | 84 |
| Rigors and chill | 25 | 50 |
| Jaundice | 15 | 30 |
| Vomiting | 12 | 24 |
| Cough | 3 | 6 |

**Table 7: Management of liver abscess**

| Management | Frequency | Percentage |
|---|---|---|
| Conservative | 23 | 46 |
| USG-guided pigtail drainage | 21 | 42 |
| Open drainage | 06 | 12 |

## CONCLUSION

The advent of modern radiological techniques such as USG and CECT abdomen coupled with history and clinical examination has led to an early diagnosis of liver abscess. Medical management and percutaneous drainage (USG guided) has become the mainstay of treatment, thereby significantly reducing the morbidity and mortality associated with the disease. Open surgical drainage is employed in patients with ruptured liver abscess presenting as peritonitis.

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Original Article

# Study of Non-Invasive Predictors of Esophageal Varices in Chronic Liver Disease

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## Abstract

**Introduction:** Chronic liver disease is a process of progressive destruction and regeneration of the liver parenchyma leading to fibrosis and cirrhosis.[1]

**Aims and Objectives:** The aims of the study were to study the ultrasonographic parameters and platelet count, to study platelet count and spleen diameter ratio in prediction of esophageal varices in chronic liver disease.

**Materials and Methods:** The study comprised 100 portal hypertensive patients who were admitted in Mahatma Gandhi Memorial Hospital between February 2017 and October 2018.

**Discussion:** Cirrhosis is the most advanced form of liver disease and variceal hemorrhage is one of its lethal complications. Over half of the patients with cirrhosis will develop varices. The risk of bleeding once OV formed is 20–35% within 2 years.

**Conclusion:** Ultrasonography of abdomen is a simple, convenient, and non-invasive method for assessing the severity of portal hypertension in patients and to predict the severity of esophagogastric varices indirectly.

**Key words:** Chronic liver disease, Esophageal varices, Portal hypertension

## INTRODUCTION

Chronic liver disease is a process of progressive destruction and regeneration of the liver parenchyma leading to fibrosis and cirrhosis.[1] Portal hypertension is the significant complicating feature of decompensated cirrhosis and is responsible for the development of ascites and esophageal varices, results in the development of collaterals to bypass the increased resistance to flow within the portal vein to return blood to systemic circulation.[2] PH refers to elevated HVPG >5 mm of hg. The increased hepatic resistance to blood flow caused by architectural disruption combined with intrahepatic vasoconstriction and vasodilatation in splanchnic vascular bed with increased splanchnic blood flow is the underlying pathology. Portal hypertension becomes clinically significant when the PPG increases above the threshold value of 10 mm Hg (e.g., formation of varices) or 12 mm Hg (e.g., variceal bleeding and ascites). PPG values between 6 and 10 mm Hg represent subclinical portal hypertension.[3,4] Bleeding from ruptured esophageal or gastric varices is the main complication of portal hypertension and a major cause of death. Most cirrhotic patients develop esophageal varices, with a lifetime incidence as high as 90%.[5] As per existing guidelines in a case of cirrhosis of liver, we are screening with upper gastrointestinal endoscopy to look for any esophagogastric varices present or not and grade the severity of varices and to start the prophylactic B. blockers. Doubts are expressed regarding the cost-effectiveness of universal screening with upper gastrointestinal endoscopy. A study done by Spiegel *et al.* published in journal HEPATOLOGY[6] concluded… "Empiric β blocker therapy for the primary prophylaxis of variceal hemorrhage is a cost-effective measure as the use of screening endoscopy to guide the therapy adds significant cost with only marginal increase in effectiveness." In this setting, if we can predict the severity of portal hypertension by a low cost and non-invasive method then we can use the upper gastrointestinal endoscopy for only high risk patients. Although the occurrence of esophageal varices and the

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time of gastrointestinal bleeding in portal hypertension cannot be exactly predicted, there are some endoscopic, ultrasonographic, laboratory parameters. and clinical signs associated with high risk of bleeding. Some studies have shown good correlation between ultrasonographic findings and platelet count and severity of esophagogastric varices. "In this study, we make an attempt to predict the esophageal varices based on ultrasonographic findings, platelet count, and platelet count spleen diameter ratio and its correlation with upper GI endoscopy.

### Aims and Objectives

The aims of the study were as follows:

1. To study the ultrasonographic parameters and platelet count.
2. To study platelet count and spleen diameter ratio in prediction of esophageal varices in chronic liver disease.

## MATERIALS AND METHODS

The study comprised 100 portal hypertensive patients who were admitted in Mahatma Gandhi Memorial Hospital between February 2017 and October 2018.

A detailed clinical history was recorded regarding age, sex, and duration of symptoms such as jaundice, distension of abdomen, hematemesis, and melena. All patients underwent complete clinical examination including detailed examination of gastrointestinal system. Routine biochemical investigations and liver function tests were done in every patient. Every recruited patient underwent ultrasonography and fiberoptic upper gastrointestinal endoscopy. Platelet count spleen diameter ratio was calculated.

### Inclusion Criteria

Cases of portal hypertension admitted in the Department of General Medicine and Gastroenterology in MGM Hospital.

### Exclusion Criteria

The following criteria were excluded from the study:

1. Cases of portal hypertension who are on blockers.
2. Cases of portal hypertension who underwent EST or EVL.
3. Cases of portal hypertension who underwent TIPS or shunt surgery.
4. Hepatocellular carcinoma.
5. Primary hematological disorders.
6. Active gastrointestinal bleeding on admission.
7. Previously known gastrointestinal bleeding.
8. Unstable medical condition.

### Study Proforma

Laboratory testing, ultrasonography, and fiberoptic upper gastrointestinal endoscopy were done in every recruited patient.

### Laboratory Testing

Hematological and biochemical workup included measurement of hemoglobin, total leukocyte count, platelet count, prothrombin time, and serum concentrations of bilirubin (total and conjugated), serum albumin, alanine aminotransferase, and aspartate aminotransferase. For each patient, a modified Child-Pugh score was calculated.45 All patients were tested for HBsAg and antibodies to hepatitis C virus to determine the cause of liver cirrhosis. Tests for other causes of cirrhosis (serum ceruloplasmin and slit lamp examination for Wilson's disease, tests for autoantibodies for autoimmune liver disease, and iron studies for hemochromatosis) were carried out only if there was a suggestive clinical clue.

### Ultrasonography

(a) Measurement of liver size: Liver size is measured using sagittal approach in the midclavicular line. It is measured from diaphragm to the inferior border on b-mode image.

(b) Measurement of splenic size: Spleen size was measured by placing the patient in supine position, using 2–5 MHz curvilinear transducer in the coronal plane of section, posteriorly in one of the lower left intercostal spaces. The patient was examined in various degrees of inspiration to maximize the window to the spleen. The spleen parenchyma is extremely homogenous and it has uniform mid to low echogenicity. When the spleen enlarges, it can be more echogenic. A maximum cephalocaudal measurement exceeding 13 cm indicates enlargement with high degree of reliability.

(c) Measurement of portal vein diameter: The portal venous supply to the left lobe of liver can be visualized using an oblique, cranially angled subxiphoid view (recurrent subcostal oblique projection). The main and right portal veins are best seen in the sagittal or oblique sagittal plane. It is measured in supine position, during quiet respiration where the portal vein crosses anterior to the IVC43.

(d) Presence of collaterals: Five major sites of portosystemic venous collaterals are

1. Gastroesophageal junction between coronary and short gastric veins and systemic esophageal veins.
2. Paraumbilical vein-connects left portal vein to the systemic epigastric veins near umbilicus.
3. Splenorenal and gastrorenal.

4. Intestinal – regions in which GIT becomes retroperitoneal collaterals form (e.g.: ascending, descending colon, duodenum, and liver).

Duplex Doppler provides additional information. Increase of <20% in the diameter of the portal vein with deep inspiration indicates portal hypertension with 81% sensitivity and 100% specificity.

Ultrasonography is the preferred initial investigation because of its low cost and high accuracy [Table 1].

### Endoscopy

Endoscopy is important to assess semi-quantitatively the number, appearance and size of any esophageal varices

I. Esophageal varices
- Grade I: Small varices without luminal prolapsed [Table 2].
- Grade II: Moderate-sized varices with luminal prolapsed with minimal obscuring of gastroesophageal junction.
- Grade III: Large varices showing luminal prolapsed substantially obscuring of gastroesophageal junction [Table3].
- Grade IV: Very large varies completely obscuring GE junction
- Grade 1 and 2 are considered as small varices and Grade 3 and 4 as large varices 47.

II. Gastric varices [Table 4]
These are classified as continuation of esophageal varices along the lesser curve of the stomach (GOV-1) or in the fundus (GOV-2); more rarely "Isolated gastric varices" may be found in the fundus (IGV-1) or in the rest of stomach (IGV-2) [Table 5]. The prevalence of gastric varices in portal hypertension is about 20%. They cause 5–10% of all episodes of upper gastrointestinal bleeding in portal hypertension.

III. Portal hypertensive gastropathy (PHG)
2 types of gastric mucosal changes are seen in portal hypertensive gastropathy [Table 6]. Mosaic pattern of gastric mucosa indicates mild PHG and cherry red spots in gastric mucosa reflect severe PHG.

### Statistical Analysis

This is an observational study where 100 patients were included, of which 50 are cases (with esophageal varices) and 50 are controls (without esophageal varices). The cases were again divided into large and small varices based on endoscopic findings. Detailed history taking and clinical examination were done.

Descriptive statistics of normally distributed variables is reported as mean and SD and that of non-normally distributed variables were subjected to Mann–Whitney test and median with range was calculated and $P < 0.05$ is taken as significant. All variables which were found to be significant on univariate analyses were included as candidate variables for logistic regression analysis to identify independent predictors for the presence of esophageal varices and their size.

## RESULTS

### Age Distribution

Median age with range among 50 cases was 43.18 (range 24–86), and among 50 controls was 42.16 (range 22–68),

**Table 1: Age distribution among cases and controls**

| Age | Cases | Controls | Large varices | Small varices |
|---|---|---|---|---|
| 20–30 | 6 | 10 | 3 | 3 |
| 31–40 | 24 | 15 | 12 | 12 |
| 41–50 | 12 | 14 | 6 | 6 |
| 51–60 | 4 | 7 | 3 | 1 |
| 61–70 | 3 | 4 | 1 | 2 |
| >70 | 1 | 0 | 1 | 0 |
| Total | 50 | 50 | 26 | 24 |

**Table 2: Sex distribution among cases and controls**

| | Females | | Males | | Total | |
|---|---|---|---|---|---|---|
| | Number | % | Number | % | Number | % |
| Cases | 11 | 22 | 39 | 78 | 50 | 100 |
| Controls | 8 | 16 | 42 | 84 | 50 | 100 |
| Large varices | 6 | 23 | 20 | 77 | 26 | 52 |
| Small varices | 5 | 21 | 19 | 79 | 24 | 48 |

**Table 3: Distribution of various etiologies among cases and controls**

| Etiology | Patients |
|---|---|
| Alcoholic liver disease | 62 |
| Hepatitis B | 10 |
| Hepatitis C | 2 |
| Non-alcoholic fatty liver | 6 |
| Wilsons disease | 1 |
| Cause remained unknown | 19 |

**Table 4: Distribution of cases and controls according Child-Pugh score**

| Column 1 | Class A | Class B | Class C | Total |
|---|---|---|---|---|
| Cases | 4 | 18 | 28 | 50 |
| Controls | 7 | 23 | 20 | 50 |
| Large | 3 | 10 | 13 | 26 |
| Small | 1 | 8 | 15 | 24 |
| Total | 15 | 59 | 76 | |

**Table 5: Sensitivity, specificity, positive, and negative predictive values for significant parameters for presence of varices**

| Parameters | Sensitivity | Specificity | Positive predictive value | Negative predictive value |
|---|---|---|---|---|
| Portal vein diameter (>13.05 mm) | 65% | 54% | 55.58% | 45.26% |
| Spleen Diameter(>15.4cm) | 78.80% | 64% | 56.06% | 44.63% |
| Platelet Count(<102000) | 82.69% | 58% | 59.68% | 41.03% |
| Platelet count/splenic diameter(<815) | 80.77% | 64% | 56.67% | 44.01% |

**Table 6: Sensitivity, specificity, positive, and negative predictive values for the significant parameters for the presence of large varices**

| Parameters | Positive predictive value | Negative predictive value |
|---|---|---|
| Portal vein diameter(>14.m) | 60.43% | 40.32% |
| Spleen diameter(>16.25cm) | 52.84% | 47.85% |
| Platelet count(<93500) | 54.29% | 46.42% |
| Platelet count/spleen diameter(<548) | 58.36% | 42.28% |

for large varices it is 44.46 (range 29–86) and for small varices is 41.79 (range 24–65).

### Sex Distribution

Of 100 patients, 81 were male and 19 were female. Among cases 39 were male and 11 were female (no. of males/females in large varices is 20/6 and small varices is 19/5) and in controls 42 were male and 8 were female.

### Distribution of Patients Based on Etiology

Alcoholic liver disease is the most common etiology in this study corresponding to 62% of cases followed by hepatitis B with 10%.

Relationship of cases and controls based on Child-Pugh score:

Child-Pugh score was calculated for all the patients with most of the patients with varices fall in Group C and without varices in Group B

Platelet count shows highest sensitivity for the detection of esophageal varices with 82.69% followed by platelet count/splenic diameter of 80.77%. Specificity is highest for splenic diameter and platelet count/splenic diameter.

Platelet count/splenic diameter shows highest sensitivity of 88% and specificity is highest for splenic diameter with 69.23% for detection of large varices.

## DISCUSSION

Cirrhosis is the most advanced form of liver disease and variceal hemorrhage is one of its lethal complications. Over half of the patients with cirrhosis will develop varices. The risk of bleeding once OV formed is 20–35% within 2 years.

The reported mortality rate from first episode of variceal bleeding is 17–57%. Of those who survive the initial episode of bleeding and who do not receive active treatment, the risk of recurrent bleeding is approximately 66% and usually occurs within 6 months of the initial bleeding episode.

Since cirrhotic patients with large esophageal varices are at a high risk for bleeding, preventive efforts have concentrated on identifying cirrhotic patients with large varices.

In 1997, The American College of Gastroenterology (ACG) recommended screening endoscopy for cases with established cirrhosis who were candidates for medical therapy.

Also, in 1998, The American Association for the study of liver disease (AASLD) recommended screening endoscopy for varices and to be in particular routine in child Class B and C patients, but in child class A to be limited to patients with evidence of portal hypertension (thrombocytopenia or large portal vein/collaterals on abdominal imaging).

Prophylactic therapy initiated when large varices were discovered on screening endoscopy, had shown a decrease in the incidence of bleeding and an effect on bleeding – related mortality.

It was estimated that 100 screening endoscopies need to be performed to prevent 1–2 cases of variceal bleeding.

Therefore, identification of clinical features that can accurately predict esophageal varices and help identifying patients at greatest risk is important to improve the yield and cost-effectiveness of endoscopic screening.

Bleeding occurs in significant proportion of patients with severe PHG which accounts for most nonvariceal bleeding episodes in patients with cirrhosis and portal hypertension. PHG bleeding is a serious complication, which is usually chronic and insidious but occasionally massive and life-threatening. Overt hemorrhage from the gastric mucosa occurred in 60% of patients with severe PHG with a cumulative risk of bleeding of 75% over a 5-year follow-up period.

Several studies in the past have shown independent parameters such as splenomegaly, ascites, Spider nevi, Child's grade, platelet count, prothrombin time/activity, portal vein diameter, platelet count/ spleen diameter ratio, serum albumin, and serum bilirubin as significant predictors for the presence of esophageal varices. Our study found that 50% of the cirrhotic patients had EV diagnosed by endoscopy. This result is similar to the range of 24–80% showed in literature and reminds us that a significant part of cirrhotic patients are unnecessarily submitted to this procedure.

Relationship of esophageal varices with clinical and laboratory parameters:

a) Ascites and hepatic encephalopathy: In a study done by Fook-Hong NG *et al.* showed that low platelet count and presence of ascites were the significant independent predictors for high-grade EGV.

In present study, ascites and hepatic encephalopathy were not significantly associated with the presence of varices. Similar results were obtained by Cherian *et al.* in predicting esophageal varices.

a) Serum albumin, total bilirubin, prothrombin activity:

In a study done by D'Amico *et al.* showed that a serum albumin concentration of < 3.3 g/dL was predictors of esophageal varices.

In a cross-sectional study done by Schepis *et al.* has shown that prothrombin activity of 70% was used as an independent predictor of esophageal varices with an odds of 9.85. In our study, we did not get significance for serum albumin and prothrombin activity in prediction of esophageal varices. Similar results were obtained by Cherian *et al.*, where no significance was obtained for the above parameters.

No studies in the past have shown that total bilirubin as a predictor of esophageal varices. The present study also did not show any statistical significance for the prediction of esophageal varices based on total bilirubin levels.

4. Child-Pugh score:

The Child-Pugh score consists of two clinical features and three laboratory parameters and is used to assess the prognosis of chronic liver disease.

The Child-Pugh score was originally developed in 1973 to predict surgical outcomes in patients presenting with bleeding esophageal varices.

In our study, Child-Pugh score was not significantly associated with presence of esophageal varices but most of the cases belong to class C and controls (no esophageal varices) belong to Class B.

The study done by Jijo *et al.* shows significance and has a highest sensitivity of 95% for Child-Pugh Class B and C in predicting esophageal varices and postulated an algorithm where patients with Child-Pugh Class B and C were given primary prophylaxis and for Class A, they have seen platelet count and spleen diameter and then initiated prophylaxis accordingly.

5. Platelet count

Pathogenesis of thrombocytopenia includes productive, consumptive, or distributional mechanisms. It is commonly believed to be due to pooling and destruction of platelets in the spleen which may be mediated by platelet-associated IgG. Reduced levels of thrombopoietin either due to impaired production or rapid degradation may also add to thrombocytopenia.

Thus, platelet count depends on multiple factors not just portal hypertension.[47] Garcia- Tsao *et al.* (180 patients), Pilette *et al.* (116 patients), and K. C. Thomopoulos *et al.* (184 patients) reported a low platelet count to be an independent risk factor for the presence of varices. Mohammad Khuram *et al.* (200 patients) found OV in 146 with 121 having thrombocytopenia (94.5%).

We report that platelet count of <10200/mm$^3$ is 82.67% sensitive and 58% specific predictor of OV with positive predictive value of 59.64% and negative predictive value of 41.02 % in predicting presence of varices and a platelet count of 93500/mm$^3$ is 75% sensitive, 65.37% specific with 54.28, and 46.43 positive and negative predictive values, respectively, in predicting large varices.

Similar results were obtained in a study done by Cherian *et al.* with platelet count of 90000/mm$^3$ with 59.3% sensitivity, 64.2% specificity, and 47.5 PPV and 74.2 is NPV.

Chalasani *et al.* (346 patients) found that a platelet count <88,000 was an independent risk factor for the presence of large varices.

In retrospective analysis of 143 patients with compensated cirrhosis, Schepis *et al.* reported OV in 63 patients (44%) with platelet count of <100,000 as predictor of OV.

Most of the studies in the past have shown platelet count as a significant individual predictor of esophageal varices. In the present study, platelet count has shown highest sensitivity of 82.69 in predicting presence of esophageal varices among all the parameters studied with odds of 6.65.

Relations of Esophageal Varices with Ultrasonographic Parameters

Upper GI endoscopy of the study population revealed that a total of 50 patients had developed gastroesophageal varices.

Ultrasonography showed that median portal vein diameter (PVD) of the patients with gastroesophageal varices (GEV) was 13.9 mm with range of 8–18 mm and without gastroesophageal varices (GEV-0) was 12.1 mm with range of 7.8–16 mm. This difference was statistically significant ($P < 0.0322$).

Radiologically, median spleen diameter of the patients with OV was 16 cm with range of 8–26 cm and spleen size in the no varices group was 13.8 cm with range of 9–19 cm, and the difference was highly significant ($P < 0.001$). Hence, it can be concluded that gastroesophageal varices developed in cirrhotic patients with portal vein diameter more than 13.9 mm and larger than 16 cm spleen size.

These observations were more or less similar to other studies. In the study by Prihatini *et al.*, portal vein diameter 11.5 mm and spleen size of 10.3 cm were predictive factors for esophageal varices in liver cirrhosis. Here, spleen size and portal vein diameter was smaller than our study.

Portal vein diameter and spleen size for development of gastroesophageal varices were also nearer to Cherian *et al.* study (portal vein 14 mm and spleen size 17 cm). Thomopoulos *et al.* showed that the majority of patients with gastroesophageal varices had spleen size more than 13.5 cm which was nearly similar to ours.

In our study, as the portal vein diameter and spleen size increased, gastroesophageal varices also transformed to higher grades. Median portal vein diameter and spleen size with range in higher grade varices were 14.7 mm (8.5–16.8 mm) and 17.2 cm (8–26 cm), respectively.

In a study by Schepis *et al.,* portal vein diameter 13 mm was associated with higher grade varices.

Sharma and Aggarwal had noted that a clinically palpable spleen was associated with high grade varices; however, they did not measure the splenic size radiologically.

The fact that different studies conclude different best cutoff values of the portal vein diameter may be explained at least in part by that the physique of Asian populations is smaller than that of European populations. It has been reported that the normal mean portal vein diameter in Chinese populations is ± 1.3 mm, while it is 11.0 ± 0.3 mm in French populations.

Our data showed that spleen diameter and portal vein diameter measured by ultrasonography were independent predictors for the presence of varices.

Contrary to what was suggested in previous reports, no correlation between splenomegaly and EV was found in other studies. These differences may be due to the variations among studies regarding the etiology and the stage of liver cirrhosis studied.

Moreover, splenomegaly is found more frequently in post hepatitis cirrhosis than in alcoholic cirrhosis.

Some of these patients with splenomegaly and dilated portal vein may not have EV. One of the possible explanations for this result could be the development of spontaneous intra-abdominal shunts that decrease the blood flow of varices while maintaining congestive splenomegaly and dilated portal vein.

### Relationship of Esophageal Varices with Platelet Count and Splenic Diameter

The parameter connects thrombocytopenia to splenomegaly to introduce a variable that takes into consideration the decreased platelet count most likely attributed to hypersplenism caused by portal hypertension.

This method uses two easily obtained parameters, which are part of the routine in a cirrhotic patient and, thus, would not increase costs.

The platelet count to spleen diameter ratio, proposed by Giannini *et al.* in 2003, reported that the platelet count/spleen diameter ratio to be the only independent variable associated with presence of OV on multivariate analysis and identified a cutoff value of 909, giving a PPV of 96% and NPV of 100%. Moreover, it appears to be the best noninvasive predictor of EVs that have been developed so far.

Several studies have been performed in an attempt to validate this new parameter as a new noninvasive screening tool for EVs.

In the present study, on univariate analysis, a platelet count-spleen diameter ratio of 608 was significantly associated with the presence of esophageal varices and it was found significant even in multivariate analysis with odds of 10.92 (CI-4.07-29.26).

Similar results in univariate analysis were found in study done by Jijo *et al.* but did not found significance in multivariate analysis.

## CONCLUSION

Ultrasonography of abdomen is a simple, convenient, and non-invasive method for assessing the severity of portal hypertension in patients and to predict the severity of esophagogastric varices indirectly.

Patients having
- Portal vein diameter >13.9 mm,
- Spleen size >16 cm and
- Platelet count of <98000/microL

Platelet count and spleen diameter ratio <608 were found to have varices which were indirect evidences of severity of portal hypertension. The above said parameters tend to predict varices when they occur in combination than they occur individually.

These predictors may be of help
- To the physicians practicing in rural areas where endoscopy facilities are not readily available, in helping them to initiate appropriate primary pharmacological prophylaxis in these patients.
- In an urban setting where the endoscopy workload is high, a noninvasive predictor, as in this study, can help one to initiate drug therapy while waiting for the endoscopy procedure.

## SUMMARY

Chronic liver disease is a process of progressive destruction and regeneration of the liver parenchyma leading to fibrosis and cirrhosis.[1]

Portal hypertension is the significant complicating feature of decompensated cirrhosis. Most cirrhotic patients develop esophageal varices, with a lifetime incidence as high as 90%, and the reported mortality from variceal bleeding ranges from 17% to 57%.[7-10] Of those who survive the initial episode of bleeding and who do not receive active treatment, the risk of recurrent bleeding is approximately 66% and usually occurs within 6 months of the initial bleeding episode.

As per existing guidelines in a case of cirrhosis of liver, we are screening with upper gastrointestinal endoscopy to look for any esophagogastric varices present or not and grade the severity of varices. And then we start the prophylactic measures like propranolol to prevent the first bleed.

To restrict upper GI endoscopy to those patients who have ultrasonographic or laboratory indicators able to predict the presence of esophageal varices would result in a better risk/benefit ratio for the endoscopic study.

In this study, we make an attempt to predict the esophageal varices based on ultrasonographic findings, platelet count and platelet count spleen diameter ratio, and its correlation with upper GI endoscopy.

The present study was carried out in the Department of Medicine, Mahatma Gandhi Memorial Hospital, Warangal, between February 2017 and October 2018.

A hundred patients included in the study, of which 50 are cases (with esophageal varices) and 50 are controls (without esophageal varices). The cases were again divided into 26 large varices and 24 small varices based on endoscopic findings. Laboratory testing, ultrasonography, and fiberoptic upper gastrointestinal endoscopy were done in every recruited patient.

We conclude that ultrasonography of abdomen is a simple, convenient, and non-invasive method for assessing the severity of portal hypertension along with laboratory testing in patients with chronic liver disease and to predict the severity of esophagogastric varices indirectly.

Patients having portal vein diameter >13.9 mm, spleen size >16 cm, and presence of collaterals on ultrasonography and platelet count of <98000/microL, platelet count and spleen diameter ratio < 608 were found to have varices which were indirect evidences of severity of portal hypertension. The above said parameters tend to predict varices when they occur in combination than they occur individually.

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Original Article

# The Comparative Study of Transvaginal Sonography and Endometrial Biopsy

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## Abstract

**Introduction:** Dysfunctional uterine bleeding (DUB) is a common disorder of reproductive age group of females.

**Aims:** The aim of the study was to correlate transvaginal ultrasonography and histopathological findings of endometrial biopsy in patients of DUB in age group of ≥35 years.

**Materials and Methods:** It was a comparative study conducted from November 1, 2009, to March 31, 2011. A total of 150 new patients of DUB were included in this study. They underwent transvaginal ultrasonography in pre- and post-ovulatory phase and endometrial biopsy in premenstrual phase and their findings were correlated.

**Results:** Transvaginal sonography has 96% sensitivity and 96% specificity for endometrial thickness of <12 mm for predicting normal endometrium on histopathology. Furthermore, the presence of findings such as trilaminar pattern, hypoechoic endometrium, absence of any linear abnormalities, and normal interface between endometrium and myometrium has a good correlation with secretory endometrium on histopathology.

**Conclusion:** Transvaginal ultrasonography can be used as first line non-invasive diagnostic modality for evaluating patients of DUB in ≥35 years of age group.

**Key words:** Dysfunctional uterine bleeding, Ultrasonography, Women

## INTRODUCTION

Dysfunctional uterine bleeding (DUB) is the abnormal uterine bleeding without any clinically detectable organic, systemic, and iatrogenic cause. It commonly occurs in extremes of reproductive age group.[1] It has been evaluated by both invasive and non-invasive diagnostic methods. Invasive methods include endometrial biopsy, dilation and curettage, and hysteroscopy in which endometrial biopsy (EB) is the gold standard painful procedure which has less patient acceptability. Non-invasive methods include transvaginal sonography (TVS) and saline infusion sonography which are painless diagnostic methods and provide good information regarding endometrium and endometrial cavity.

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Endometrial biopsy has histopathological findings which can range from secretory endometrium to proliferative/disordered proliferative/simple hyperplasia/complex hyperplasia and atypical hyperplasia in patients of DUB.[2] TVS has certain characteristic endometrial findings for normal and abnormal endometrium. The presence of trilaminar pattern, hypoechoic endometrium, absence of linear abnormalities, normal interface between endometrium and myometrium, absence of focal and diffuse thickening in proliferative phase predicts normal endometrium, and vice-versa. Endometrial thickness (ET) in premenstrual phase also get affected in patients with abnormal endometrium on histopathology.

Since EB is a painful invasive procedure, there is a need to establish a diagnostic modality which should be painless and non-invasive and thus can be used as a first line diagnostic method in patients of DUB. Hence, this study was conducted to correlate TVS and EB histopathological findings so that above need could be met.

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## MATERIALS AND METHODS

This was a comparative study of TVS and histopathological findings of EB which was conducted in the Gynae Outpatient Department of Smt. Sucheta Kriplani Hospital, N. Delhi, from November 1, 2009 to March 31, 2011. A total of 150 new patients of DUB in age group of ≥35 years were recruited by randomization procedure.

All 150 patients with c/o heavy or prolonged bleeding with regular or irregular cycles which is not due to any organic, systemic, or iatrogenic cause were included in this study. Patients having intrauterine contraceptive device or having any organic, systemic, or iatrogenic cause were excluded from this study. A written and verbal informed consent was obtained from all the patients and approval was obtained from ethical committee.

These patients were clinically evaluated by detailed history, general physical, systemic, and pelvic examination. Thereafter, certain blood investigations were carried out such as complete Hemogram, serum estradiol (measured in first half of menstrual cycle), and serum progesterone levels (measured on day 21 of menstrual cycle). Levels were evaluated using enzyme-linked immunosorbent assay method.

These patients then underwent TVS in both preovulatory and postovulatory phase of cycle. TVS was done with a probe of 4–9 Hz. Scan was performed through the anterior vaginal wall, anterior vaginal fornix, posterior vaginal fornix, and lateral fornices. Following features such as trilaminar pattern of endometrium in preovulatory phase, type of echogenicity of endometrium, any linear abnormalities, regularity of interface between endometrium and myometrium, homogenicity of myometrium, any focal thickening of endometrium, cystic spaces in endometrium, and fluid in endometrial cavity in both the half of menstrual cycle were looked for.

Normal findings in proliferative phase were described as presence of trilaminar pattern and hypoechoic endometrium. Normal findings in secretory phase were described as endometrial thickness of 7–14 mm and hyperechoic endometrium. Furthermore, findings like no linear abnormalities, regular interface between endometrium and myometrium, normal homogenous myometrium, no focal or diffuse thickening, and absence of cystic spaces in endometrium in both the phases of menstrual cycle were considered as predictor of normal endometrium.

EB was then performed in premenstrual phase. Biopsy was taken by EB curette. It was fixed in 10% neutral buffered formalin and then specimen was embedded in wax to make blocks. A microtome was used to slice off the block in form of ribbon. It was then transferred to warm water bath and placed in dry oven. Slides were then stained with hematoxylin and eosin stain and were then examined. Following histology were looked for – normal proliferative endometrium, normal secretory endometrium, disordered proliferative endometrium, simple hyperplasia, complex hyperplasia, atypical hyperplasia, endometrial atrophy, and endometrial carcinoma.

The results of TVS and EB findings were correlated and analyzed using Pearson's Chi-square rest and sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and *P* value were calculated and interpreted.

## RESULTS

A total of 150 patients of DUB in age group of ≥35 years excluding those with any organic/systemic/iatrogenic cause were recruited in this study. They were clinically evaluated and TVS and EB was performed after informed consent. The findings of TVS and EB were correlated then. Correlation was also done with respect to their hormonal levels, that is, serum estradiol and serum progesterone levels.

In this study, trilaminar pattern in TVS finding was present in 54% of patients. Hypoechoic endometrium in preovulatory phase was present in 56% of patients. endometrial thickness (ET) in premenstrual phase of ≥12 mm and ≥15 mm was present in 63% and 87%, respectively. Mean ET was 12.6 ± 1.46 mm.

In EB findings, secretory endometrium was present in 35%, proliferative endometrium in 47%, disordered proliferative endometrium in 17%, and simple hyperplasia in 1% was present. Hence, ovulatory DUB constituted 35% and anovulatory DUB constituted 65% of patients.

During correlation of TVS and EB findings, it was seen that trilaminar pattern was present in 75% of secretory endometrium, 34% of proliferative endometrium, and 68% of disordered proliferative endometrium and was absent in case of simple hyperplasia. Hence, the sensitivity, specificity, PPV, NPV, and *P* value of TVS using trilaminar pattern as criteria for detecting normal and abnormal endometrium were 58%, 75%, 81%, 49%, and <0.01, respectively.

Regarding echogenicity, hypoechoic endometrium in preovulatory phase was present in 74% of secretory endometrium, 44% of proliferative endometrium, and 56% of disordered proliferative endometrium and was absent in simple hyperplasia. Sensitivity, specificity, PPV, NPV, and

*P* value of TVS using echogenicity as criteria for detecting normal and abnormal endometrial histopathology were 54%, 74%, 79%, 46%, and 0.002, respectively.

ET of <12 mm in premenstrual phase was present in 96% of secretory endometrium, 4% of proliferative endometrium, 4% of disordered proliferative endometrium, and absent in simple hyperplasia. ET of <15 mm was present in 100% of secretory endometrium, 79% of proliferative endometrium, and 84% of disordered proliferative endometrium.

Combined mean ET of anovulatory DUB (proliferative/disordered proliferative/simple hyperplasia) was 13.4 ± 1.06 mm and mean ET in ovulatory DUB (secretory endometrium) was 11.1 ± 0.80 mm. Sensitivity, specificity, PPV, NPV, and *P* value using ET as criteria for detecting normal and abnormal endometrial histopathology were – for 12 mm – 96%, 96%, 98%, 93%, and <0.01 and for 15 mm – these values were 21%, 100%, 100%, 41%, and <0.01, respectively.

It was also observed that serum estradiol was raised in 93% of anovulatory DUB and only 2% of ovulatory DUB. Serum progesterone was lower than normal in 94% of anovulatory DUB and only 2% of ovulatory DUB. The sensitivity, specificity, PPV, NPV, and *P* value for serum estradiol in detecting abnormal histopathology were 93%, 98%, 99%, 88%, and <0.01, respectively. Sensitivity, specificity, PPV, NPV, and *P* value of serum progesterone in detecting abnormal endometrial histopathology were 94%, 98%, 99%, 90%, and <0.01, respectively.

## DISCUSSION

This was a comparative study of TVS findings with histopathological findings of EB in patients of DUB in age group of ≥35 years. For detection of endometrial histopathology, EB has been recommended as a gold standard by American college of Obstetricians and Gynecologists (ACOG) (2004) for patients of age group ≥35 years and for patients who are chronic anovulatory and have been bleeding which is refractory to medical management.[3] Since it is an invasive and often painful procedure, studies on alternate non-invasive diagnostic modality like TVS were thought of which can reduce number of unnecessary EBs in patients of DUB.

Earlier studies have focused only on ET which is subjected to extensive changes during the reproductive period. These studies have shown that using ET as only criterion proved to have low sensitivity (64–88%) and low specificity (46–75%). Recently, few studies have been done on the use of TVS as an initial non-invasive diagnostic modality using other parameters for detection of endometrial pathology in different age groups.

In this study, parameters of TVS such as trilaminar pattern in late proliferative phase, echogenicity of endometrium, fluid in endometrial cavity, homogenicity of myometrium, and interface between endometrium and myometrium and central linear abnormalities were studied and their findings were collaborated with histopathological findings of EB.

In this study, 54% of patients had normal trilaminar pattern in late proliferative phase. It was further seen that in patients with ovulatory DUB, 75% of them had normal trilaminar pattern. This might be due to some of the women presenting very early in proliferative phase when endometrium has not converted into normal trilaminar pattern.

In women with anovulatory DUB with proliferative type of endometrium, 66% had absent trilaminar pattern. This can be because of wrong interpretation or wrong timings of EB and few of the patients may actually be of ovulatory type of DUB as seen by presence of normal serum estradiol and serum progesterone levels in them.

In a study conducted by Abe *et al.*[4] on the use of non-triple layer ultrasonic finding in biopsy recommendation for premenopausal women, they found that the application of TVS using non-triple layer criteria is a highly accurate first step for the selection of premenopausal patients of DUB for EB which may reduce the number of unnecessary EBs by 25%.[4] They found that "abnormal" TVS criteria could detect disease states in 90% of patients with sensitivity of 94.6% and specificity of 77.2% ($P < 0.01$).

In ovulatory DUB, normal hypoechoic endometrium was present in 74% of patients while in anovulatory DUB, 46% had normal hypoechoic endometrium. Normally endometrium is hypoechoic in proliferative phase and gets hyperechoic in secretory phase. A change in echogenicity of endometrium during proliferative phase is suspicious of endometrial pathology. These echogenic criteria were also used by Abe *et al.* in his study.

In present study, sensitivity, specificity, PPV, NPV, and *P* value of TVS using ET as criteria for detecting normal and abnormal endometrial histopathology were – for 12 mm as cut off, these values were 96%, 96%, 98%, 93%, and <0.01 and for 15 mm as cut off, these values were 21%, 100%, 100%, 41%, and <0.01, respectively. Hence, it was seen that a cut off of 12 mm has high sensitivity and specificity in differentiating normal from abnormal endometrium. Increasing the cut off to 15 mm decreases the sensitivity to 21% but specificity and PPV increases to 100%.

In a study conducted by Nazeeb *et al.*,[5] on role of transvaginal sonography in assessment of abnormal uterine bleeding in premenopausal age group, cut off of

8 mm was taken for suscipicious endometrial pathology and transvaginal sonography was able to detect most of the endometrial pathologies. They found sensitivity to be 74% and specificity to be 72%.

In another study conducted by Islam *et al.*,[6] on transvaginal sonography regarding its sensitivity and specificity, cutoff of endometrial thickness was taken as 14 mm and below that no serious endometrial pathology was found. It was found that the sensitivity, specificity, negative predictive value and positive predictive value for proliferative endometrium were -79%, 100%, 78% and 100% respectively, for secretory endometrium – 100%, 96%, 100% and 79% respectively, for endometrial hyperplasia - 100%, 93%, 100% and 79% respectively and for endometrial carcinoma – 100%, 99%, 100% and 33% respectively.

In this study, 98% of ovulatory DUB had S. estradiol levels in normal range while in anovulatory DUB, 93% had high estradiol levels. The high estradiol levels in anovulatory DUB are the cause of anovulation leading to presence of proliferative, disordered proliferative endometrium, and simple hyperplasia. In one patient who had simple hyperplasia, serum estradiol level was very high (>525 pg/ml). There is a good correlation with high estradiol levels and presence of non-secretory endometrium in histopathology.

## CONCLUSION

From this study, it can be concluded that in the absence of other significant findings such as loss of interface between endometrium and myometrium, heterogeneous myometrium, heterogeneous echotexture of endometrium in proliferative phase, and ET of <12 mm has a good correlation with secretory endometrium on histopathology. Hence, patients with these findings can be managed without any invasive diagnostic procedure.

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Original Article

# A Prospective Study of Uterine Myomas in CKM Hospital Warangal

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## Abstract

**Aims and Objectives:** The objectives of this study were to study 100 cases of fibroid uterus admitted to CKM Hospital, Warangal attached to Kakatiya Medical College, Warangal, with respect to clinical spectrum, pathological correlation, with type of fibroid endometrial and ovarian pathology, associated conditions (medical and surgical comorbidities).

**Materials and Methods:** A clinical study of 100 cases of fibroid uterus was made in CKM Hospital, Warangal attached to Kakatiya Medical College, Warangal. The cases are selected by random allocation. On admission, a detailed history, clinical examination, and investigations were made.

**Results:** Leiomyoma is the most common benign tumor of the uterus and commonly found in the premenopausal women, most commonly in the fourth decade about 46%. The most common mode of presentation is menstrual disturbances 65%, among which menorrhagia was seen in 83.4% of the cases. Intramural fibroids are the most common variety, accounting to 79%. The endometrial pattern was proliferative in 49%. Cystic ovaries were seen in 6% of the patients adenomyosis in 8% indicating hyperestrogenism.

**Conclusion:** Fibromyoma (Leiomyoma) most common benign tumor of the female genital tract. Commonly affecting premenopausal women, most common in the fourth decade. Most commonly seen in multipara. Most common mode of presentation is menstrual disturbances. Intramural is the most common variety. The proliferative and hyperplastic endometrium was commonly reported. The presence of proliferative endometrium, adenomyosis, and cystic ovaries all is indicative of hyperestrogenic state associated with the development of fibroids.

**Key words:** Leiomyoma, Benign, Menorrhagia

## INTRODUCTION

Leiomyoma of uterus forms the most common type of benign tumor of uterus, and also most common pelvic tumor in women.[1] It occurs once in every four or five women of reproductive age. Unfortunately, symptomatology continues to be variable. It is believed that symptomatology depends on number, size, and location of tumor[2] although most leiomyomas are believed to be asymptomatic and progress slowly.

Due to their wide spectrum of clinical symptoms such as menstrual irregularities, pelvic pain, and infertility, they represent tremendous public health burden and economic costs to the society. They assume importance, particularly in our country as they are an important cause for anemia. Hence, strategies are needed to limit the growth and to treat non-surgically.

Surgery has for long been the main mode of therapy for the myomas. For women who have completed childbearing, hysterectomy forms an attractive option as it eliminates both symptoms and chances of recurrence.

For women who wish to retain, the uterus for future pregnancies or other menstrual function myomectomy is known.

The recent trend has been toward non-surgical approaches such as GnRH hormone analogs/agonists. RU 486,[3] LNG-IUS, SERM like ulipristal asoprisnil, HIFU (high-intensity focused ultrasound) selective uterine artery embolization[4]

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laparoscopic cryoablation,[5-7] radiofrequency thermal ablation,[6] and MRGUs.[8,9]

This study is an attempt to analyze the clinicopathological spectrum in cases of leiomyoma of the uterus at CKM Hospital, Warangal and to know regarding the pattern of presentation, mode of treatment and associated conditions in this region.

### Aims and Objectives

The objectives of this study were to study 100 cases of fibroid uterus admitted to Government Maternity Hospital Hanamkonda attached to Kakatiya Medical College, Warangal, with respect to:

1. Clinical spectrum.
2. Pathological correlation, with the type of fibroid endometrial and ovarian changes.
3. Associated conditions (medical and surgical comorbidities).

## MATERIALS AND METHODS

A clinical study of 100 cases of fibroid uterus was made in CKM Hosptial, Hanamkonda attached to Kakatiya Medical College, Warangal.

The cases are selected by random allocation. On admission, a detailed history, clinical examination and investigations were made. The following points were noted in the history.

1. Age and socioeconomic status of the patient.
2. History of presenting complaints was taken in detail: Noting down the following:
   a. Menstrual disorder (detailed menstrual history is taken) menorrhagia/
   b. Metrorrhagia/polymenorrhea/dysmenorrhea/ postmenopausal bleeding.
   c. White discharge per vagina – amount, duration, and whether blood stained.
   d. Bladder and bowel symptoms such as frequency, retention, dysuria and dyspepsia, and indigestion.
   e. Mass per abdomen – when she noticed the mass, rate of growth, presence of pain, and type of pain.

3. Menstrual history: The following points were noted:
   (i) Age of menarche.
   (ii) Past menstrual cycle – regularity of periods, duration of cycles menstrual flow-scanty, moderate or excessive, associated with pain or not, presence of any intermenstrual bleeding.
   (iii) Last menstrual period.
   (iv) Age of menopause

4. Obstetric history: The following points were considered.
   a. Duration of marriage
   b. Abortions – if any, and gestational age
   c. Deliveries – preterm/term
   d. Others: Malpresentation

Incoordinate uterine action, plan.
   (i) Mode of delivery
   (ii) Third stage complications
   (iii) Puerperium – fever and subinvolution of uterus.

5. Past history of diabetes, hypertension tuberculosis epilepsy bleeding disorders thyroid disorders and infertility were noted.
6. Past surgical history of myomectomy.
7. Family history of myomas in the mother aunt and siblings.

### Clinical Examination

1. Under general examination: Importance was given to following points
   (a) Evidence of anemia
   (b) Presence of edema of feet
   (c) Vitals and examination of cardia and respiratory system

2. Local examination

(i) Per abdomen:
   (a) Inspection: Presence of mass, dilated veins over the surface of abdomen.
   (b) Palpation: Whether the mass arises from the pelvis, that is, lower border not made out, tenderness, size, surface, boundaries, consistency of mass, and mobility.
   (c) Percussion: For the presence of ascites.
   (d) Auscultation: For uterine souffle.

(ii) Per speculum examination
   (a) Condition of vagina.
   (b) Condition of cervix – for the presence of erosions, descent of cervix, for any growth.
   (c) Any discharge if present, presence of excoriations
   (d) Presence of cystocele, rectocele or enterocele

(iii) Bimanual examination:
   (a) Direction of cervix and its consistency.
   (b) Size, position, and consistency of uterus.
   (c) Mobility of uterus and transmission of the movement of the cervix to the growth and vice versa.
   (d) Mass felt separate from the uterus.
   (e) Tenderness in the fornix.

(iv) Sounding of the uterus was done.

The diagnosis of fibroid uterus was made by clinical examination in the majority of our patients, considering

the menstrual history, firm mass in the hypogastric region, transmitting movement from the cervix to mass, and vice versa.

Examination under general anesthesia was not made in our studies. The diagnosis was confirmed by scanning in all cases. Diagnostic curettage was done to rule out any endometrial pathology, especially in elderly patients and to know the hormonal status in infertile patients. In patients with infertility, semen analysis of husband and tubal testing was made before undertaking conservative surgery.

### Investigations

The following investigations were made before taking the patient for surgery:

Blood – Complete blood picture

- Grouping and Rh typing
- ESR
- FBS and PLBS
- Blood urea and serum creatinine
- Urine – albumin, sugar and microscopy, culture, and sensitivity.
- Stool – Ova and cysts
- Pap smear and endometrial sampling.

Intravenous urography and hysterosalpingography in selected cases.

### Scanning

At laparotomy: Size of uterus, number, and situation of fibroids, condition of tubes, and ovaries were noted.

In cases posted for myomectomy, chromotubation was made utilizing methylene blue.

The ovaries were conserved in cases of hysterectomies unless associated with pathology and in elderly patients.

The hysterectomy specimen was cut anteriorly in the midline and near the cornu to inspect the cavity and seedling fibroids. The specimen was sent for histopathological examination of endometrium and myometrium.

Microscopic examination done

(i) To confirm the diagnosis.
(ii) For degenerative changes.
(iii) Associated endometrial pathology.
(iv) Associated with adenomyosis and
(v) For changes in the ovaries, tubes, and cervix.

## RESULTS

Leiomyoma is the most common benign tumor of the pelvis. It accounts to maximum gynecology admissions in our institute and forms the most common indication for hysterectomy. A hundred cases were selected randomly for the study.

From Table 1, it is evident that leiomyomas are occurring with almost equal incidence in reproductive and the premenopausal age group, most commonly occurring in the fourth decade. The mean age being 42 years. The youngest patient in our study was 26 years old, and the oldest was 58 years old. Although leiomyoma is a disease of low parity, in our study, we have noted it to be more common in multiparous women, as illustrated in Table 2.

Which show that, there is a long period of secondary infertility before the symptoms could develop, that is, the interval between last delivery and development of symptoms in most of the cases is significantly long, in which 46% of the cases was 16–20 years back, and in 25% of the cases, it was more than 20 years back. There are just 2% cases with last childbirth <5 years.

Mean age of the sterilization – 23.48+-
4.84 Minimum – 3 years
Maximum – 28 years

Early age at marriage and early sterilization also play a role [Table 3]. The mean age at which the patients were sterilized was 23 years. In 33% of the patients, the duration between sterilization and development of symptoms was 16–20 years.

Incidence of various symptoms in combination in the present study dysmenorrhea was seen in 14% of the cases. Spasmodic dysmenorrhea occurs in intramural and submucous fibroid. Congestive dysmenorrhea results from increased vascularity in the pelvis, due to associated pelvic pathology.

White discharge per vaginum was seen in 6% of the cases, which was most commonly associated with chronic

**Table 1: Incidence of leiomyoma in relation to age**

| Age (in years) | Percentage |
|---|---|
| 21–30 | 7 |
| 31–40 | 42 |
| 41–50 | 46 |
| 50+ | 5 |

**Table 2: Interval between last childbirth and development of symptoms**

| Last childbirth in years | Percent patients |
|---|---|
| <5 | 2 |
| 6–10 | 7 |
| 11–15 | 20 |
| 16–20 | 45 |
| >20 | 24 |

**Table 3: Interval between sterilization and development of symptoms**

| Period since sterilization in years | Percent patients |
|---|---|
| <5 | 2 |
| 6–10 | 3 |
| 11–15 | 15 |
| 16–20 | 33 |
| >20 | 17 |
| Not tubectomized | 29 |

**Table 4: Distribution of menstrual symptoms**

| Distribution of menstrual symptoms | Percentage |
|---|---|
| HMB | 83.4 |
| Metrorrhagia | 7.81 |
| Polymenorrhagia | 6.25 |
| Polymennorhea | 1 |
| PMB | 1.6 |

**Table 5: Size of fibroid uterus in studied cases**

| Size of the uterus | Percentage |
|---|---|
| <16 weeks | 76 |
| 16–20 weeks | 22 |
| >20 weeks | 2 |

cervicitis, also seen in cases of fibroid polyp and prolapse. Pain abdomen was seen in 41% of the cases, in most of the cases, the pain was associated with cystic ovaries, in others, the pain was due to endometriosis, PID, urinary tract infection, or cholelithiasis. The presence of a mass was complained in 8% of the cases. Urinary problems were noticed in 2% of the cases, which were typically associated with cervical fibroid/broad ligament fibroid.

None of the patients presented with infertility as the chief complaint. About 1% of the patients presented with bowel discomfort. Other symptoms such as vomiting, fever, postcoital bleeding, swelling of lower limbs, mass per vaginum, and abdominal discomfort were observed in 3% of the cases.

Anemia was seen in 50% of the cases, of which 40% were severely anemic, 30% were moderately anemic, and another 30% had mild anemia.

All the patients were hospitalized, after detailed examination and investigations, the patients were treated for anemia and other medical disorders.

Patients underwent surgery or were treated medically with progesterone therapy for 6 months or levonorgestrel intrauterine contraceptive device. The type of surgery was chosen depending on the age of the patient, parity, associated adnexal, and pelvic pathology.

**Table 6: Incidence of various types of leiomyomas**

| Type of Thyroid | Percentage |
|---|---|
| Subserous | 11 |
| Intramural | 79 |
| Submucous | 15 |
| Broad ligament | 2 |
| Cervical | 7 |

**Table 7: Histopathological abnormalities in combination associated with myoma**

| Associated pelvic | Percentage |
|---|---|
| Cystic ovaries | 6 |
| Chronic cervicitis | 85 |
| Adenomyosis | 8 |
| Pelvic inflammatory | 4 |
| Fibroid polyp | 5 |
| LSIL | 1 |
| Granulosa cell | 1 |

In the present study, it is noted that most of the patients presented with menstrual disturbances, among which menorrhagia was comparatively more, though statistically not significant Table 4. Menstrual disturbances are the most common modality of presentation (65%), among which heavy menstrual bleeding (83.4%) was seen most commonly, typically associated with intramural and submucous fibroids, in cases with a subserous fibroid, menorrhagia was due to associated endometrial hyperplasia. Metrorrhagia was found in 7.81% of the cases and polymenorrhagia in 6.25%. Only one case of postmenopausal bleeding was found.

### Incidence of Various Management Done

About 43% patients underwent total abdominal hysterectomy (TAH), 24% TAH with unilateral salpingo-oophorectomy, 11% underwent TAH with bilateral salpingo-oophorectomy, 1% underwent myomectomy, 2% underwent TAH with bilateral salpingectomy, 2% underwent TAH with unilateral salpingectomy, 6% cases resolved with medical management, 10% cases were inserted with levonorgestrel eluting IUS, and 1% cases underwent subtotal hysterectomy.

Myomectomy was performed in young and nulliparous women, to conserve the fertility, the results of myomectomy could not be evaluated as the study duration is short. Subtotal hysterectomy had to be done in a case due to dense adhesions between bladder and uterus. The size of the specimen was noted, following which the specimen was dissected in the center and at the cornual ends, to look for the situation, type, and number of fibroids.

In our series, it was noted that the size of the fibroid uterus varied from a few centimeters to 24 weeks of gravid uterus. It is seen that about 76% were of the size of 16 weeks

**Table 8: Incidence of leiomyoma in relation to age**

| Age group in years | Present study | Maitri *et al.* (2015) | Baruah (1961) | Bhaskar Reddy (1963) | Usha *et al.* (1992) % |
|---|---|---|---|---|---|
| 21–30 | 7.0 | 10.0 | 3.0 | 21.5 | 10.53 |
| 31–40 | 42.0 | 55.0 | 3.5 | 50 | 48.95 |
| 41–50 | 46.0 | 32.0 | 10 | 23 | 37.95 |
| 50+ | 5.0 | 3.0 | 4 | - | 3.09 |

gravid uterus, 22% were of the size between 16 and 20 weeks, and huge fibroids of >20 weeks were encountered in 2% of the patients.

All the leiomyomata were corporeal, no extrauterine fibroids were encountered. Among the uterine about 93.75% were in the body and 7% were cervical, intramural fibroid was the most common variety comprising about 79% of the cases, 15% submucous, 11% subserous, 2% were broad ligament fibroids, and all were pseudo broad ligament fibroids.

### Incidence of Histopathological Pattern of Endometrium

Histopathological pattern of endometrium was studied. It showed proliferative endometrium in 49%, secretory changes were noted in 13%, endometrial hyperplasia was seen in 13% cases, and simple proliferative glandular hyperplasia was seen in 25%.

The associated pathology in the adnexa and other pelvic structures was studied, which showed cystic ovaries in 6% of the cases. A variety of cysts were noted such as simple serous cyst, follicular cyst, serous/papillary cystadenoma, dermoid cyst, and corpus luteal cyst. Adenomyosis was found in 8% of the cases, chronic cervicitis was seen in 85% of the cases and PID in 4% of the cases. Fibroid polyp was seen in 5% cases, 1% had a Granulosa cell tumor, and 1% had Low grade squamous intraepithelial neoplasia.

## DISCUSSION

Incidence of leiomyoma is highest in the fourth decade, with not a significant difference between the incidence in the third decade. This is probably because the areas in and around CKM Hospital, Warangal, are rural to suburban and women do not seek health care until very late into the disease course. Similarly, the incidence of leiomyoma was highest among the multiparous group in most of the studies, as depicted in table below. Although the literature states that, leiomyoma is a disease of low parity. This is probably due to early age at marriage, and long gap between the last childbirth and development of symptoms.

The analysis of symptoms shows that the menstrual complaints were predominant among all the study groups with comparable results [Table 5]. Other complaints such as pain/abdomen and mass/abdomen were also found.

Different authors have quoted varying incidence of the size of fibroids, this depends on the stage at which the patients present.

About 79% were intramural fibroids, which is the most common variety [Table 6]. Similar results were obtained by other authors such as Maitri *et al.* (60.6%), Usha *et al.* (77%), Chhabra *et al.* (47%), and Shaw (73%). Although the incidence of cervical fibroid has been coated as very low, 4% (Shaw) and 0.6% (Tiltman), the incidence in our study is comparatively high 7%.

### Incidence of Various Operations Performed

Compared to the statistics from the study conducted by Maitri *et al.*, it has been seen that the number of TAH with unilateral salpingo-oophorectomy has increased. Furthermore, the usage of LNG IUCD has risen and has proven to be both efficient and acceptable to the patients. Few cases have resolved with the usage of progesterone for 6 months [Table 7].

### Incidence of Histopathological Pattern of Endometrium

The histological pattern of endometrium observed was proliferative type in 49% of the cases, these results are comparable to that quoted by other authors. The incidence of simple proliferative glandular hyperplasia was very high in our study which is contrary to the incidence quoted by the other studies. This indicates the hyperestrogenic states associated with fibroids, endometrium was secretory in 13% of the cases.

### Histopathological Abnormality in Combination Associated with Myoma

The association with cystic ovaries and adenomyosis also indicates hyperestrogenism [Table 8].

### Incidence of Various Degenerations in Studied Cases

The incidence of cystic and hyaline degeneration was 2% each which is similar to the other studies. Other degenerations were not found.

## CONCLUSION

Fibromyoma (Leiomyoma) most common benign tumor of the female reproductive tract. The trends in the age incidence have remained the same, the occurrence of fibroid is rare before 20 years of age, and they cease to grow after menopause. Although previous studies have

shown the incidence to be maximum in the reproductive age group, our study showed it to be occurring with almost equal incidence in the third and fourth decade. Although fibroid is a disease of low parity, it was most commonly seen in multipara, a significantly long period of infertility following last childbirth predispose to the development of fibroids. Most common mode of presentation is menstrual disturbances. Since most of the patients were referred by local doctors, the patients ascribed any symptoms to the presence of fibroid, retrospectively.

Intramural is the most common variety, followed by combination leading to multiple fibroids, then submucous, and subserous fibroids. The proliferative and cystic glandular hyperplastic endometrium were commonly reported. The presence of proliferative endometrium, adenomyosis, and cystic ovaries all is indicative of hyperestrogenic state associated with the development of fibroids. There is a need for greater education and awareness among the women of reproductive and premenopausal age group. Since most of the cases are referrals from peripheries, there is also a need for the local physicians and gynecologists to detect fibroid early in its course and start appropriate management. Most of the women have come to the tertiary center with severe anemia or the complications of fibroid uterus.

Early detection will help in immediate institution of medical management and uterus conserving procedures. This will reduce the hysterectomy rate which continues to be high. The women also need to be educated about medical management as the acceptance of uterus conserving procedures continues to below. The effect of fibroid uterus on the quality of life, morbidity of surgery, and post-operative complications can be reduced by medical management.

In conclusion, the emerging drugs such as SERMs and SPRMs must be available throughout the tertiary centers as most of the patients are from low socioeconomic background and cannot afford the drugs. LNG IUS also continues to be out of reach for most of these women as it needs regular follow-up.

The concerned authorities must educate the women from rural background regarding the need for routine gynaecological visits starting from the third decade. All these measures will bring down the hysterectomy rate and ensure greater compliance with medical management.

### Summary

- Leiomyoma is the most common benign tumor of the uterus.
- In our series commonly found in premenopausal women in the fourth decade, 46% cases. No cases were seen below 20 years.
- There is a long period of childlessness (infertility) between the last childbirth and appearance of symptoms, in 46% of cases. This interval was 16–20 years.
- The mean age at which the patients underwent sterilization is 23 years and the interval between sterilization and development of symptoms in 33% of patients was 16–20 years and 17% above 20 years.
- Most common mode of presentation is menstrual disturbances 65%, among which menorrhagia was seen in 83.4% of the cases.
- Intramural fibroids are the most common variety, accounting to 79%, followed by submucous in 15%, subserous in 11%, and cervical in 7%.
- Cystic and hyaline degeneration was noted in small numbers.
- Endometrial pattern was proliferative in 49%, secretory in 13%, hyperplasia was noted in 13%, simple proliferative glandular hyperplasia in 25%.
- Cystic ovaries were seen in 6% of the patients adenomyosis in 8%, PID 4%, and 1% each of LSIL and granulosa cell tumor.
- Chronic cervicitis in 85% of the cases.

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