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Contents

CASE REPORTS

- Silence Becomes Violent – An Unnatural Event in Cerebral Arachnoid Cyst
Bhavanam Hanuma Srinivas, A S K Ahamed Sharief, Bommisetty Trinath Kumar, N V Sundara Chary 1
- Laparoscopic Management of a Cholecystocutaneous Fistula: A Rare Case
R Murugesan, S Muthuraj, P Karthikeyan, K Ashok Kumar, Shivanshu Misra 4
- Kissing Vertebral Arteries – A Technical Note on Vasculopexy of Vertebral Arteries
Srinivasa Rao Nutakki, Ahamed Sharief ASK, Vijaya Pamidimukkala 7
- Cast Hollow Obturator Prosthesis in a Patient with Squamous Cell Carcinoma Following Hemimaxillectomy – A Case Report
R Ravichandran, Lino Paul, K Harsha Kumar, Litty Francis 11

REVIEW ARTICLES

- Women in the Motherland Gender Health Inequalities in India
Rashmi Mehra 15
- Median Mandibular Flexure
Arkaprava Saha, Nirmal Raj, Ajanpeni, Rajeshwari Tambolkar, Pratik Bumb 19

ORIGINAL ARTICLES

- An *In vitro* Study to Evaluate the Shear Bond Strength of an “Amorphous Calcium Phosphate”-Containing Orthodontic Adhesive
Nihar Ranjan Sahoo, Rashmita Sahoo 23
- Clinical Pattern of Multiple Myeloma in Low Socioeconomic Group Patients of South India
K Sivasubramaniam, K V S Latha, Abhishek Ranjan 30
- Prevalence and Associated Factors of Anxiety Disorders among Cancer Patients Presented to Madras Medical College Chennai
M V Tintu, T S Rahul, K V S Latha, K Siva Subramaniam 35

Gamma-Glutamyl Transferase an Oxidative Stress Marker in Metabolic Syndrome <i>P. Sunithapriya, N. Sasivathanam</i>	42
Efficacy of 2 mm Three-dimensional Locking Titanium Miniplates in Management of Anterior Mandibular Fractures <i>Deepa Pande, Jyothi B, Jerin Jose</i>	47
Esthesioneuroblastoma Treatment Results From a Tertiary Care Center <i>K V S Latha, K Sivasubramaniam, T S Rahul</i>	54
Renal Function in Cirrhosis of Liver: Hospital-based Study in Tripura <i>Paul Subhadip, Bhaumik Pradip</i>	57
To Compare the Intubating Conditions of Cisatracurium with Rocuronium – A Prospective, Randomized Double-blind Study <i>Yerramsetti Atchyutha Ramaiah, S Priyadharsini, M Santhi Sree</i>	61
Low-cost Negative Pressure Therapy for Wound Healing <i>T Srinivas, M Aparna, A Nagaraju, K Sreevani</i>	67
Comparative Study of Medical Management of Anal Fissure between Topical Application of Minoxidil and Diltiazem <i>A Patidar, V Tiwari, A Silodia</i>	73
Sonological Findings of Interstitial Lung Disease and Its Comparison with HRCT in Bhopal, India <i>Lovely Kaushal, Sandeep Kumar</i>	77
Comparison of High-resolution Computed Tomography Findings in Drug-Sensitive and Drug-Resistant Pulmonary Tuberculosis Patients <i>Lovely Kaushal, Pooja Rajput</i>	88
Assessment of Acromiohumeral Interval in A-P Radiograph as an Indicator of Rotator Cuff Injury and Its Comparison with High-frequency USG in Bhopal, Central India <i>Lovely Kaushal, Shubhendra Singh, Poornima Maravi</i>	98

The Effect of Pulp and Paper Industry Effluent on the Biological and Bacteriological Parameters of River Hindon

Asha Mishra, Rakesh Kumar Pande

110

Assessment of Impact of Nonsurgical Periodontal Therapy on Serum Homocysteine Levels in Patients with Chronic Periodontitis

Vineet Kotwal, Shivani Jandial, Bhanu Kotwal, Rajiv Mengi, Manik Sharma, Vinod Tomar

114

Parity and Menarche as Factors Associated With Age at Natural Menopause

Priyanka Parihar, Sanjeev Singh, Ravi Kumar Parihar, Harleen Kour, Neha Majotra

118

Silence Becomes Violent – An Unnatural Event in Cerebral Arachnoid Cyst

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Abstract

Intracranial arachnoid cysts usually account for 1% of the intracranial mass lesions. Their most frequent location is the middle cranial fossa. Most are asymptomatic or present with headache, convulsions, and hemorrhage. We herein report a clinical case, radiology, and discussion of previously asymptomatic middle cranial fossa arachnoid cyst in a 9-year-old male child who presented with raised intracranial features following a trivial trauma.

Key words: Arachnoid, Rupture, Subdural

INTRODUCTION

Intracranial arachnoid cysts usually had an indolent course; they account for 1% of the intracranial mass lesions.^[1] Arachnoid cysts are common childhood developmental anomalies; their most frequent location is the middle fossa.^[2] They are benign lesions and may be associated with complications such as subdural hematoma, subdural hygroma, and intracystic hemorrhage. Minor head injury is known to result in subdural hygroma or hematoma due to rupture of arachnoid cyst; however, spontaneous rupture of arachnoid cyst may occur rarely.^[2] They are more common in males as compared to females.^[3] In children, they are frequently associated with seizures and cranial deformity.^[4,5] Rupture of arachnoid cyst causing subdural hygroma is very rare, with few case reports.

CASE REPORT

A 9-year-old, previously healthy boy, is presenting to the emergency department of a tertiary care hospital with the

complaints of severe left hemicranial headache and multiple episodes of vomiting for past 2 days. There was no history of loss of consciousness, seizures. The child had H/O trivial trauma 2 weeks back. No significant past medical or surgical history. He achieved all developmental milestones normally. On examination vital data normal, he was drowsy on examination with the GCS 14/15. Power was 5/5 on both sides, all cranial nerves were intact, and no sensory loss was observed. There were no meningeal signs, but there was left side papilledema. His blood investigations, including blood glucose, full blood count, serum creatinine, and electrolytes, were normal. Magnetic resonance imaging (MRI) brain done which showed left middle cranial fossa cyst with left frontotemporoparietal, extra-axial collection of CSF-like intensity (T1 hypo, and T2 hyper) compatible with arachnoid cyst [Figures 1 and 2]. Left pterional craniotomy, evacuation of subdural hygroma, fenestration of cyst into suprasellar cistern, and marsupialization of the cyst were performed [Figure 3]. The patient developed pseudomeningocele, which was managed with lumbar CSF drainage for 4 days and was discharged without any deficits. The post-operative imaging showed resolution of the subdural hygroma.

DISCUSSION

Arachnoid cysts are CSF collections between the two layers of arachnoid membrane and are usually benign

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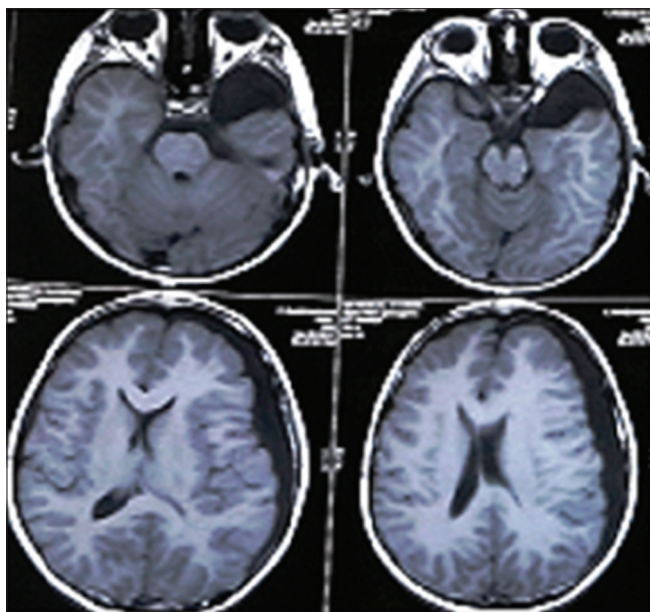


Figure 1: Magnetic resonance imaging brain T1W image showing subdural hypointensity in the left frontotemporal region and left middle cranial fossa suggestive of arachnoid cyst with subdural hygroma and mass effect

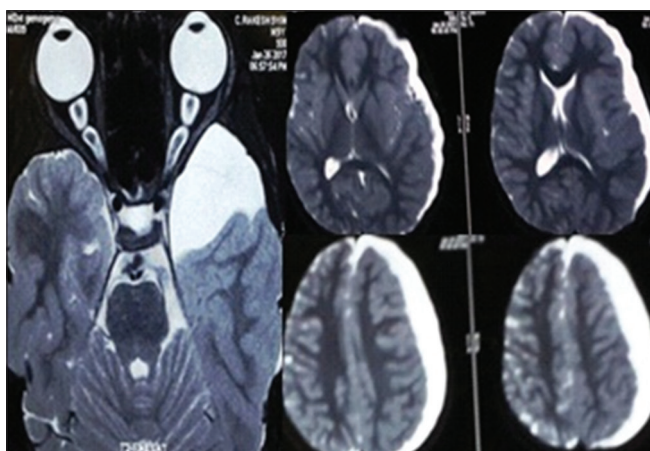


Figure 2: Magnetic resonance imaging brain T2 W image showing subdural hyperintensity in the left frontotemporal region and left middle cranial fossa suggestive of arachnoid cyst with subdural hygroma and mass effect

lesions. About 1% of intracranial space occupying lesions are arachnoid cysts. They usually grow slowly and occasionally disappear without treatment.^[6] Arachnoid cysts complicated, with cystic expansion, intracystic hemorrhage, subdural hematoma, and subdural hygroma, are usually symptomatic. Their association with subdural hygroma is rare.^[7,8] In 1924, first time Naffziger described, the possible mechanism of subdural hygroma formation, according to which a tear in the arachnoid membrane resulting in one-way valve mechanism with accumulation of CSF is thought to be responsible for subdural hygromas.^[9,10] Tears of outer cyst membrane are the main cause of subdural

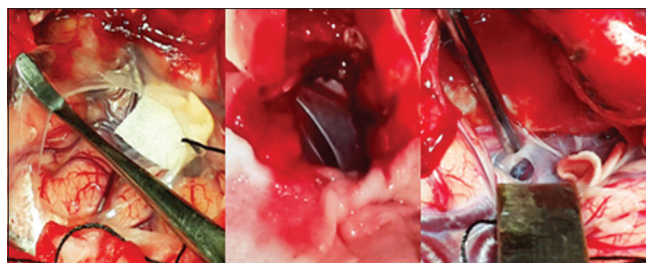


Figure 3: Intraoperative image showing left FTP area, slit like tear between left middle cranial fossa and FTP area, after marsupialization opening of cyst into suprasellar cisterns

hygroma in arachnoid cyst patients. The rupture is either spontaneous or traumatic in origin. Raised intracranial pressure with Valsalva maneuver is another possible cause of cyst rupture leading to hygroma. Most of the cases present with symptoms of raised intracranial pressure such as nausea, vomiting, headache, and rarely 6th cranial nerve palsy. Parsch *et al.* reported subdural hemorrhage in 2.43% and subdural hygroma in 0.46% of patients with arachnoid cyst reported on MRI. Mild head injury is the most common cause of arachnoid cyst rupture; however, rarely do they rupture spontaneously. Gradual increase in size of hygroma is due to the continuous transudation of cerebrospinal fluid in the ruptured cyst. CSF itself is less expansive and compressive than blood due to its low osmotic and hydrostatic pressure. Patients with arachnoid cyst may have complications by subdural hematoma as they are predisposed to it. Various management options of cerebral arachnoid cysts have been described in the literature. Surgical treatment of symptomatic cysts is generally acceptable. Craniotomy and fenestration of cyst, subdural evacuation, and CSF diversion are procedures performed in arachnoid cyst rupture depending on the size, location, and clinical presentation. For asymptomatic arachnoid cysts, prophylactic surgical treatment is not recommended.

CONCLUSIONS

Traumatic subdural hygroma should be suspected in symptomatic arachnoid cyst patients with any history of trivial head injury. MRI brain is investigation of choice. Features of raised intracranial pressure warrant for surgical treatment.

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Laparoscopic Management of a Cholecystocutaneous Fistula: A Rare Case

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Abstract

Introduction: Cases of cholecystocutaneous fistulas are rare as a result of rapid diagnosis and treatment. We present a case of cholecystocutaneous fistula developed after removal of drain placed after lap cholecystostomy for the treatment of acute calculus cholecystitis.

Case Presentation: A 37-year-old female presented with abdominal pain, purulent discharge, and passage of stones from the drain fixed-site after 6 years of cholecystostomy. A computerized tomography scan showed a biliary fistula. Laparoscopic cholecystectomy was successfully carried out.

Conclusion: Laparoscopic cholecystectomy is attempted in cholecystocutaneous fistula and it is a safe and feasible technique to manage cholecystocutaneous fistulas.

Key words: Cholecystitis, Cholecystocutaneous fistula, Laparoscopic cholecystectomy, Percutaneous drainage

INTRODUCTION

We report this case for many reasons. First, there is very less incidence of the disease. Second, the long history of this patient before diagnosis also makes this case very interesting; and lastly we wanted to share our surgical experience with colleagues. Cholecystocutaneous fistulas are rare complication following cholecystitis. Fewer than 20 cases have been reported in the published literature over the past 50 years.^[1] Fistulas are more commonly associated with Gallstones, although it occurs with acalculous cholecystitis and carcinoma gallbladder.

CASE REPORT

A 37-year-old female was admitted with complaints of abdominal pain and vomiting. She was diagnosed

to have acute calculus cholecystitis, and laparoscopic cholecystectomy was attempted. However, due to dense adhesions with surrounding structures, cholecystostomy was done at a private hospital in Kerala, India. The drain was kept and bile was drained. Drain removed after 15 days. Post-operative period was uneventful and the patient discharged. Follow-up ultrasound after 6 months revealed stone in gallbladder with complaints of pus discharge and passage of stones from the previous drain fixed-site in September 2018 for which Incision and drainage were done in that hospital. Then, she again presented with abdominal pain and passage of stones [Figure 1] from the same site in November 2018 and referred to our hospital.

Treatment at our hospital CECT abdomen was taken and it showed cholecystocutaneous fistula with cholelithiasis [Figure 2]. Laparoscopic cholecystectomy with excision of fistulas tract was planned and operated on 28th November, 2018. Per-operatively, dense adhesions noted. Fundus of gallbladder found adhesive to the anterior abdominal wall. Calot's triangle dissected. Lap cholecystectomy done after ligating cystic duct and cystic artery with clip. Gallbladder dissected out from the liver bed. Fistulous tract seen from fundus inside the muscle with a defect of size 1cm. Tract extends

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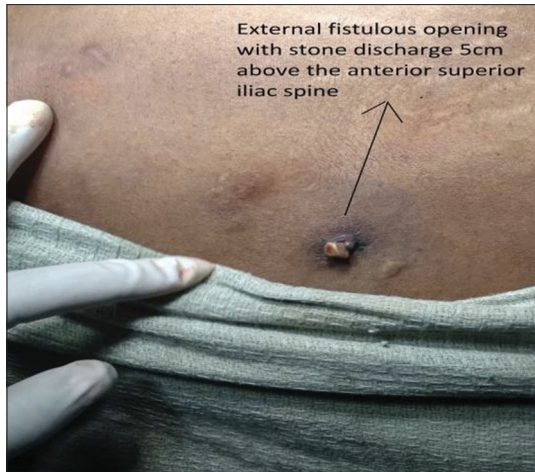


Figure 1: Patient complains of passing stones

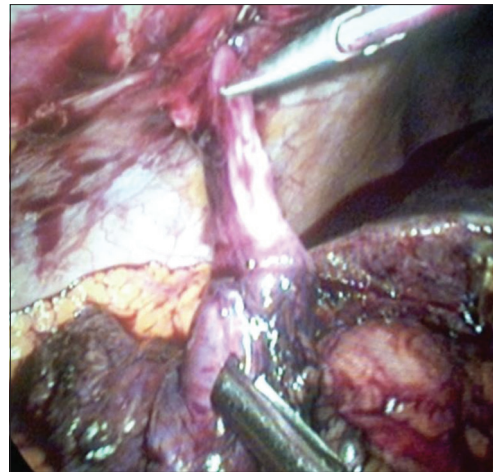


Figure 4: Dissection of the track

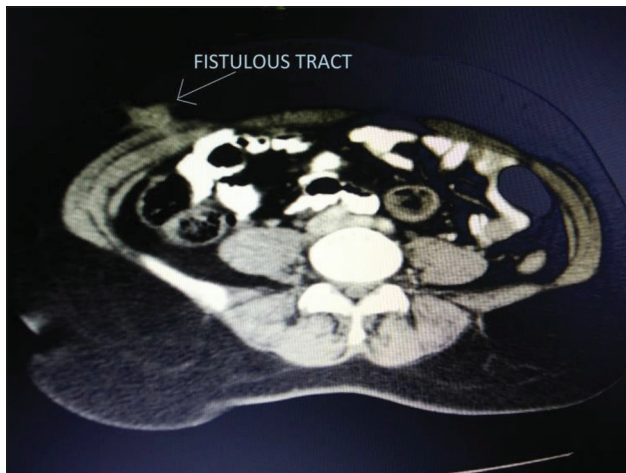


Figure 2: CT scan of fistulous tract

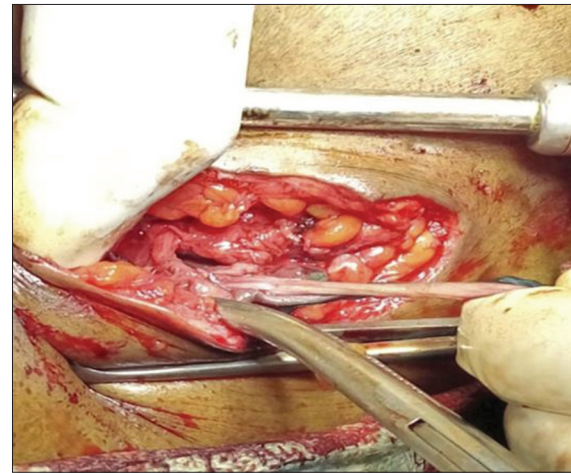


Figure 5: Fistulous track removed anteriorly along with gallbladder through skin incision

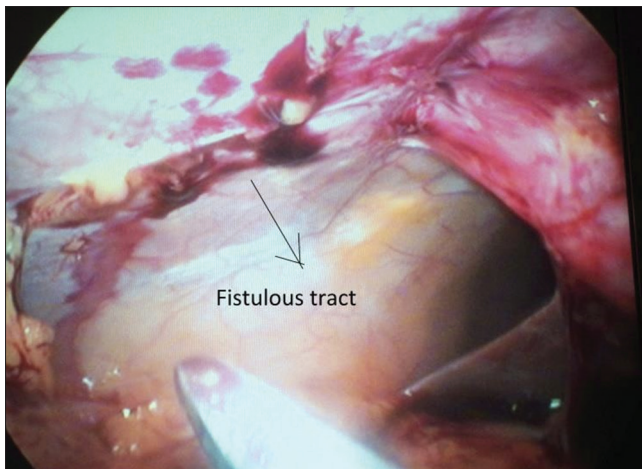


Figure 3: Fistulous track

up to skin [Figures 3 and 4]. Fistulous tract dissected laparoscopically till the skin. The external opening seen 5 cm above the anterior superior iliac spine. Stone extracted from external opening. Fistulous tract excised

into externally from skin [Figures 5]. Postoperative period was uneventful.

DISCUSSION

Since the beginning of the 20th century, the number of diagnosed cases of cholecystocutaneous fistula has declined dramatically. In 1890, Courvoisier reported 499 cases of perforated gallbladders; of these, 169 resulted in the formation of external fistulas through the abdominal wall.^[2] In contrast, between 1900 and 1975, only 31 cases were reported in the literature. Fewer than 20 cases have been reported in the published literature over the past 50 years.^[1]

We present a case of a 37-year-old female who was diagnosed with a cholecystocutaneous fistula developed after 6 years following removal of percutaneous drain fixed during laparoscopic cholecystostomy to treat her acute cholecystitis. Cholecystectomy with excision of fistula tract is the definitive treatment for this condition.^[3] Laparoscopic

approach is another option whenever feasible.^[4] Post-operative histopathological examination of gall bladder with fistulous tract shows chronic calculus cholecystitis with fibrosis and fistulous tract shows the structure of the skin and fibrous tract lined by granulation tissue. Although fistula formation is a rare complication following cholecystitis, it should be kept in mind as a differential diagnosis for any fistulous tract in the right abdominal wall.^[5]

CONCLUSION

Cholecystocutaneous fistulas are rare complication following cholecystitis. Fewer than 20 cases have been reported in the published literature over the past 50 years.^[1] Fistulas are more commonly associated with gallstones, although it occurs with acalculous cholecystitis and carcinoma gallbladder. Laparoscopic cholecystectomy is attempted in cholecystocutaneous fistula and it is a safe and feasible technique to manage cholecystocutaneous fistulas.

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- All authors have equally contributed to collecting the data and preparing this article and are in agreement for publishing it.

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Kissing Vertebral Arteries – A Technical Note on Vasculopathy of Vertebral Arteries

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Abstract

The authors report an extremely rare cause of cervicomedullary cord compression by anomalous course of bilateral vertebral arteries and its management options. A 40-year-old female patient presented with 1 year history of progressive quadriparesis and left upper limb radicular pain. Investigations revealed that the vertebral arteries on both sides had a mirror-like course and caused a deep indentation into the high cervical cord. Bilateral vasculopathy was done using Teflon slings. The treatment resulted in good recovery from symptoms. Anomalous course of the vertebral artery can result in symptoms of high cervical cord compression. Vasculopathy can result in lasting cure from symptoms.

Key words: Anomalous vertebral arteries, Cervicomedullary junction, Compressive myelopathy, Vasculopathy

INTRODUCTION

Cervicomedullary (CM) compression due to a variety of bony and soft-tissue abnormalities has been frequently identified.^[1-3] We report an extremely rare cause of cervical cord compression by abnormally coursing vertebral arteries on both sides. Vertebral arteries on both sides deeply indented into the spinal cord and resulted in symptoms of myelopathy and radiculopathy. The management issues of the case are discussed.

CASE REPORT

A 40-year-old woman presented with symptoms of insidious onset and gradually progressive imbalance on walking and weakness of all four limbs for about 1 year. She was also complaining of left upper limb radicular pain. She was unable to perform fine motor activities with both of her hands and was able to walk only with support. Clinical examination revealed Grade 3 spastic

quadriparesis, power in the left side limbs being worse. A sensory examination showed impaired proprioception and pinprick sensation bilaterally, worse on the left side. All kinesthetic sensations were severely impaired. Romberg's sign was positive. MR imaging revealed large flow voids in the region of the craniovertebral junction that resulted in cord compression [Figure 1]. MR and CT angiography revealed bilateral anomalous vertebral arteries which did not pass through the transverse foramen of the atlas but turned medially after exiting the axis [Figure 2]. The arteries entered the C2-C3 interlaminar space below the inferior border of C2, pierced the dura, and looped medially "kissing" each other on the dorsal surface of the CM region deeply indenting into the cord substance [Figure 3]. There was no other bone or soft-tissue anomaly in the region.

There was no evidence of instability.

Surgery Details

A midline suboccipital craniectomy with C1 and C2 laminectomy was performed. The extradural vertebral arteries were identified as they exited the transverse foramen of the axis. Vertebral arteries on both sides were visualized coursing posteromedially between the axis and C3. The vessels then pierced the dura mater underneath the lamina of C3. Intracranially, the vessels again looped medially "kissing" each other over the dorsal aspect of

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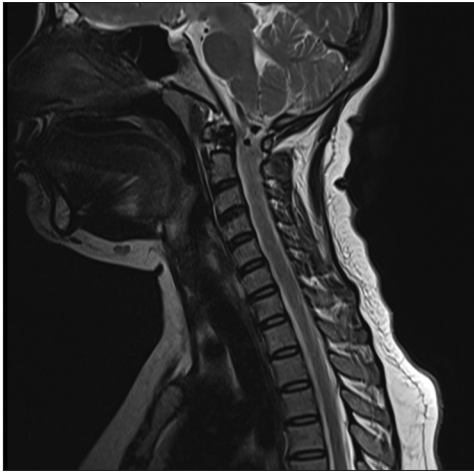


Figure 1: Sagittal MRI, T2 image showing CVJ compression by both vertebral arteries



Figure 2: Coronal cuts MRI showing anomalous course of vertebral arteries

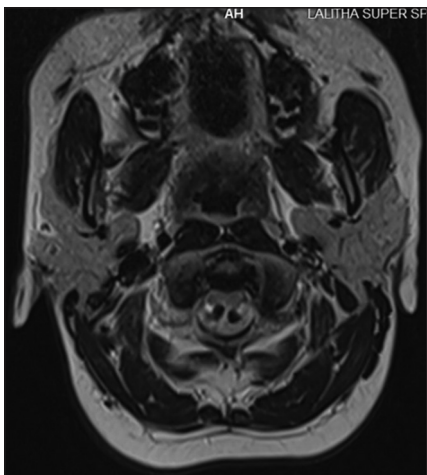


Figure 3: Axial T2 MRI image with CVJ compression

CM junction [Figure 4]. The arteries traversed between the rootlets of the C2 nerve. The cervical cord at this level was indented and flattened and appeared grayish and soft.

The indentation and effects on the cord appeared more severe on the left side.

Microvascular techniques were used to separate the arteries from the C2 roots and from the cord. The arteries could be relatively easily lifted away from the neural tissue and the rootlets. A window was created between the neural tissue and the vessels and a Teflon sponge was passed around the arteries on each side creating a sling [Figure 5]. Then, a non-absorbable 3-0 Prolene suture was taken through the sling arms and brought out through the dura mater and vessel along with the sling was taken aside from the spinal cord and was fixed to the dura initially and then to the adjacent muscle. This maneuver elevated the vessels away from cord without causing any kinking or lumen compromise [Figure 6]. The hitching also ensured that the vessels would remain separated from the cord and cervicomedullary junction underneath the dura.

Post-operative Course

The patient improved in the post-operative period and made a rapid neurological recovery.

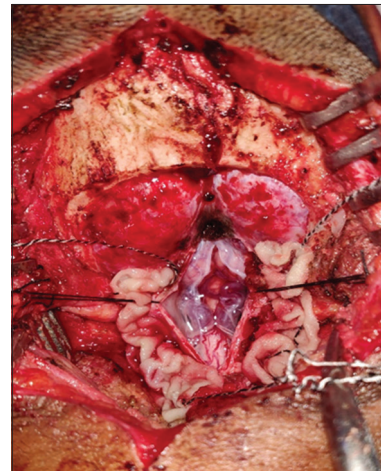


Figure 4: Kissing vertebral arteries

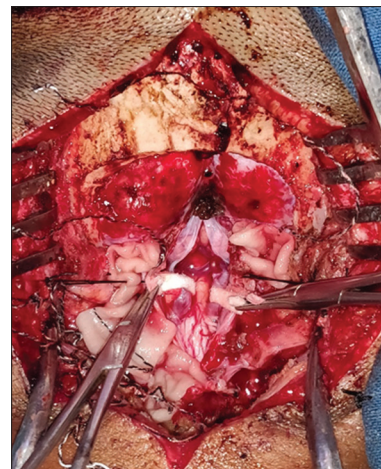


Figure 5: Teflon slings around the vertebral arteries

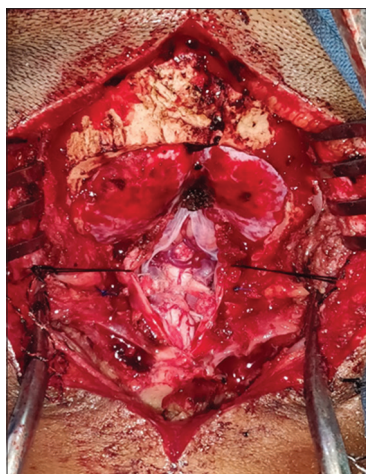


Figure 6: Vasculopexy completion with both vertebral arteries shifted away relieving compression

DISCUSSION

Vascular loops and ectatic vertebrobasilar arteries are common causes of trigeminal neuralgia, hemifacial spasm, glossopharyngeal neuralgia, vertigo and/or tinnitus, and spasmodic torticollis.^[4,5] Although rare primary and secondary reductions of posterior cranial fossa volume, tumors both infratentorial and supratentorial have been reported to cause vascular compression syndromes.^[4,6] Microvascular decompression of the affected cranial nerve has been the accepted modality of treatment in such cases. Even in cases with local or remote tumors, it has been speculated that vascular compression at the root entry zone ultimately causes the pain. Resection of the tumor with or without directly manipulating the vessel loop has been associated with lasting relief of symptoms. Ectatic and anomalous vertebral arterial loops resulting in cord compression have been identified only rarely.^[7,8]

Cacciola *et al.* studied the normal anatomy of vertebral artery in the region of craniovertebral junction on cadavers.^[9] The vertebral arteries run a vertical course from the transverse foramina of C3–C6. After its exit from the transverse foramen of the C3 vertebra, the V1 segment of the artery courses posterosuperiorly and forms a loop within the groove on the inferior surface of the superior articular facet, turns back inferiorly, and then exits from the transverse foramina of the C2 vertebra. The extent of extension of the vertebral artery loop within the C2 facet varies. The vertebral artery exits from the transverse process of the C2 vertebra and takes an initial lateral bend and then traverses superiorly to enter the transverse foramen of C1. In its third segment, after exiting the transverse process foramen of C1, the vertebral artery takes an approximately 90° posterior bend and turns medially to engage in the groove on

the superior surface of the posterior arch of the atlas, where turning around the superior facet of the atlas, it bends anteriorly to enter the spinal canal in front of the posterior atlanto-occipital membrane. In its fourth segment, the artery pierces the dura mater and arachnoid between the occipital bone and atlas and enters the cranial cavity through the foramen magnum. From the reported literature, it appears that there is approximately 2–3% incidence of vertebral artery anomalies in the region of craniovertebral junction. Although rare, vertebral artery course and its dural entry below the posterior arch of atlas exist.^[9,10] In our case, the vertebral artery on both sides entered into the intradural compartment between C2 and C3 lamina bilaterally. It appeared that due to abnormal course, the extradural course of the vertebral artery was probably shortened and the extra length of the vertebral artery was present intradurally. This excess length of the artery formed a loop on the dorsal surface of the cord. Continuous pulsation of the large arteries over long period of time was apparently the cause of myelopathy. Anomalous vertebral arteries in most instances do not cause any symptoms. From our literature survey, we look at isolated 13 cases of symptomatic cord compression due to anomalous vertebral arteries, out of which, 6 had unilateral compression and 7 had bilateral compression.^[10,11] While two patients had evidence of myelopathy, rest of the cases had symptoms that could be related to nerve root compression and manifested as neck pain, arm pain, or torticollis.^[10-12] Intermittent stimulation of the dorsal root entry zone of the cervical nerve with pulsations of the vertebral artery can explain the neck pain and occipital neuralgia. Compression of the Lissauer's tract might be the mechanism of the shoulder and arm pain.^[11] Takahashi *et al.*^[13] reported a case where the radiological and clinical features were remarkably similar to our presented case. It was suggested by Suzuki *et al.*^[14] that the vertebral arteries entering the spinal canal at a lower level, may lead to cord compression as the intraspinal subarachnoid space at that level may be narrow. Hasegawa *et al.*^[8] reported a patient with an abnormal course of the vertebral artery, platybasia, and hypoplasia of the atlas. They postulated that the canal stenosis associated with hypoplasia of the atlas contributed to the cord compression by the vertebral artery. MRI and 3D CT angiography are the investigations of choice to diagnose such patients. The reconstructed CT image demonstrated the course of the vertebral arteries and its bony relations obviating the need for a four vessel angiography. Treatment options for patients with anomalous vertebral arteries with root or cord compression include vessel transposition, duroplasty, detachment of roots from the vertebral arteries, or the placement of inert material between the vessel and the cord. Since the vertebral arteries are large and adequate decompression may not

be achieved with mere insertion of prosthetic material between the vessel and neural tissue, transposition of the vertebral arteries and vasculopexy may be the preferred technique. Various materials such as Gore-Tex, silicon tapes, and nylon threads have been used to lift the arteries from the cord. All the previously reported patients with bilateral vertebral artery compression have been treated with vertebral artery transposition and duroplasty.^[10,11-16] In one patient, an additional prosthesis was also placed between the arteries and the cord.^[15] All the patients improved following surgery except the one who developed a right hemiparesis postoperatively following a frontal infarct.^[16] In our patient, a Teflon sponge was inserted in the space between the vertebral artery and the cord. Since the artery was in contact with a long segment of the cord, a wider sponge was used. After the elevation, the arteries were maintained in this position using the Prolene sutures that passed through the arms of the Teflon sling and hitching them to the outer surface of the dura. This was further anchored to the adjoining muscles. This method allowed primary closure of the dura except for a small patch in the region of the dural hitching which was repaired with a local pedicled muscle flap. Although duroplasty and laminectomy could have been “sufficient” and probably safer for indirect decompression of the spinal cord, the ease with which the arteries could be dissected free and elevated off the spinal cord favored an aggressive surgical strategy. Following bilateral vasculopexy, the cervicomedullary junction was relieved of compression resulting in lasting relief of the symptoms of the patient.

CONCLUSIONS

Anomalous course of vertebral arteries may rarely cause cervicomedullary junction compression. Careful pre-operative investigations and planning for vertebral artery vasculopexy may provide lasting relief from symptoms.

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Cast Hollow Obturator Prosthesis in a Patient with Squamous Cell Carcinoma Following Hemimaxillectomy – A Case Report

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Abstract

Maxillary defects are created by surgical treatment of benign or malignant neoplasms, congenital malformation, and by trauma. The size and location of the defects influence the degree of impairment and difficulty in prosthetic rehabilitation. Lack of support, retention, and stability are common prosthodontic treatment problems for patients who have had a maxillectomy. The defects of maxilla apart from affecting the functions of the speech, swallowing, and mastication also cause cosmetic disfigurement. This clinical report describes the prosthodontic treatment of a patient diagnosed with squamous cell carcinoma who underwent a hemimaxillectomy, rehabilitated with a definitive hollow cast obturator.

Key words: Hemimaxillectomy, Hollow cast obturator, Squamous cell carcinoma

INTRODUCTION

Numerous epithelial subtypes of malignancies are found on the maxillary sinus: Adenocarcinoma, squamous cell carcinoma (SCC), adenoid cystic carcinoma, malignant melanoma, or salivary gland carcinoma. In SCC cases, concurrent chemoradiation, along with debulking, can be considered.^[1,2] A surgical treatment alone without reconstruction or obturation of the defect will result in air, food, and liquid escaping into the sinus and nasal cavities, leading to severe dysfunction of speech and deglutition with a significant reduction in quality of life of the patient.^[1] Post-surgical maxillary defects predispose the patient to hypernasal speech, fluid leakage into the nasal cavity, and impaired masticator function. The prosthesis needed to repair the defect is known as a maxillary obturator. An obturator (Latin: *obturare*, to stop up) is a disc or plate,

which closes and opening or defect of the maxilla as a result of partial or total removal of the maxilla.^[2]

Indications for the use of an obturator are as follows:

- To serve as a temporary prosthesis during the period of surgical correction
- To restore the esthetic appearance of the patient rapidly for social contact
- When surgical primary closure is contraindicated
- When the age of the patient contraindicates surgery
- When the size and extent of the deformity contraindicates surgery
- When the local avascular condition of the tissues contraindicates surgery
- When the patient is susceptible to recurrence of the original lesion which produced the deformity.^[3]

The patient is first treated with an interim obturator prosthesis, which is usually placed 7 to 10 days after surgery.^[6-11] A definitive obturator is fabricated approximately 3–4 months after surgery when the healing is complete. The definitive obturator impression should include the skin graft mucosal junction, lateral aspect of the orbital floor, and the velopharyngeal area depending on the extent of the defect.^[4-7] This case report describes the prosthetic

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rehabilitation of a maxillectomy patient with a cast hollow obturator.

CASE REPORT

A 62-year-old male patient was referred from the Regional Cancer Center, Thiruvananthapuram, to the Department of Prosthodontics, Government Dental College, Thiruvananthapuram, for prosthetic rehabilitation of a maxillectomy defect on the right side. The patient had undergone surgical maxillectomy 7 months back for the treatment of SCC. The chief complaints reported by the patient were nasal regurgitation of food and fluids while eating, along with difficulty in speaking. An extraoral examination revealed facial asymmetry, with a lack of support for the lips and cheek on the right side [Figure 1]. The mouth opening of the patient was slightly restricted, with defective hypernasal speech. Intraoral examination revealed an Aramany Type II palatal defect involving the right side of the arch [Figure 2].



Figure 1: Pre-treatment

Impressions were made using irreversible hydrocolloid impression material, the maxillectomy defect was outlined, and the cast was surveyed for designing the titanium metal framework. A special tray with a uniform 2 mm wax spacer was fabricated for the final impression procedure. Rest seats were prepared on disto-occlusal of 26 and mesio-occlusal of 27, to receive rests of embrasure clasp. The rest seat was also prepared for 24 mesio-occlusal fossa with a canine extension. After completion of the mouth preparation, the extension into the defect was molded using an admix of impression compound and greenstick in the ratio of 3:7 [Figure 3].

Border molding of the defect side was done using polyvinyl siloxane putty in an incremental manner. The final impression was made using polyvinyl siloxane light body material [Figure 4].

The design was transferred onto the master cast. A refractory cast was made by duplicating the blocked-out master cast using reversible hydrocolloid. An inlay wax pattern of the framework was made on the refractory cast [Figure 5].



Figure 3: Defect molded with admix mixture



Figure 2: Intraoral view

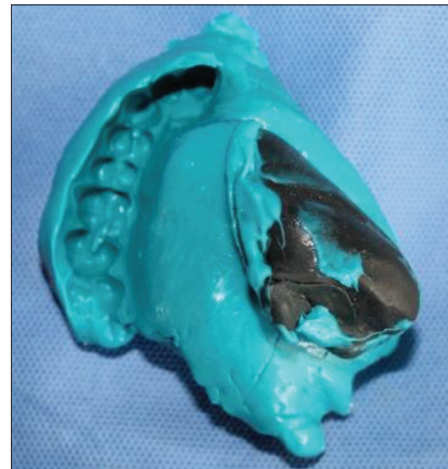


Figure 4: Addition silicone impression

The wax pattern was cast in cobalt-chromium [Figure 6].

The try-in of the metal framework was done in patient's mouth. The master cast was mounted on to a semiadjustable articulator using the jaw relation record. The try-in of the prosthesis was done after teeth setting [Figure 7].

The try-in prosthesis was then acrilized keeping the bulb hollow to reduce the weight of the obturator. The hollow bulb was made by making an acrylic shim from the duplicated cast and then fusing it with the acrilized obturator. After standard finishing and polishing procedures, the prosthesis was inserted [Figure 8].

The patient showed considerable improvement in phonation, and the obturator was very effective in preventing nasal regurgitation of food and fluids. The patient was very much satisfied with the prosthesis [Figure 9]. Periodic recall appointments were scheduled for the evaluation

of the prosthesis. The follow-up appointments showed satisfactory results with no deterioration of comfort and function with the prosthesis.

DISCUSSION

Prosthetic management of palatal defects has been employed for many years. Ambrose Pare was the first to use artificial means to close a palatal defect as early as the 1500s. The early obturators were used to close congenital rather than acquired defects. Claude Martin described the use of a surgical obturator prosthesis in 1875. Fry described the use of impressions before surgery in 1927, and Steadman described the use of an acrylic resin prosthesis lined with gutta-percha

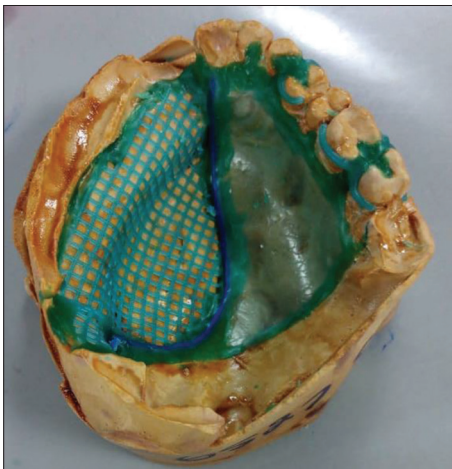


Figure 5: Wax pattern



Figure 7: Try-in

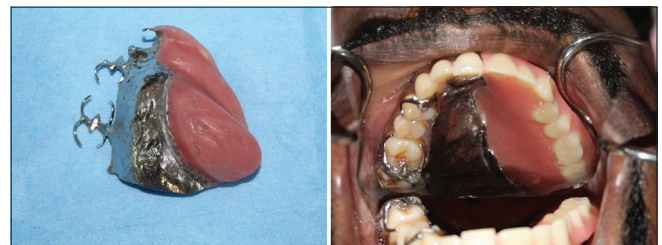


Figure 8: Cast hollow obturator inserted



Figure 6: Framework



Figure 9: Post-treatment

to hold a skin graft within a maxillectomy defect in 1956.^[8,9] In the total rehabilitation of the maxillectomy patient, the maxillofacial-prosthodontist has two primary objectives:

- i. To restore the functions of mastication, deglutition, and speech and
- ii. To achieve normal oro-facial appearance.^[4]

In this case, the support was gained from the remaining teeth and palate. Complete coverage of the remaining palate was planned to ensure maximum distribution of the load during the function. Successful obturation of the maxillectomy defect is guided by the volume of the defect and the positioning of post-surgical hard and soft tissues to be used for retention, stabilization, and support of the obturator.^[10] The weight of the prosthesis must be reduced to increase the retention of the obturator.^[11] Here, the obturator was made hollow, thus reducing its weight.

The advantages of a hollow bulb obturator are as follows:^[1]

- i. The weight of the obturator is reduced, making it more comfortable and efficient
- ii. Improves one of the fundamental problems of retention and increases physiological function so that teeth and supporting tissues are not stressed unnecessarily
- iii. The decrease, in pressure to the surrounding tissues, aids in deglutition and encourages the regeneration of tissue
- iv. The lightweight of the hollow bulb obturator reduces the self-consciousness of wearing a denture.

Referral to a speech pathologist will contribute to its success by improving the ability of the patient to adequately speak and swallow.^[12]

CONCLUSION

Although it is difficult to improve the quality of life for hemimaxillectomy patients compared with patients with conventional prostheses, this can be achieved with the skill, knowledge, and experience of specialists. A proper diagnosis and a well-designed treatment plan will result in pleasant outcomes. Rehabilitation with obturator prosthesis appears to be a functional and effective treatment modality. The problem experienced by hemimaxillectomy patients are reduced if a team approach is adopted, and specialists are careful to apply skill and experience at all stages and keep the patient under regular review.

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Women in the Motherland Gender Health Inequalities in India

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Abstract

Gender-related health inequalities in India have not received much attention from health program developers, implementers, and researchers. This paper attempts to put forth the current prevailing issues related to gender and health in India which could form the basis of a number of health program reforms and future research. It also mentions certain health behaviors and diseases for which gender differences remain largely unacknowledged. This article further highlights gender inequalities in the provision of health technology and services. It also presents inequalities associated with utilization of health services which is perpetuated by lack of gender-sensitivity in the planning and provision of these services. It also points out the health policies in place which have not been able to alleviate gender-related health inequities and inequalities. A number of issues requiring urgent attention have been raised which should be addressed to improve over-all gender-related and gender-associated health inequalities.

Key words: Gender inequalities, Gender, Health inequalities, India, Women's health

INTRODUCTION

Health is a multidimensional, composite construct of biological, and socioeconomic factors (Cheng and Goodman, 2014). Extrapolation of the variations in these factors results in difference or disparity in health statuses. Inarguably, such a disparity represents an inequality that has been described as “unfair, unjust, or avoidable” (Adler and Rehkopf, 2008). To improve our understanding of the societal disparities in health and healthcare, it is imperative to study the different factors at play, widening our focus to include not only income but also other markers of deprivation such as gender, religion, caste, and occupation (Murray *et al.*, 1999; Braveman and Tarimo, 2002). Out of these, gender is inherent to each individual and is considered a social construct even though the terms “sex” and “gender” have long been used interchangeably (Pryzgodna and Chrisler, 2000). Gender varies with societies and eras in terms of the gender roles, behaviors, biases, and norms prevailing in society at that time. Gender has had

a varied impact on health outcomes. Such impacts range from the lop-sided access (in favor of men) to resources such as food, healthcare, education, and finances to the subjugation and powerlessness, especially among women from lower and middle-income countries like India (Basu, 1989; Nichter *et al.*, 2010; Duflo, 2012; Aurino, 2017). Therefore, this essay will address if the inequalities in health associated with gender are increasing in India in the 21st century.

Mortality rates among females of all age groups are lower than males in most populations resulting in a greater number of women (Hill and Upchurch, 1995; Pongou, 2012; Regan and Partridge, 2013). Contrastingly, India has long presented with a skewed male-female child sex ratio (Jha *et al.*, 2006). Furthermore, the infant sex ratio in India has deteriorated from early 20th century to its current state in the 21st century [Figure 1]. The situation has been appalling for children aged 0–6 years with a maximum decline in sex ratios and a consistently decreasing number of girls in the past 50 years [Figure 2] which at present stands at 914 girls for a thousand boys. Comparing two consecutive census data has revealed that “made-to-order pregnancies” and “sex selection” have increased over the past 10 years, with an annual rate of 0.57% ($P = 0.02$) (Jha *et al.*, 2011). Skewed child sex ratios have been primarily linked with the sex differentials in the infant and child mortalities. India has long been established as a largely

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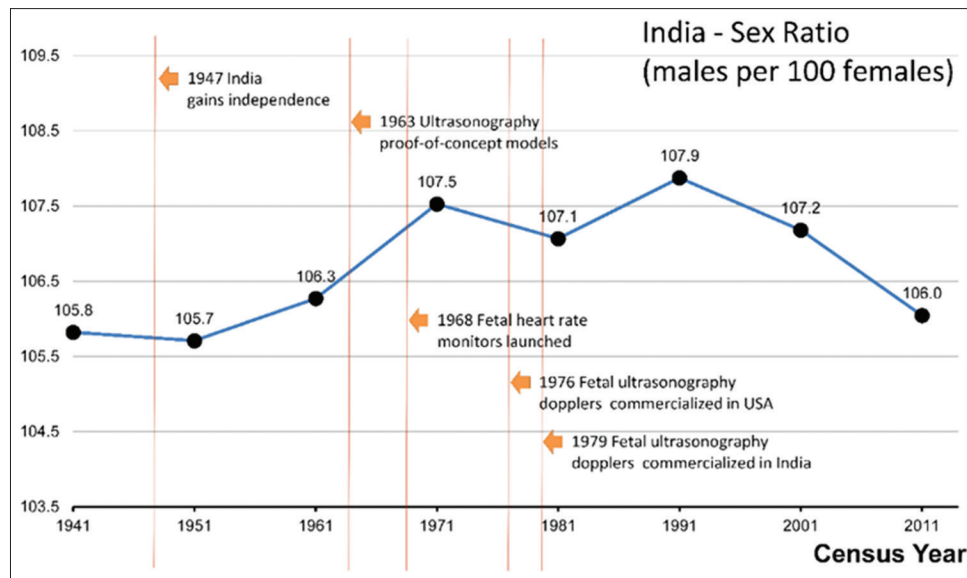


Figure 1: Infant sex ratio in India from 1941 to 2011 using census data. Extracted from Jha *et al.*, 2011

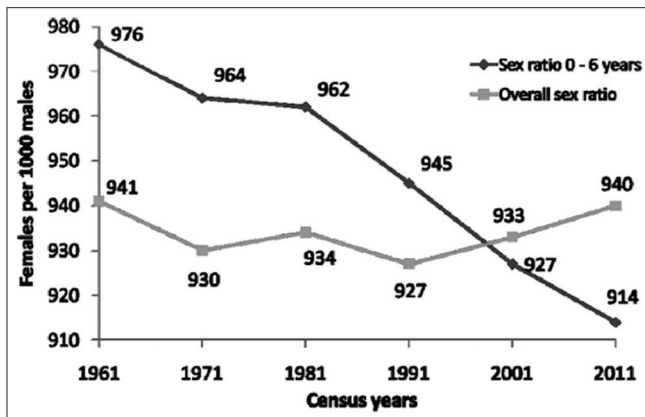


Figure 2: Dwindling child sex ratio in the 0-6 year age group (As adapted from National Census data from 1961 to 2011—Census India, 2011)

“patriarchal, patrilocal, and patrilineal” society (Silva *et al.*, 2017). Female foeticide and infanticide plagues, the Indian society due to the much prevalent “son mania” and girl-child considered a “burden” the geography, ethnicities, and socio-economic status of the population. Surprisingly, research has shown that an average educated Indian woman is also more likely to actively choose a male child (Aravamudan, 2007; Ansari, 2018). The distribution of power, resources, on the one hand, and occupations and risk factors, on the other hand, are all governed by the prevailing gender bias (Johnson, 2001).

Even for the surviving female child, an acute differential in the child care exists. Analysis of breastfeeding patterns among the Indian population showed significant differences between the length of breastfeed received by sons in comparison to daughters (Jayachandran and Kuziemko, 2011). This is in line with existing literature

showing that Indian parents choose to allocate greater resources to the male child (Pande, 2003; Osters, 2009). This trend continues through into the 21st century as the costs of living rises, reducing family size with the son seeming to be the more “profitable investment” (Hesketh and Xing, 2006). A similar inequity is seen between immunization coverage for the male and female children in a family, seen by comparing the coverage from 1992–1993 to 2005–2006. Despite increased incentivization and immunization programs introduced by the government, there is a steadily lower immunization coverage among females, even though the overall percentage coverage has increased (Corsi *et al.*, 2009). A number of studies have shown a distinct parental discrimination against the girl child in providing basic food and health care which has been understood as a major cause for existing gender disparity in health-care provision, nutrition, and child survival (Gupta, 1987; Basu, 1989; Mishra *et al.*, 2004). Despite the inherent biological advantage, females in the Indian context are dealt a tough hand in terms of the existing oppressive patriarchal social structure which has marginalized women through the centuries into the 21st century as well giving them an environmental, material, and psychosocial disadvantage (Banerji, 2016; Purewal, 2018). Since only a small percentage of the women are involved in monetarily fruitful work, an average woman is at the mercy of the male head of the family to allocate funds and resources for her health and well-being (Santow, 1995; Banerji, 2006). Even with a rise in the employability, education, and economic status of women, there has been only a small reduction in the gender disparities, despite the overall improvement of the health status of the Indian population (Corsi *et al.*, 2009; Saikia *et al.*, 2016).

The gender associated health inequity is not restricted to certain age groups. This disparity persists through older ages, with women being more likely to suffer from a disability and chronic health conditions. In addition, older women are at a higher risk of dependency, isolation, poverty, and neglect. They have higher chances of being left out of various social security programs due to low literacy, confinement at home, and gender relations, as experienced in daily life (Case and Paxson, 2005; Sen and Östlin, 2008; Pandey and Ladusingh, 2015).

An accepted historical generalization has been that “Women get sick and men die” which has been reiterated with time (Oksuzyan *et al.*, 2008). Saikia *et al.* (2016) illustrated that this gap has persisted through the 20th into the 21st century, although it has narrowed. Several studies have revealed the existing and widening disparity in the prevalence of common non-communicable diseases (NCDs) (such as obesity, diabetes, heart disease, stroke, cancer, and chronic respiratory diseases) between the genders (Anish *et al.*, 2013; Bonita and Beaglehole, 2014). According to the 2014 National-level data, overall NCD prevalence has been found to be higher among women (63%) as compared to men (47%). It was also seen that rural women (86%) had a higher risk of NCDs in comparison to rural men (64%) and urban men (53%) (Patra, 2016). Factors such as differential exposure to risk factors (such as stress, tobacco use, and occupational hazards), division of labor on the basis of gender, accessibility to preventive services, and treatment culminate in poor health outcomes for women (McDonough and Walters, 2001; Hosseinpoor *et al.*, 2012; Silva *et al.*, 2014). The perpetuating state of women is further reiterated by the social role theory, which suggests a vicious cycle between the social role played by a gender in society and their occupation which mutually and reciprocally affect each other (Eagly, 2012; Koenig and Eagly, 2014).

Gender does not affect health in isolation; instead, it is a complex interplay of other social determinants. Poverty and social class are other important factors which affect the health outcome of a population. Batra *et al.* (2018) and Pandey *et al.* (2018) noted the unfavorable gender differential toward women in terms of expenditure for hospitalization and cancer treatment. Pathak *et al.* (2010) analyzed national-level health surveys from 1992 to 2006 and found that the utilization of unskilled home delivery has reduced only by 1.8% among the poor pregnant women in comparison to 11.3% among the non-poor. Such a marked difference perhaps is influenced by the cost of service, distance to health facilities, cultural beliefs, level of education among the poor and non-poor women, and their families. This perhaps indicates that with improved socio-economic status, there is improvement

in the health status of women. Similarly, Saikia (2016b) assessed the gender difference in health-care expenditure (HCE) using national level data from 2004 to 2012 and found that female HCE to be significantly lower than male HCE with other demographic and socioeconomic factors controlled. Distinctly lower HCE was found for females for both chronic and short-term morbidity, with the disparity widening from 2004 to 2012. This HCE discrimination persists from youth to adulthood and widening in old age. Such a consistent disadvantage for the women probably stems out from the complex web of deeply entrenched patriarchy, poverty, and social position of women eliminating her health from priorities of the household since the women are traditionally more invested in household activities that are not directly associated to economic gains. Thus, they would postpone addressing their own health needs giving priority to the males of the household who are the “bread earners” and bring income (Santow 1995; Das *et al.*, 2018).

It has been reiterated time and again by the Black report (1980), the Acheson Report (1998) and the Marmot Report (2012), that significant health inequalities are seen through the 20th into the 21st century associated with gender, social class, ethnicity, and other factors. Inequities corresponding with gender are further magnified with the complex of socioeconomic status and the prevailing health services situation and poverty status of India. Even though there have been general improvements in health indicators in the population, the most deprived women remain the unhealthiest. Despite an improved health status among women, they still lag behind when compared to their male counterparts. Despite the efforts of the government in terms of newer reforms, national-level health programs and incentivization of a number of health services for the women, the sheer magnitude of centuries of social disadvantage, prejudice, and continued bias to the male child looms large on the health disparity faced by women in India.

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Median Mandibular Flexure

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Abstract

Mandibular flexure is a multifactorial phenomenon that occurs instantaneously and concurrently with jaw movements. The mandibular flexure can affect the prognosis and treatment outcome for various dental and implant-related procedures. Therefore, it is very important to take appropriate measures and adopt correct technique that helps negate the flexural movement of the jaw during any prosthetic rehabilitation. Mandibular flexure occurs during unilateral loading and extra strain is transmitted at the bone-implant interface. However, the amount of strain introduced by mandibular flexure alone may not be significant enough to stimulate bone modeling or remodeling.

Key words: Centric relation, Mandibular flexure, Occlusal mounting

INTRODUCTION

Median mandibular flexure (MMF) is a functional elastic deformation characterized by medial convergence of hemimandibles during jaw opening and protrusive movements.

The muscles, ligaments, and tendons attached to mandible exert force on the bone which causes a change in the shape of mandible at different levels of movement of jaws.

The muscles responsible for this event are:

1. Lateral pterygoid: Main muscle responsible
2. Mylohyoid
3. Platysma
4. Superior constrictor of pharynx.

These muscles, being originated medially, pull the mandible medially during different kinds of jaw movement. Since mandible is a “U” shaped bilaterally symmetrical bone, this bending force of muscles during excessive mouth opening and protrusive movement causes stress concentration in symphysis region which in turn changes mandibular arch

width. Dental arch width and facial form are important factors for determining success and stability of orthodontic treatment.

Three basic types of facial morphology exist; short, average, and long. Those with long faces have excessive vertical facial growth which is usually associated with an anterior open bite, increased sella-nasion mandibular plane angle, increased gonial angle, and increased maxillary/mandibular plane angle. The short face types have reduced vertical growth that is accompanied by a deep overbite, reduced facial heights, and reduced sella-nasion mandibular plane angle. Between the two types lies the average face. The mandible has a property to flex inwards around the mandibular symphysis with a change in shape and decrease in mandibular arch width during opening and protrusion of the mandible. The mandibular deformation may range from a few micrometers to more than 1 mm. The movement occurs because of the contraction of lateral pterygoid muscles that pulls mandibular condyles medially and causes a sagittal movement of the posterior segments.^[1]

MMF is the mandibular deformation characterized by the property of mandible to flex inward during opening and protrusion movements of the jaw with a reduction in the width of the mandibular arch. These movements occur in the frontal plane of the mandible and are caused by the contraction of lateral pterygoid muscles. The mandible flexes around the mandibular symphysis with medial pull on the mandibular condyles and sagittal movement of

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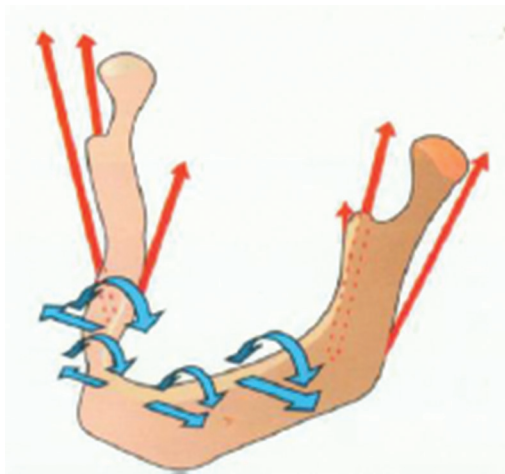
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the posterior segments. The deformation of mandible during flexure is so minimal that it is often overlooked and considered to have no practical significance. However, this trivial amount of mandibular deformation has emerged as a significant factor that can influence the prognosis and treatment outcomes for various dental and implant-related procedures.

MMF MECHANISM

The contraction of the two pterygoid muscles: Medial and lateral pterygoid have the same effect where the mandible flexes around the mandibular symphysis with medial pull on the mandibular condyles and sagittal movement of the posterior segments.

Internal pterygoid muscles due to the orientation of its fibers determine the principal vertical direction of mandible displacement (lower fibers insertion on the internal gonion; upper fibers, insertion on the posteroinferior extremity of the maxillary tuberosity and palatine pyramidal process). Furthermore, secondary propulsion and laterality movements are realized. A number of authors consider that rotation of the horizontal mandibular ramus to the midline and the slightly mandibular translation toward the front is due to the pterygoid internal muscles obliqueness (front, from the inside out, and sagittal, from anterior to posterior). The distortion of the mandible occurs early in the opening cycle, and the maximum changes may occur with as little as 28% opening or about 12 mm of mandibular movement.



The mandible being a single bone along with the muscle attached to it is able to perform various complex movements. The medial mandibular flexure (MMF) is a deformation of the mandible resulting from these movements performed during normal physiological functions such as talking and chewing. The muscle action during these movements makes both mandibular rami approach toward each other.

The MMF has become an important aspect in dentistry, especially in the field of conventional and over implants prostheses. When the use of conventional fixed prosthesis was started, as a means of rehabilitating lost teeth, a lot had been studied on this topic. There was a need, in many cases, to extend the metallic structure to regions distally to the mental foramen when the patient did not agree with the rehabilitation through removable dentures.

There are several studies about the possible consequences of bilateral rigid connection with distal extension in conventional prostheses. Some dentists associate MMF with muscle pain, limited mouth opening, absence of prosthesis passivity, bone loss and prosthesis fractures. With the onset of implantology, the replacement of fixed dentures in mandible by implant-supported fixed prostheses became a reality and with it the demand to resolve the problem of medial mandibular flexure.

MMF is a multifactorial phenomenon. The mandible changes its shape through the extended pressure caused by the contraction of various muscles and ligament attachments.

The pull applied by these attached structures not only causes alteration of the shape of mandible with a reduction in arch width but also affects the relative position of the teeth which are located on the mandibular arch. The most important factor causing mandibular deformation is the contraction of external or lateral pterygoid in a frontal plane during opening and protrusion of the mandible. A “U-” or horseshoe-shaped mandible is considered as a curved beam that is subjected to bilateral and unilateral loading. The lateral pterygoid contraction pulls the condyle and condylar neck medially and produces bending torque in the mandible.^[2]

According to Hylander, the bending force was exerted mainly by the medial component of force exerted by the obliquely arranged lateral pterygoid symphyseal bone torque by bonding strain gauges to the symphysis of an adult *Macaca fascicularis* and postulated that the functional contraction of the lateral pterygoid muscle caused a high strain in the symphyseal region and the symphyseal bending occurred by adduction of the mandible during mouth opening.

BASED ON HIS WORK, FOUR PATTERNS OF JAW DEFORMATION DURING MANDIBULAR FLEXURE WERE POSTULATED

Symphyseal Bending

This type of bending is associated with medial convergence or corporal approximation: This type of strain is associated with contraction of the lateral pterygoid muscle during jaw opening movements.^[1]

Dorsoventral Shear

This produces a shear force in the sagittal plane [Figures 1 and 2]. It is a result of the vertical components of muscle forces from the lateral pterygoid muscles and the reaction forces at the condyles. The magnitude of the shear force is dependent on the points of application. During symmetrical loading, the amount of shear force is equal on both sides of the mandible; however, during unilateral loading, the amount of deformation differs between the working and balancing sides.^[1]

Corporal Rotation

It occurs during rotation of the body of the mandible, usually during the lower stroke of mastication. The resultant force causes the narrowing of the dental arch.^[1]

Anteroposterior Shear

It occurs as a result of contraction of the lateral components of the jaw elevating muscles. It occurs late in the power stroke, and the bending moment increases from the posterior to the anterior region.

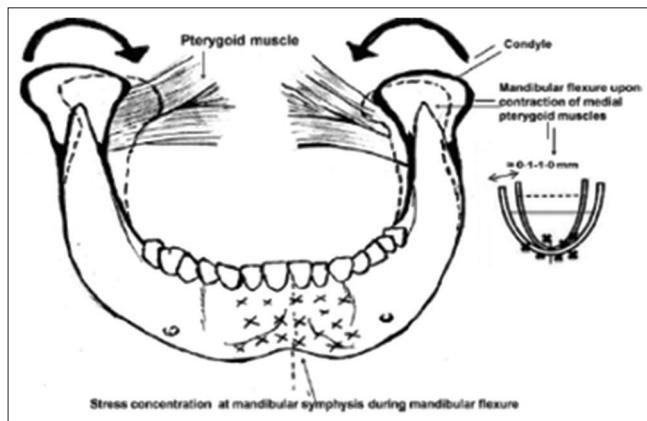


Figure 1: Medical rotation of the mandible and decrease in arch width during mandibular flexure caused by contraction of lateral pterygoid muscle

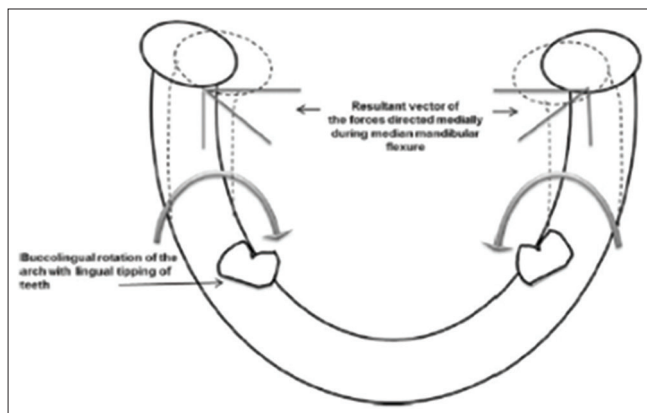


Figure 2: Bucco-lingual tipping of the teeth in lower arch and stress concentration at mandibular symphysis area during mandibular flexure

RELEVANCE OF MMF IN CD PATIENT

Following prosthetic procedures and guidelines should be followed to reduce the effect of MMF:

Considerations in Impression Making

As musculature strongly influences the amount of mouth opening and closure, the effect of MMF cannot be precluded in the impression-making process. Moreover, the changes in mandibular width due to the application of pressure on the rigid bone during various procedures for prosthesis reconstruction cannot be neglected.^[3] The strong influence of MMF may lead to inaccurate construction of fixed prostheses and removable prosthesis at the time of placement. The usual tendency is to attribute the misfit of the prostheses to the variability of dental procedures without considering the influence of MMF.

The medial convergence of the mandible due to contraction of the muscles by the conventional open mouth impression technique may alter the accuracy of the master cast and result in compromised prosthesis. Moreover, when impressions are obtained with mandible at a position of maximum mouth opening, the teeth will be recorded in a more lingual position than they would actually be found at rest or in occlusion. If an impression of the lower arch is made in such a position, the removable prosthetic appliance fabricated on the corresponding cast would be physiologically acceptable only when the mouth is open. When the mandible is closed, the denture would not fit the outwardly expanding arch as it was constructed on a constricted arch form. Such an ill-fitting denture applies pressure on teeth and the accommodating structures in the immediate vicinity.

Considerations while Recording Centric Relation (CR)

Mandibular flexure occurring either during patient-guided CR registrations or during function may influence the fit of the prosthesis and make it difficult for the clinician to achieve good occlusal contact.^[4] This is further complicated by the use of rigid dental casts mounted within rigid articulators. This often results in severe discrepancies as a closed-mouth CR record may not accurately fit onto a dental cast made from an open mouth impression technique. Second, the framework of a fixed dental prosthesis fabricated on a cast made from an open mouth impression technique would not fit accurately in patients' mouth. Such prosthesis would have occlusal interferences and result in pain when the patient applies a biting force. Therefore, a "closed-mouth" impression technique and a dentist-guided CR recording technique should be used to reduce such discrepancies. Tylmann (2001) supported a closed bite double arch method to avoid mandibular flexure effects with open mouth techniques.

Considerations while Occlusal Mounting

Mandibular flexure in the horizontal plane often results in discrepancies between cusp tip indentations in the jaw registration records and cusp tip location on the dental casts. The articulation of the casts is affected due to the lingual movement of mandibular teeth. This type of occlusal mount will not represent the correct occlusal relationship. The restorations fabricated to such recordings could present with occlusal interferences and articulators may require modification so as to allow for mandibular resilience.

RELEVANCE OF MMF FOR FIXED PARTIAL DENTURE (FPD) PATIENTS

In contrast to the flexure of the mandible, there may be flexure of the FPD framework during function. This may result in the intrusion of teeth. All beams flex as forces are placed on them. As an FPD is placed in function, the framework can flex. As discussed earlier, one of the functions of the PDL is to act as a shock absorber for the teeth. When natural teeth are used as abutments on both ends of a fixed partial denture, mandibular flexure and flexure of FPD frameworks do not result in intrusion of teeth. Lack of intrusion can be attributed to the fact that the teeth have PDLs to absorb the forces.

RELEVANCE OF MMF FOR IMPLANT PATIENT

Mandibular flexure potentially affects the accuracy of different stages of implant treatment, including osseointegration of the surrounding bone, implant prosthesis fabrication, strain distribution within the framework during mastication, and crestal bone around implants.^[5] The flexural forces cause lateral stresses on the implant body resulting in bone loss around implants, loss of implant fixation, material fracture, and discomfort on mouth opening.

Therefore, it is essential to consider MMF while planning any implant-supported prosthesis. MMF causes microdamage at the crestal region and poor osseointegration due to micromovements around implants. Fischman (1990) explained the importance of rotational aspect of mandible on the osseointegration of implants.^[6,7] Hobkirk and Schwab (1991) have also confirmed that the posterior implants could be subjected to stress-induced

microdamage at the bone-implant interface in cantilever situations due to mandibular flexure. Relative displacement of up to 420 μ and force transmission of up to 16 N between linker implants with jaw movements is possible during mandibular flexure. The forces were more during the opening and protrusive movements than lateral excursion.

The following procedure should be adopted to reduce the effect of mandibular flexure while placing implants: Impressions should be made with the patient's mouth in a partially closed unstrained mandibular position; short spans of fixed prosthesis are advisable whenever possible; large spans of porcelain should be avoided. At sites where implant size or bone quality is compromised, posterior mandibular osseointegrated implants should be free-standing with a short span of fixed prosthesis or related to tooth abutments through stress breakers. Thus, fixed implants and non-rigid connectors with the splitting of the restorations should be avoided in the mandible as two or more independent prosthesis are more favorable when implants are placed in the anterior region.

CONCLUSION

Mandibular flexure is a multifactorial phenomenon that occurs instantaneously and concurrently with jaw movements. The mandibular flexure can affect the prognosis and treatment outcome for various dental and implant-related procedures. Therefore, it is very important to take appropriate measures and adopt the correct technique that helps negate the flexural movement of the jaw during any prosthetic rehabilitation.

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An *In vitro* Study to Evaluate the Shear Bond Strength of an “Amorphous Calcium Phosphate”-Containing Orthodontic Adhesive

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Abstract

Introduction: Decalcification of tooth enamel around orthodontic brackets continues to be a perennial problem in orthodontics. The success of fluoride as a cariostatic agent is attributed to two functions: (1) Bactericidal effect at higher concentrations and (2) remineralization of enamel to form fluorohydroxyapatite. Amorphous calcium phosphate (ACP)-filled methacrylate composites have demonstrated the potential to remineralize carious enamel lesions by releasing supersaturated levels of calcium and phosphate ions in proportions favorable for the formation of hydroxy apatite over an extended period of time. Aegis OrthoTM, an ACP-containing adhesive, has been marketed for the use as a light-cured orthodontic adhesive with similar properties to previously used resins. However, to even be considered for clinical use, they must first provide satisfactory shear bond strength.

Purpose: The purpose of the study was to determine whether an ACP-containing adhesive (Aegis Ortho) provides an acceptable level of shear bond strength to function as an orthodontic adhesive.

Materials and Methods: Sixty extracted premolars were randomly divided into three groups for orthodontic bonding. Group 1 used a composite resin adhesive (Transbond XT), Group 2 was bonded with an ACP-containing adhesive (Aegis Ortho), and Group 3 used a resin-modified glass ionomer (Fuji Ortho LC). All bonded teeth were stored in distilled water at 37°C for 24 h before debonding. Shear bond strength and adhesive remnant index (ARI) were recorded for each specimen.

Results: The mean shear bond strengths for the three test groups were as follows: Group 1 (10.83 ± 3.03 MPa), Group 2 (4.04 ± 2.12 MPa), and Group 3 (10.99 ± 2.48 MPa). The statistical analysis showed that there was no statistically significant difference in bond strength between Group I and Group III. Groups II and III exhibited lower ARI scores than Group I, but a majority of specimens had greater than 50% of the cement removed along with the bracket during debonding except Group I.

Conclusion: Orthodontic resin containing ACP has significantly lesser shear bond strength to function as an orthodontic adhesive.

Key words: Amorphous calcium phosphate, Orthodontic adhesive, Shear bond strength

INTRODUCTION

The introduction of the acid etch technique by Buonocore^[1] in 1955 and the development of orthodontic resins by Newman *et al.*^[2] in 1965 has replaced banding with bonding, marking a new era in orthodontic history. Today, direct

bonding has become the most popular method and clinical standard for attaching orthodontic brackets. A common requirement for all resin-based composite adhesive systems is some form of enamel etching due to which there is loss of surface enamel and subsequent caries susceptibility. Because of this glass ionomer has been suggested as an alternative due to their distinct advantage of fluoride release. Despite this advantage, studies have reported poor bracket bond strength in the range of 2.4–5.4 MPa^[3] and higher bracket detachment rate than composite resin systems. This was a major shortcoming. Addition of small amount of light-activated resin to glass ionomer cements (GICs) was found to improve the physical and mechanical properties of GICs. These came to be known

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as “resin-modified GICs” and were introduced to the dental profession in 1988. Studies in orthodontic literature reported improvement of bond strength from 5.4 to 18.9 MPa with these resin-modified GICs.^[4,5]

Decalcification of tooth enamel around orthodontic brackets continues to be a perennial problem in orthodontics. The success of fluoride as a cariostatic agent is attributed to two functions:^[6] (1) A bactericidal effect at higher concentrations and (2) remineralization of enamel to form fluorohydroxyapatite which is less soluble in an acidic medium than hydroxy apatite.

Thus far, our specialty had focused mainly on protocols for fluoride intervention. However another mechanism can also favor remineralization dynamics: Amorphous calcium phosphate (ACP)-filled methacrylate composites have demonstrated the potential to remineralize carious enamel lesions by releasing supersaturated levels of calcium and phosphate ions in proportions favorable for the formation of hydroxy apatite over an extended period of time. This was considered a novel approach and a departure from the many fluoride-containing resin-based materials. The first commercially available ACP-containing orthodontic resin received FDA approval in February 2004.

ACP has the properties of both preventive and restorative materials that justify its use in dental cements, sealants, composites, and more recently, orthodontic adhesives. ACP-filled composite resins have been shown to recover 71% of the lost mineral content of decalcified teeth.^[7] One ACP-containing adhesive, Aegis Ortho™* has been marketed for use as a light-cured orthodontic adhesive with similar properties to previously used resins.

Studies have demonstrated their mineralization potential of ACP-containing materials.^[7-9] However, to even be considered for clinical use, they must first provide satisfactory shear bond strength. There are hardly any studies in orthodontic literature which investigate the bond strength of ACP-containing materials. Therefore, the aim of this study was to determine whether Aegis Ortho adhesive provides an acceptable level of shear bond strength to function as an orthodontic adhesive. This product was compared with the commonly used orthodontic adhesives/cements, Transbond XT™** and Fuji Ortho LC™*** in India. Similar to the claims made by the ACP adhesive manufacturer, the use of resin-modified GIC (Fuji Ortho LC) has been said to be more effective in preventing white spot lesions than conventional composite resins.^[10] Using this cement as another comparative group allows comparison of adhesives marketed for the purpose of white spot prevention. The efficacy of the

ACP-containing adhesive in preventing demineralization was not the focus of this study, but if proven to have adequate bond strength, this feature will be explored in future research.

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- **-3M Unitek, 2724, South Peck Road, Monrovia, CA 91016, USA
- ***-GC America Inc., Alsip, Ill.

MATERIALS AND METHODS

Sixty extracted human premolars, free of visible caries, decalcification, fractures, peculiar morphology, fractures, and other defects were collected and stored in distilled water at room temperature and remained in distilled water at all times except when brackets were being bonded and debonded. The distilled water was changed periodically to inhibit bacterial growth.

The teeth were randomly divided into three groups – Group I, Group II, and Group III, all containing 20 specimens.

- Group I – Samples were bonded using Transbond XT (3M/Unitek Corp, Monrovia, Calif.)
- Group II – Samples were bonded using Aegis Ortho (Harry J Bosworth Co., Skokie, Ill) [Figure 1], and
- Group III – Samples were bonded using Fuji Ortho LC (GC America Inc., Alsip, Ill).

Grooves were made on the root surface of each sample and then embedded in a cylindrical colored acrylic block of polymethyl methacrylate so that only the coronal portion of the specimen was exposed [Figure 2]. The crowns were oriented along the long axis of the blocks and were stored in distilled water at room temperature in a closed airtight container. Sixty 022-MBT metal maxillary premolar



Figure 1: Aegis Ortho™ amorphous calcium phosphate-containing adhesive

brackets were used (Gemini Series, 3M Unitek). The base area of each bracket was calculated (mean = 10.12 mm²) using image analysis equipment.

Before bonding, all teeth were cleaned using coarse, oil free pumice with a rubber prophylaxis cup, rinsed with water, and dried for 10 s using an air-water syringe. The teeth were etched with 35% phosphoric acid gel (Harry J. Bosworth Co.) for 30 s and then thoroughly rinsed with sterile water from an air/water syringe and dried with oil free and moisture free air until enamel had a frosty appearance.

For Group I, a layer of Transbond XT primer was applied to the tooth surface and photopolymerized for 10 s. Then, Transbond XT paste applied to the base of the bracket which was then placed on the tooth with firm pressure. Excess adhesive was removed from around the base of the bracket and the adhesive was then light cured for 40 s, positioning the light source on each interproximal side for 20 s with the help of QHL75, Dentsply halogen curing light.

For Group II, a layer of Aqua Bond was applied on the etched enamel and gently air dried for 5 s. Then, a thin layer of ACP-containing orthodontic adhesive (Aegis Ortho™, Harry J. Bosworth Co.) was applied to the orthodontic bracket and immediately pressed into the adhesive on the tooth surface. Excess adhesive was removed. For Group III instead of frosty appearance, the tooth surface kept moist after acid etching. The powder and liquid were mixed. The mixed cement was applied to the bracket bases and immediately the brackets were pressed on to the prepared tooth surface. The excess cement was removed. The cement was photopolymerized using the same light and following the same protocol as the first group. The manufacturer's instructions were followed throughout the procedure.

After bracket bonding, all the samples were stored in distilled water at 37°C for 24 h.

Method of Shear Bond Strength Evaluation

The shear strength of bonded teeth was tested using an Instron Universal Testing Machine (UTM) Model No: 1195-5500R [Figure 3]. The sample testing was carried out using a sensitive load cell value of 5000 Newton. This technique of testing shear bond strength has been widely reported in the literature.

Each tooth was oriented with the testing device as a guide and held firmly between the lower cross head of the UTM [Figure 4] so that its labial surface would be parallel to the applied force during the shear bond strength tests. A gingivo-occlusal load that produced a shear force at



Figure 2: Acrylic blocks with teeth embedded



Figure 3: Instron universal testing machine



Figure 4: Shear bond strength jig mounted on universal testing machine

the bracket-tooth interface was applied to the bracket by means of a looped soft stainless steel wire of size 21 gauge attached to the upper cross head of the machine. The results of each test were recorded in Newton (N) on a graphic plotter. Shear bond strengths were measured at a crosshead speed of 0.5 mm/min. The bond strength was calculated in megapascals.

After debonding, each tooth was examined under stereomicroscope named Carl Zeiss Jena to determine the amount of adhesive remaining on each tooth according to adhesive remnant index (ARI).^[11]

OBSERVATIONS AND RESULTS

The values obtained on testing the shear bond strength of samples in Groups I, II, and III were recorded in Newton and then converted into MPa (megapascal). Routine statistical analysis such as mean, maximum and minimum, range, and standard deviation was calculated for each group.

Data were analyzed using computer software, Statistical Package for the Social Sciences (SPSS) version 10. Data are expressed in its mean, median, and standard deviation. Analysis of variance (one-way ANOVA) was performed as parametric test to compare different groups. Duncan's multiple range (DMR) test was used as *post hoc* analysis to elucidate individual comparisons between groups. For all statistical evaluations, a two-tailed $P < 0.05$ was considered statistically significant.

The shear bond strength for brackets bonded with Transbond XTTM in Group I was 10.83 ± 3.03 MPa, for Aegis OrthoTM in Group II was 4.04 ± 2.12 MPa, and for Fuji Ortho LC in Group III was 10.99 ± 2.48 MPa. Fuji Ortho LC was found to have the highest and Aegis OrthoTM the lowest shear bond strength. *Post hoc* DMR test for individual group showed that there was no statistically significant difference in bond strength between Group I and Group III. One-way ANOVA showed that Group II (Aegis Ortho) has significantly lower bond strength than both Group I (Transbond XT) and Group III (Fuji Ortho LC) [Table 1], [Figure 5].

ARI

After debonding, the enamel surface of each tooth was examined with a stereomicroscope under $\times 10$ to determine the amounts of residual adhesive remaining on each tooth. A modified ARI suggested by Artun and Bergland^[11] was used to quantify the amount of remaining adhesive using the following scale: 0, no composite left on enamel surface; 1, less than half of composite left on enamel surface; 2, more than half of composite left on enamel surface; and 3, all composite left on enamel surface [Table 2].

The mean ARI score for Transbond XT was 1.4 in Group I, for Aegis Ortho, it was 0.67 in Group II, and for Fuji Ortho LC, it was 0.87 in Group III. Kruskal–Wallis ANOVA was used as non-parametric tool to compare ARI scores

Table 1: Analysis of variance (one-way ANOVA) of shear bond strength (MPa) comparing different groups

Group	Mean	±SD	F value	p value
I	10.83 ^b	3.03	71.389	<0.001
II	4.04 ^a	2.12		
III	10.99 ^b	2.48		

^{a,b}Means with same superscript do not differ each other (Duncan's multiple range test)

Table 2: Number of samples and their distribution according to adhesive remnant index

Group	Adhesive remnant index scores			
	0	1	2	3
I	2	5	9	4
II	5	10	3	2
III	5	9	3	3

ARI scores: 0 – no composite left on enamel surface; 1 – less than half of composite left on enamel surface; 2 – more than half of composite left; and 3 – all composite left

Table 3: Kruskal–Wallis ANOVA comparing adhesive remnant index scores between different groups

Group	Mean	Median	±SD	H value	p value
I	1.40	2.00	0.74	9.841	< 0.05
II	0.67	1.00	0.49		
III	0.87	1.00	0.52		

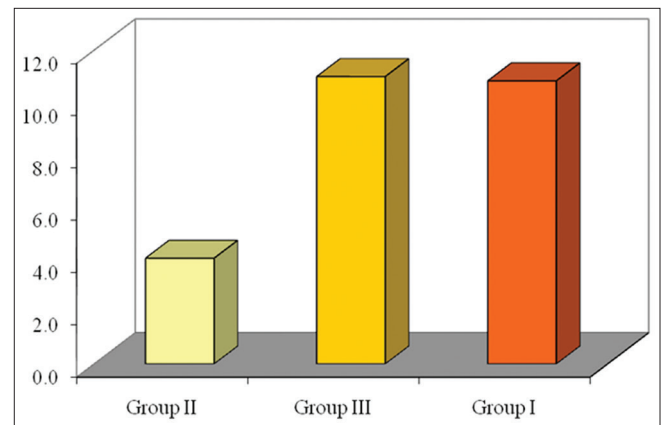


Figure 5: Comparison of mean shear bond strength

between different groups [Table 3], [Figure 6]. It showed that there was statistically significant difference between the mean ARI values of Group I and Groups II and III. For all statistical evaluations, a two-tailed $P < 0.05$ was considered statistically significant.

DISCUSSION

Until recently, most of the attention has been on fluoride, either placed topically in various concentrations or incorporated into restorative materials with varying

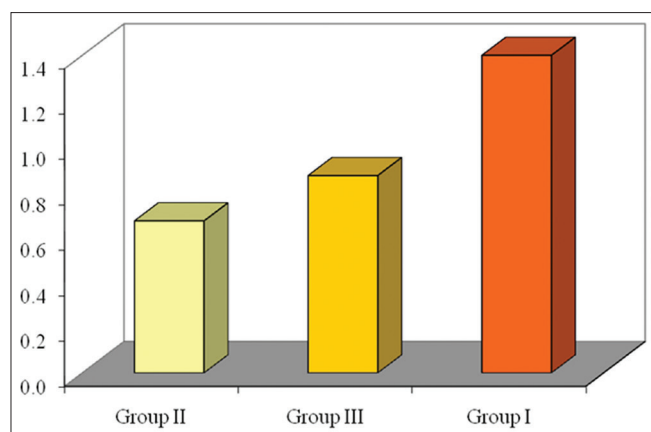


Figure 6: Comparison of adhesive remnant index

degrees of fluoride release, but the development and incorporation of ACP materials in dentistry is a different approach to reverse the effects of demineralization on enamel surfaces. There is no doubt that fluoroapatite is less soluble than hydroxyapatite, but exactly how much fluoride released from a restorative material to inhibit caries is still unknown.^[6]

ACP-containing materials are a new class of “smart” materials which get self-activated in low pH oral environments and return to a dormant state when the pH returns to normal. Skrtic *et al.*^[9] demonstrated that ACP accelerates the tooth’s natural calcium phosphate remineralization process to prevent demineralization that could be due to microleakage or poor oral hygiene.

It is one of the first “smart” materials in dentistry to receive lukewarm reviews. Ariston pHc™ (Vivadent, Schaan, Lichtenstein) was marketed in Europe as a restorative material that released calcium, hydroxyl, and fluoride ions, but little scientific information was generated about its actual ion-release effects.^[12] Again, van Dijken^[13] reported a clinically unacceptable failure rate using Ariston pHc™, which contained a calcium source but no phosphate. The calcium release was largely ineffective because the resin chemistry did not favor continuous release.

The first commercially available ACP-containing materials were a sugar-free chewing gum containing casein phosphopeptide-ACP (CPP-ACP) known as Recaldent™ (Recaldent Pty. Ltd., Melbourne, Australia) and an ACP-containing toothpaste, Enamelon™ (Enamel, Cranbury, NJ).^[14] Studies showed that CPP-ACP chewing gum resulted in a dose-related increase in enamel subsurface remineralization. This increased enamel remineralization was consistent with the previous studies showing the anticariogenic and remineralization potential of CPP-ACP in solution.^[15,16] Although there is a growing body

of evidence to support ACPs remineralizing potential, there is concern over the mechanical properties of ACP-containing materials.

In the early 1990s, the first bioactive mineral ion-releasing composites were developed, based on a polymer matrix phase and a filler phase of ACP.^[8] The ACP had to be stabilized by pyrophosphate ions to retard conversion of ACP back to apatite, and because of ACPs high solubility, a substantial release of calcium and phosphate ions was possible. These levels were found to be sustainable and could promote remineralization in tooth enamel.

Unfortunately, pyrophosphate-stabilized ACP-filled composites are mechanically weak because ACP does not reinforce the composite like silanized fillers do in most resin-based composites. Previous investigators suggested that ACP-containing dental materials should be limited to situations when mechanical demands are less, such as in pit and fissure sealants or bases and liners.^[17] Skrtic *et al.*^[9] demonstrated that ACP-containing composites can be made stronger by the addition of glass-forming agents and with silica or zirconia-hybridized ACP in Bis-GMA/TEGDMA/HEMA/ZrDMA-based composites.

The most clinically relevant property of an adhesive system is its bond strength as it determines the clinical longevity of the bonded attachments. In the current study, the mean shear bond strength of Group I (Transbond XT), Group II (Aegis Ortho), and Group III (Fuji Ortho LC) was 10.83 ± 3.03 , 4.04 ± 2.12 , and 10.99 ± 2.48 MPa, respectively. One-way ANOVA was done to evaluate for significant difference at $P < 0.05$ in the mean shear bond strengths of three groups and *post hoc* DMR test for individual group comparison.

One-way ANOVA analysis showed that there is a statistically significant difference in shear bond strength between Group II and the other two groups (Groups I and III) ($P < 0.001$). However, a *post hoc* Duncan’s analysis revealed no statistically significant difference between Groups I and III. Group III showed highest shear bond strength among three groups and Group II showed lowest shear bond strength.

It has been reported that clinically adequate shear bond strengths for metal orthodontic brackets to enamel should range from 5.9 to 7.8 MPa in terms of clinical and 4.9 MPa in terms of laboratory performances as suggested by Reynolds.^[18]

The bond strength (10.83 MPa) at which failure was observed for the brackets in the Transbond XT control

group falls within acceptable limits reported in the orthodontic literature.^[3-5] The corresponding value for shear bond strength of the Aegis Ortho group was only 4.04 MPa, which is just below the range in terms of laboratory performances as suggested by Reynolds.^[18] Fuji Ortho LC exhibited sufficient bond strength to be used as an orthodontic adhesive.

Only a few articles have investigated the incorporation of calcium phosphates into orthodontic adhesives. Dunn^[19] examined the bond strength of the same ACP adhesive used in this study and observed that brackets failed at a significantly lower force level (14.2 N) when compared to a traditional composite resin adhesive, as was found in the current study. Kawabata *et al.*^[20] investigated the bond strength of a resin cement containing varying amounts of α -tricalcium phosphate and concluded the formulations possessed a clinically acceptable bond strength.

On examining the enamel surfaces of the debonded samples, it was found 45% of Group II brackets and 50% of Group III brackets gave an ARI score of 1 (<50% of adhesive remained on the enamel surface) while 45% of Group I brackets gave ARI score of 2 (more than 50% of adhesive remained on the enamel). This implies in both Groups II and III the bond failure occurred at enamel-adhesive interface and for Group I at adhesive-bracket interface.

Less resin on the enamel surface after debonding corresponds to less work and time spent by the orthodontist to remove the resin. Hence, a lower ARI score is favorable in this situation. Group II did have a significantly ($P < 0.05$) lower ARI score compared to the other two groups. Therefore, the clinician would have to spend very little time removing the ACP-containing adhesive from the tooth. In addition, this difference in ARI scores suggests the ACP-containing adhesive exhibited more of a cohesive failure compared to the composite resin and resin-modified glass ionomer adhesives.

No clinical studies have examined the survival rate of brackets bonded with ACP-containing adhesives. It should be stressed. This study suggests that, if this adhesive is found to have remineralization capabilities, it may be acceptable to some clinicians and patients who have higher caries susceptibility if it prevents white spots. However, as per this study, from the viewpoint of bond strength, Aegis OrthoTM cannot be recommended, as the mean shear bond strength obtained for this material was only 4.04 MPa (± 2.12) which is well below the accepted range suggested by Reynolds.^[18]

Being an *in vitro* bond strength study, caution is advised in extrapolating the results of the present study to the clinical situation.

CONCLUSION

The result of the present study showed that orthodontic resin containing ACP has significantly lesser shear bond strength as compared to conventional resin-based composite and resin-modified GICs ($P < 0.001$). This would suggest greater tendency for earlier debonding which would be clinically unacceptable.

Fuji Ortho LC displayed acceptable bond strength similar to Transbond XT. Both these groups showed significantly higher bond strength than Aegis Ortho.

Aegis Ortho and Fuji Ortho LC displayed lower value of ARI score compared to Transbond XT.

The complete characterization of this adhesive system will be incomplete without an *in vivo* evaluation.

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Clinical Pattern of Multiple Myeloma in Low Socioeconomic Group Patients of South India

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Abstract

Background: Multiple myeloma (MM) forms \square 10% of hematological malignancies. Our aim and objective were to find the clinical profile, and presenting feature of MM in patients presented in a government hospital that treats below poverty line group of patients.

Materials and Methods: Medical records of all patients diagnosed with plasma cell neoplasm between December 2014 and December 2019 were taken from data registry and analyzed.

Results: One hundred and forty-two patients fit into MM diagnosis. Eighty-three were male (58.5%) and 59 were female (41.5%) with male to female ratio of 1.4. The median age of the study patients was 59 years (range 33–82 years). About 3.5% (5) patients were <40 years of age. One hundred and five patients (73.9%) had bone pathology, including lytic lesions and osteopenia with lumbar vertebra being the most common site, followed by thoracic vertebra and pelvis. The neurological compromise was present in 32 patients (22.5%). One hundred and twelve patients (78.8%) had Grade 1 or 2 anemia. Seventy-eight patients (54.9%) had creatinine >2 mg/dl with 25 of them had acute kidney injury. Twenty-seven patients (19%) had hypercalcemia. Twenty-three patients (16.2%) had infection during presentation with most common focus as lungs. Serum protein electrophoresis showed M band in 85.2% of patients and urine Bence Jones protein was positive in 61.3% of patients. Serum lactate dehydrogenase was elevated in 41.5% of patients and beta-2 microglobulin was elevated in 72% of patients.

Conclusions: MM patients presented at an early age, with an advanced stage and more end-organ damage that requires much attention.

Key words: Clinical pattern, Low socio-economic group, Multiple myeloma

INTRODUCTION

Plasma cell dyscrasias include various disorders that result from monoclonal proliferation of plasma cells. The clinical behavior of each disorder varies from benign to malignant. The common among them, known as monoclonal gammopathy of undetermined significance (MGUS) is asymptomatic and can be diagnosed in the general population. Other related disorders include smoldering multiple myeloma (SMM), MM, and Waldenstrom macroglobulinemia. MM is a malignant

proliferation of terminally differentiated plasma cells. Dr. Henry Bence Jones first described clinical features of myeloma in a patient in 1850, and the term MM was later coined by Rustizky in 1873. It forms around 17% of all hematological malignancies and around 1.8% of all malignancies.^[1] It is a disease of the elderly with a median age of presentation being 69 years^[2] and median age of death being 74 years. In India, it is noted that the median age of presentation is 60–69 years, which is earlier than that of west.^[3] Only 5% of the patients are below 40 years of age. MM is almost always preceded by MGUS^[4] which is asymptomatic and can be diagnosed incidentally in the general population. The spectrum of disease starts from MGUS to SMM and then to MM.^[5] The rate of progression from MGUS to SMM is 0.5% to 1% per year, while it is around 10% per year for SMM to MM.^[6] The exact etiology for MGUS or MM is unknown. Some of the risk factors identified are older age, male sex, and African American and African compared to Americans

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Mexican Americans and also Europeans.^[7] The reason may be due to the genetic susceptibility and molecular biology involving the pathogenesis of MM. Some familial cause for MM is also reported, but the exact extent is unknown. First degree relatives have a 3.7-fold increased risk than that of the general population.^[8] Some of the presenting features of MM in the descending order of frequency are anemia, bone pain, elevated creatinine, fatigue, hypercalcemia, and weight loss.^[9] Patients from India present in an advanced stage compared to the western population.^[10-13] The analysis of the descriptive nature of plasma cell dyscrasias in India is important as there is variation between the patient characteristics and disease presentation between the western population and Indian population. This study will help us in understanding the lack of knowledge among our population and possibly improve early diagnosis and treatment.

MATERIALS AND METHODS

Patients registered between December 1, 2014, and December 31, 2019 (5 years) were searched from the database and analyzed. This is a retrospective study where all details were taken from the patient's master case sheets from the Department of Medical Oncology, Madras Medical College, Chennai. The diagnosis of MM, SMM, MGUS, solitary plasmacytoma, and plasma cell leukemia was searched and analyzed. The updated International Myeloma Working Group (IMWG) criteria are used for the diagnosis of MM [Table 1]. Conditions where reactive plasma cells are seen such as metastasis, long-standing infections, connective tissue diseases, and liver disease were removed. Laboratory results were checked whether it is done within 1 month of diagnosis of plasma cell disorder to avoid error. All myeloma work-up was checked whether it is done in same institution laboratory to avoid any interlaboratory errors. If any extra information was needed apart from those available in master case sheets of individual patients, the patients or their attenders were communicated through telephone or letter and requested to provide the missing details. Data including name, age, sex, address, and contact details of patients were tabled in the master sheet. All statistical analysis was made with the help of IBM SPSS statistical software version 23. Percentage, ratio, mean, median, mode, and range were calculated. Microsoft office version 2016 was used for tables and appropriate charts wherever required.

RESULTS

One hundred and sixty-eight patients were registered as plasma cell neoplasm in the 5-year period. Among 168 patients, three had solitary plasmacytoma involving

mandible, clavicle, and lung, respectively, four patients had SMM, and six patients had MGUS. Data could not be analyzed for 13 patients due to various reasons, and hence they were excluded [Table 2]. There were 142 patients who met the revised IMWG^[14] criteria, as shown in Table 1. There were 83 (58.5%) male patients and 59 (41.5%) female patients with a M:F ratio of 1.4. The majority of the patients were in their sixth decade with a median age of 59 years (range 35–84 years) at the time of presentation. Five (3.5%) patients were below 40 years of age and the majority were between 50 and 60 years of age (41.5%), age-wise distribution is listed in Table 3. Fifteen patients (10.6%) were smokers and 28 patients (19.7%) were alcoholic.

Clinical Profile

The neurological compromise was present in 32 patients (22.5%). They had the various extents of paraparesis, paraplegia, quadriplegia, and uncontrolled bladder function depending on the site of cord compression with the majority of patients presenting as quadriplegia (22 patients). About 66.1% of patients ($n = 94$) had fatigue, which is defined in NCCN guidelines as cancer or its treatment-related distressing, persisting feeling of tiredness which is not proportional to the activity done and interferes with our daily living. Back pain was seen in 45.1% of patients with most of them having low backache and spine tenderness was present in 40.1% of patients. Significant weight loss with $\geq 10\%$ of their body weight was present in 38.2% of patients. Bony pain in any part of the body, including back pain, was present in 64.1% of patients. Pallor was present in 62.7% of patients, and 23 patients (16.2%) had an infection during the presentation with the most common site as lung. Fever was present in 19 patients, and 42 patients had pedal edema [Table 4].

Lab and Radiological Profile

One hundred and five patients (73.9%) had bone pathology, including lytic lesions and osteopenia, with lumbar vertebra being the most common site, followed by thoracic vertebra and pelvis. The percentage of involvement in each bone site is mentioned in Table 5. The most common method used to diagnose bone involvement was skeletal radiography (54%), followed by computed tomography (CT) scan (40%) and remaining cases were by positron emission tomography CT and magnetic resonance imaging scan. One hundred and twelve patients (78.8%) had anemia of all grade, with 47.8% (68 patients) had Hb < 10 g/dl as per IMWG end-organ damage definition. Seventy-eight patients (54.9%) had creatinine > 2 mg/dl, with 25 of them having acute kidney injury (AKI), and 50.7% of patients had uremia. The median creatinine clearance among patients with kidney involvement was 35 ml/min. Twenty-seven patients (19%) had hypercalcemia which is defined in IMWG as > 11 mg/dl and 13 among them had symptoms related to hypercalcemia, while

Table 1: IMWG revised diagnostic criteria

Revised International Myeloma Working Group diagnostic criteria for multiple myeloma and smoldering multiple myeloma	
Definition of multiple myeloma	
Clonal bone marrow plasma cells $\geq 10\%$ or biopsy-proven bony or extramedullary plasmacytoma* and any one or more of the following myeloma-defining events:	
<ul style="list-style-type: none"> ■ Evidence of end-organ damage that can be attributed to the underlying plasma cell proliferative disorder, specifically: <ul style="list-style-type: none"> • Hypercalcemia: serum calcium >0.25 mmol/L (>1 mg/dL) higher than the upper limit of normal or >2.75 mmol/L (>11 mg/dL) • Renal insufficiency: creatinine clearance <40 mL per min[†] or serum creatinine >177 μmol/L (>2 mg/dL) • Anemia: hemoglobin value of >20 g/L below the lower limit of normal, or a hemoglobin value <100 g/L • Bone lesions: one or more osteolytic lesions on skeletal radiography, CT, or PET-CT[‡] ■ Any one or more of the following biomarkers of malignancy: <ul style="list-style-type: none"> • Clonal bone marrow plasma cell percentage* $\geq 60\%$ • Involved:uninvolved serum free light chain ratio[§] ≥ 100 • >1 focal lesions on MRI studies[§] 	
Definition of smoldering multiple myeloma	
Both criteria must be met:	
<ul style="list-style-type: none"> ■ Serum monoclonal protein (IgG or IgA) ≥ 30 g/L or urinary monoclonal protein ≥ 500 mg per 24 hours and/or clonal bone marrow plasma cells 10 to 60% ■ Absence of myeloma defining events or amyloidosis 	
Definition of monoclonal gammopathy of undetermined significance	
All three criteria must be met:	
<ul style="list-style-type: none"> ■ Serum monoclonal protein <30 g/L ■ Bone marrow plasma cells $<10\%$ ■ Absence of myeloma defining events or amyloidosis (or Waldenström macroglobulinemia in the case of IgM MGUS) 	

PET-CT: ¹⁸F-fluorodeoxyglucose positron emission tomography with computed tomography.

* Clonality should be established by showing kappa/lambda-light-chain restriction on flow cytometry, immunohistochemistry, or immunofluorescence. Bone marrow plasma cell percentage should preferably be estimated from a core biopsy specimen; in case of a disparity between the aspirate and core biopsy, the highest value should be used.

† Measured or estimated by validated equations.

‡ If bone marrow has less than 10% clonal plasma cells, more than one bone lesion is required to distinguish from solitary plasmacytoma with minimal marrow involvement.

§ These values are based on the serum FreeLite assay (The Binding Site Group, Birmingham, UK).

The involved free light chain must be ≥ 100 mg/L.

§ Each focal lesion must be 5 mm or more in size.

Table 2: Distribution of plasma cell disorders

Diagnosis	Number (%) n=168	Male	Female
Solitary plasmacytoma	3 (1.8)	2	1
SMM	4 (2.4)	4	0
MGUS	6 (3.5)	4	2
MM	142 (84.5)	83	59
Missing data	13 (7.7)	7	6

SMM: Smoldering multiple myeloma, MM: Multiple myeloma, MGUS: Monoclonal gammopathy of undetermined significance

others were asymptomatic. Serum protein electrophoresis showed M band in 85% of patients and urine Bence Jones

protein (BJP) was positive in 61% of patients. Serum lactate dehydrogenase (LDH) was elevated in 42% of patients, and beta-2 microglobulin was elevated in 72% of patients. Platelets less than a lakh were present in 15 patients (10.5%), and erythrocyte sedimentation rate was high in 36.6% of patients as per the lab cutoff for males and females. M band is identified in 121 patients (85.2%) with serum protein electrophoresis and seven patients (4.9%) were picked up by immunofixation electrophoresis in serum or urine. Urine BJP was identified in 87 patients (61.3%), and elevated LDH was present in 59 patients (41.5%). Serum hypoalbuminemia (albumin <3.5 g/dl) was present in 41 patients (28.9%).

Patients were classified as per the International Staging System for myeloma, as shown in Table 6. Stage 3 was the most common presentation, and 88 patients (61.9%) presented in that stage, while 32 patients (22.6%) and 22 patients (15.5%) presented in stage 2 and stage 1, respectively.

Table 3: Age-wise distribution of MM

Age group	Number (%) n=142	Male (%) n=83	Female (%) n=59
Below 40	5 (3.5)	4	1
40–50	52 (36.6)	27	25
50–60	59 (41.5)	35	24
60–70	19 (13.4)	12	7
70–80	6 (4.2)	4	2
Above 80	1 (0.7)	0	1

Table 4: Clinical and Lab profile of MM

Symptom/sign	Number (%) total n=142	Lab profile	Number (%) total n=142
Fatigue	94 (66.1)	Lytic bone lesion	105 (73.9)
Neurological deficit	32 (22.5)	Creatinine >2 mg/dl	78 (54.9)
Back pain	64 (45.1)	Acute kidney injury	25 (17.6)
Spine tenderness	57 (40.1)	Uremia	72 (50.7)
Recent weight loss	54 (38.2)	Hypercalcemia	27 (19)
Bone pain	91 (64.1)	Anemia all grades	112 (78.8)
Pallor	89 (62.7)	Thrombocytopenia	15 (10.5)
Infection	23 (16.2)	Erythrocyte sedimentation rate elevation	52 (36.6)
Fever	19 (13.4)	M band in SPE	121 (85.2)
Edema	42 (29.5)	Urine BJP	87 (61.3)
		Elevated LDH	59 (41.5)
		Hypoalbuminemia	41 (28.9)
		$\beta 2M >3.5$ mg/L	102 (71.8)

LDH: Lactate dehydrogenase, BJP: Bence Jones protein, SPE: Serum protein electrophoresis

Table 5: Individual bone involvement in MM

Site of bone lesion	Number (%) total n=105
Lumbar	77 (73.3)
Thoracic	43 (40.9)
Pelvis	39 (37.4)
Cervical vertebra	9 (8.5)
Femur	28 (26.6)
Tibia	14 (13.3)
Humerus	19 (18.1)
Small bones	5 (4.7)

Table 6: International Staging System of MM

ISS stage (old)	Definition	Number (%) total n=142
1	$\beta 2M <3.5$ mg/L; ALB ≥ 3.5 g/dL	88 (61.9%)
2	$\beta 2M <3.5$ mg/L; ALB ≥ 3.5 g/dL; or $\beta 2M$ 3.5–5.5 mg/L	32 (22.6%)
3	$\beta 2M >5.5$ mg/L	22 (15.5%)

ALB: Albumin

Treatment

Most of the patients (67%) received cyclophosphamide, vincristine, and prednisolone (CVP) regimen, which includes CVP once in 3 weeks. About 28% of patients received CVP along with thalidomide while remaining patients received bortezomib based regimen. When patients received thalidomide, they were put on antiplatelet therapy to prevent thromboembolic events. Patients also received bone modifying agents along with chemotherapy such as zoledronic acid or ibandronate if the creatinine clearance is very low.

DISCUSSION

This study included a good number of patients over a period of 5 years and analyzed their clinical and laboratory profile. Fousad *et al.*^[15] in their prospective study which is from South India showed a slight male predominance with a M:F ratio of 1.3 and our study also showed a ratio of 1.4. The median age in our study was 59 years while it is a bit late in western study which reports as seventh decade^[16,17] and a little higher percent of patients younger than 40 years of age (3.5%) compared to 2%^[17] as described in western literature. Neurological involvement and spinal compression are rare in western population but it is very high in Indian scenario and especially in low socioeconomic group (22.5% in this analysis) where there is very late presentation with frank paraplegia and many patients with paraplegia do not recover with spinal decompression surgery or radiotherapy to the involved compression site. Although fatigue is less reported in large studies, our study found 66.1% of patients had fatigue probably due to late and advanced stage of presentation in our population. Most of the back pain and bone pain in any site is being managed symptomatically without working up for the cause in initial treatment centers. Renal involvement was more in our study group (54.9%) with higher percentage of AKI (17.6%), where it was the presenting feature as mentioned by Dr. Winearls in his study.^[18] Kidney involvement was due to either light chain nephropathy of hypercalcemia, with many of them not requiring biopsy since the light chain was elevated in many patients. There was around 9% lesser incidence of hypercalcemia (19%) compared to that reported by Kyle *et al.*^[16] and the reason is unknown, which may need a prospective study. Many patients with anemia (72%) had increased number of plasma cell percentage with a mean of $29\% \pm 8.7\%$, which could explain the cause of anemia in the majority of patients. The most common type of anemia was normocytic and normochromic. Weight loss was more by 10% compared to that reported by Kyle *et al.*^[16] MM patients are prone to many infections because of the impaired functioning of immunoglobulin and plasma cells. In our study, 16.2% of patients had an infection during the

initial workup among which pneumonia was found in many. Hypoalbuminemia was present in 28.9%, and increased beta-2 microglobulin was found in 71.8% of patients, both of which determine the stage of the disease in the International Staging System, and hence more patients had stage 3 at the time of presentation which leads to poor overall survival.

CONCLUSION

MM patients present in an advanced disease condition compared to the West. Increased awareness is needed for this increasing hematological malignancy among the general public and also to primary physicians so that early treatment can prolong the progression-free survival and probably the overall survival.

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ETHICAL APPROVAL

Obtained as per the institution protocol.

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Prevalence and Associated Factors of Anxiety Disorders among Cancer Patients Presented to Madras Medical College Chennai

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Abstract

Background: The prevalence of anxiety disorders and its associated factors among cancer patients in India and Tamil Nadu are less studied. As untreated anxiety can lead to significant morbidity, there is a strong need to address these issues with an evidence-based knowledge.

Objective: The objective of the study was to determine the prevalence and associated factors of anxiety disorders among cancer patients presented to Madras Medical College, Chennai, India.

Methodology: This cross-sectional study was carried out among cancer patients presented to Madras Medical College. Sample consisted of 200 cancer patients, out of this ten were excluded due to missing data, only 190 patients were included for analysis. We used Tylor scale for anxiety.

Results: The mean age of cancer patients was 56.11 years and median duration of cancer was 12.79 months. The prevalence of anxiety among cancer patients presented to Madras Medical College Chennai was 64%. The majority have moderate degree of anxiety (51%). We observed a significant association between anxiety and duration (time since diagnosis) of cancer and socioeconomic status of patients with $P = 0.00001$, 0.035 , respectively. There was no significant association between anxiety and marital status, age, sex, educational level, and cancer type.

Conclusions: The prevalence of anxiety disorder was high among cancer patients attending care at Madras Medical College Hospital. The majority were having moderate degree anxiety. There was significant association between anxiety and cancer duration and patient's socioeconomic status that needs to be addressed and requirement of a trained staffs or clinical psychologist's availability is warranted.

Key words: Anxiety disorders, Cancer patients, Madras Medical College Chennai

INTRODUCTION

Cancer is now considered as a chronic health condition. Cancer directly or indirectly influences physical, psychosocial well-being, and overall quality of life of these patients. For all individuals, the diagnosis of cancer is a life altering experience. Many psychiatric conditions may occur in cancer patients, commonly diagnosed are depression, anxiety,

adjustment disorders, stress related disorders, and other neurocognitive disorders. Sometimes that anxiety becomes a clinically debilitating condition in its own right. Hence, initial recognition and management of anxiety disorders are utmost important. Cancer care professionals should be aware of these mental health problems and should take a responsible step for its initial recognition and management.

Patients may experience fear, stress, loneliness, and uncertainty about the future, once cancer diagnosis is established. It is one of the most stressful events that a person may experience in his or her life. They may also experience various bouts of stress and anxiety during their treatment. Within 1 year of diagnosis around one-third of cancer patients will experience psychological morbidity such as major depression, generalized anxiety disorder.^[1]

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As per many studies, as high as 50% of cancer patients can develop anxiety. As per studies, anxiety may affect mood of patient, adherence to treatment, thereby the success of cancer treatment, and the quality of life.^[2]

Patients experience high level of anxiety soon after the diagnosis of cancer, but many of them adapt to this over time.^[3] As cancer progresses, anxiety may start to increase such that more extensive disease is often associated with a higher prevalence of anxiety in the majority of studies.^[4]

Cancer patients usually experience more than one type of anxiety; among this, generalized anxiety disorder is the most common. Most of these patients also experience panic disorders. Severe stress itself can also trigger a panic attack.^[5]

Variables such as age, gender, marital status, social class, and education variants have influence on anxiety in the general population but in cancer patients degree of susceptibility with these variants may become less important, because the stressor is more severe.^[6]

Apart from diagnosis of cancer, treatment of cancer with surgery, chemotherapy, radiotherapy also leads to anxiety. Association between anxiety and self-reported quality of life particularly impaired social functioning, fatigue, and physical impairment has been demonstrated in cancer care.^[7]

The aim of our research is to understand the prevalence and nature of anxiety and factors associated with anxiety.

Objectives

The objectives of the study were to determine the prevalence and associated factors of anxiety disorders among cancer patients presented to Madras Medical College Chennai.

1. To know the grade of anxiety disorders among cancer patients presented to Madras Medical College, Chennai
2. To know the association between the medical variables such as type of cancer and duration of cancer (time since the diagnosis has made) and anxiety
3. To know the association between the socio-demographic variables such as age, gender, level of education, and socioeconomic status of patient and anxiety.

METHODOLOGY

Study Design, Area, and Time

A cross-sectional study conducted at the Madras Medical College, Chennai, during the period from November 2, 2019, to March 2, 2020.

Study Population

Both adult male and female patients (over 20 years of age) undergoing chemotherapy were included in this study at Madras Medical College, Chennai, during the period from November 2, 2019, to March 2, 2020, was included in this study.

The patients' details were collected from the registration Department of Madras Medical College, Chennai.

Data Collection Tools and Analysis

Structured questionnaire was used to interviewing patients for data collection. It contains personal data such as sex, age, marital status, educational level, socioeconomic status, and some medical variables such as type of cancer and time since diagnosis.

The different types of questionnaires used were Hospital Anxiety and Depression Scale (HADS-A), HADS-D, GAI, and geriatric depression short form. HADS-A displayed sensitivity 91%, and specificity 70%. HADS-D displayed sensitivity 82% and specificity 83%. GAI displayed sensitivity 91% and specificity 65%.^[8]

We used Taylor scale for anxiety (modified HADS-A questionnaire). This scale contains 30 questions, with yes or no answers. And every yes answer means one degree in the scale. The scale divided into five categories as follow:

- 0–9 free from anxiety
- 10–12 mild anxiety
- 13–16 moderate anxiety
- 17–19 severe anxiety
- 20–30 very severe anxiety

Computer program (SPSS) version 19 was used for analysis of the data.

Ethical Consideration

This study was started after obtaining Ethical Committee approval from Madras Medical College, Chennai. Patients were clearly explained the objectives of the study. Patients were double ensured that all this information will be kept in a strictest confidence. Information will be used for benefit of the community only.

RESULTS

The overall response rate to the questionnaires was 95% (190 of 200 questionnaires), while ten were excluded from the analysis either due to missing data or below or above the required age. The mean age of patients in this study was 56.11, as shown in Table 1. The overall prevalence of the anxiety among cancer patients was 64 % [Figure 1].

We observed that the highest prevalence of the anxiety was among the age group between 20 and 40 years, it was 65.62%, and lowest prevalence was among the age group above 60 years, it was 63.33%, as shown in Table 1 and Figure 2.

In this study, of 190 patients, 105 (55.26%) were male, while the remaining were female 85 (44.74%) [Figure 3].

Considering the marital status of patients, 164 (86.32%) of them were married, 14 (7.37%) were single, 10 (5.26%) were widow, and only 2 (1.05%) of them were divorced [Figure 4].

Education level of patients in this study, most of them 126 (66.32%) were illiterate, while 46 (24.21%) of them were having primary school degree, and 15 (7.89%) of the patients were having secondary school degree, only 3 (1.58%) with university degree [Figure 5].

Considering the socioeconomic status, the majority of patients in this study were belong to poor class 102 (53.68%) and 86 (45.26%) of them were middle class while the remaining 2 (1.06%) were rich [Figure 6].

The most common tumor's type among the patients was: Breast cancer, lung cancer, head and neck cancer, and colon cancer, 52 (27.37%), 36 (18.95%), 30 (15.79%), and 30 (15.79%), respectively, while the lower types were: Non-Hodgkin Lymphoma, stomach cancer, and esophagus, 12 (6.32%), 18 (9.47%), and 12 (6.31%), respectively [Figure 7].

We observed that anxiety was highly prevalent among patients who had the cancer for around 19–24 months [Table 2] as it was 81.82%, and least prevalent among the patients who had the cancer for around 6 months, as it was 42.86%.

The mean duration of the cancers was 12.79 days.

We observed from Figure 8 that the most common form of the anxiety is the moderate form 51%, followed by the mild form of anxiety 26%, while the lowest is the very severe form of anxiety (8%).

Table 1: Presence of anxiety or not among patients receiving chemotherapy at Madras Medical College, Chennai, in relation to their age distribution data

Age	Anxiety number	Normal number	Anxiety percentage	Normal percentage	Total %
20–40 years	21	11	65.62	34.38	32 (16.84)
41–60 years	44	24	64.71	35.29	68 (35.79)
61–80 years	57	33	63.33	36.67	90 (47.37)
Total	122	68	64	36	190 (100)

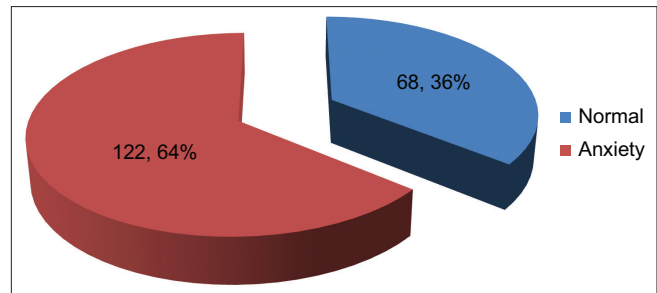


Figure 1: Distribution of anxiety in the patients attending chemotherapy at Madras Medical College Chennai

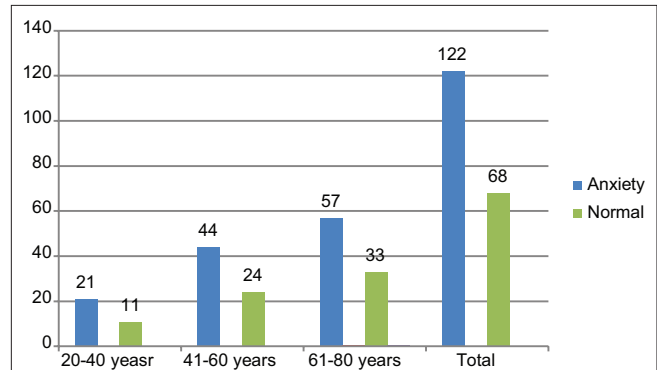


Figure 2: Presence of anxiety or not among patients receiving chemotherapy at Madras Medical College Chennai, in relation to their age distribution data

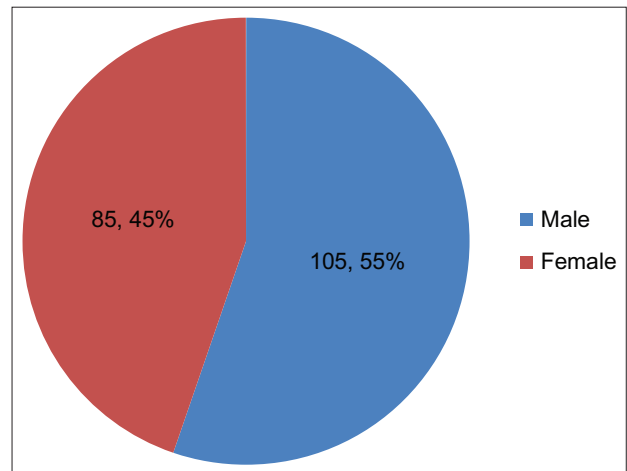


Figure 3: Distribution patients attending chemotherapy at Madras Medical College Chennai according to their sex

t-test is used to investigate the relationship between patients age and presence of anxiety or not [Table 3].

Another *t*-test was used to investigate relationship between duration of cancer and presence of anxiety or not. We got $P = 0.00001$ and result of *t*-test = 5.39, significant association, as shown in Table 4.

Chi-square test was used to investigate the association between categorical variables (such as marital status,

sex, education, socioeconomic status, and cancer type) in regarding to the presence of anxiety or not in these patients.

For marital status regarding to anxiety, the Chi-square test resulted in $P = 0.632$, as shown in Table 5. For patients sex regarding to anxiety the test resulted in $P = 0.432$, as shown in Table 6. For patients education regarding to anxiety ($P = 0.0669$), as shown in Table 7. For patients socioeconomic status regarding to anxiety the result of

test was $P = 0.035$, as shown in Table 8. Finally, for patients cancer type regarding to anxiety the result of test was $P = 0.166$ [Table 9].

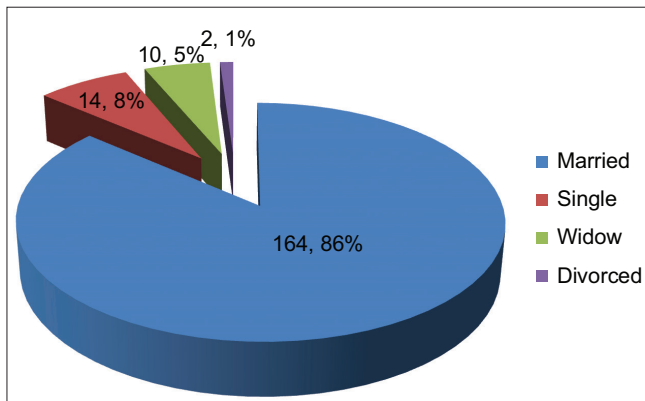


Figure 4: Distribution of marital status of patients attending chemotherapy at Madras Medical College Chennai

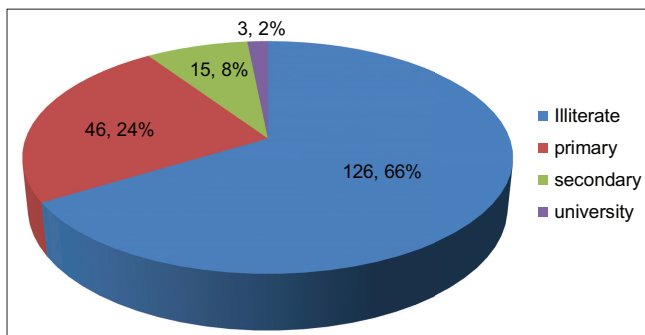


Figure 5: Distribution of educational level of patients attending chemotherapy at Madras Medical College Chennai

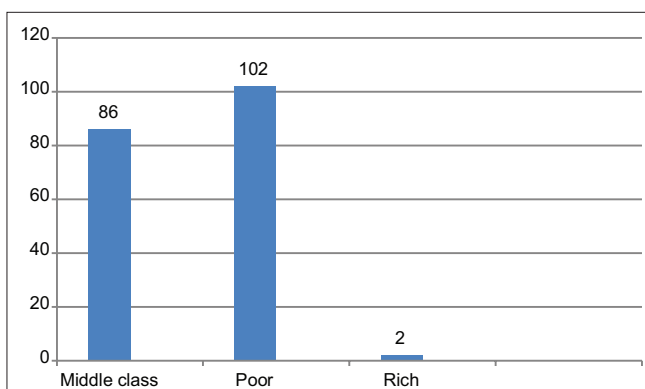


Figure 6: Distribution of patients attending chemotherapy at Madras medical college according to their socioeconomic status

Table 2: Distribution of cancer's duration in-relation to presence of anxiety or not among patients attending chemotherapy at Madras Medical College

Duration	Anxiety number	Anxiety percentage	Normal number	Normal percentage	Total %
6 months	15	42.86	20	57.14	35 (18.42)
7-12 months	32	72.73	12	27.27	44 (23.16)
13-18 months	39	58.21	28	41.79	67 (35.26)
19-24 months	36	81.82	8	18.18	44 (23.16)
Total	122	64	68	36	190 (100)

Table 3: Comparison of the using t-test, relationship between patients age and presence of anxiety or not

Anxiety	Mean±SD	t	df	P value
Age				
Anxiety	55.90±3.34	0.733	188	0.464
Normal	56.47±7.35			

We got a $t = 0.733$ and $P = 0.464$. Not significant.

Table 4: Comparison of the patients state of presence anxiety or not in-relation to their cancers duration using t-test

Anxiety	Mean±SD	t	Df	P value
Duration				
Anxiety	13.72±3.47	5.39	188	0.00001
Normal	11.18±2.34			

Table 5: Comparison of the patients state of anxiety or not in-relation to their marital status using Chi-square test

Variables	Anxiety	Normal	X ²	P value
Marital status				
Married	103 (62.8)	61 (37.2)	1.719	0.632
Single	10 (71.43)	4 (28.57)		
Widow	8 (80)	2 (20)		
Divorced	1 (50)	1 (50)		
Total	122 (64)	68 (36)		

Table 6: Comparison of the patients state of anxiety or not in-relation to their sex using Chi-square test

Variables	Anxiety	Normal	X ²	P value
Sex				
Male	70 (66.67)	35 (33.33)	0.6161	0.432
Female	52 (61.18)	33 (38.82)		
Total	122 (64)	68 (36)		

DISCUSSION

The study aimed to find out the prevalence of anxiety and its relation to medical variables, and sociodemographic variables.

We found a high prevalence of anxiety among cancer patients in this study, 64% patients with cancer had anxiety. This is in par with other studies, as shown (2007) in Iran study 57% of cancer patient have anxiety.^[9] Studies from developed countries usually showed a low prevalence of anxiety. Compared to developing countries, developed countries have low prevalence of mental health problems.

The most of the patients in our study are with moderate type anxiety (51%). Our results are in par with UK (2013) and Iran (2013) studies.^[10] This shows that cancer patients are more prone for mental health problems such as anxiety and since anxiety can affect quality of life of patient and treatment outcome this should be taken seriously.

We observed that there was no statistically significant relationship between anxiety and cancer type ($P = 0.166$) in our study. However, we find significant association between cancer duration ($P = 0.00001$) and anxiety. Those with cancer duration of 19–24 months are more prone for development of anxiety in our study. Our result was consistent with the Pakistani study (2010)

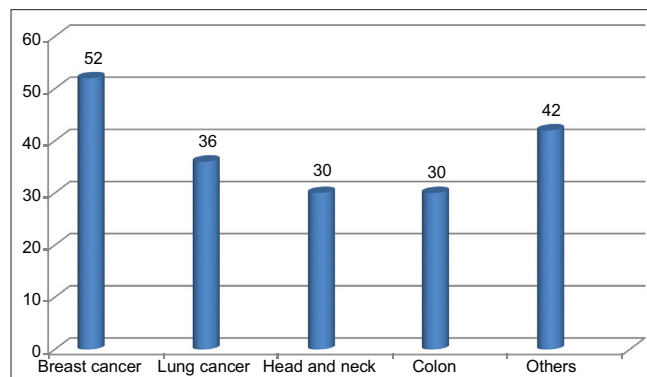


Figure 7: Distribution cancer type among patients attending chemotherapy at Madras Medical College Chennai

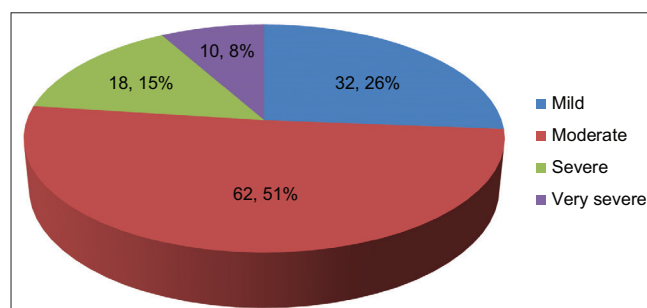


Figure 8: Distribution of anxiety grades in patients attending chemotherapy at at Madras medical college

showing a significant association of cancers duration on predisposition to anxiety.^[11]

There was no statistically significant relationship between anxiety and gender, and anxiety and the educational status in our study. Other studies also confirmed our results. We observed a statistically significant relationship between anxiety and socioeconomic status in our study, which was not consistent with most of the other studies. Most of the patients in our study belong to poor class, 102 of 190 patients, only two patients belong to rich class. So their financial stress, poor social support may lead to less hospital visits and less attention to mental health may be reason for these significant associations in our study.

In our study, we not observed significant association ($P = 0.464$) between anxiety and patients age. However,

Table 7: Comparison of the patients state of anxiety or not in-relation to their educational level using Chi-square test

Variables	Anxiety	Normal	X2	P value
Education				
Illiterate	88 (69.84)	38 (30.16)	7.1591	0.0669
Primary	22 (47.83)	24 (52.17)		
Secondary	10 (66.67)	5 (33.33)		
University	2 (66.67)	1 (33.33)		
Total	122 (64)	68(36)		

X2=Chi-square test

Table 8: Comparison of the patients state of anxiety or not in-relation to their socioeconomic status using Chi-square test

Variables	Anxiety	Normal	X2	P value
Socioeconomic status				
Poor	74 (72.55)	28 (27.45)	6.6816	0.035
Middle class	47 (54.65)	39 (45.35)		
Rich	1 (50)	1 (50)		
Total	122 (64)	68 (36)		

X2=Chi-square test

Table 9: Comparison of the patients state of anxiety or not in-relation to their cancer types using Chi-square test

Variables	Anxiety	Normal	X2	P value
Tumour type				
Breast	40 (76.92)	12 (23.08)	9.1340	0.166
Lung	20 (55.56)	16 (44.44)		
Head and neck	18 (60)	12 (40)		
Non-Hodgkin Lymphoma	8 (66.67)	4 (33.33)		
Colon	16 (53.33)	14 (46.67)		
Esophagus	10 (83.33)	2 (16.67)		
Stomach	10 (55.56)	8 (44.44)		
Total	122	68		

some of the previous studies showed a significant association between patients' age and anxiety. They observed that young patients having a higher likelihood of suffering from anxiety. In our study, also we observed a numerically high value for young patients regarding their anxiety, but it found to be not statistically significant. Older patients also experience same amount of anxiety in our study, contribution of other external factors may be reason for this variation compared to other studies in developed countries.

There was no statistically significant relationship between anxiety and marital status ($P = 0.632$) in our study. This is comparable to other studies.^[12]

Limitation

In this study, patients were interviewed using a questionnaire. Different studies tend to phrase questions differently which may influence the patient answers. We might unintentionally direct the patients to specific answers.

CONCLUSIONS

The prevalence of anxiety disorder among cancer patients presented to Madras Medical College was high.

1. Moderate grade of anxiety is observed in majority of patients
2. There was significant association between anxiety and duration of cancer
3. There was significant association between the anxiety and socioeconomic status of the patients
4. There was no significant association between the anxiety and marital status, sex, and educational level, age of patient and cancer type.

Recommendations

We like to suggest the following recommendations based on the result of our study:

1. We recommend that all cancer patients should undergo a complete and thorough baseline psychological screening as a part of standard cancer care
2. We recommend that all cancer patients should undergo periodic psychological assessment during treatment and follow-up period by psychiatric consultants
3. There is need for giving psychological awareness to cancer patients and their family to decrease the risk of anxiety development.

Questionnaire about the prevalence of anxiety disorders

Dear patient:

We doctors of Madras Medical College, medical oncology department are conducting a research on the prevalence

of anxiety disorders among cancer patients. Reconducting out the answers of these questions, and your sincere answers will be very useful for our research result. All these information will be kept strictly confidential and will be used for scientific purposes only and you have complete freedom in the non-acceptance to answer any questions.

Our sincere thanks and appreciation.....

*Personal Information:

Sex:..... Age:.....

Marital status:.....

Educational level:.....

Socioeconomic state:.....

Type of cancer:.....

Time since diagnosis:.....

N	Question	Yes	No
1	Is your sleep disturbed and not continued?		
2	Do you have great fears compared to your friends?		
3	Have you had periods in which you lost sleep over worry?		
4	Do you complain of severe diarrhea or constipation?		
5	Do you see yourself lacking self confidence?		
6	Do you have uncomfortable feelings in your stomach?		
7	Do you blush from yourself or from others?		
8	Do you feel anxious about work or money?		
9	Do you complain from nausea?		
10	Do you feel hungry almost all the time?		
11	Do you feel unhappy all the time and you wish to be as happy as others.		
12	Did you frequently notice hands shaking when you try to do something?		
13	Do you feel worried beyond reason over small things?		

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Gamma-Glutamyl Transferase an Oxidative Stress Marker in Metabolic Syndrome

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Abstract

Introduction: Metabolic syndrome refers to the Co-occurrence of a cluster of risk factors, including abdominal obesity, insulin resistance, atherogenic dyslipidemia, and hypertension. MetS, also labeled as “Insulin resistance syndrome,” “syndrome X,” “hypertriglyceridemic waist,” and “the deadly quartet,” is increasingly being recognized as an important cardiovascular risk factor. Metabolic syndrome is often characterized by oxidative stress, a condition where there is an imbalance result between the production and inactivation of reactive oxygen species. The present study is done to determine the association of γ -glutamyl transferase (GGT) in metabolic syndrome.

Materials and Methods: A total of 50 individuals were selected based on the criteria for metabolic syndrome as the study group and control group included 50 normal individuals free from any major illness. Both the control and study groups were age- and sex-matched. Blood samples were analyzed for GGT, fasting blood glucose, and lipid profile. GGT was estimated by the carboxy substrate method.

Statistical Analysis: Results were expressed as mean \pm S.D. and were statistically analyzed using SPSS software version 16 and Microsoft Excel. A significant increase in serum GGT levels was observed in the study group (85.19 ± 35.32) when compared to the control group (33.31 ± 10.92) and P value was statistically significant.

Conclusion: Our study showed elevated levels of GGT in individuals with metabolic syndrome which indicates that there is underlying oxidative stress in these individuals. The evaluation of GGT is simple and cost effective, it not only helps in early identification of high-risk individuals, but also provides an insight to plan lifestyle modification in ameliorating oxidative stress in metabolic syndrome.

Key words: Fatty liver, Gamma-glutamyl transferase, Lipid profile, Metabolic syndrome, Oxidative stress

INTRODUCTION

Metabolic syndrome, also known as syndrome X, is defined by the WHO as a pathological condition characterized by abdominal obesity, insulin resistance, hypertension and dyslipidemia.^[1]

According to National Cholesterol Education Program (NCEP) ATP3 2005:

Presence of any three or more of the following is needed for the diagnosis

1. Blood glucose > 5.6 mmol/L (100 mg/dl) or drug treatment for elevated blood glucose
2. High-density lipoprotein (HDL) cholesterol < 1.0 mmol/L (40 mg/dl) in men, < 1.3 mmol/L (50 mg/dl) in women, or drug treatment for low HDL-C
3. Blood triglycerides > 1.7 mmol/L (150 mg/dl) or drug treatment for elevated triglycerides
4. Waist > 102 cm (men) or > 88 cm (women)
5. Blood pressure $> 130/85$ mmHg or drug treatment for hypertension.

It is estimated that around 20–25% of the world's adult population have metabolic syndrome. In other words, over a billion people in the world are now affected by metabolic syndrome. With the metabolic syndrome driving the twin global epidemics of type 2 diabetes and cardiovascular diseases, there is always a felt need to diagnose those

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individuals with metabolic syndrome early so that lifestyle modification and treatment may prevent the development of complications.

Recently, epidemiology studies have shown that gamma-glutamyltransferase (GGT) is involved in pathophysiological processes such as oxidative stress and lipid peroxidation which are important to the pathogenesis and development of metabolic syndrome.^[2]

GGT, a marker of alcohol consumption and liver disease, has been strongly associated with obesity-related outcomes including metabolic syndrome, diabetes, hypertension, dyslipidemia, cardiovascular diseases and cancer.^[3]

GGT is the enzyme found in the liver, kidney, lungs, pancreas and prostate. GGT catalyzes the transfer of γ -glutamyl group from glutathione (GSH) to another peptide or amino acids in γ glutamyl cycle. GGT is concerned with the metabolism of GSH which is a potent intracellular antioxidant. GGT also has a critical role in cysteine metabolism and is linked to insulin resistance as well.

In view of the above facts, the present study is done to determine the association of GGT as a oxidative stress marker in individuals with metabolic syndrome.

MATERIALS AND METHODS

The study was conducted at the Department of Biochemistry, Thanjavur medical college hospital, after getting approval from the ethical committee. Written informed consent was obtained from the participants.

A total of 50 individuals diagnosed as metabolic syndrome based on the NCEP criteria were chosen as study group and control group included 50 normal individuals free from any major illness. Both the control and study groups were age- and sex-matched. Both the groups were analyzed for GGT, fasting blood glucose and lipid profile which included total cholesterol, triglycerides, low-density lipoprotein (LDL), HDL and Very low density lipoprotein (VLDL).

Exclusion Criteria

Patients with diabetes mellitus, hypertension, renal diseases, hepatitis and alcoholism were excluded from the study.

Sample Collection

Under strict aseptic precautions, 5 ml of fasting venous blood were collected from each subjects. The vacutainers containing the blood samples were kept at room temperature for $\frac{1}{2}$ h, allowed to clot, and then centrifuged at 2000 g for 15 min for a clear separation of the serum.

Standing body height and body weight were measured. The waist circumference was measured in a horizontal plane midway between the inferior margin of the ribs and the superior border of the iliac crest. Body mass index (BMI) (kg/m^2) was calculated by dividing weight (in kilograms) by the square of height (in meters).

Estimation of GGT

Methodology

Carboxy substrate method.

Principle

GGT catalyzes the transfer of amino group between L- γ -Glutamyl-3-carboxy-4 nitro anilide and glycylglycine to form L- γ -glutamylglycylglycine and 5-amino-2-nitrobenzoate. The rate of formation of 5-amino-2-nitrobenzoate is measured as an increase in absorbance which is proportional to the GGT activity in the sample.

Normal reference ranges of GGT 11–50 U/L for men and 7–32 U/L for women.

Estimation of Blood Glucose

Fasting blood glucose was estimated by glucose oxidase-peroxidase enzymatic endpoint method.

Estimation of Lipid Profile

In fasting blood samples, serum total cholesterol and triglycerides are estimated by standard enzymatic procedures and HDL cholesterol by direct assay method.

- LDL is calculated by Friedewald's formula
- $\text{LDL} - c = \text{Total cholesterol} - (\text{HDL} + \text{VLDL})$
- $\text{VLDL} = \text{Triglycerides}/5$.

Statistical Analysis

Results were expressed as mean \pm S.D. and were statistically analyzed using SPSS software version 16 and Microsoft Excel. Student's *t*-test was used to analyze the difference between the study and the control groups. The relationship between the variables was evaluated using Karl Pearson's correlation coefficient. $P < 0.05$ is considered to be statistically significant.

RESULTS

Baseline characters, namely, the anthropometric measurements, BMI, the biochemical data and results of GGT, fasting blood glucose, and lipid profile, are shown in Table 1

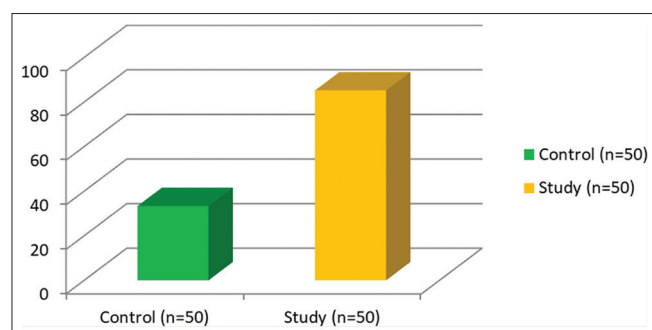
Table 2 and Figure 1 show Student's *t*-test analysis of GGT levels between the control and study group.

Table 2 shows that the mean serum GGT levels in the study group are 85.19 ± 35.52 , which is higher than the

Table 1: Descriptive statistics

Parameters	Control (n=50)				Study (n=50)			
	Min.	Max.	Mean	S.D	Min.	Max.	Mean	S.D
Age	25	50	35.58	6.899	27	50	39.44	6.828
HT	1.45	1.68	1.5520	.05421	1.46	1.65	1.5528	.05280
WT	38	68	55.00	6.587	65	89	77.44	6.600
BMI	18.02	28.30	22.83	2.55	29.9	38.46	32.15	1.70
WC	85.2	97.6	90.6	6.7	102.4	107.2	105.6	9.8
GGT	11.93	56.78	33.31	10.92	31.19	189.40	85.19	35.52
FBG	64	117	88.14	13.339	69	120	91.10	13.715
T.CHO	127	200	167.60	17.607	142	298	220.78	37.335
TGL	65	170	124.64	22.89	156	447	266.96	74.056
HDL	24	66	44.66	9.962	26	44	37.0	4.876
LDL	46.00	135.00	96.16	23.59	66.60	242.00	131.24	42.35
VLDL	13.00	47.00	25.40	5.536	31.20	89.40	53.39	14.81

WC: Waist circumference, BMI: Body mass index, GGT: Gamma-glutamyltransferase, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoprotein, FBG: Fasting blood glucose, TGL: Triglycerides

**Figure 1: Mean gamma-glutamyltransferase levels between the study and the control group**

control group mean 33.31 ± 10.92 which is statistically significant.

Table 3 shows Student *t*-test analysis of lipid profile parameters between control and study group.

Table 4 shows student's *t*-test analysis of BMI levels between control and study group.

Table 4 shows that the mean serum BMI levels in the study group are 32.15 ± 1.70 which is higher than the control group mean 22.83 ± 2.55 which is statistically significant.

Table 5 shows Pearsons correlation between GGT and other study parameters. A positive correlation is observed between GGT and BMI which are statistically significant.

DISCUSSION

Obesity is a disorder of body weight regulatory mechanisms characterized by the accumulation of excess body fat. Visceral adipose tissue releases bioactive substances such as non-esterified fatty acids, cytokines and proinflammatory substances which are responsible for inflammation, dyslipidemia, and atherogenesis. The prevalence of obesity

Table 2: Student *t*-test analysis of GGT between control and study group

S. NO	GGT	Mean \pm S.D	Statistical inference
1	Control (n=50)	33.31 \pm 10.92	T=-9.869
2	Study (n=50)	85.19 \pm 35.52	0.0001<0.05 Significant

GGT: Gamma-glutamyltransferase

Table 3: Student *t*-test analysis of lipid profile parameters between control and study group

Sample	Mean	S.D	Statistical inference
T.CHOL			
Control (n=50)	167.60	17.60	T=-9.110
Study (n=50)	220.78	37.33	0.0001 <0.05 Significant
TGL			
Control (n=50)	124.64	22.89	T=-12.983
Study (n=50)	266.96	74.05	0.0001 <0.05 Significant
HDL			
Control (n=50)	44.66	9.96	T=4.871
Study (n=50)	37.02	4.87	0.0001<0.05 Significant
LDL			
Control (n=50)	96.16	23.59	T=-5.117
Study (n=50)	131.24	42.35	0.0001<0.05 Significant
VLDL			
Control (n=50)	25.40	5.53	T=-12.518
Study (n=50)	53.39	14.81	0.0001 <0.05 Significant

HDL: High density lipoprotein, LDL: Low density lipoprotein, VLDL: Very low density lipoprotein, TGL: Triglycerides

and metabolic syndrome is rapidly increasing in India and other South Asian countries.

Obesity often predisposes to insulin resistance, where there is the decreased response of the peripheral tissues to the normal circulating concentration of insulin. The

condition that exists between insulin resistance and the development of overt type 2 diabetes mellitus is called metabolic syndrome. The intracellular redox imbalance, along with persistent chronic inflammatory conditions, results in metabolic syndrome^[4] [Figure 2].

Oxidative stress arises as a result of an imbalance in the oxidative and antioxidative status. Oxidant molecules are produced endogenously and they are also taken exogenously from the outer environment. Major sources of reactive oxygen species are from electron transport chain and from a range of oxidase enzymes, including xanthine oxidase, glycolate oxidase and monoamine oxidases.^[5]

In our present study, we measured serum GGT in individuals with metabolic syndrome and compared

the same with healthy controls. The mean GGT in the study group was significantly high (85.19 ± 35.32) when compared to the control group (33.31 ± 10.92) and *P* value was statistically significant. The elevated levels of GGT in the study group suggest that these individuals may be in the early stages of metabolic syndrome where there is oxidative stress, but the defense mechanism is active so that oxidative damage is not detected. This study also correlates with the previous studies done by Kasapoglu *et al.*

A positive correlation is observed between GGT and BMI which are statistically significant, which correlates with the studies done by Blaj *et al.*^[6] Similarly, Rantala *et al.* investigated the relationship between GGT and MS and revealed a highly significant relationship between GGT and the components of the metabolic syndrome.^[7]

Table 4: Student *t*-test analysis of BMI between control and study group

S. No.	BMI	Mean±S.D	Statistical inference
1	Control (n=50)	22.83±2.55	T=-21.421
2	Study (n=50)	32.15±1.70	0.0001<0.05 Significant

BMI: Body mass index

Table 5: Pearsons correlation between GGT and other study parameters

GGT	Correlation value	Statistical inference
Age	0.015	<i>P</i> >0.05 Not Significant
Height	-0.034	<i>P</i> >0.05 not significant
Weight	0.120	<i>P</i> >0.05 not significant
BMI	-0.162(*)	<i>P</i> <0.05 significant
FBG	0.033	<i>P</i> >0.05 not significant
T.CHOL	-0.107	<i>P</i> >0.05 not significant
TGL	-0.161	<i>P</i> >0.05 not significant
HDL	-0.220	<i>P</i> >0.05 not significant
LDL	-0.032	<i>P</i> >0.05 not significant

BMI: Body mass index, HDL: High density lipoprotein, LDL: Low density lipoprotein, TGL: Triglycerides, FBG: Fasting blood glucose, GGT: Gamma-glutamyltransferase

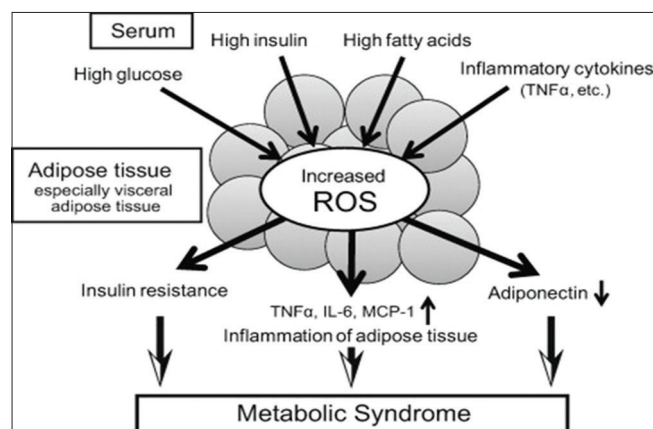


Figure 2: Oxidative stress in metabolic syndrome

GGT is an extracellular membrane bound glycoprotein that contributes to extracellular catabolism of GSH. GGT is a heterodimeric glycoprotein that is typically anchored to the cell membrane by an amino terminal hydrophobic region. The enzyme may be considered as a type II transmembrane protein because it has a large carboxyl-terminal ectodomain, which exhibits the catalytic activity, and a single transmembrane domain consisting of about 20 amino acid residues that include an apparent signal peptide.^[8]

Although the enzyme is produced in various tissues such as liver, kidney, lungs, pancreas and prostate, most of the GGT in serum is derived from the liver. GGT has a central role in the maintenance of intracellular antioxidant defenses through extracellular catabolism of GSH the principal thiol antioxidant in humans. By this action, it enhances the availability of cysteine to promote intracellular GSH resynthesis, thereby counteracting oxidant stress.^[9]

Increased expression of GGT can be a response to oxidative stress, facilitating increased transport of GSH precursors into cells. Excess GGT leaked into the serum may be a result of normal cell turnover, due to oxidative stress, proteolysis, increased GGT synthesis, and endothelial cell damage.^[10] Thus, increased serum concentrations of GGT could identify people with a low but persistent increase of oxidative and other cellular stresses.^[11]

Non-alcoholic fatty liver disease, a condition seen in metabolic syndrome, is one of the common cause for chronic liver diseases worldwide. Excess deposition of fat in the liver causes hepatocellular damage which stimulates increased synthesis of GGT.^[12] Secondary to low-grade inflammation triggered by hepatic steatosis GGT level increases, thereby impairing insulin signaling both in the liver and systemically.^[13-16] In the view of above facts, GGT

has a potential role as a marker of oxidative stress and subclinical inflammation in metabolic syndrome.

CONCLUSION

Our study confirms that GGT is a sensitive oxidative stress marker and a mediator of low-grade systemic inflammation associated with metabolic syndrome. The test for GGT is readily available, easy to perform and cost effective and can be frequently used in clinical practice. Early diagnosis promotes lifestyle modification and treatment interventions, hence, can alleviate the development of complications in metabolic syndrome.

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Efficacy of 2 mm Three-dimensional Locking Titanium Miniplates in Management of Anterior Mandibular Fractures

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Abstract

Purpose: The current study aimed to evaluate the efficacy of 2 mm three-dimensional (3D) titanium locking miniplates in the management of anterior mandibular fractures.

Materials and Methods: Twenty patients who fulfilled the inclusion criteria with displaced and undisplaced anterior mandibular fractures, open reduction, and internal fixation were done under general anesthesia using 2 mm 3D titanium locking miniplates. Patients were further evaluated for the stability of fracture segments and measured the bone density at 1st, 6th, and 12th week on a radiograph using Digora software. In addition, post-operative complications such as wound dehiscence, infection, plate/screw fracture, and screw loosening were also assessed. The results were then subjected to statistical analysis.

Results: The current study showed first, a satisfactory occlusion in all 20 patients. Second, satisfactory healing of the fracture site was observed on a radiograph at 1st, 6th, and 12th weeks. The results were statistically significant at $P < 0.05$. However, 1 (5%) case of infection was noted and none of the cases had any wound dehiscence, plate/screw fracture, or screw loosening.

Conclusion: The use of 2 mm 3D titanium locking plate has proven to be effective in the management of anterior mandibular fractures.

Key words: Mandibular anterior fracture, Miniplate, Titanium three-dimensional locking plate

INTRODUCTION

The individuality of a man is represented by his face, and his identity is the key to his personality and interaction. Facial injury is devastating psychological and is accompanied by functional disturbances. Mandible is the strongest and largest facial bone. By virtue of its position on the face and its prominence and peculiar curved pattern and prominent contour forming the so-called jawline makes it very susceptible to trauma. From the time of Hippocrates, there have been many different techniques

for treating mandibular fractures, and repositioning and immobilization of the bony fragments have been the prime principle.^[1] Earlier, the jaw was immobilized for a prolonged period of time and the patient had to maintain a liquid diet.^[2] However, the changing society and reluctance of many patients to wear IMF for a prolonged period have forced surgeons to change the treatment modality from closed reduction to open reduction. Open reduction with internal fixation (ORIF) includes many techniques starting from wire osteosynthesis, Luhr's vitallium compression plates, Schmoker and Spiessl's dynamic compression plate (DCP), eccentric DCP reconstruction plate, monocortical non-compression mini plates, lag screw, and dimensional (three-dimensional [3D]) plates.^[3]

Mandibular fractures are divided anatomically into different categories. Among them, the angle is the most common 26.7% followed by condylar and subcondylar 26% then by symphyseal/parasymphyseal.^[4] However, two modalities

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of treatment of mandibular fracture have been evolved; one is rigid stabilization, given by Spiessl^[5] and the other semi-rigid fixation suggested by Champy *et al.*^[6,7] Ideal location for plate fixation is at the region of maximum tension, that is, superior border, but due to presence of tooth root and inferior alveolar bundle, this is not possible, thus the plate is fixed at the lower border, but this fails to control the superior border fanning so tension band is required for better stability.^[8] Moreover, the conventional miniplate techniques requires maxillomandibular fixation for a short period of time and fail to provide 3D stability.^[9] These limitations are overcome by the introduction of 3D plates.^[10] The design of the 3-D plates mainly consists of two linear plates connected by reinforcing vertical struts, 3D plates; therefore, it provides greater resistance against the gap opening at either the superior or inferior border. In addition, it uses lesser foreign materials, reduces the operation time and overall cost of treatment.^[11] Very few studies have reported previous clinical experiences with these plates in mandibular fractures. The present study aimed to evaluate the efficacy of 2 mm 3D titanium locking miniplates in the management of anterior mandibular fractures.

MATERIALS AND METHODS

A prospective clinical study was conducted on 20 consecutive patients who reported to department of oral and maxillofacial surgery with anterior mandibular fractures. The study was approved by the ethical committee and informed consent was obtained from all patients who agreed to participate in the study. All 20 patients underwent ORIF under general anesthesia using 2 mm 3D titanium locking miniplates and 2 mm × 10 mm length monocortical locking screws.

Inclusion and Exclusion Criteria

The patients for this study were selected on the basis of the inclusion and exclusion criteria. Inclusion criteria were as follows: Patients within the age group of 20–50 years, patients with a displaced or undisplaced anterior mandibular fracture that needed an open reduction and internal fixation, and patients under the Anesthesiologists-1 category. The exclusion criteria were those patients with comminuted fractures, patients with pathological fractures and bone pathology, patients with an immune-compromised state, and fractures associated with infection.

Pre-operative Assessment

The pre-operative assessment included detailed case history to evaluate age, sex, type of fracture, etiology, pre-surgical occlusion, which was categorized as either deranged or not deranged, associated fracture of the mandible and whether

the fracture was displaced or undisplaced. Subsequently, patients were subjected to radiographic investigation, which included extraoral radiography (orthopantomograph, posterior anterior view of mandible) and intraoral radiograph (occlusal view of mandible) followed by routine complete blood investigations.

Study Variables

In the present study, patients were evaluated first for the stability of fracture segments after fixation. Second, for any post-operative complications such as wound dehiscence, infection plate/screw fracture, and screw loosening. Third, bone densities were measured on a radiograph at 1st, 6th and 12th weeks postoperatively using Digra software.

Surgical Technique

After intubation of the patient, neosporin ointment was applied to both the eyes and sterile gauze pads were placed over the eyes followed by the placement of the throat pack. The patient was scrubbed with 2% cetrimide hydrochloride, painted with 5% povidone-iodine, and draped according to the standard protocol. Irrigation of the oral cavity was done with 0.2% chlorhexidine gluconate solution. The surgical approach for the fractures was through the intraoral vestibular incision in thirteen patients and in seven patients through the extension of existing laceration. Infiltration was done using 2% lignocaine hydrochloride with 1:80,000 adrenaline. The lip was then retracted and the marking of incision was made using Bonny's Blue Ink. A curvilinear incision was made perpendicular to the mucosal surface. Care was taken to place the incision out into the lip, leaving at least 1 cm of attached gingiva. The mentalis muscle was identified and incised perpendicular to bone, leaving a flap of muscle attached to bone for closure. Dissection was carried out subperiosteally and the mental neurovascular bundle was identified approximately midway between the alveolar ridge and inferior border, below the second premolar or slightly anterior. The fracture site was then identified and reduced. Intra-oral occlusion was achieved with intermaxillary fixation. The bone plates were adapted and held with a plate holding forceps to make bur holes for the screws. The fractured segments were then fixed with 2 mm 3D titanium locking miniplates and 2 mm × 10 mm length monocortical screws [Figure 1]. The bur hole was made using a drill bit of 1.5 mm × 10 mm. Care was taken to avoid damage to the roots of the teeth and the mental nerve. The other associated fractures of the mandible were treated as per routine. Guiding elastics were placed as per treatment protocol. Once adequate fixation was achieved, the area was irrigated with povidone-iodine and normal saline. Intra-operative stability of fracture segments after fixation was checked by clinical manipulation in three directions. No further intervention

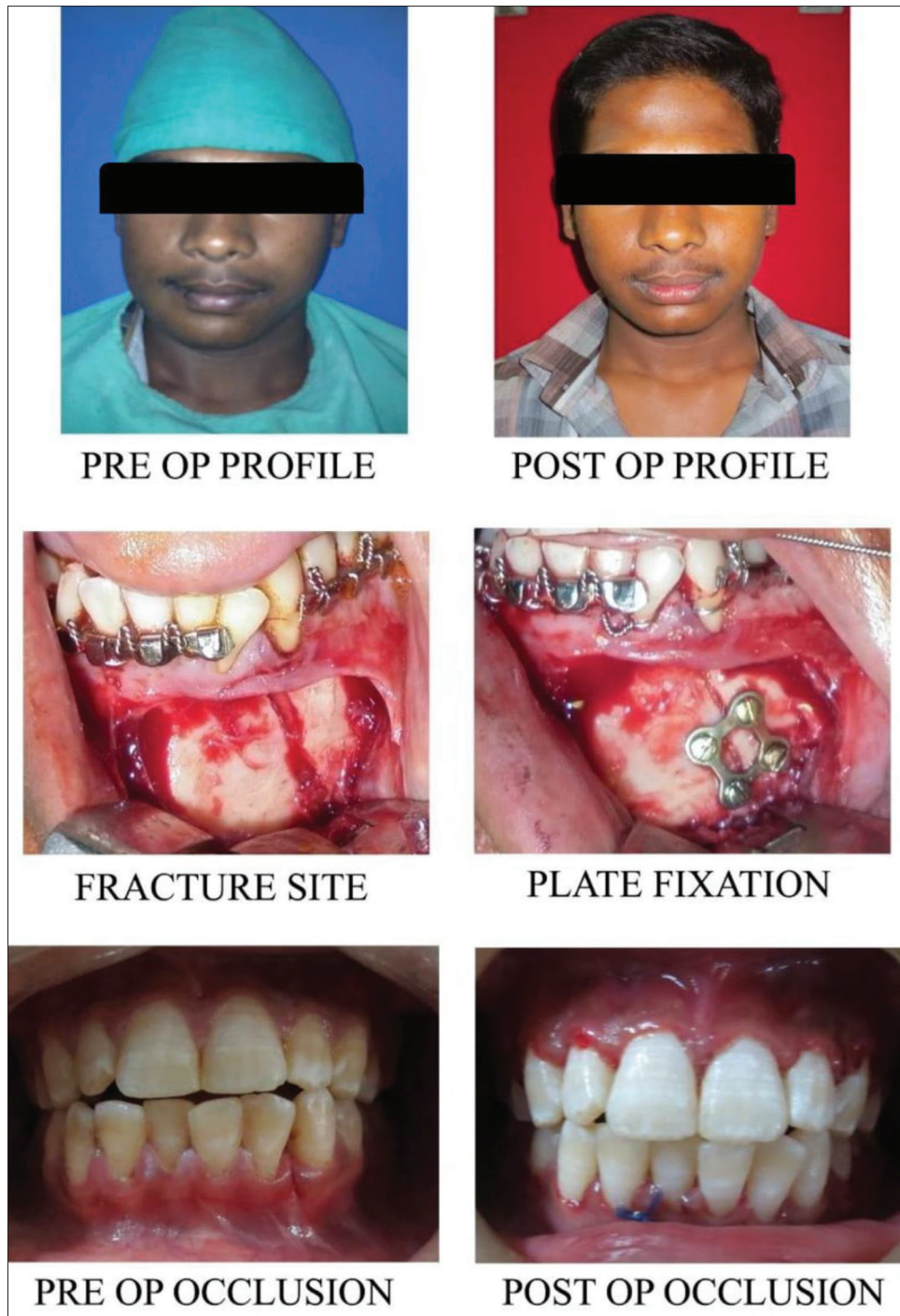


Figure 1: The placement of the three-dimensional locking plate in the treatment of anterior mandibular fracture by open reduction and internal fixation

was required, as adequate stability was obtained. After achieving adequate hemostasis, the wound was closed in two layers with 3-0 vicryl. Then, intermaxillary fixation was released. Fractures with minor occlusion discrepancies were managed by intermaxillary fixation for 2 weeks. The adhesive bandage was applied to the chin to support the mentalis muscle and prevent its drooping. Extubation was done uneventfully and the throat pack removed.

All patients were kept postoperatively on intravenous antibiotics for 5 days and analgesics for 3 days. In addition, 0.2% chlorhexidine gluconate mouthwash was prescribed for 30 days to maintain oral hygiene.

Statistical Analysis

Comparison of presurgical and post-surgical occlusion was done using the Chi-square test. Comparison of the

radiographic healing at 1 week, 6 weeks, and 12 weeks was analyzed using students *t*-test.

RESULTS

Demographically, of 20 patients, 13 were between 21 and 30 years, six between 31 and 40 years, and one between 41 and 50 years. Patients older than 50 years were excluded from the current study as there could be comorbid systemic conditions associated and, moreover, there could be chances of nonunion. In the current study, of 20 patients, 1 was female (05%) and 19 were male (95%). The distribution of the number of patients according to the etiology for the anterior mandibular fractures was four patients with road traffic accidents (20%) followed by five patients with assault (25%) and 11 patients with falls (55%). Fracture distribution consisted of six symphysis fractures (30%), nine parasymphysis fractures (45%), and five parasymphysis fractures associated with subcondylar fracture (25%). On clinical examination, 4(20%) patients had undisplaced fractures and 16 (80%) patients had displaced fractures with resultant derangement in occlusion [Table 1].

The reduction was adequate in all 20 patients. The two subcondylar fractures of the mandible were managed by ORIF with a 3D trapezoidal locking plate and three subcondylar fractures of the mandible were managed by inter-maxillary fixation for 4 weeks. All 20 patients were evaluated for post-operative occlusion. Postoperatively, the release of inter maxillary fixation and occlusion was satisfactory in all 20 patients. Table 2 depicts the comparison of pre- and post-surgical occlusion in all 20 subjects. Pre-surgical and post-surgical occlusion was compared statistically using Chi-square test; the Chi-square value was

40 (>5.99 for $P = 0.05$). The results showed satisfactory post-operative occlusion in all 20 patients (100%) and the results were statistically significant [Table 2].

The radiographic bone density at 1st, 6th, and 12th-week postoperatively was calculated using Digora software. Digora calculated the density of the region of the interest, that is, the chosen area along the fracture line. The respective pixel values obtained with the Digora software were compared statistically using student *t*-test [Table 3]. Comparison of preoperative and postoperative radiographic healing at 1st, 6th and 12th weeks. The results showed that the radiographic bone density between the pre-operative and 1st week was 1.81. This was not statistically significant. However, the comparison of pre-operative radiographic bone density at 6th and 12th weeks postoperatively showed 8.91, 10.54, respectively. These results were statistically significant [Figure 2].

Table 4 demonstrates the distribution of patients according to the post-operative complications. The results suggested that postoperatively only 1 (5%) patient presented with infection. None of the cases had wound dehiscence, plate/screw fracture, or screw loosening [Table 4].

DISCUSSION

Over the years, the methods to treat mandibular fractures have undergone many refinements. The strategic position of the mandible on the facial skeleton and its unique role in mastication, deglutition, phonation, and esthetics compels the clinician to give immediate attention whenever it is fractured. The primary goal of treatment of mandibular fractures is to achieve satisfactory occlusion.

Table 1: The pre-operative study variables

1	25	M	Right parasymphysis fracture	Deranged	No	Displaced
2	24	M	Left parasymphysis fracture	Deranged	No	Displaced
3	35	F	Left parasymphysis and right low subcondylar fracture	Deranged	Yes	Displaced
4	40	M	Right parasymphysis and left subcondylar fracture	Deranged	Yes	Displaced
5	24	M	Left parasymphysis fracture	Normal	No	Undisplaced
6	20	M	Left parasymphysis and right subcondylar fracture	Deranged	Yes	Displaced
7	21	M	Left parasymphysis and right subcondylar fracture	Deranged	Yes	Displaced
8	23	M	Right parasymphysis and left subcondylar fracture	Deranged	Yes	Displaced
9	23	M	Symphysis fracture	Normal	No	Undisplaced
10	50	M	Right parasymphysis fracture	Deranged	No	Displaced
11	30	M	Left parasymphysis fracture	Deranged	No	Displaced
12	32	M	Symphysis fracture	Deranged	No	Displaced
13	27	M	Symphysis fracture	Deranged	No	Displaced
14	22	M	Symphysis fracture	Deranged	No	Displaced
15	38	M	Left parasymphysis fracture	Deranged	No	Displaced
16	35	M	Right parasymphysis fracture	Deranged	No	Displaced
17	27	M	Symphysis fracture	Deranged	No	Displaced
18	22	M	Left parasymphysis fracture	Deranged	No	Displaced
19	29	M	Symphysis fracture	Normal	No	Undisplaced
20	35	M	Right parasymphysis fracture	Normal	No	Undisplaced

Table 2: The distribution of number of patients according to the pre-surgical and post-surgical occlusion

Occlusion	Pre-surgical		Post-surgical	
	Number	Percentage	Number	Percentage
Deranged	16	80	00	00
Not deranged	04	20	00	00
Satisfactory	00	00	20	100

Chi-square value 40.00 (>5.99 for $P=0.05$), there is association between occlusion and pre-surgical and post-surgical

Table 3: The comparison of radiographic healing preoperatively and in 1st, 6th, and 12th weeks postoperatively

Between pre-operative and 1 st week	1.81(NS)
Between pre-operative and 6 th week	8.91(S)
Between pre-operative and 12 th week	10.54(S)

*S-Denotes statistically significant, NS: Denotes statistically not significant

Table 4: The distribution of patients according to the post-operative complications

Post operative complication	Number	Percentage	Number	Percentage
Wound dehiscence	20	100	00	00
Infection	19	95	01	05
Plate/screw fracture	20	100	00	00
Screw loosening	20	100	00	00

The current study aimed to evaluate the efficacy of 2 mm 3D titanium locking miniplates in the management of anterior mandibular fracture. For this purpose, a total of 20 patients with symphysis and parasymphysis fractures of the mandibles who fulfilled the inclusion and exclusion criteria were chosen for the study. Of the 20 patients, six patients had symphysis fractures, nine patients had parasymphysis fractures, and the remaining five patients had parasymphysis fractures associated with subcondylar fractures.

Conventional indirect wiring techniques for closed reduction achieve satisfactory occlusion with good bone healing, but may not reestablish the anatomical reduction. However, in the past, different techniques of (ORIF) have shown varying success rates. Michelet *et al.* in 1973 developed small plates and monocortical screws to fix mandibular fractures.^[12] Furthermore, Champy's technique of placing plates along ideal lines of osteosynthesis using intraoral incisions, mini plates, and monocortical screws is well known. Although this technique avoids the placement of cutaneous incisions, reduces the operative time, and nerve injury, the lack of absolute rigidity with the smaller plates and the requirement for patient compliance with a liquid to soft diet during healing is a major limitation of this technique.^[13] In contrast, the limitation of rigid and semi-rigid fixation led to the development of 3D plates.

The design of the 3D plate is basically quadrangular, geometrically consisting of two horizontal plates interconnected as vertical struts by which provide stability in all three dimensions. The strut plates provide greater resistance against gap opening at the inferior border with biting forces compared with a single plate at the external oblique ridge or superolateral border. The 3D plate provides three-dimensional stability and carries a low infection rate.^[14] The stability achieved by the geometric shape of the 3-D plates, it is better than that of standard miniplates. In the current study, 18 patients were treated with ORIF using a four-holed 3D plate and two patients with oblique fractures with a six-holed 3D plate. The results showed satisfactory post-surgical occlusion in all 20 patients (100%). A statistically significant correlation ($P < 0.05$) was obtained between pre-surgical and post-surgical occlusion. Babu *et al.*^[15] also reported satisfactory post-operative occlusion and healing with no paresthesia or no soft tissue infection in subjects when treated under open reduction and internal fixation using 2 mm 3D locking titanium miniplate.

Munhoz *et al.*^[16] used Digora software to measure bone density in the sockets of mandibular third molars after extraction of the tooth and grafting. Bone density and crest healing were measured immediately at 2 months and 6 months after surgery. Bone density increased significantly, and there was a statistically significant difference between the experimental and control groups. The current study also showed a gradual increase in bone density at 1st, 6th, and 12th weeks using Digora software. The radiographic bone density between the pre-operative and 1st week was 1.81. This was not statistically significant. However, the radiographic bone density at 6th and 12th-week postoperatively was statistically significant.

Loosening of screws and plates is considered to be one of the main risk factors for increased rates of infection because it is known that loose hardware propagates an inflammatory response. The possible advantage of this property of a locking plate/screw system is the decreased incidence of inflammatory complications from the loosening of the hardware and reduced period of inter-maxillary fixation postoperatively.^[17] The present study used a modified locking system with a 2 mm 3D titanium locking miniplate/screw system and 2 mm × 10 mm monocortical screws where the threads in the head of the screw are tapered and there is a bevel within the plate. On the last turn, while seating in the screw, the thread in screw head will engage the bevel in the plate. This tapered screw design eliminates the need for meshing of the screw and plate threads, thus providing the freedom to place the screw up to a 100 angulation from the plane perpendicular to the plate.^[12] Furthermore, locking plate/screws have certain

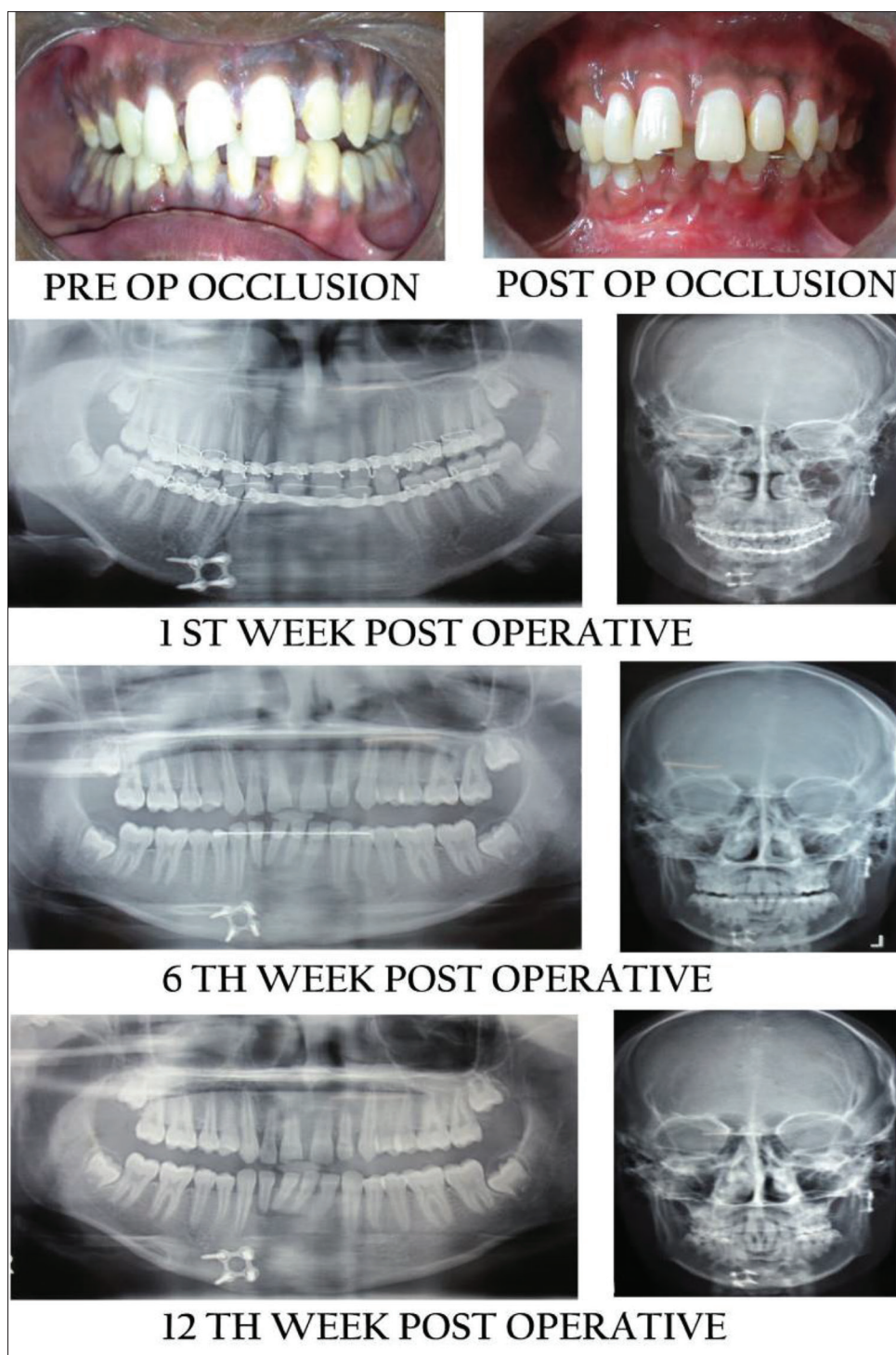


Figure 2: The post-operative occlusion and radiographic fracture healing after the placement of three-dimensional locking plate at 1st, 6th, and 12th weeks postoperatively

advantages over conventional plate/screws. They include greater stability across the fracture site with less chance of screw loosening as the screw head locks into the congruent thread of the plate transforming the screws and plate into a single unit. Moreover, intimate contact of the plate to the bone is not necessary with the use of these plates, and the cortical perfusion is preserved with a decrease in the

incidence of bone necrosis, thus enhancing bony healing and regeneration.

There are several reasons for post-operative infection which includes the presence of teeth in the line of fracture, delay in antibiotic therapy, poor oral hygiene, and patients on immunosuppressive drug therapy. However,

the current study showed one minor complication of plate infection. However, the plate infection got resolved with the administration of IV antibiotics. Further studies with a larger sample and follow-up would give a possible explanation for this particular observation. Furthermore, none of the cases showed wound dehiscence, plate/screw fracture, and screw loosening and all 20 patients (100%) showed satisfactory occlusion and good post-radiographic healing. This suggests that 3D locking titanium miniplates are a promising and effective method for the management of ORIF of anterior mandibular fracture.

CONCLUSION

Our study firstly showed a decreased incidence of inflammatory complications from loosening of the hardware. Second, fixation of mandibular fractures with 3D self-locking titanium plates facilitated stabilization at both the superior and inferior borders and thereby preventing displacement of the segment postoperatively. Third, a 100% satisfactory occlusion and a good post-radiographic healing were obtained.

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Esthesioneuroblastoma Treatment Results From a Tertiary Care Center

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Abstract

Background: Esthesioneuroblastomas (ENB) or olfactory neuroblastomas are extremely rare malignant tumors of the head and neck region. Surgery is the primary modality of treatment. Adjuvant radiotherapy (RT) is used from Kadish stage B onward. RT is used as a single modality whenever surgery is not possible. Chemotherapy is used in residual, inoperable, advanced, and metastatic diseases.

Materials and Methods: Patients diagnosed with ENB between January 2012 and December 2017 in our institute were analyzed retrospectively.

Results: Five patients were treated in the study period (5 years). The median age of the patients was 54 years with M:F ratio of 1.5. Most of the patients had nasal block as presenting symptom followed by epistaxis. All the patients presented in the advanced stage (Kadish C and D). Surgery was possible in only two-third of patients in stage C, and they received adjuvant RT. One-third of patients in stage C received radical RT. Half of the patients in stage D were fit for palliative RT alone, and the other 1/2 received radical RT dose. Chemotherapy was given for four patients with four cycles of cisplatin and etoposide. After chemotherapy, there was partial response in two patients, complete response in one patient, and progressive disease in one patient.

Conclusion: Since ENBs are rare, the standard of care and chemotherapy role remains to be explored a lot. Radiation and chemotherapy help in many patients, especially as palliation.

Key words: Esthesioneuroblastoma, Hyams pathological grading, Kadish stage, Olfactory neuroblastoma

INTRODUCTION

Esthesioneuroblastomas (ENB) or olfactory neuroblastomas are uncommon malignant tumors of the head and neck region and were first described by Berger and Luc.^[1] They usually arise from nasal mucosa and cribriform plate and the cell of origin is thought to be olfactory receptors. Due to proximity to the central nervous system and locally aggressive nature,^[1] they become inoperable or complete excision that is difficult, and many patients require radical or adjuvant radiotherapy (RT). The incidence is very rare, and it forms 3% of endonasal neoplasms. The median age

of the patient is 53 years, and bimodal distribution is seen with most patients presenting in the 4th–6th decade and some cases in the 2nd decade.^[2-6] Male predominance is seen. The presentation can include nasal block, epistaxis, nasal discharge, pain, and nodal spread or distant metastasis can occur rarely. Special staging system, known as the Kadish system and its modification,^[7,8] is used unlike other head and neck malignancies, where AJCC system is used. The most commonly computed tomography (CT) scan is performed to find the bony extension, and magnetic resonance imaging (MRI) gives the detailed picture of intracranial extension and orbital invasion of disease, and both are complementary to each other. Since this is a neuroendocrine tumor octreotide scan and positron emission, tomography/CT has a role and can be useful in picking up nodal or distant metastasis. A pathological examination only will confirm the diagnosis. Whenever surgery is possible, it should be done first with a craniofacial approach yielding superior local control and survival than transfacial approach.^[9] Combined surgery and adjuvant RT improved survival over surgery or RT

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alone.^[9] The role of adjuvant chemotherapy is unclear. Chemotherapy with cisplatin and etoposide combination is used in disseminated and locally advanced disease with or without local treatment.^[10]

MATERIALS AND METHODS

This manuscript was written to find the presentation and treatment outcome of this uncommon malignancy in our population and also the treatment outcome. Details of all head and neck cancer patients registered between January 2012 and December 2017 were searched, and those who were histologically proven to be ENB were identified and analyzed. Six patients were identified, and details of one patient were incomplete, and hence, those five patients were analyzed individually. Statistical analysis was made with the help of SPSS software version 23. Mean, mean, mode, standard deviation, range, percentage, and disease response at the end of primary and subsequent treatment were analyzed.

RESULTS

Five patients with a diagnosis of ENB were analyzed. Three were male and two were female. The median age of presentation was 54 years (range 39–62 years). The median follow-up period was 61 months (range 33–83 months). Symptom duration ranged from 1 month to 26 months. About 80% ($n = 5$) of the patients had nasal block (right side being more common) and 60% ($n = 3$) patients had bleeding from nose. Other symptoms and signs and their median duration of time are depicted in Table 1. The median duration for diagnosis after the presenting complaint was 35 days (range 20–48 days). Three (60%) patients had Kadish stage C and 2(40%) patients had Kadish D stage. Eastern cooperative oncology group (ECOG) performance score was 1 for 2 patients, score 2 for 2 patients, and score 3 for 1 patient. Hyams' grading system was used for histopathological reporting. Grade of the individual patient is shown in table 3, and 1 patient's grading could not be done (Patient 1), as slides and blocks could not be traced. All the patients were worked up initially with CT and MRI, and the feasibility of surgery was assessed in tumor board with head and neck team and neurosurgeons. CT and MRI of two patients are shown in Figure 1a and b, respectively. Only two patients with Kadish stage C were taken up for surgery, and both of them had residual disease after surgery (Patient 1 and 4), and they received adjuvant RT. Patient 2 was in poor ECOG and, hence, received only palliative RT of 30 Gy followed by palliative care. The other two patients (Patient 3 and 5) received a radical radiation dose of 66 Gy. Four patients received chemotherapy after radiation was completed with cisplatin 100 mg/m² D1 and etoposide 100 mg/m² D1-D3q21 days. Three patients received four

cycles, and one patient could receive two cycles only and stopped due to disease progression. A complete response could be achieved in only one patient, and he received all three modalities of treatment. Individual patient responses to initial treatment and subsequent treatment with chemotherapy are shown in Tables 3 and 4, respectively.

DISCUSSION

All five patients presented in an advanced stage (Kadish stage C or D) which makes complete excision difficult. Surgery being the primary modality of treatment, when not adequate, it leads to poor treatment outcome. RT, when used after surgery as an adjuvant treatment, will produce better treatment outcome than surgery alone for Kadish stage B onward.^[11] Doses <54 Gy usually produce inferior local control.^[12] Radiation alone usually has poor survival, as shown in the literature.^[11] RT helped in palliation of

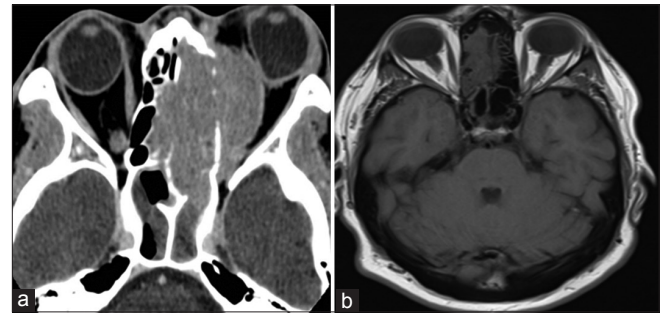


Figure 1: (a and b) Computed tomography and magnetic resonance imaging of Patient 3 and 4, respectively

Table 1: Kadish staging of olfactory neuroblastomas

Stage	Definition
A	Confined to nasal cavity
B	Involves the nasal cavity and one or more paranasal sinuses
C	Extending beyond the nasal cavity or paranasal sinuses
D	Regional lymph node or distant metastasis

Table 2: Presentation

Signs/Symptom	Number (%) $n=5$	Median duration (months)
Nasal obstruction	4 (80)	21
Epistaxis	3 (60)	1.5
Right:Left:Bilateral	2:1:1	
Nasal discharge	3(60)	9
Loss of smell (anosmia)	2(40)	5
Neck swelling	3 (60)	26
Nasal swelling	4 (80)	7
Pain	-	-
Visual disturbance	1 (20)	2
Diplopia	1(20)	1
Epiphora	1(20)	3
Otagia	-	-

Table 3: Hyams' grading system

Grade	Lobular preservation	Mitotic index	Nuclear polymorphism	Fibrillary matrix	Rosettes	Necrosis
1	+	None	None	Prominent	HW rosettes	None
2	+	Low	Moderate	Present	HW rosettes	None
3	±	Moderate	Prominent	Low	HW rosettes	Rare
4	±	High	Marked	Absent	None	Frequent

Table 4: Initial treatment

P. No.	Age	Sex	Grade	Stage	Initial treatment	RT dose	Response
1	54	M	NR	C	SX + RT	54 Gy/30#	SD
2	62	M	3	D	RT	30 Gy/10#	PD
3	58	F	2	C	RT	66 Gy/33#	SD
4	51	M	2	C	SX + RT	55.8 Gy/31#	PR
5	39	F	4	D	RT	66 GY/33#	PR

P. No: Patient number, M: Male, F: Female, NR: Not recorded, SX: Surgery, RT: Radiotherapy, SD: Stable disease, PD, Progressive disease, PR: Partial response

Table 5: Subsequent treatment

P. No.	Subsequent treatment	Number of cycles	Response
1	CIS+ETO	2	PD
2	PALLIATIVE CARE	-	-
3	CIS+ETO	4	PR
4	CIS+ETO	4	CR
5	CIS+ETO	4	PR

P. No: Patient number, PD: Progressive disease, PR: Partial response, CR: Complete response, PR: Partial response

symptoms such as nasal block, epistaxis, nasal discharge, and pain, especially when debulking is not possible and in patients with poor performance status. The mode of RT is very important due to the presence of critical structures such as optic nerve, optic chiasma, and brain stem since more than 54 Gy is required in the adjuvant setting and 66–70 Gy in radical setting for better disease control. Intensity-modulated RT and proton therapy will be helpful in this scenario. Concurrent chemo is not a standard of care, unlike squamous cell carcinoma of head and region, where it is given routinely along with RT. Chemotherapy is given only as an adjunct to surgery and RT and not helpful as a single modality as these tumors are not much chemosensitive. The most commonly used drugs are cisplatin, etoposide, vincristine, cyclophosphamide, and Adriamycin. There are no large randomized control trials comparing various drug combinations as its extremely difficult to recruit the patients due to the rarity of incidence. Each institution has various policies of choosing chemotherapy schedule. In our institute, cisplatin and etoposide are given for residual disease and inoperable setting after RT. It produced partial response in 50% of patients and some patients poorly respond to chemotherapy. Hence, disease response after

two cycles is important both clinically and by imaging to avoid cisplatin toxicity for non-responders.

CONCLUSION

Esthesioneuroblastomas are still challenging, due to the rarity of the tumor and proximity to critical structures. More Indian data are required to compare results from different institutions and will help in developing the standard of care.

ETHICAL APPROVAL

Obtained as per the institution protocol.

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Renal Function in Cirrhosis of Liver: Hospital-based Study in Tripura

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Abstract

Introduction: Liver disease is a common disorder affecting multiple system. It accounts for approximately 2 million deaths every year worldwide and 1 million due to complications of cirrhosis. Current epidemiological trends show that common liver diseases in Asia-Pacific countries are alcohol-related liver diseases, non-alcoholic fatty liver disease (NAFLD), hepatitis B and C, etc. Most of them lead to cirrhosis of liver. Renal dysfunction is one of the most common complications of cirrhosis with high morbidity and mortality.

Objectives: The objectives of the study were to evaluate the state of renal function in patients with cirrhosis of liver among hospitalized patients.

Methodology: This study was cross-sectional hospital-based study in a period of 1½ year.

Results: The study was done on 200 consecutive patients of diagnosed cirrhosis of liver. Male preponderance of 72% observed in the study. The mean age of cirrhosis of liver was 52.28 ± 8.983 years. The most common etiology of cirrhosis was alcohol-related liver cirrhosis (67%). Diabetes was found among 58% of cirrhotic. Chronic kidney disease (CKD) was found among 24% cirrhosis of liver patients. Among CKD patients, 16% were in Stage 3a of CKD, 8% in Stage 3b, 22% were in Stage 4, and 54% were in Stage 5. Prevalence of CKD among non-alcoholic liver cirrhosis was more compare to alcohol-related cirrhosis. CKD was more common among cirrhosis with diabetes. Hypokalemia and hyponatremia were closely related to hepatic encephalopathy.

Conclusion: End stage CKD is an important complication of cirrhosis. NAFLD-related cirrhosis is more prone to develop CKD. Regular evaluation of renal function among cirrhotic is of prime importance.

Key words: Alcohol-related liver disorders, Chronic kidney disease, Cirrhosis of liver, Hepatitis B, Hepatitis C, Non-alcoholic fatty liver disease, Renal function

INTRODUCTION

Cirrhosis is a condition that is defined histopathologically and has a variety of clinical manifestations and complications, some of which can be life threatening. In the past, it has been thought that cirrhosis was never reversible; however, it has become apparent that when the underlying insult that has caused the cirrhosis has been removed, there can be reversal of fibrosis. The pathologic features of cirrhosis consist of architectural distortion with the formation

of regenerative nodules. This results in a decrease in hepatocellular mass and alteration of blood flow. This leads to induction of fibrosis with activation of hepatic stellate cells.^[1] Liver disease accounts for approximately 2 million deaths per year worldwide. Cirrhosis is currently the 11th most common cause of death globally and liver cancer is the 16th leading cause of death; combined, they account for 3.5% of all deaths worldwide. Cirrhosis is within the top 20 causes of disability-adjusted life years and years of life lost. According to the WHO, alcohol consumption accounts for 3.8% of the global mortality.^[2,3] Regarding hepatitis B as of 2016, 27 million people (10.5% of all people estimated to be living with hepatitis B) were aware of their infection, while 4.5 million (16.7%) of the people diagnosed were on treatment.^[4] Globally, an estimated 71 million people have chronic hepatitis C virus infection. A significant number of those who are chronically infected will develop cirrhosis or liver cancer. The WHO estimated that in 2016,

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approximately 399,000 people died from hepatitis C, mostly from cirrhosis and hepatocellular carcinoma.^[5]

Current epidemiological trends of the most common liver diseases in Asia-Pacific countries reveal that alcohol consumption, non-alcoholic fatty liver disease (NAFLD), and hepatitis B virus (HBV) remain the primary cause of cirrhosis. The expanding implementation of HBV vaccination has been effective in reducing the incidence of liver cancer, especially in countries like India, China, and other countries.^[3]

NAFLD prevalence is increasing owing to increasingly urbanized lifestyles and dietary changes; as a result, the rising trend of NAFLD is becoming comparable to that of Western countries. NAFLD is associated with the development of cardiovascular and kidney diseases, patients with this disease should receive tailor-made advice and continuous support for lifestyle modification.^[3,6,7]

Cirrhosis is described as either compensated or decompensated. Decompensation means one or more of the following: Ascites, bleeding varices, hepatic encephalopathy, and jaundice. Acute kidney injury, chronic kidney injury, hyponatremia, and spontaneous bacterial peritonitis are also features of decompensation. Child Turcotte-Pugh (CTP) staging and model of end stage liver disease score used for prognosticating cirrhotic patients. However, CTP is clinically convenient and easy to use.^[8]

Renal dysfunction is one of the most common complications of cirrhosis with high morbidity and mortality.^[9-13] Renal dysfunction in this population may present acutely, or may be a result of underlying chronic kidney disease (CKD). An accurate assessment of renal function is recommended in all patients with cirrhosis. Indeed, the renal function assessment guides the management of patients, helps to define prognosis and to plan transplant strategies. Despite its limitations, serum creatinine is still the most used biomarker for the estimation of glomerular filtration rate (GFR) in patients with cirrhosis.^[12-15] The most important chronic liver diseases (CLDs) associated with chronic renal disease are alcohol-related liver disease, NAFLD, and hepatitis B and C.^[16] The prevalence of CKD among patients with cirrhosis has increased due to the increased prevalence of CKD-associated comorbidities such as diabetes.^[3,17] There were CKD patients who had significantly higher serum creatinine and higher prevalence in non-alcoholic steatohepatitis (NASH) -related cirrhosis.^[18]

Hence, evaluation of renal function is of immense value in the management of cirrhosis of liver and outcome of intervention and planning for liver transplantation have definite role with variations in renal function.

Objectives

The objectives of the study were as follows:

1. To assess renal function by estimating serum urea, serum creatinine, serum uric acid, urine analysis, and estimated GFR among the patients of cirrhosis of liver
2. To evaluate the association of etiological factors causing liver cirrhosis with CKD.

METHODOLOGY

This is a cross-sectional hospital-based study (IPD) of consecutive 200 patients of cirrhosis liver of different etiology admitted for management which was evaluated for renal function as per pre-defined protocol approved by Institutional Ethics Committee.

Operational Definitions

Cirrhosis of liver

Cirrhosis is defined anatomically as a diffuse process with fibrosis and nodule formation. It is the end result of the fibrogenesis that occurs with chronic liver injury. The most common causes include alcohol excess, viral hepatitis, NASH, and autoimmune diseases.^[6]

CKD

CKD encompasses a spectrum of pathophysiologic process associated with abnormal kidney function and a progressive decline in GFR. The risk of CKD progression is closely linked to both the GFR and the amount of albuminuria.^[1] The kidney disease improving global outcome definition and classification were accepted, with clarifications. CKD is defined as kidney damage or GFR <60 mL/min/1.73 m² for 3 months or more, irrespective of cause.^[19]

RESULTS AND ANALYSIS

A total of consecutive 200 patients of cirrhosis of liver were evaluated for renal function during period of 1 year and data analyzed systematically.

Etiology

The present study reveals that most common cause of cirrhosis of liver in Tripura at present is alcohol-related liver disorder (67%), followed by NAFLD (20%), hepatitis B (8%), and hepatitis C (3%). This is big shift [Figure 1].

Demography

The present study shows that 72% total patient of cirrhosis of liver are male and 28% are female. On the contrary, 70% on NAFLD-related cirrhotic are female. The study reveals high prevalence of diabetes among patients of cirrhosis of liver (58%). The mean age of cirrhosis of liver was 52.28 ± 8.983 years in the present study.

Stages of CLD

In the study group, 42% of patients were from CTP C, 57% were from CTP B, and rest 1% was from CTP A. Most of the patients in this study belong to advanced Liver disease group [Figure 2].

CKD and Cirrhosis of Liver

In the present study, 24% of total cirrhosis patients was in CKD [Figure 3]. Among patients with CKD, 16% were in Stage 3a of CKD, 8% in Stage 3b, 22% were in Stage 4, and 54% were in Stage 5. It shows that most of the cirrhotic are having advance stage of CKD. It has also observed that cirrhotic without history of significant alcoholism is having higher prevalence (45%) of CKD.

Metabolic Changes

In this study, hypokalemia (55.6%) and hyponatremia (35.6%) were noted only in patients of cirrhosis with higher grade of encephalopathy and were not noted among patients without encephalopathy. Hyperuricemia was noted in 23.5% of patient with cirrhosis of liver.

DISCUSSION

CLD has got a wide spectrum. Cirrhosis of liver and hepatocellular carcinoma is two end stage conditions. Cirrhosis is associated with various multiorgan dysfunction and CKD is one of them. This cross-sectional study on 200 consecutive hospitalized cirrhosis of liver patient was done at a tertiary care hospital of Tripura, a state of Northeast region of India.

The study reveals the changing etiology of CLD. At present, alcohol-related chronic liver disorder is the most

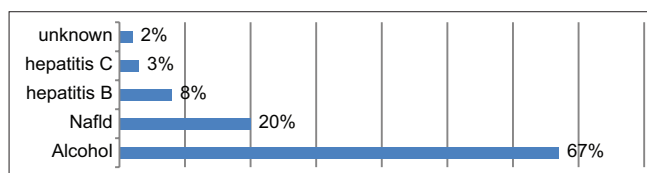


Figure 1: Etiology of cirrhosis of liver in Tripura

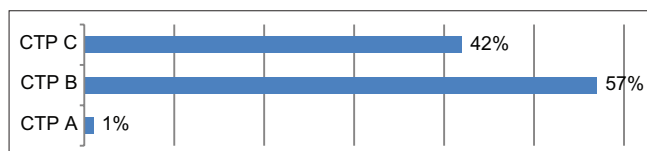


Figure 2: Stages of chronic liver disease

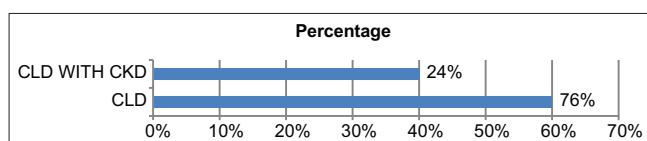


Figure 3: Chronic kidney disease among patients with cirrhosis of liver

common cause in this region (67%), which is a matter of concern from public health point of view (Mukherjee *et al.*, 2017; Ram *et al.*, 2019).^[20,21]

In this evaluation, there is male preponderance in overall cirrhosis but NAFLD-related cirrhosis is more in female (70%). Florence also showed female preponderance (72.7%). As it has also been observed in some other recent studies from Tripura (Subarna and Pradip, 2018).^[22]

Florence^[23] conducted a cross-sectional study with 2346 patients, which showed male preponderance (63.2%) of total cirrhotic patient. The mean age of all liver cirrhosis patients in the present study was 52.28 years and it was 50.4 years in the study of Florence.

The present study shows that 58% patients of cirrhosis are having diabetes mellitus.

In this study, it was observed that 24% patients of cirrhosis of liver are having significant CKD and 54% of CKD patients are in Stage 5 disease. Florence^[23] showed higher prevalence of CKD (46.8%) in cirrhosis.

It was noted in the present study that CKD is more among patients with NAFLD. It can be attributed that probably metabolic syndrome/NAFLD-related CLD patients are having more kidney disease. In the present study group, there is preponderance of alcohol-related liver disease; hence, CKD is less. Pearson Chi-square test is applied to find out the association between non-alcoholic liver cirrhosis and CKD, shows that there is a strong association ($P = 0.003$ [<0.05]) that is patients with non-alcoholic liver cirrhosis are more prone to develop CKD than alcohol-related liver cirrhosis. Diabetes (a component of metabolic syndrome) was more common among non-alcoholic liver cirrhosis than alcohol-related liver cirrhosis and CKD, has got a strong association with a $P = 0.039$ (<0.05). Rajender *et al.*, 2019^[24] got similar result.

Hypokalemia and hyponatremia are associated with encephalopathy in Cirrhosis of liver. Hyperuricemia is associated with cirrhosis with advance CKD (Afzali *et al.*, 2010).^[25]

More parameters and imaging to be performed to evaluate renal dysfunction in cirrhosis of liver with CKD.

CONCLUSION

This study has clinical and public health implications, this study reveals that prevalence of CKD is more common in those who are suffering from non-alcoholic liver cirrhosis and females are more prone to develop non-

alcoholic liver disease compared to males. Researcher should look for NAFLD in diabetics, especially in the presence of metabolic syndrome. Once found, aggressive management of cardiovascular and renal morbidity should be the primary goal. It has only recently been appreciated that CKD represents an important burden of disease for patients with non-alcoholic liver cirrhosis.^[26]

The study reveals that early evaluation of renal abnormalities at the time of diagnosis of CLDs and at a frequent interval thereafter is of paramount importance to reduce multiter trouble of CLDs, CKD, and metabolic syndrome.

Patients with CKD should be treated as a high-risk group among hospitalized patients with cirrhosis due to their poor survival, impact on liver transplantation and they should be monitored carefully for the development of superimposed AKI (Wong *et al.*, 2019).^[16]

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To Compare the Intubating Conditions of Cisatracurium with Rocuronium – A Prospective, Randomized Double-blind Study

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Abstract

Background: Neuromuscular blocking agents are usually administered during anesthesia to facilitate endotracheal intubation and to provide muscle relaxation during surgery. There are few studies comparing cisatracurium versus rocuronium for the assessment of intubation conditions and hemodynamic response. In this study, we have compared the intubating conditions, hemodynamic events between cisatracurium and rocuronium.

Materials and Methods: This prospective, randomized, double-blind, controlled study includes 70 adult patients of both sexes aged between 20 and 60 years with ASA Grade I and II. These patients were randomly allocated into two groups of 35 each. Group A received 0.1 mg/kg of inj. cisatracurium (2 ED95). Group B received 0.6 mg/kg of inj. rocuronium (2 ED95). The intubating conditions, hemodynamic variables, and adverse reactions were compared between these groups.

Results: In our study, the mean percentage depression of adductor pollicis at 180 s was 66.43% ($\pm 24.94\%$) in cisatracurium group against 18.29% ($\pm 15.19\%$) in the rocuronium group which was statistically significant. The blockade at adductor pollicis was more intense with rocuronium compared to cisatracurium at 180 s in our study.

Conclusion: In our study, it is concluded that the suppression of muscle twitch at adductor pollicis muscle was significantly more with rocuronium than cisatracurium. The intubating conditions assessed as per Copenhagen conference score system were superior with rocuronium than with cisatracurium. The hemodynamic parameters such as heart rate and MAP were similar in both the groups.

Key words: Cisatracurium, Intubation, Rocuronium

INTRODUCTION

Neuromuscular blocking agents are usually administered during anesthesia to facilitate endotracheal intubation and to provide muscle relaxation during surgery. An ideal neuromuscular blocking agent should have quick onset of action that provides the best intubating conditions and also enable the reversal of blockade within a short period of time. They should not possess cumulative effects that may

lead to residual paralysis. The poor intubating conditions may increase the incidence of difficult intubation, trauma to the airway and can cause laryngeal injury, as manifested by voice hoarseness and vocal cord damage. Since laryngoscopy and intubation are associated with hemodynamic responses^[1] such as tachycardia and hypertension routinely, suboptimal relaxation of vocal cords can further exaggerate. Hence, an ideal muscle relaxant should provide vocal cord immobility quickly, adequate relaxation of jaw, and less hemodynamic responses that make placement of endotracheal tube easy with direct laryngoscopy. The ideal neuromuscular blocking agent is one which has brief duration of action, provides profound relaxation, and is free from hemodynamic changes.

Succinylcholine^[2] was used routinely to aid intubation for its rapid onset of action and reliable neuromuscular blockade

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that causes profound relaxation of the cords. The side effects such as muscle pain, hyperkalemia, and pressure changes in the ocular and intracranial compartments led to the use of non-depolarizing muscle relaxants. The non-depolarizing muscle relaxants which are currently in use in clinical practice are vecuronium, atracurium, and rocuronium.^[3] The potency of the drug is determined by the dose–response curves which describe the relationship between twitch depression and dense. The effective dose 50 or ED50 is the median dose corresponding to 50% twitch depression to supramaximal electric stimulus. The ED95 is the dose of neuromuscular blocking agent that is expected to produce 95% block at the adductor pollicis. Several multiples of the ED95 are usually administered to ensure adequate neuromuscular blockade for intubation and to minimize the time to maximum block that is more commonly used for dosing muscle relaxants. Therefore, equipotent doses are usually compared to find the pharmacodynamic properties.^[4] The time of onset is shortened by increasing the dose at intubation but at the expense of prolonged time to recovery. Cisatracurium and rocuronium are non-depolarizing muscle relaxants belonging to different classes of intermediate acting muscle relaxants, with cisatracurium belonging to benzylisoquinolinium group and rocuronium to steroidal group.

Cisatracurium is 4 times as potent as atracurium. It is eliminated by Hoffman elimination (77%). At physiological pH and temperature, cisatracurium is converted to laudanosine and monoquaternary acrylate. The amount of laudanosine produced is 5 times less than atracurium. Histamine release is also nil with cisatracurium making it more suitable for intubation as it does not cause hypotension like atracurium. The elimination is not dependent on liver and renal function. The effective dose ED95 is 0.05 mg/kg and doses in the range of twice to 4 times of ED95 have been studied for intubation with varying time for suppression of twitch response.

Rocuronium, an intermediate acting non-depolarizing muscle relaxant, has a structure similar to vecuronium and pancuronium. It is approximately 6–10 times less potent and the ED95 dose for suppression of twitch is observed at 0.3 mg/kg. The recommended dose for intubation within 1 min is 1 mg/kg. However, the duration of action is prolonged up to 90 min with such higher dosage. Hence, the drug has been investigated for their intubating conditions starting from 0.3 mg/kg to 0.9 mg/kg.

The intubating conditions measured in terms of vocal cord mobility and jaw relaxation were found to be satisfactory even with the lowest dose of 0.3 mg/kg. The suppression of twitch response was 5–6 min with 0.3 mg and was 2.6–3 min with 0.6 mg/kg. However, the incidence of

tachycardia and hypertension was more with lowest dose used that demanded additional doses of fentanyl and propofol.

Literature data on rocuronium and cisatracurium showed studies where comparison of different dosages has been done with succinylcholine as a relaxant^[5] for intubation.

There are few studies comparing cisatracurium versus rocuronium for the assessment of intubation conditions and hemodynamic response.^[6,7] When two drugs are compared, it is meaningful to compare only equipotent doses and usually clinically relevant doses (twice the ED95%) of both.

MATERIALS AND METHODS

This prospective randomized double-blind study was conducted in the TOT complex, Govt. General Hospital, Kakinada, attached to Rangaraya Medical College between January 2019 and June 2019. After obtaining the Institutional Ethical Committee approval and informed written consent, 80 adult patients belonging to ASA I and II, of both sexes, aged between 20 years and 60 years were taken up for this study.

The sample size was calculated assuming the mean time for onset time of blockade with cisatracurium which was 50.45 s with a standard deviation of 20 and 70.75 s and with a standard deviation of 27.31 for rocuronium. The sample size was calculated for a power of 90% and 5% alpha error. The required sample size was 29 subjects in each group. To account for non-participation or loss to follow up of 20%, another 6 subjects were included to the study groups. Hence, the final sample size was 70 which divided into two groups.

Inclusion Criteria

The following criteria were included in the study:

1. Surgeries planned under general anesthesia with endotracheal intubation
2. ASA I and II patients
3. Elective surgeries.

Exclusion Criteria

The following criteria were excluded from the study:

1. Myopathies
2. Chronic liver disease
3. Chronic renal disease
4. Obesity with BMI >30 mg/kg/m²
5. Patients with anticipated difficult airway.

These 70 adult patients are randomly allocated into two groups

Group A: 0.1 mg/kg of inj. cisatracurium (2 ED95).
Group B: 0.6 mg/kg of inj. rocuronium (2 ED95).

The study drugs were loaded by an independent anesthesiologist as per the computer generated random numbers. The person who loaded the drug did not participate in monitoring the study parameters.

Inj. cisatracurium and inj. rocuronium twice the ED95 were loaded according to patients body weight and diluted to 10 ml.

The patient was then shifted to the operating room, all the standard monitors were connected, and the electrodes for TOF monitoring were attached to the right wrist for stimulation of ulnar nerve. After securing iv access, patients were pre-oxygenated with 100% oxygen for 3 min, inj. midazolam 1 mg iv, and inj. fentanyl 2 µg/kg given. After 3 min, patient induced with inj. propofol 2 mg/kg iv. and checked for ease of mask ventilation. The study drug was given based on computer generated numbers.

After 180 s, TOF count was monitored and the percentage depression of adductor pollicis was noted. Then, intubation conditions were assessed according to the Copenhagen conference score (CCS) and were intubated with ETT size 7 mm ID PVC in female and with 8 mm ID PVC in male patients. The position of ETT was confirmed with capnography and bilateral air entry.

Then, physiological parameters, heart rate and mean arterial pressure, were noted at pre-induction, post-induction, and for every 3 min for the first 15 min. The side effects such as any skin reactions and idiosyncratic anaphylactic reactions were also noted.

Study Parameters

1. Percentage depression of adductor pollicis twitch at 180 s
2. The CCS
3. Physiological parameters – heart rate and mean arterial pressure.

At the end of surgery, anesthesia was reversed with inj. neostigmine 0.05 mg/kg and inj. glycopyrrolate 0.01 mg/kg and shifted to PACU.

RESULTS

This randomized comparative trial was conducted to compare the intubating conditions between equipotent doses of cisatracurium and rocuronium (2×ED95) in elective surgeries requiring general anesthesia with endotracheal intubation and controlled ventilation. A total

of 70 subjects were included in the study – 35 subjects in each group [Tables 1 and 2].

Group A received an intubating dose of inj. cisatracurium 0.1 mg/kg (2×ED95) and Group B received an intubating dose of inj. rocuronium 0.6 mg/kg (2×ED95).

The collected data were analyzed with IBM.SPSS statistics software 23.0 version. To describe about the data, descriptive statistics, frequency analysis, and percentage analysis were used for categorical variables and the mean and S.D were used for continuous variables. To find the significant difference between the bivariate samples in independent groups, the unpaired sample *t*-test was used. To find the significance in categorical data, Chi-square test was used. In all the above statistical tools, the *P* = 0.05 is considered as statistically significant.

DISCUSSION

The onset time, duration of action of muscle relaxants, and the type of surgery are important factors in choosing the appropriate drugs to achieve rapid, successful tracheal intubation. Rocuronium, atracurium, and cisatracurium^[8] are frequently used muscle relaxants for short to intermediate duration surgical procedures. The adequacy of conditions for tracheal intubation is a function of several factors, such as depth of anesthesia at the time of intubation attempt and the level of neuromuscular block at the time of attempt.

Cisatracurium,^[9] at higher doses – 4 times the ED95 dose, provides neuromuscular blocking property at 90 s that ensures optimal intubating conditions. The intubating conditions measured in terms of vocal cord mobility and priming^[10,11] rocuronium 0.3 mg/kg. However, the suppression of twitch response is delayed up to 5–6 min with 0.3 mg/kg of rocuronium^[12] and 2.6–3 min with 0.6 mg/kg rocuronium. The objective of the present study was to compare the 16 undergoing elective surgery. In our study, the intubating conditions and the percentage depression of adductor pollicis^[13] twitch were assessed at 180 s following twice the ED95 dose of cisatracurium or rocuronium.

The study groups were comparable with respect to age, gender, and weight. None of the patients were excluded from the study and did not have any complications in the intraoperative period.

The Percentage Depression of Adductor Pollicis [Tables 3 and 4]

In our study, the mean percentage depression of adductor pollicis at 180 s [Figure 1] was 66.43% (±24.94%) in cisatracurium group against 18.29% (±15.19%) in the

Table 1: Comparison of demographic profile between the study parameters

S. No.	Parameters	Group A n=35	Group B n=35	P-value
1	Age	33.97±13.19	40.89±13.7	0.478
2	Sex			0.328
	Male	19(34.3%)	24(65.6%)	
	Female	16(45.7%)	11(31.4%)	
3	Weight (in kg)	62.24±12.1	59.53±10.97	0.392
4	BMI (kg/m ²)	22.88±2.51	22.29±2.38	0.402
5	ASA			0.329
	Status 1	62.9%	37.1%	
	Status 2	37.1%	62.9%	

Table 2: Duration of surgery

Parameter	Group A (n=35) (mean ±SD)	Group B (n=35) (Mean ±SD)	Unpaired t-test
Duration of surgery (in hours)	2.17±0.62	2.43±0.81	0.141

Table 3: Median of percentage depression of adductor pollicis twitch at 180 s

Parameter	Group A (n=35) Median (IQR)	Group B (n=35) Median (IQR)
Percentage depression of adductor pollicis twitch at 180 s	75 (2, 96)	21 (0, 47)

Table 4: Mean of percentage depression of adductor pollicis twitch at 180 s

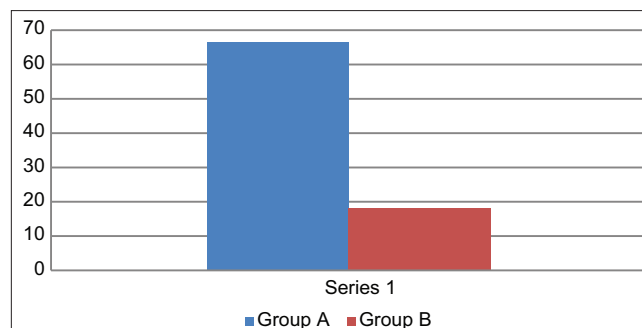
Percentage depression of adductor pollicis twitch at 180 s comparison between groups by unpaired t-test						
Groups		<i>n</i>	Mean	S.D	<i>t</i> -value	<i>P</i> -value
Percentage depression of adductor pollicis twitch at 180 s	Group A	35	66.43	24.94	9.753	0.0005**
	Group B	35	18.29	15.19		

**Highly significant at $P < 0.01$ level

rocuronium group which was statistically significant. The blockade at adductor pollicis was more intense with rocuronium compared to cisatracurium^[14] at 180 s in our study.

Omera *et al.*^[15] found the onset time of action for cisatracurium at 160.4±14.3 s following twice the ED95 dose of cisatracurium and the intubating conditions were acceptable only after 150 s following cisatracurium.

Naguib *et al.*^[6] reported early onset of neuromuscular blockade at 1.3 min with 0.6 mg/kg of rocuronium compared to equipotent dose of cisatracurium. However,


Figure 1: Bar diagram showing mean of percentage depression of adductor pollicis twitch at 180 s

Kim *et al.*^[7] reported the onset time for blockade as 2.7 (2.2–3.2) min at the larynx and 3.9 (3.0–4.8) min at the adductor pollicis following administration of cisatracurium at 0.1 mg/kg. They noted that the onset time and the recovery time were fast at the laryngeal muscle compared to adductor pollicis. Hyunjung *et al.*^[12] reported that twice the ED95 dose of rocuronium produce T1 suppression at 102 ± 49 s compared to 197 ± 53 s with cisatracurium.

In our study, we found similar results where the percentage of twitch suppression was significantly low for rocuronium than cisatracurium indicating more blockade.

The Copenhagen Consensus Conference Score [Tables 5 and 6 and Figure 2]

Omera *et al.*^[15] demonstrated the intubating conditions to be acceptable after 150 s with twice the ED 95 dose of cisatracurium. However, the intubating conditions at 60 s were clinically acceptable in about 80% of patients who received 0.6 mg of rocuronium. We found similar results as evidenced by the excellent and good scores in majority of subjects who received rocuronium.

Hyunjung *et al.*^[12] reported excellent intubating conditions with both rocuronium and cisatracurium. However, the onset time was significantly longer with cisatracurium (197 ± 53 s), compared to that of rocuronium (102 ± 49 s).

Heggeri *et al.*^[13] reported that none of the patients at 60 s showed a TOF count of 0 with 2×ED95 dose of rocuronium. However, the intubating conditions were excellent at 60 s with 0.9 mg/kg of rocuronium in 97% of subjects. Bhandari *et al.*^[16] reported excellent to good intubating conditions in 93.33% of patients at 60 seconds with rocuronium 0.9 mg/kg.

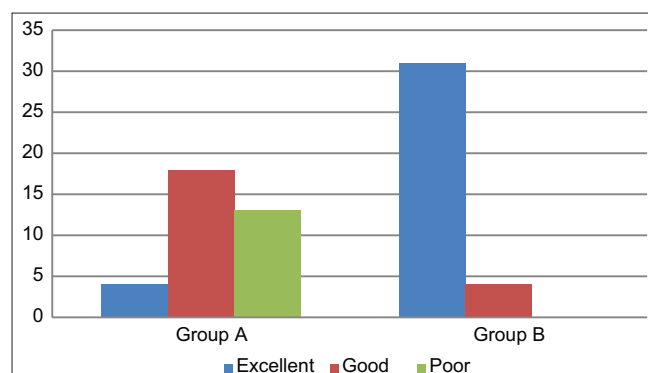
In our study, the Copenhagen consensus conference score with rocuronium was excellent in 88.6% of patients and good in 11.4% of patients. None of the patients had poor score with rocuronium, whereas 37.1% of subjects had poor score with cisatracurium. The Copenhagen consensus

Table 5: Comparison of CCS score among the two groups

Comparison between CCS with groups					
CCS	Groups		Total	t-value	P-value
	Group A	Group B			
Excellent					
Count	4	31	35	42.738	0.0005
%	11.4	88.6	50.0		
Good					
Count	18	4	22		
%	51.4	11.4	31.4		
Poor					
Count	13	0	13		
%	37.1	0.0	18.6		
Total					
Count	35	35	70		
%	100.0	100.0	100.0		

Table 6: The Copenhagen consensus conference score

Score	Jaw relaxation	Vocal cords	Diaphragmatic response
Excellent	Relaxed jaw	Abducted immobile vocal cords	No diaphragmatic movement
Good	Relaxed jaw	Abducted immobile vocal cords	Some diaphragmatic movement (bucking)
Poor	Relaxed jaw	Moving vocal cords	Coughing on intubation
Inadequate	Jaw is not relaxed	Abducted vocal cords	Impossible intubation.


Figure 2: Comparison of Copenhagen conference score between the groups

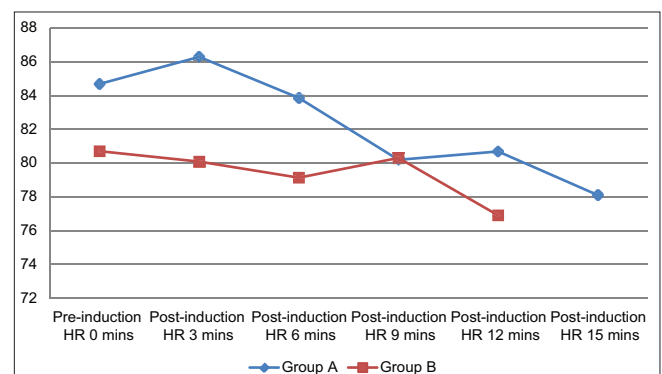
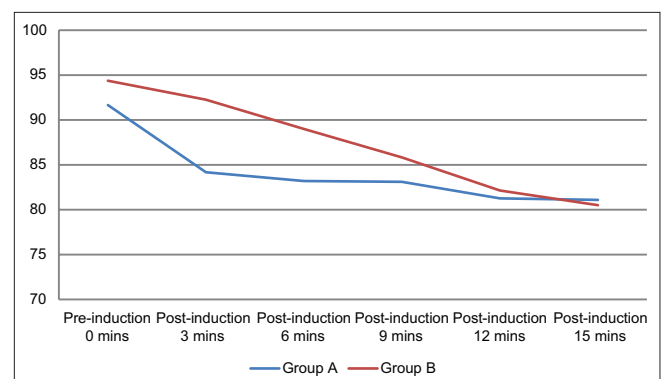
conference score with cisatracurium was excellent in 11.4% of patients and good in 51.4% of patients in our study. However, there were no patients with a score of inadequate CCS. The poor scores noted in the cisatracurium group could be due to the lower dose that was used in our study.

Table 7: Heart rate at different time intervals between the groups

Parameter (per min)	Group A (n=35) (Mean±SD)	Group B (n=35) (Mean±SD)	Unpaired t-test P-value
Pre-induction HR 0 min	84.69±18.49	80.71±13.47	0.308
Post-induction HR 3 min	86.29±17.83	80.09±15.75	0.128
Post-induction HR 6 min	83.86±15.9	79.14±10.46	0.148
Post-induction HR 9 min	80.2±14.01	80.31±12.75	0.972
Post-induction HR 12 min	80.69±16.94	76.91±16.76	0.352
Post-induction HR 15 min	78.11±16.3	74.63±14.96	0.355

Table 8: Mean arterial pressure at different time intervals between the study groups

Parameter (in mm Hg)	Group A (n=35) (Mean±SD)	Group B (n=35) (Mean±SD)	Unpaired t-test P-value
Pre-induction 0 min	91.66±13.41	94.37±16.65	0.455
Post-induction 3 min	84.17±16.22	92.26±18.26	0.654
Post-induction 6 min	83.2±15.09	89±14.25	0.385
Post-induction 9 min	83.11±14.09	85.83±12.45	0.396
Post-induction 12 min	81.26±12.48	82.14±14.17	0.782
Post-induction 15 min	81.09±12.46	80.51±12.44	0.848


Figure 3: Heart rate at different time intervals between the groups

Figure 4: Mean arterial pressure at different time intervals between the study groups

Hyunjung *et al.* observed ideal intubating conditions with cisatracurium at higher doses in the range of 3–4 times the ED95 dose of cisatracurium.

Physiological Parameters [Tables 7 and 8, Figures 3 and 4]

There were no differences between the changes in the heart rate and blood pressure at different time intervals between both the groups in our study. Jammer *et al.* reported that 2×ED95 and 3×ED95 of cisatracurium did not show statistically significant change in HR and MAP. Hyunjung *et al.*^[12] reported no difference in hemodynamics at equipotent doses of cisatracurium and rocuronium.

Limitations of the Study

The recovery characteristics of the neuromuscular blockade were not assessed. In our study, comparing equipotent dose of cisatracurium and rocuronium, the intubating conditions were optimal with rocuronium as compared to that of cisatracurium at 180 s. The intensity of blockade as measured by TOF was more for the group that received rocuronium.

CONCLUSION

In our study, we compared the intubating conditions between cisatracurium and rocuronium given at twice the ED95 dose at 180 s, we found

- The suppression of muscle twitch at adductor pollicis muscle was significantly more with rocuronium than cisatracurium
- The intubating conditions assessed as per CCS scoring system were superior with rocuronium than with cisatracurium
- The hemodynamic parameters – heart rate and MAP were similar in both the groups.

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Low-cost Negative Pressure Therapy for Wound Healing

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Abstract

Background and Objective: Wounds are a major source of morbidity, lead to considerable disability, and are associated with increased mortality; therefore, they have a significant impact on public health and the expenditure of healthcare resources. Vacuum-assisted closure (VAC) uses negative pressure to assist wound healing. Negative pressure drains fluid from the wound, thus removing the substrate for growth of microorganisms. Negative pressure may also accelerate granulation tissue formation and promote angiogenesis. The mechanical stimulation of cells by tensile forces may also play a role by increasing cellular proliferation and protein synthesis. Negative pressure wound therapy (NPWT) involves the use of a negative pressure therapy or suction device to aspirate and remove fluids, debris, and infectious materials from the wound bed to promote the formation of granulation tissue.

Methodology: A total of 50 cases clinically presenting as ulcer between January 2019 and December 2019 in Government Medical College, Mahabubnagar, were taken for study. Each case was examined clinically in a systematic manner for the study of all patients presenting with ulcers. VAC dressing was done and outcome was measured by recording wound scores on days 3, 7, and 10.

Results: In our clinical study of 50 cases managed by VAC dressing, 50% of the cases were of traumatic, 36% diabetic, and 14% cases of vascular etiology. Wound healing was better in the non-diabetic group compared to diabetic and in non-smokers compared to smokers. The most common organisms isolated were *Staphylococcus*, *Pseudomonas*, and *Proteus*.

Interpretation and Conclusion: In our study, VAC therapy enhanced granulation tissue formation leading to better wound healing and faster recovery. VAC is thus a promising new technology that can be used in both acute and chronic wounds as an adjuvant therapy to improve the results of various surgical procedures.

Key words: Negative pressure wound therapy, Vacuum-assisted closure, Wound healing

INTRODUCTION

Vacuum-assisted closure (VAC) is a new technique in the challenging field of management of contaminated, acute, and chronic wounds. Negative pressure wound therapy (NPWT) also called vacuum-assisted wound closure and refers to wound dressing systems that continuously or intermittently apply sub-atmospheric pressure to the surface of a wound. The application of controlled levels of negative pressure has been shown to accelerate

debridement and promote healing in many different types of wounds. The optimum level of negative pressure appears to be around 125 mmHg below ambient and it is believed that negative pressure assists in the removal of interstitial fluid, decreasing localized edema and increasing blood flow. This, in turn, decreases tissue bacterial levels. Despite the significant costs involved, the technique is said to compare favorably in financial terms with conventional treatments in the management of difficult wounds.^[1]

It involves the application of sterile, open-pore foam dressing directly on the wound. The wound is then sealed with an occlusive drape to create a closed, controlled environment. A fenestrated vacuum tube is connected to a vacuum source; fluid is drawn from the wound through the foam into a reservoir for subsequent disposal. Negative pressure is applied at 50–125 mm/Hg, resulting

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in a decrease in the local interstitial pressure, and effluent from the wound is drawn out into the collection device. Initially, the vacuum pressure is applied continuously. As the amount of drainage decreases, the vacuum may be applied on an intermittent basis. The vacuum dressing is usually changed at the approximately 48-h interval.^[2,3] Wound progress is recorded using parameters in the wound scoring system. The objectivity of assessments used to generate the wound score makes this scoring system ideal for evaluating treatment and outcome of wounds.^[4]

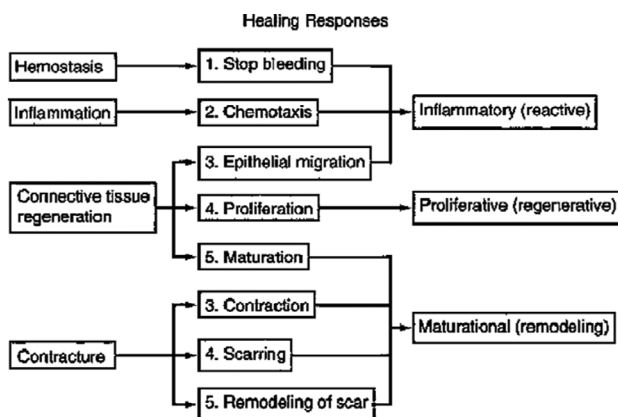
Objectives of the Study

1. To study the outcome of vacuum-assisted closure of wounds.

A wound is defined as a discontinuity of the skin, mucous membrane, or tissue caused by physical, chemical, or biological insult. Surgeon's goal in wound management is to create an environment where the healing process can proceed in an optimal fashion. Wound healing is a fundamental hemostatic process in response to injury. It involves the activation of a basic cellular process of inflammation, cell proliferation, and cell growth as well as regeneration of these processes once the repair is complete. The processes of wound healing take place in an overlapping and sequential manner.

Phases of Wound Healing

1. Hemostasis and inflammatory phase
2. Proliferative phase
3. Maturation and remodeling phase.^[5]



Management of Wounds

Wound healing is a highly orchestrated process, which commences with the removal of debris and control of infection. Subsequently, the wound heals through deposition of granulation tissue, wound contraction, and maturation. Factors such as pressure, trauma, venous insufficiency, diabetes mellitus, vascular disease,

and prolonged immobilization will influence wound healing.^[6]

Standard wound management consists of initial surgical debridement, then either wet-to moist (WM) gauze dressings, which need to be changed at least twice daily, can be used to cover the wound. These dressings are relatively inexpensive, readily available, and easy to apply. Vacuum-assisted closure has been suggested as an alternative that may promote faster wound healing with fewer painful dressing changes.

Vacuum-assisted Closure

Vacuum-assisted closure is a potential alternative for treating of skin wounds. It uses negative pressure to assist wound healing.^[7]

Indications and Contraindications for the use of VAC

The principal indications for the use of VAC are:

- Acute and traumatic wounds
- Pressure ulcers
- Chronic open wounds (stasis ulcers and diabetic ulcers)
- Meshed grafts
- Flaps
- Lower extremity diabetic ulcers

Contraindications are:

- Fistulas to organs or body cavities
- Necrotic tissue in eschar
- Osteomyelitis(untreated)
- Malignancy in the wound

MATERIALS AND METHODS

A total of 50 cases clinically presenting as ulcers between January 2019 and December 2019 were included in the study. A clinical examination of each case was done systematically for the study.

Wound Preparation

Any dressings from the wound were removed and discarded. A culture swab for microbiology was taken before wound irrigation with normal saline. Surgical debridement was done and adequate hemostasis achieved.

Method of use of NPWT Dressing

The sterile hydrocolloid sheet of the approximate size of the wound is placed gently into position.

The perforated drain tube is then placed on top of the sheet and a second hydrocolloid sheet placed over the top. The wound, together with the first few inches of the drainage tube and the surrounding area of healthy skin,



is then covered with the adhesive transparent membrane supplied. At this stage, it is important to ensure that the membrane forms a good seal, both with the skin and the drainage tube. The distal end of the drain is connected to the suction device. This was achieved by Romo Vac suction device; suction was applied continuously or intermittently based on the amount of wound discharge.

RESULTS

An interventional study involving 50 cases of wounds was done in the Department of Surgery, Government Medical College, Mahabubnagar between January 2019 and December 2019.

Gender Distribution of Wounds

Wounds were more common in males 38 cases (76%) than in females 12 cases (24%) male to female ratio 3.167: 1.

Duration of Wounds

Based on the duration of wounds, cases were grouped into three categories: <10 days, 10–30 days, and >30 days. Most cases fall in the group 10–30 days 30 (60%), 19 cases (38%) in the group <10 days, and 1 case (2%) in the group > 30 days [Table 1].

Wounds were most commonly located in the foot 20 (40%) followed by the leg 16 (32%) and the ankle and sole 4 (8%) each. One case of wound in the abdomen was included in the study. [Chart 2 and Table 2].

Smokers and Non-smokers

Twenty-seven (54%) of cases were smokers, 23 (46%) were non-smokers [Table 3].

Table 1: Duration of wound – evaluation of wound healing score on day 7

Duration in years	n	Day 7		
		Mean	SD	Median
<10 days	16	4.94	0.85	5
>10 days	25	4.84	1.21	5
Total	41	4.88	1.08	5

Mann–Whitney test, $P=0.7$

Table 2: Location of wound – evaluation of wound healing score on day 7

Location	Wound score					
	3.00	4.00	5.00	6.00	7.00	Total
Forearm	0	2	3	0	0	5
Abdomen	0	0	0	0	1	1
Leg	1	2	7	4	0	14
Ankle	1	0	1	1	0	3
Foot	2	5	2	5	1	15
Sole	1	0	2	0	0	3
Total	5	9	15	10	2	41

$P=0.024$. Significant difference in wound healing depending on the location of the wound.

Table 3: Smoking – evaluation of wound healing score on day 7

Smoking	n	Day 7		
		Mean (18)	SD	Median
Yes	24	4.50	0.89	5
No	17	5.41	1.12	6
Total	41	4.88	1.08	5

Mann–Whitney test, $P=0.006$

Table 4: Etiology – evaluation of wound healing score on day 7

Location	n	Day 3		
		Mean	SD	Median
Traumatic	20	5.25	0.78	5
Diabetic	16	4.44	1.21	4
Vascular	05	4.80	1.30	5
Total	41	4.88	1.08	5

Kruskal–Wallis test, $P=0.08$ Mann–Whitney test. Traumatic versus diabetic – 0.03

Table 5: Age-wise evaluation of wound healing score on day 7

Age in years	n	Day 7		
		Mean	SD	Median
<40	11	5.09	0.94	5
41–50	15	4.73	1.22	5
>50	15	4.87	1.06	5
Total	41	4.88	1.08	5

Kruskal–Wallis test, $P=0.8$

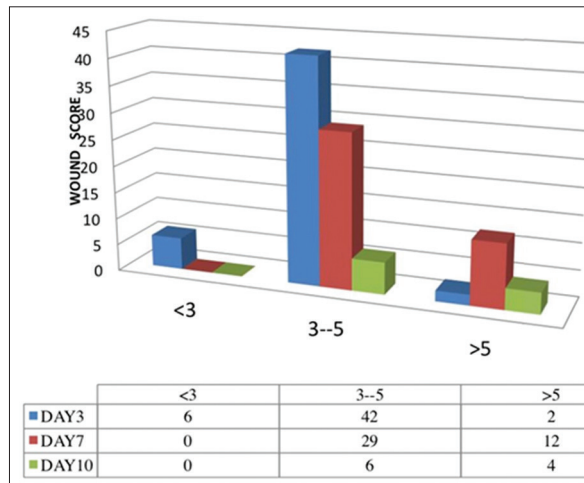


Chart 1: Wound scores on days 3, 7, and 10

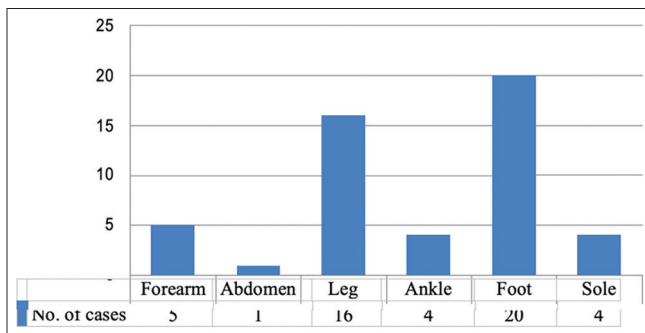


Chart 2: Distribution of location of wounds

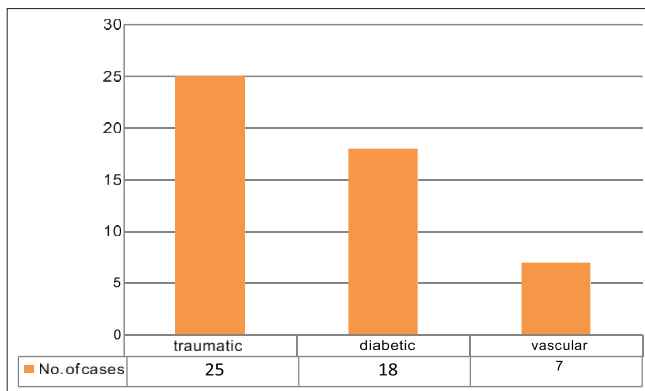


Chart 3: Etiology of wounds

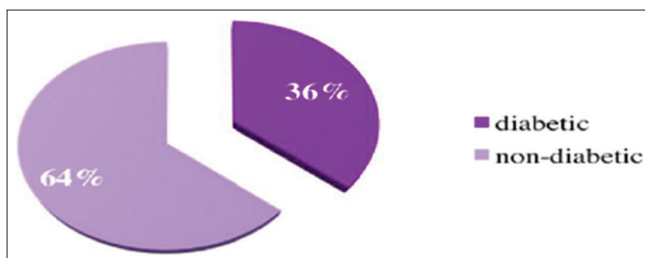


Chart 4: Diabetic and non-diabetic wounds

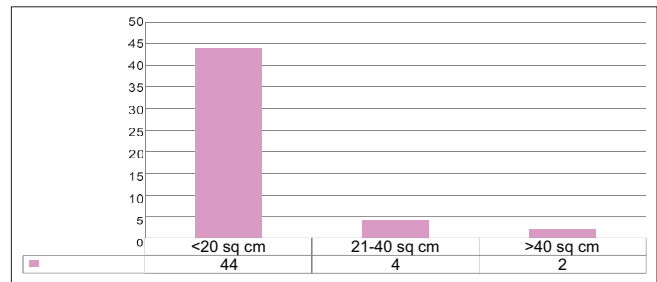


Chart 5: Wound area in square CM

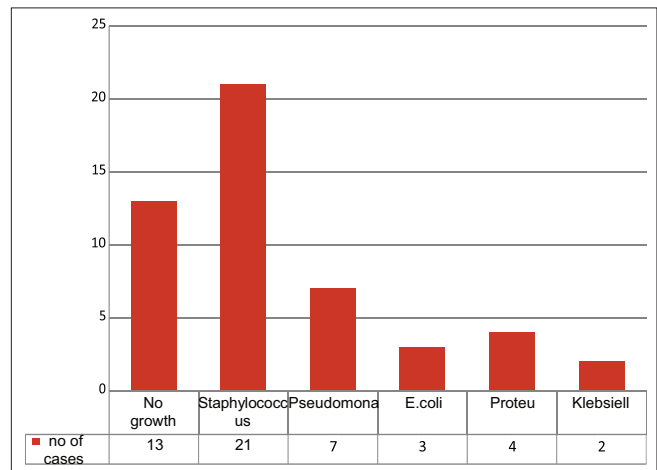


Chart 6: Organisms cultured from wound

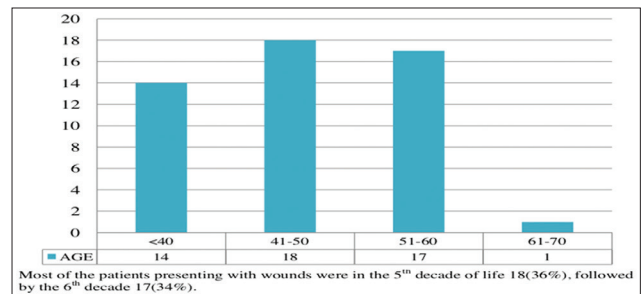


Chart 7: Age distribution of wounds

Based on etiology of wounds, which were determined by history and clinical examination, wounds were divided into traumatic, diabetic and vascular [Chart 3]. A major portion 25 (50%) of cases fell into traumatic group and 18 (36%) into diabetic and 7 (14%) into vascular group [Chart 4 Table 4].

Wounds of area <20 cm² constitute maximum number of cases – 44 (88%) [Chart 5].

The most common organism cultured from the wounds was *Staphylococcus aureus* 21 (42%) [Chart 6]

CONCLUSION

VAC therapy is a recent modality of treatment of wounds. Its introduction has changed the course of

management of wounds. Based on the data from the present study and other studies available, VAC does appear to result in better healing, with few serious complications, and thus looks to be a promising alternative for the management of various wounds. The application of VAC is simple but requires training to ensure appropriate and competent use.

In patients treated with negative pressure wound therapy (NPWT), the following was noted:

- Earlier appearance of granulation and epithelialization
- Rapid decrease in wound size
- Shorter duration of hospitalization
- Early achievement complete wound score.

On correlating the wound outcome variables, we also noticed that presence of diabetes mellitus increased the duration of formation of granulation tissue and epithelialization.^[8] This study confirms that negative pressure wound therapy is safe, has a faster response in wound healing, and gives better efficacy as compared to conventional wound therapy in the management of lower limb ulcers. Hence, it is a better choice for the management of lower limb ulcers.

SUMMARY

The negative pressure wound therapy (NPWT) is a feasible and excellent option for the management of different types of wounds. At present, NPWT has become an established method in wound management.

The application of sub-atmospheric pressure decreases the bacterial colonization over the wound and increases blood flow.^[9] Increased oxygenated blood flow to the wound healing promotes the oxidative bursts in neutrophils and thereby promoting the killing of microbes and preventing infection.

Most of the commercially available NPWT devices are foam-based systems. In our study, we used our own NPWT by using a Romo Vac suction drain which is cost-effective for reproducing the same results and for the benefit of patients, as the majority of our patients are from rural area.

- The present interventional study involved 50 cases of wounds.
- Patients affected were most commonly in the 5th (36%) decade followed by 6th decade (34%) [Chart 1 Table 5].
- There was a male preponderance with male:female ratio of 3.2:1.
- Most of the patients in the study presented early, presenting between 10 and 30 days of onset.

- VAC dressing was done in wounds occurring in a variety of locations such as foot 20 (40%), leg 16 (32%), forearm 5 (10%), ankle and sole 4 (8%), and abdomen 1 (2%). Twenty-seven (54%) of patients were smokers.
- Trauma was the most common etiology 25 (50%) followed by diabetes 18 (36%) and vascular causes 7 (14%).
- Wound area was recorded before treatment and grouped into <20 cm² (44 cases [88%]), 21–40 sq cm (4 cases [8%]) and > 40 sq cm (4 cases [8%]).
- *Staphylococcus aureus* was the most common organism cultured 21 (42%) followed by *Pseudomonas aeruginosa* 7 (14%). No growth was observed in 13 cases.
- Wound scores were recorded on days 3, 7, and 10 of VAC therapy. The scoring system used was based on the area of granulation tissue, its color, and consistency [Chart 7].
- Of 18 diabetic wounds, wound scores of 5 and above were observed in nine cases following VAC therapy. VAC dressing of longer duration is required for diabetic wounds for a good outcome.
- There was a significantly better outcome in non-smokers compared to smokers, with 75% of non-smokers and 58% of smokers showing wound scores >5 on day 7 of VAC therapy.^[10]

Thus, the outcome of VAC therapy depends on various factors such as age, etiology of wounds, and existence of comorbid conditions such as diabetes and factors like smoking. The candidates for VAC therapy should be chosen after considering these factors with care.

From our study, it can be concluded that VAC is a promising new technology in the field of wound healing with multiple applications in a variety of wounds.

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Comparative Study of Medical Management of Anal Fissure between Topical Application of Minoxidil and Diltiazem

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Abstract

Aims and Objectives: The aim of the study was to compare the outcome in the medical management of anal fissure with topical application of 2% minoxidil and 2% diltiazem for anal fissure.

Materials and Methods: Prospective study of 100 patients of anal fissure was done from October 2017 to August 2019 done at the Department of General Surgery NSCB Medical College Jabalpur. One subgroup of 49 patients treated with topical 2% minoxidil and other groups of 49 were treated with 2% diltiazem for 6 weeks and regularly followed every 2 weeks and assessed through pain visual analog scale from 0 to 10.

Results: Complete healing of fissure was seen in 34/49 patients used diltiazem and 42/49 who used minoxidil and use of minoxidil also associated with faster pain relief.

Conclusion: Minoxidil is a better alternative of diltiazem for medical management of anal fissure.

Key words: Fissure, Management, Topical application

INTRODUCTION

An anal fissure is linear, longitudinal tear, or split in the epithelial lining of the distal anal canal distal to the dentate line. Anal fissure is one of the most common anorectal problems. It is often associated with severe sharp pain upon defecation described as “tearing” or “passing broken glass” and sometimes bleeding followed by a less severe burning pain which may last for several hours afterward.^[1-4]

Fissures can be classified as acute if they have been present for <6 weeks chronic if they persist for more than 6–8 weeks. Acute fissures are often superficial and well-demarcated edges. Chronic anal fissures on the other hand

are wider and deeper and marked by ulcer with keratinous edges, presence of a sentinel tag at the external apex, and hypertrophy of the anal papillae.^[5-7]

Minoxidil (2,4-diamino-6-piperidinopyrimidine-3-oxide) is a vasodilator which an effective vasodilator which acts directly on vascular smooth muscle cells, producing a decreasing in peripheral vascular resistance and reduces blood pressure. Minoxidil acts through opening the potassium channels. The potassium efflux leads to hyperpolarization of the smooth muscle and reduction in calcium influx through voltage-operated calcium channels. These pharmacological properties suggest potential benefits for minoxidil in the medical management of anal fissure. Diltiazem (calcium channel blocker) has a role in the treatment of anal fissure as they have shown to reduce resting anal pressure (RAP).^[8-12]

Aims and Objective

In this study, we had compared the medical management of anal fissure with topical agent 2% minoxidil and 2% diltiazem.

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MATERIALS AND METHODS

After a detailed history clinically examination, the diagnosis of anal fissure was confirmed. Some of the cases of anal fissure had given ointment based topical minoxidil and some cases were given ointment based topical diltiazem to apply it circumferentially inside anal verge thrice a day for 6 weeks and ask to avoid laxative and stool softer and patient ask to visit the hospital every 2 weeks and assessed through pain visual analog scale (VAS). Pain score was recorded on a VAS from 0 to 10.0 being minimum pain and 10 being maximum (intolerable) pain which hampers routine activity.

This is a prospective, randomized controlled study for the duration of September 2017 to August 2019 and was conducted in Netaji Subhash Chandra Bose Medical College and Hospital Department of General Surgery Jabalpur (M.P.).

The ethics committee of our hospital approved the protocol and all patients provided written informed consent.

A total of 100 patients were enrolled for study, divided into two subgroups one subgroup (n=50) given treatment with 2% minoxidil, and another subgroup (n=50) received treatment with 2% diltiazem for medical management of anal fissure.

Patients were advised to apply ointment circumferentially inside the anal orifice every 8 hourly for 6 weeks and the patient was asked for follow-up on OPD basis every alternate week for a period of 6 weeks.

Anal pain was assessed before starting the treatment and at alternate week follow-up visit through using a linear visual analog pain score (0–10).

All the demographic and technical data related to patients included in the study were collected, entered in Pro forma, and master chart in excel sheet.

Statistical Analysis

All the data were entered in Microsoft Excel and then transferred to IBM SPSS version 21.0 for analysis. Data were analyzed and $P < 0.05$ was taken as the level of significance.

OBSERVATION AND RESULTS

We did this study in 98 patients which were divided into two groups consisting of 49 patients in each group. One group of 49 patients received 2% diltiazem, while other groups

received 2% minoxidil for local application on perianal and anal orifice for 6 weeks for medical management of anal fissure.

Pre-treatment chief complaints like pain which was the main chief complaint were assessed with VAS and score was given from 0 to 10, another complaint was bleeding per rectum was assessed subjectively. After receiving treatment, the patient was reassessed every alternate week in a follow-up visit on OPD basis and after examination pain and healing of anal fissure was assessed. For 6 weeks, complete healing was defined as the presence of scar or disappearance of fissure after maximum 6 weeks of treatment, while partial healing was defined as persistence of fissure but improvement in symptoms (pain relief and/or control of bleeding).

Majority of patient participated in our study were mainly young male presented with complains of pain on defecation (70.4%) and pain on defecation with bleeding per rectum (26.5%) mainly.

Mean age of patients participated in our study was 31.63 years in one group (D) and 33.31 years in another group (M), while pre-intervention grade of pain in one group (D) is 4.69 while in another group (M) it was 4.76. The mean time complete healing was found 3.5 weeks in one group (D), while the meantime of complete healing in another group (M) was found to be 2.7 weeks. Complete healing was seen in 34 out of 49 patients (69.4%) in one group (D) and seen in 42 out of 49 patients (85.5%) in other groups (M). The main side effect seen within the group using diltiazem for anal fissure locally were perianal excoriation seen in two patients (4.1%), itching seen in eight patients (16.3%), and itching with excoriation seen in one patient (2%) while main complications seen with the group using minoxidil were excoriation in two patients (4.1%), haring in perianal and anal region in three patients (6.1%), and perianal itching in two patients (4%) [Figure 1, Graphs 1 and 2, Tables 1 and 2].

DISCUSSION

In Awan *et al.* prospective study, randomized, double-blind study, a total of 100 patients with anal fissure were recruited (50 patients in each group). The patient in Group A received local ointments containing 0.5% minoxidil while the patient in Group B received topical 2% diltiazem. Healing of anal fissure and symptomatic relief were observed and analyzed. The rate of healing was similar in two groups, meantime taken for healing was significantly shorter with minoxidil with no systemic or local side effect.^[13]

Table 1: Distribution of complaints according to treatment option selected

Complaints	Treatment option selected		Total
	Diltiazem	Minoxidil	
Pain on defecation			
Count	38	31	69
% Within treatment option selected	77.6%	63.3%	70.4%
Pain on defecation with bleeding			
Count	11	15	26
% Within treatment option selected	22.4%	30.6%	26.5%
Pain on defecation with itching			
Count	0	3	3
% Within treatment option selected	0.0%	6.1%	3.1%

Chi-square=4.326; P=0.115

Table 2: Distribution of healing according to treatment option selected

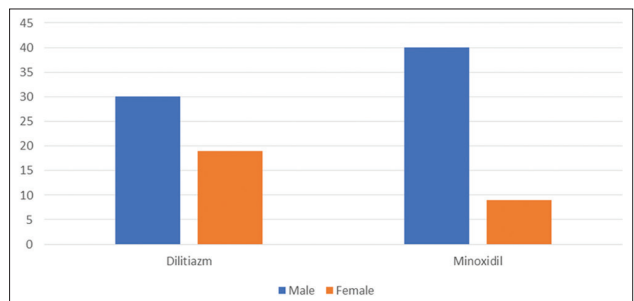
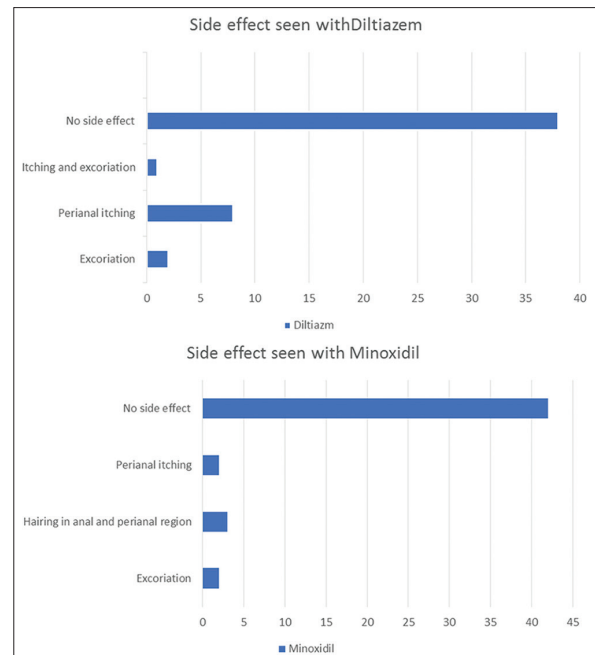
Healing	Treatment option selected		Total
	Diltiazem	minoxidil	
Complete			
Count	34	42	76
% Within treatment option selected	69.4%	85.7%	77.6%
Partial			
Count	15	7	20
% Within treatment option selected	30.6%	14.3%	22.4%

Chi-square=4.64; P=0.098

In Alvandipour *et al.*, in a double-blind, randomized clinical trial, including 88 patients of anal fissure were randomly assigned to either 0.5% minoxidil ointment or 2% diltiazem cream for local application. In the study, diltiazem and minoxidil reduced the pain, bleeding and improved fissure healing with no significant difference with slight higher local complication, that is, itching was slightly higher with minoxidil.^[14]

In Muthukumarassamy *et al.* in a prospective, randomized, double-blind study in 90 patients with anal fissure were recruited. The patient received a local application of an ointment containing 5% lignocaine (28), 0.5% minoxidil (36), or both (26). In this study, rate of healing was similar in three groups, while meantime taken for healing was significantly shorter in mix and minoxidil alone group compare to lignocaine alone group. The rate of pain relief was similar in the three groups. Stoppage of bleeding occurred more often with combination treatment than with lignocaine alone.^[15]

Our study is in agreement with that of previous similar studies. The minoxidil group had a slightly higher rate of pain relief compare to diltiazem and more cases of complete healing of anal fissure compare to diltiazem.


Figure 1: Pre-treatment anal fissure clinical pic

Graph 1: Distribution of gender according to treatment option selected

Graph 2: Distribution of side effects according to treatment option selected

The small sample size was the main limiting factor of our study.

CONCLUSION

Complete healing anal fissure was seen in 34/49 patients used diltiazem while complete healing seen in 42/49 patients used minoxidil. The rate of pain relief was found to be faster in a group using minoxidil compare to a group using diltiazem. This difference between rate of pain relief and fissure healing between diltiazem and minoxidil local application for anal fissure was found statistically significant. Hence, we conclude that the use of 2% minoxidil local application for medical management of anal fissure has advantages of a faster rate of pain relief and complete healing and hence may be considered as an alternative treatment modality for medical management of anal fissure.

Hence, in view of faster pain relief and complete healing and less side effect, we conclude that minoxidil is a better alternative for medical management of anal fissure compare to diltiazem.

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Sonological Findings of Interstitial Lung Disease and Its Comparison with HRCT in Bhopal, India

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Abstract

Introduction: Interstitial lung disease (ILD) refers to a group that is characterized by varying combinations of inflammation and fibrosis involving the space between the epithelial and endothelial basement membranes.

Aim and Objective: This study was conducted to the comparison of B line distance (vertical hyperechoic reverberation artefacts) in high-frequency sonography in ILD with high-resolution computed tomography (HRCT).

Materials and Methods: Prospective analytical cross-sectional study conducted on patient ILD, thoracic sonography, and HRCT were included in our study. USG was performed through intercostals space on all patients using a 7.5–10MHz linear probe for lung. HRCT studies were performed with 128-MDCT scanner. USG B line distance compare with HRCT scans were assessed for the presence of consolidation, ground-glass opacity, nodular, reticular, reticulonodular, bronchiectasis, and honeycomb appearance. Student's *t*-test and ANOVA were used to compare the means. Chi-square test was used to compare the categorical data. *P*-value of < 0.05 is considered as statistically significant.

Results: In the present study, ILD was more prevalent in the age between 51–60 (31%) and 61–70 years (31%) followed by 41–50 years (16%). Study on USG findings, it was found that all patients had B line (100%). Negative correlation between B line distance and consolidation, ground-glass appearance with HRCT finding. Positive correlation between B line distance and reticular pattern, reticulonodular pattern, bronchiectasis, and honeycombing pattern with HRCT findings.

Conclusion: Ultrasound is useful in situations where HRCT is not available or undesirable, as in pre-hospital emergencies and in pregnancy and when a patient cannot be transported out of the intensive care unit because of severe disease.

Key words: B line, High frequency USG, High-resolution computed tomography, Interstitial lung disease

INTRODUCTION

Interstitial lung disease (ILD) refers to a group of disorders that are characterized by varying combinations of inflammation and fibrosis involving the space between the epithelial and endothelial basement membranes. ILD has different etiologies, clinical presentations, radiological patterns, and histological appearance.^[1]

The causes of ILD can be classified into one of the following four categories: (1) Diseases associated with

the condition that affects other parts of the body (e.g., autoimmune or collagen vascular disease), (2) diseases associated with specific exposure to an agent known to damage the lungs (e.g., medications such as bleomycin, occupational exposures such as asbestos, tobacco smoke, or agents in the environment that causes an immune reaction called hypersensitivity pneumonitis), (3) diseases associated with known genetic abnormalities (e.g., Hermansky–Pudlak syndrome), and (4) idiopathic diseases (diseases of an unknown cause). The most common ILDs are idiopathic.^[2]

ILD may be idiopathic or caused by exposure to organic and inorganic substances (hypersensitivity pneumonitis and pneumoconiosis), medical conditions such as connective tissue diseases (CTDs), multisystemic diseases and obstructive sleep apnea, drugs, infection, and radiation therapy. The overall estimated prevalence of ILD is about

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25–74/100,000 population and up to 80.9 per 100,000 in men and 67.2 per 100,000 in women.^[3]

Diagnosis of ILD is usually made based on a combination of clinical, functional, radiological, and histological data.

Reticular pattern involving the subpleural regions, ground-glass opacities, nodular and micronodular pattern, and honeycombing are the common high-resolution computed tomography (HRCT) signs of pulmonary fibrosis.^[4]

Chest ultrasonography has many uses, both diagnostic and interventional. It is used in the diagnosis of diseases of the pleural space such as pleural effusion, pleural thickening, pleural masses, and pneumothorax. It is also used in the diagnosis of diseases caused by lung parenchymal lesions such as pneumonia, lung abscesses, neoplasms, pulmonary embolism, and arteriovenous malformations.^[5]

However, some studies have demonstrated that transthoracic sonography (TS), as a consequence of its well-known advantages (absence of radiation exposure, ready availability, and cost-effectiveness), can play a complementary role in the diagnosis of ILD, especially when chest radiography or HRCT is not readily available or undesirable for instance during pregnancy. Moreover, TS can be useful in monitoring the course of the disease in patients with confirmed ILD (thus avoiding unnecessary overload of radiation exposure).^[6]

Diffuse parenchymal lung diseases as pulmonary fibrosis, characterized by the presence of multiple diffuse bilateral B-lines that appear as discrete laser-like vertical hyperechoic reverberation artifacts that arise from the pleural line, extend to the bottom of the screen without fading, and move synchronously with lung sliding.^[7]

The ultrasound assessment of ILD is determined by the presence and quantification of B-lines, which consist of tails generated by the reflection of the ultrasound beam from thickened subpleural interlobar septa at the lung surface interface.^[8]

In radiologic imaging, the term “artefact” describes any part of an image which does not accurately represent the anatomic structures present within the subject being evaluated. B-lines are defined as discrete laser-like vertical hyperechoic reverberation artefacts that arise from the pleural line, extend to the bottom of the screen without fading, and move synchronously with respiration.^[7]

B-lines are visible when the lung parenchyma air content is partially decreased and/or the interstitial space is volumetrically expanded, such as in pulmonary edema of

various etiologies and ILD. It is important to underline that B-lines cannot be clearly correlated to a specific anatomical structure, but rather they are correlated to the changes in the physical properties of the lung.^[8]

The present study is an attempt to evaluate high-frequency sonological findings in ILD and its comparison with HRCT.

Aims and Objectives

The aim of the study was as follows:

- To evaluate high-frequency sonological findings in ILD
- To compare these sonological signs with HRCT.

MATERIALS AND METHODS

This study was prospective analytical cross-sectional study type.

Study Place

This study was conducted at Gandhi Medical College, Hamidia Hospital, Bhopal.

Study Duration

This study duration was 18 months.

Methodology

One hundred adult patients with ILD who were referred to our department from TB and chest department for thoracic sonography and HRCT were included in our study.

Inclusion Criteria

The following criteria were included in the study:

- Patients with complaints of ILD and referred from the TB and chest and medicine department.

Exclusion Criteria

The following criteria were excluded from the study:

- Patients with lung neoplasm
- Patients other than ILD.

Sample Size

This study was 100 patients.

Procedure

USG chest

It was performed in our Department of Radiodiagnosis Gandhi Medical College, Bhopal, on all patients using a 7.5–10 MHz linear probe for lung and pleural examinations.

HRCT chest

All chest HRCT studies were performed in the Department of Radiodiagnosis Gandhi Medical College Bhopal with a 128-MDCT scanner.

Volumetric 1.25 mm slice thickness HRCT chest acquisition was done with the patient supine in the cranial-to-caudal direction during a single breath-hold.

From the volumetric CT, data set a series of contiguous thin-collimation 1.25 mm axial HRCT images were reconstructed using a high spatial resolution algorithm.

Investigations

HRCT is the gold standard for ILD diagnosis. HRCT scans were assessed for the presence of consolidation, pleural effusion, ground-glass opacity, nodular, reticular, reticulonodular, bronchiectasis, and honeycomb appearance.

Thoracic US examinations were performed on all patients. Patients were investigated in the supine or sitting position with their arms raised above heads to widen the intercostal space. Lung ultrasonography was performed in a series of scan lines along the chest wall with the transducer oriented either perpendicular or transverse to the chest wall. The anterior chest: Along the para-sternal lines, along the mid-clavicular, anterior axillary, and mid-axillary lines; for the posterior chest: Along the paravertebral, subscapular, and posterior axillary lines. It was done using grayscale (B-mode) and time-motion (M-mode).

Lung Ultrasound Technique

Investigations

History – Detailed chronological history was taken from patients about inflammatory lung disease.

Physical examination – Comprising systemic and local examination. Radiological examination

1. High-frequency ultrasonography chest
2. HRCT chest.

Statistical Analysis

Student's *t*-test and ANOVA were used to compare the means. Chi-square test was used to compare the categorical data. $P < 0.05$ is considered as statistically significant.

DISCUSSION

ILDs represent a heterogeneous group of lung disorders that may be acute or chronic and characterized by diffuse involvement of the interstitium and impairment of the gas exchange capacity through the alveolocapillary membrane, which may lead to respiratory failure. LDs have different etiologies, clinical presentations, radiological patterns, and histological appearance. HRCT is considered the concurrent gold standard for the diagnosis of ILD as it a sensitive method to assess the extent and the pattern of pulmonary fibrosis.^[9,10] Reticular pattern involving the subpleural regions, ground-glass opacities, nodular and

micronodular pattern, and honeycombing are the common HRCT signs of pulmonary fibrosis.^[4]

In ultrasonographic examination, the presence of a marked difference in acoustic impedance between an object and its surroundings leads to the appearance of B-line artifacts.^[11] Normal lung contains much air and little water, so no reflection of the ultrasonographic beams occurs and normally, no B-line artifacts appear. When subpleural septae are thickened by water or fibrosis, a high impedance gradient occurs between these structures and the surrounding air, causing reflection of the beams, which create a phenomenon of resonance. The beam seems to be trapped in a closed system, resulting in endless to-and-fro echoing and yielded on the screen as a narrow-based laser-like ray extending from the lung surface to the edge of the screen.^[12,13] In the present study, we evaluated high-frequency sonological findings in ILD and compared these sonological signs with HRCT.

In the present study, ILD was more prevalent in the age between 51–60 (31%) and 61–70 years (31%) followed by 41–50 years (16%). In a similar study, the age distribution of ILD patients was recorded as 54 ± 13 years by Gargani *et al.*^[14] Cömert *et al.* also recorded a similar distribution of age, that is, 59.2 ± 14.2 years.^[15] In Rotondo *et al.* study observed that mean age was 56.2 ± 13.8 .^[16]

In the present study, ILD was more prevalent in male patients (71%) followed by 29% females. Sperandeo *et al.* in a similar study found the male (61%) preponderance over female (39%) gender.^[17] In Fessi *et al.* study of ILD patients also found the male (43%) to female (57%) ratio as 1:1.3 which is contrasting to our result, this could be due to sample selection and inclusion criteria applied.^[10] The preponderance of male in our study may be due to the higher prevalence of smoking habits and exposure to pollution.

Most common presenting symptom in the present study was cough which was present in all the patients (100%), the productive cough was present in 43%, nonproductive cough was reported in 37% patients, 115 had blood in cough, more than half of the patients (53%) had breathlessness, 17% breathlessness during rest, 27% had breathlessness during walking, and 48% had breathlessness during exercise. In a similar meta-analysis by Carvajalino *et al.* reported that the highest prevalence was that for breathlessness (54–98%) and cough (59–100%) followed by heartburn (25–65%) and depression (10–49%).^[18] Alhamad *et al.* reported a cough in the majority of the patients (82%) with ILD.^[19] Araki *et al.* reported cough in 93% and dry cough in 45% of patients.^[20] Bajwah *et al.* reported dyspnoea in 93%; cough in 60%; fatigue in 29%; insomnia in 6%;

and dyspepsia 4%.^[21] All these studies are in line with the present study findings.

In the present study, 46% were smokers and 54% were non-smokers. There are strong associations between RA-ILD and older age, male sex, cigarette smoking, high rheumatoid factor titers, and increased anti-citrullinated protein antibody levels.^[22] Fraig *et al.* evaluated 156 surgical lung biopsies, and they found 109 cases of RB, corresponding 98% of cases to smoker patients.^[23] In the same way, Remy-Jardin *et al.* studied the parenchymal lesions of 41 smokers and they found the presence of pigmented macrophages in 69% of the patients.^[24] Cottin *et al.* observed diagnosis of ILD in 88.6% of smoker patients who were operated for spontaneous pneumothorax.^[12]

According to the International Consensus Conference on Pleural and Lung Ultrasound, B-lines are described as a discrete laser-like vertical hyperechoic lines arising from the pleural plane, extending to the bottom of the screen without fading and moving synchronously with the lung sliding. The presence of ≥ 3 B-lines between two ribs in a single scan is indicative for the presence of sonographic interstitial syndrome.^[7]

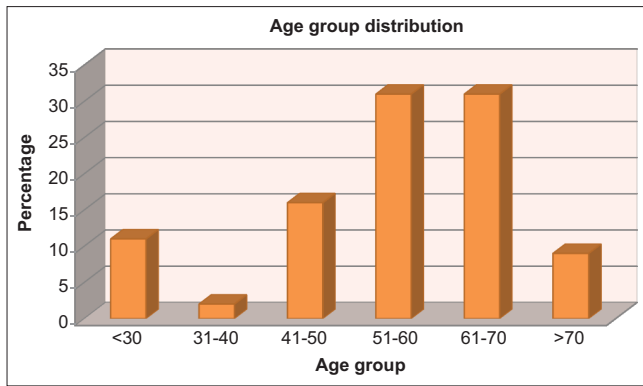
In the present study on USG findings, it was found that all patients had B line (100%), the majority had distance between B lines of 7 mm (23%) followed by 5 mm (20%) and 4 mm (19%). Sliding pleura was abolished in 16% of patients. In a similar study by Hasan and Makhlof reported that the distance between each of the two adjacent B lines correlated with the severity of the disease on chest HRCT where B3 (the distance was 3 mm) correlated with ground-glass opacity and B7 (the distance was 7 mm) correlated with extensive fibrosis and honeycombing. Furthermore, the distance between B-lines inversely correlated with FVC ($r = -0.848$, $P < 0.001$), TLC ($r = -0.664$, $P < 0.001$), DLCO ($r = -0.817$, $P < 0.001$), and PaO₂ ($r = -0.902$, $P < 0.001$).^[25] Our results are comparable with Lichtenstein, who reported the average distance between B-lines due to thickened interlobular septa by well-established fibrosis (7 mm) was wider may be due to the early stage of alveolar–interstitial affection and ground-glass attenuation (3 mm).^[12] Bouhemad *et al.* found that multiple B-lines 7 mm apart are caused by thickened interlobular septa in 30% patients and B-lines at 3 mm or less apart are caused by in 19%.^[26]

In the present study, pleural effusion was seen in 6 patients, ground-glass appearance in 45%, reticular pattern in 55 patients, nodular pattern in 25%, reticulonodular pattern in 25%, consolidation in 12%, honeycombing pattern in 40%, bronchiectasis in 37%, pleural thickening in 31%, and fibrotic band in 37% patients. Travis *et al.* reported

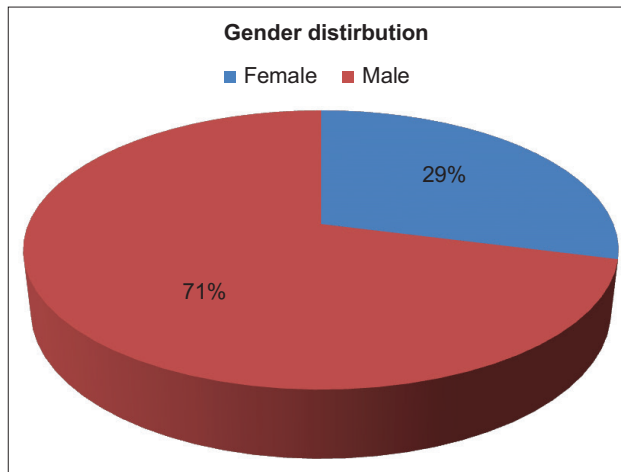
similar findings in ILD patients, HRCT scan, the lower lung zones were predominantly involved in 92% of cases; 46% had a peripheral distribution; and 47% were diffuse. Most showed a reticular pattern (87%) with traction bronchiectasis (82%) and volume loss (77%). (Travis *et al.*) Giudice *et al.* in their study revealed “comet-tail” artifacts in the anterolateral lung fields in 31 (56.36%) patients and mixed patterns consisting in increased density associated with ring-down artifacts in 24 (46.64%). Pleural involvement was also observed in 34 cases (61.82%). Thoracic US appears to be a useful adjunct to clinical, laboratory, and radiological studies in patients suspected of having infectious interstitial pneumonia.^[27] Sperandio *et al.* reported that most common USG findings as subpleural cysts seen in 57/84 (68%), reduction in physiological “gliding sign” related to disease severity (observed in 33/84–39% cases), and increased number of horizontal (and to a lesser extent vertical) reverberation artifacts (seen in 41 patients with advanced fibrosis, 34% of the total series).^[17] Sayeda *et al.* reported similar findings as sonographic features among ILD patients were B lines in 73.8%, abolished lung sliding in 23.8%, irregular and thickened pleura in 47.6% and 35.7%, respectively, and subpleural lesions in 38.1%. Increasing distance between the B lines was negatively correlated with both forced vital capacity % predicted, ground-glass opacities, and positively correlated with reticular opacities patterns on MDCT chest.^[28]

The present study found a positive correlation between B line distance and pleural effusion, where the correlation coefficient is $r = 0.154$ with insignificant $P = 0.128$. No significant correlation was obtained.

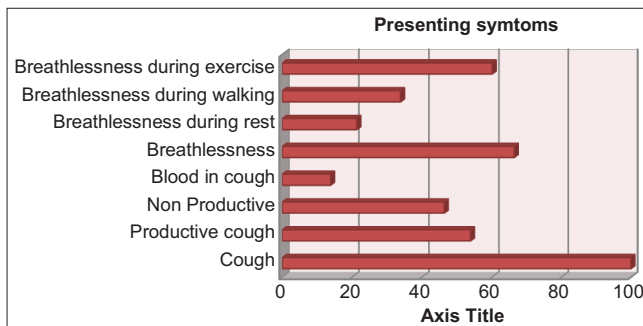
The present study found a negative correlation between B line distance and ground-glass appearance, where the correlation coefficient is $r = -0.770$ with significant $P < 0.001$. This means as the distance between B line increases and ground-glass appearance decreases. Hasan and Makhlof, in 61 patients with different CTDs, showed that the severity of ILD had a positive correlation between B-lines on LUS and the findings on chest HRCT in terms of ground-glass opacity.^[25] Early stages of ILD, even before the thickening of the subpleural interlobular septa, give ground-glass areas in HRCT. Ultrasound examination of these areas gives numerous B-lines with a narrow distance between them (3 mm), making the surface of the lung more hyperechoic, giving the description of the white lung. This may be due to the affection of the alveolar wall by inflammatory cells and edema, making it about the pleural surface between two septa giving numerous artifacts with a narrow distance between them. Bouhemad *et al.* found that multiple B-lines 7 mm apart are caused by thickened interlobular septa, characterizing interstitial edema, while



Graph 1: Age group distribution



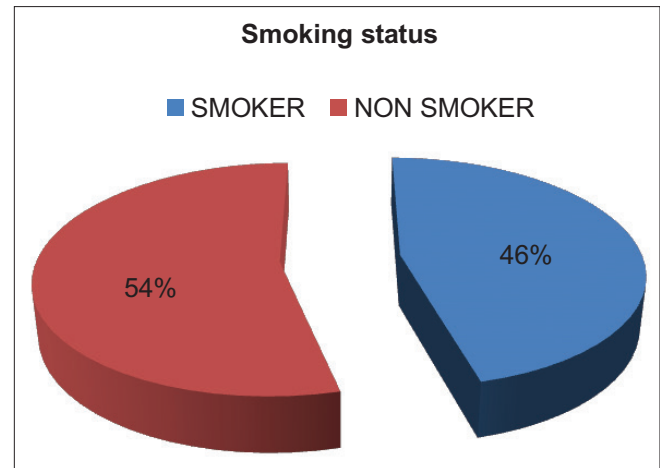
Graph 2: Gender distribution



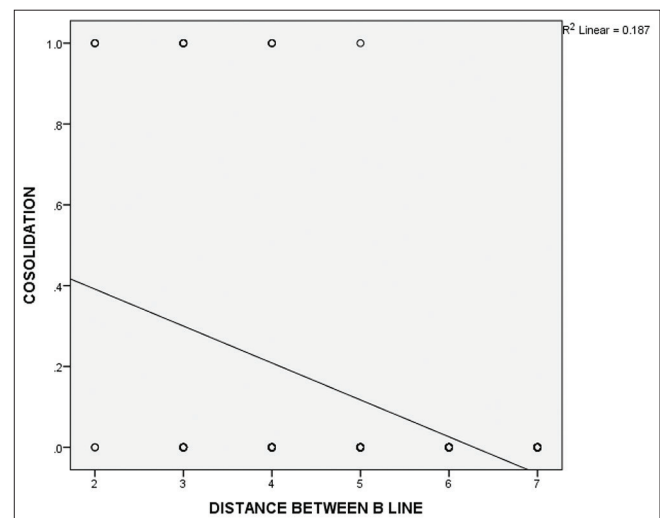
Graph 3: Presenting symptoms

B-lines 3 mm or less apart are caused by ground-glass areas characterizing alveolar edema.^[26]

The present study found a positive correlation between B line distance and pleural effusion, where the correlation coefficient is $r = 0.122$ with insignificant $P = 0.241$. No significant correlation was obtained. Sayeda *et al.* reported pleural abnormalities, thickened pleura, and pleural effusion were significantly higher among patients than among controls (35.7 vs. 0%, $P = 0.002$, 33.3 vs. 0%, $P = 0.001$, respectively). The subpleural parenchymal



Graph 4: Smoking status

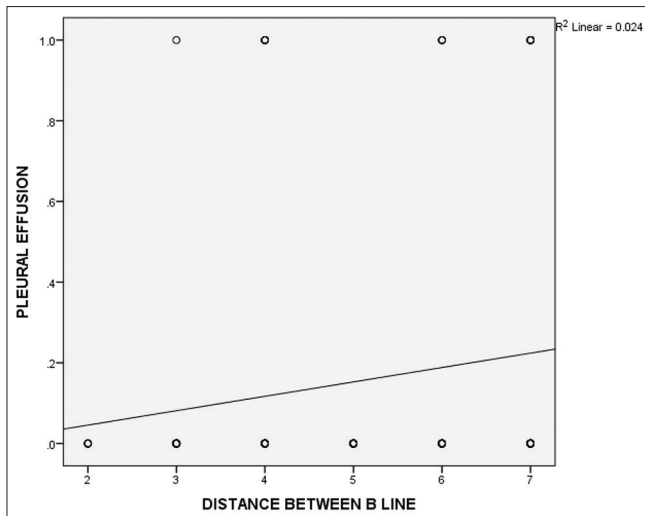


Graph 5: This graph shows a negative correlation between B line distance and consolidation, where the correlation coefficient is $r = -0.133$ with insignificant $P = 0.365$. No significant correlation was obtained

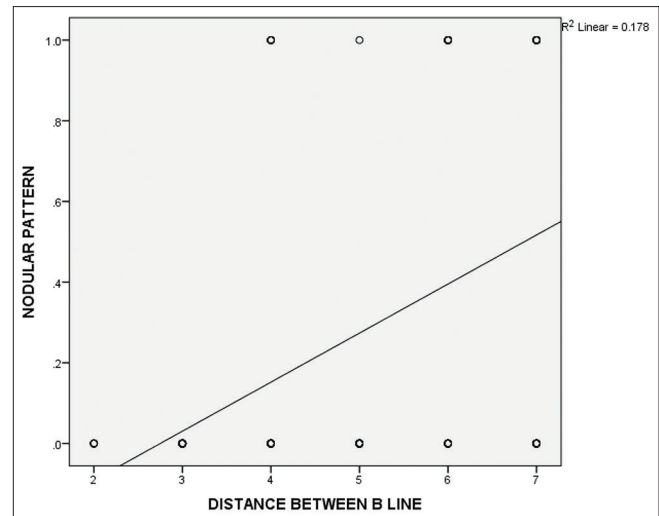
lesions were significantly higher in ILD patients compared with controls (38.1 vs. 0%, $P = 0.007$). Their sizes ranged from 15 to 20 mm.^[28]

The present study found a positive correlation between B line distance and bronchiectasis, where the correlation coefficient is $r = 0.182$ with an insignificant $P = 0.681$. No significant correlation was obtained. Barakat reported that the maximum number of B-lines seen in any positive zone was significantly correlated with type of bronchiectasis on chest HRCT ($r = 0.729$; $P < 0.0001$), and extent of bronchiectasis on chest HRCT ($r = 0.640$; $P < 0.0001$).^[29]

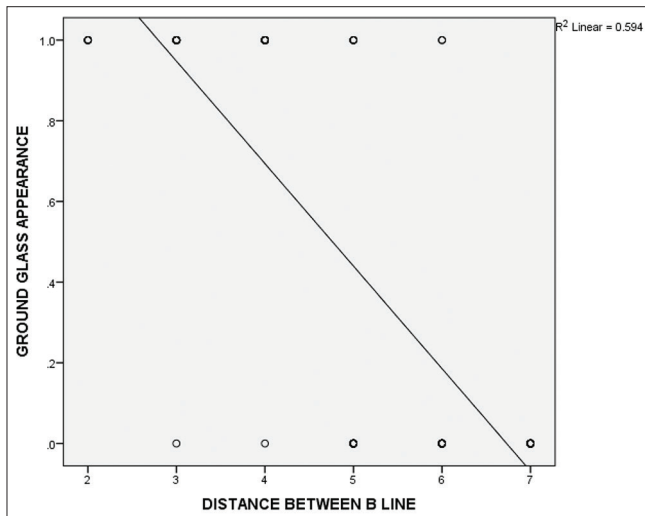
The present study found a positive correlation between B line distance and pleural thickening, where the correlation coefficient is $r = -0.164$ with insignificant $P = 0.104$. No significant correlation was obtained. Sperandeo *et al.*



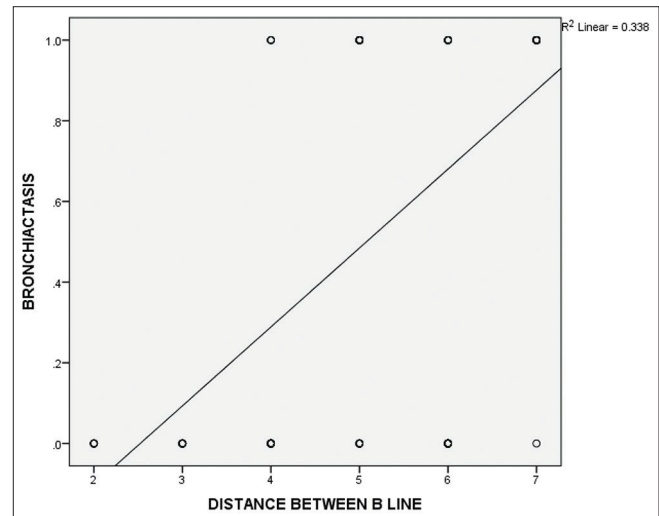
Graph 6: This graph shows a positive correlation between B line distance and pleural effusion, where the correlation coefficient is $r = 0.154$ with insignificant $P = 0.128$. No significant correlation was obtained



Graph 8: This graph shows a positive correlation between B line distance and pleural effusion, where the correlation coefficient is $r = 0.122$ with insignificant $P = 0.241$. No significant correlation was obtained



Graph 7: This graph shows a negative correlation between B line distance and ground-glass appearance, where the correlation coefficient is $r = -0.770$ with significant $P < 0.001$. This means as the distance between B lines increases ground-glass appearance decreases



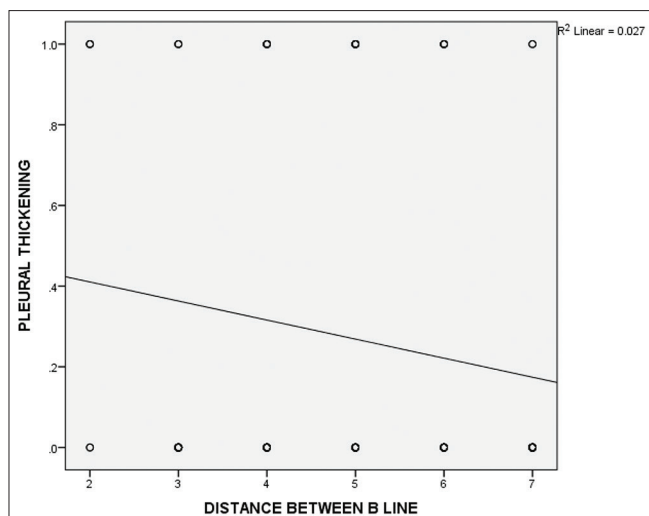
Graph 9: This graph shows a positive correlation between B line distance and bronchiectasis, where the correlation coefficient is $r = 0.182$ with insignificant $P = 0.681$. No significant correlation was obtained

enrolled 175 ILD patients who underwent LUS examination and chest HRCT. They found a good correlation between pleural and subpleural irregularities and nodules on LUS and the HRCT findings.^[17]

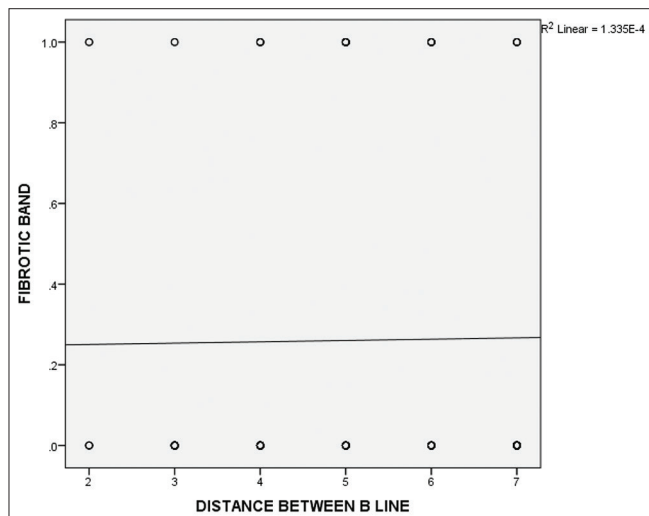
The present study found a positive correlation between B line distance and fibrotic band, where the correlation coefficient is $r = 0.012$ with insignificant $P = 0.909$. No significant correlation was obtained. Song *et al.* supported these data showing that the number of B-lines had a good correlation with the HRCT fibrosis pattern and good diagnostic accuracy in terms of sensitivity (91.5%) and specificity (81.3%) (35).^[30]

The present study found a positive correlation between B line distance and honeycombing pattern, where the correlation coefficient is $r = 0.212$ with significant $P = 0.562$. No significant correlation was obtained. Hasan and Makhoul, in 61 patients with different CTDs, showed that the severity of ILD had a positive correlation between B-lines on LUS and the findings on chest HRCT honeycombing.^[25]

The present study found a positive correlation between B line distance and reticulonodular pattern, where the correlation coefficient is $r = 0.061$ with significant $P < 0.781$. No significant correlation was obtained. Sayeda



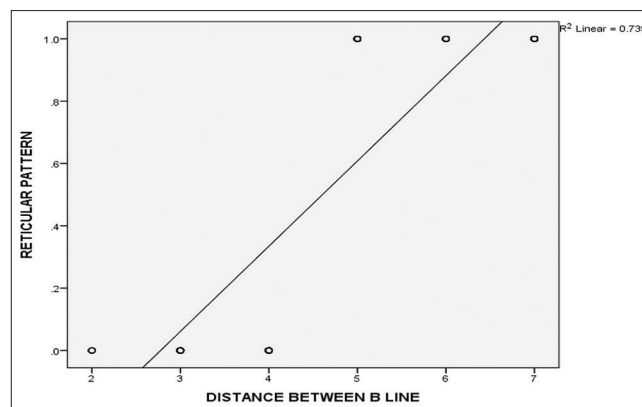
Graph 10: This graph shows a positive correlation between B line distance and pleural thickening, where the correlation coefficient is $r = -0.164$ with insignificant $P = 0.104$. No significant correlation was obtained



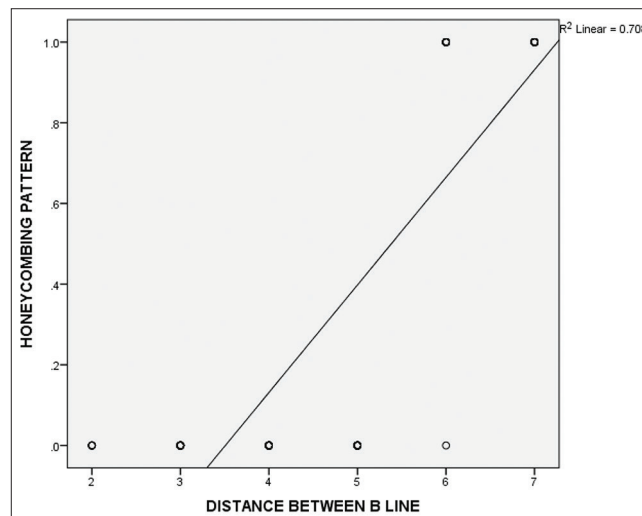
Graph 11: This graph shows a positive correlation between B line distance and fibrotic band, where the correlation coefficient is $r = 0.012$ with insignificant $P = 0.909$. No significant correlation was obtained

et al. reported the sonographic features among ILD patients were B lines in 73.8%, abolished lung sliding in 23.8%, irregular and thickened pleura in 47.6% and 35.7%, respectively, and subpleural lesions in 38.1%. Increasing distance between the B lines was negatively correlated with both of forced vital capacity % predicted, ground-glass opacities, and positively correlated with reticular opacities patterns on MDCT chest.^[28]

Cross-sectional nature and small sample size are the main limitations of the present study, a large randomized clinical trial is required to provide strength to present study findings.



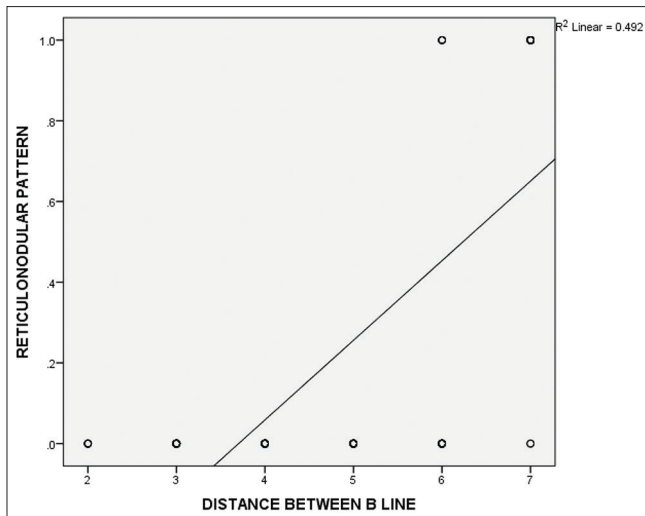
Graph 12: This graph shows a positive correlation between B line distance and reticular pattern, where the correlation coefficient is $r = 0.859$ with significant $P < 0.001$. This means as the distance between B lines increases reticular pattern also increases



Graph 13: This graph shows a positive correlation between B line distance and honeycombing pattern, where the correlation coefficient is $r = 0.212$ with significant $P = 0.562$. No significant correlation was obtained

RESULTS

1. In the present study, majority of the patients had an age between 51–60 (31%) and 61–70 years (31%) followed by 41–50 years (16%)
2. In the present study, majority of the patients were males (71%) followed by 29% females
3. Most common presenting symptom in the present study was cough which was present in all the patients (100%), productive cough was present in 43%, nonproductive cough was reported in 37% patients, 115 had blood in cough, more than half of the patients (53%) had breathlessness, 17% breathlessness during rest, 27% had breathlessness during walking, and 48% had breathlessness during exercise



Graph 14: This graph shows a positive correlation between B line distance and reticulonodular pattern, where the correlation coefficient is $r = 0.061$ with significant $P < 0.781$. No significant correlation was obtained

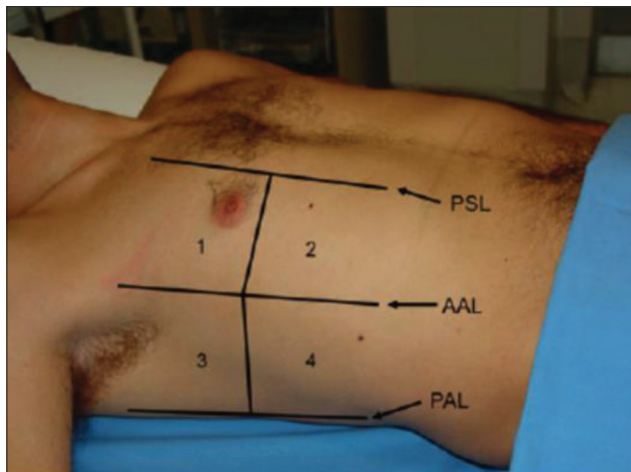


Figure 1: Markings

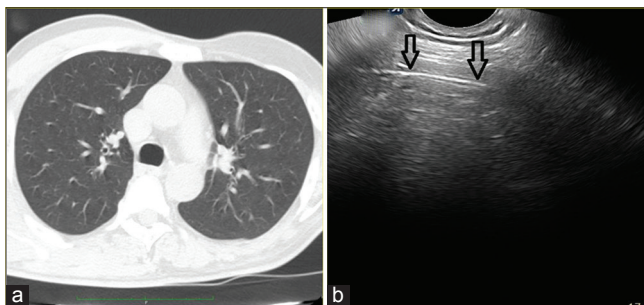


Figure 2: (a) High resolution computed sonography: Normal. (b) Transthoracic ultrasonography: Normal hyperechoic pleural line (black arrow). No B-lines visible

4. In the present study, 46% were smokers and 54% were non-smokers
5. In the present study on USG findings, it was found that all patients had B line (100%), majority had distance

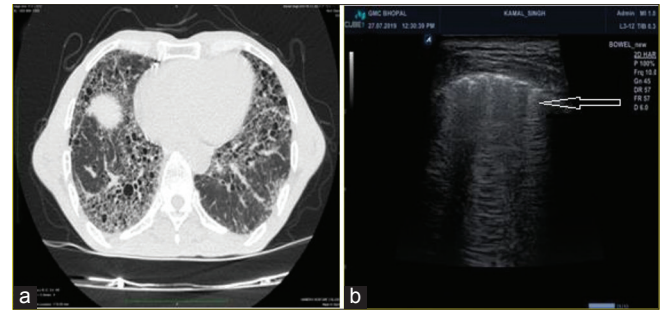


Figure 3: (a) High resolution computed tomography of the chest showing bilateral subpleural reticular and honeycomb shadows in a patient. (b) Transthoracic sonography shows B lines (white arrow) arising from the pleural line with a distance between the two B lines of about 7 mm

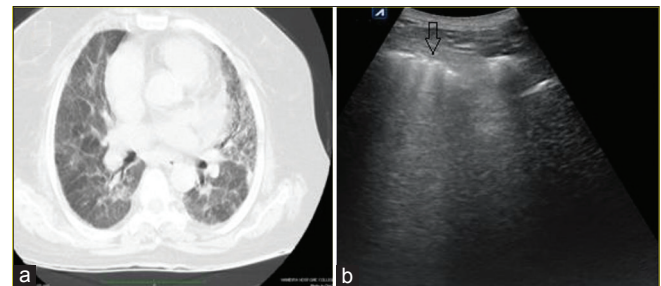


Figure 4: (a) High resolution computed tomography of the chest in a patient with interstitial lung disease showing left lung ground-glass opacity. (b) Transthoracic sonography of the same patient showing multiple B lines arising from a thickened and irregular pleural line (black arrow)

- between B lines of 7 mm (23%) followed by 5 mm (20%) and 4 mm (19%). Sliding pleura was abolished in 16% of patients
6. In the present study, pleural effusion was seen in 6 patients, ground-glass appearance in 45%, reticular pattern in 55 patients, nodular pattern in 25%, reticulonodular pattern in 25%, consolidation in 12%, honeycombing pattern in 40%, bronchiectasis in 37%, pleural thickening in 31%, and fibrotic band in 37% patients
7. Correlation between B line this graph shows a negative correlation between B line distance and consolidation, where the correlation coefficient is $r = -0.133$ with an insignificant $P = 0.365$. No significant correlation was obtained, with HRCT finding.
8. This graph shows a positive correlation between B line distance and pleural effusion, where the correlation coefficient is $r = 0.154$ with insignificant $P = 0.128$. No significant correlation was obtained
9. This graph shows a negative correlation between B line distance and ground-glass appearance, where the correlation coefficient is $r = -0.770$ with significant $P < 0.001$. This means as the distance between B line increases ground-glass appearance decreases
10. This graph shows a positive correlation between B line distance and nodular pattern, where the correlation

Table 1: Age group distribution

Age group	Frequency	Percent
<30	11	11
31–40	2	2
41–50	16	16
51–60	31	31
61–70	31	31
>70	9	9
Total	100	100

In the present study, majority of the patients had an age between 51–60 (31%) and 61–70 years (31%) followed by 41–50 years (16%)

Table 2: Gender distribution

Gender	Frequency	Percent
Female	29	29
Male	71	71
Total	100	100.0

Table 3: Presenting symptoms

	No of patients	Percentage
Cough	80	100
Productive cough	43	53.8
Non-productive	37	46.3
Blood in cough	11	13.8
Breathlessness	53	66.3
Breathlessness during rest	17	21.3
Breathlessness during walking	27	33.8
Breathlessness during exercise	48	60

Table 4: Smoking status

	Frequency	Percent
Smoker	46	46
Non-smoker	54	54

In the present study, 46% were smokers and 54% were non smokers

Table 5: USG findings

	Frequency	Percent
USG findings		
A line	00	00
B line	100	100
Distance between B line (mm)		
2	5	5
3	16	16
4	19	19
5	20	20
6	17	17
7	23	23
Sliding pleura		
Abolish	16	16
Yes	84	84

In the present study on USG findings, it was found that all patients had B line (100%), majority had distance between B lines of 7 mm (23%) followed by 5 mm (20%) and 4 mm (19%). Sliding pleura was abolished in 16% of patients

coefficient is $r = 0.122$ with insignificant $P = 0.241$.
No significant correlation was obtained

Table 6: HRCT finding

Variable	No of patients	Percentage
Pleural effusion		
No	94	94
Yes	6	6
Ground-glass appearance		
No	55	55
Yes	45	45
Reticular pattern		
No	45	45
Yes	55	55
Nodular pattern		
No	75	75
Yes	25	25
Reticulonodular pattern		
No	75	75
Yes	25	25
Consolidation		
No	88	88
Yes	12	12
Honeycombing pattern		
No	60	60
Yes	40	40
Bronchiectasis		
No	63	63
Yes	37	37
Pleural thickening		
No	69	69
Yes	31	31
Fibrotic band		
No	63	63
Yes	37	37

- This graph shows a positive correlation between B line distance and bronchiectasis, where the correlation coefficient is $r = 0.182$ with insignificant $P = 0.681$. No significant correlation was obtained
- This graph shows a positive correlation between B line distance and pleural thickening, where the correlation coefficient is $r = -0.164$ with insignificant $P = 0.104$. No significant correlation was obtained
- This graph shows a positive correlation between B line distance and fibrotic band, where the correlation coefficient is $r = 0.012$ with insignificant $P = 0.909$. No significant correlation was obtained
- Correlation between reticular pattern with B line: This graph shows a positive correlation between B line distance and reticular pattern, where the correlation coefficient is $r = 0.859$ with significant $P < 0.001$. This means as the distance between B lines increases reticular pattern also increases
- This graph shows a positive correlation between B line distance and honeycombing pattern, where the correlation coefficient is $r = 0.212$ with significant $P = 0.562$. No significant correlation was obtained
- This graph shows a positive correlation between B line distance and reticulonodular pattern, where the correlation coefficient is $r = 0.061$ with significant

Table 7: Correlation between B line with HRCT finding

	Distance between B line
Consolidation	
Pearson correlation	-0.133
Sig. (2-tailed)	0.365
<i>n</i>	100
Pleural effusion	
Pearson correlation	0.154
Sig. (2-tailed)	0.128
<i>n</i>	100
Ground-glass appearance	
Pearson correlation	-0.770
Sig. (2-tailed)	<0.001
<i>n</i>	100
Nodular pattern	
Pearson correlation	0.122
Sig. (2-tailed)	0.241
<i>n</i>	100
Pleural thickening	
Pearson correlation	-0.164
Sig. (2-tailed)	0.104
<i>n</i>	100
Fibrotic band	
Pearson correlation	0.012
Sig. (2-tailed)	0.909
<i>n</i>	100
Bronchiectasis	
Pearson correlation	0.182
Sig. (2-tailed)	0.681
<i>n</i>	100

Table 8: Correlation between reticular, reticulonodular pattern, and honeycombing pattern with B line

Reticular pattern	
Pearson correlation	0.859
Sig. (2-tailed)	<0.001
<i>n</i>	100
Honeycombing pattern	
Pearson correlation	0.121
Sig. (2-tailed)	0.562
<i>n</i>	100
Reticulonodular pattern	
Pearson correlation	0.061
Sig. (2-tailed)	0.784
<i>n</i>	100

$P < 0.781$. No significant correlation was obtained [Tables 1-8, Figures 1-4 and Graphs 1-14].

CONCLUSION

Results of the present study showed that the elder male population had a high prevalence of ILD. Cough mainly productive cough represents the most common clinical symptoms in ILD patients along with breathlessness. Smoking has a stroke association with the progression of

ILD to its severe form as in all the patients, B lines are clearly visible. The majority having 7 mm size.

Ground-glass appearance, reticular pattern, nodular pattern, reticulonodular pattern, consolidation, honeycombing pattern, bronchiectasis, etc., were the common presentations of ILD.

B line distances were positively correlated with reticular pattern and negatively correlated with ground glass appearance.

Based on the results, we conclude that transthoracic lung ultrasound has many advantages over HRCT; it is a bedside procedure widely available, easily performed, inexpensive, requires neither ionizing radiation nor a contrast medium, and is therefore readily and largely accepted by the patient. In addition, the surface of the lung can be easily studied by the US; therefore, the B-lines are quickly detected using either low-frequency or high-frequency transducers. In critically ill patients, portable machines even without Doppler power can be sufficient for a complete and detailed lung assessment. Finally, ultrasound is useful in situations where HRCT is not available or undesirable, as in pre-hospital emergencies and in pregnancy and when a patient cannot be transported out of the intensive care unit because of severe disease.

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Comparison of High-resolution Computed Tomography Findings in Drug-Sensitive and Drug-Resistant Pulmonary Tuberculosis Patients

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Abstract

Introduction: Tuberculosis is a global public health problem by the World Health Organization. The high-resolution computed tomography (HRCT) scans provide more accurate information about the extent and distribution of PTB and is the investigation of choice for PTB.

Aims and Objectives: This study aims to describe the findings of HRCT chest in drug-sensitive (DS) and drug-resistant (DR) pulmonary tuberculosis patients and compare them.

Materials and Methods: This is a cross-sectional study, comprised 114 patients (80 drug-sensitive and 34 drug-resistant patients). HRCT chest was done in the Department of Radiodiagnosis, Gandhi Medical College and Hamidia Hospital over a period of 18 months after taking proper history and consent. All the patients are either having drug-sensitive or drug-resistant tuberculosis confirmed by CBNAAT.

Results: Among 114 patients in the study, majority of them were young males. History of smoking (70.5%) and defaulters (82.4%) are the most common risk factors associated with the drug resistance patients. On HRCT of drug-sensitive patients, we found that consolidation (97.5%), tree-in-bud sign (96.25%), lymphadenopathy (93.75%), glass opacities (88.75%), and cavities (86.25%) were most common findings and among drug resistance patients, all (100%) patients were found positive for consolidation, 91.2% for ground-glass opacities, 100% cavities, all positive for (100%) tree-in-bud sign, and 94.1% for nodules.

Conclusion: Drug-resistant TB patients were comparatively younger than the drug-resistant TB patients. Smoking and drug defaultation were the major causes of MDR TB. HRCT examination shows consolidation, tree-in-bud sign, lymphadenopathy, ground-glass opacities, nodules, and cavities which were most common findings in drug-resistant tuberculosis patients, while pleural effusion, tree-in-bud opacities, and consolidation were common findings in drug-sensitive patients.

Key words: High-resolution computed tomography, Drug-sensitive and drug-resistant tuberculosis patients

INTRODUCTION

Tuberculosis, a chronic infectious disease caused by air-borne transmission of aerosolized droplets of *Mycobacterium tuberculosis* (MTB), is a major global public health problem by the World Health Organization.^[1]

There were an estimated 10.4 million new cases of tuberculosis and 1.7 million tuberculosis-related deaths every year, making tuberculosis one of the top 10 leading causes of death worldwide. Among the new cases identified, 90% were adults, 65% were men, 10% were children, and 10% had HIV coinfection. Among communicable diseases, tuberculosis is a major cause of mortality in the economically productive age group (15–49 years). The top seven countries in the world identified as having a high tuberculosis burden are India, Indonesia, China, the Philippines, Nigeria, Pakistan, and South Africa.^[1]

The problem is exemplified many folds with the advent of drug resistance in TB. Multidrug-resistant (MDR) TB is defined as disease caused by strains of *M. tuberculosis*

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that are resistant to treatment with at least isoniazid (H) and rifampicin (R). Pre-extensively drug-resistant (pre-XDR) TB refers to disease caused by MDR strains that harbor additional resistance to either any fluoroquinolone (FQ) or any of the injectable second-line aminoglycosides (AMs). While XDR-TB refers to MDR-TB with additional resistance to both FQ and AM.^[2]

The fundamental cause in the genesis of resistance to anti-tuberculosis drugs is the misuse of antibiotics to treat patients suffering from drug-susceptible tuberculosis, causing the mutation that occurs in the genome of *Mycobacterium*. Drug resistance arises mainly in areas where anti-tuberculosis programs are deficient. Moreover, immune-deficient patients of any background (both solid organ and bone marrow transplant, such as leukemia or lymphoma patients and those treated with corticosteroids) are more susceptible to infection with *M. tuberculosis*.^[3]

The management of DR-TB is critical and based on laboratory confirmation of TB and a clear understanding of drug resistance aided by drug-susceptibility testing (DST) to ensure accurate diagnosis and early intervention of appropriate treatment.^[4]

Delay in diagnosis of active cases of pulmonary TB increases the burden of the disease, and this delay in diagnosis is related to many reasons: TB can present clinically and radiologically like many other diseases as pneumonia, malignancy, and interstitial lung diseases, the yield of sputum smear is still low and needs few days to get the results. Culture for mycobacteria TB which is the gold standard in diagnosis of TB needs up to 6 weeks for sure results, even new radiometric cultures need about 2 week to give result and not available in every hospital.^[5]

The delay in diagnosis causes delay in isolation of the patient with more chance for spread of infection and increase in severity of the disease. Because of limitations in the yield of chest X-ray in diagnosis of pulmonary TB (PTB), computed tomography (CT) scans provide more accurate information about the extent and distribution of PTB through the presence of cavities and satellite lesions that cannot be visualized on chest X-ray, and moreover, CT can contribute to distinguish active from old infection.^[6]

There are data about the relationship between morphologic findings on high-resolution computed tomography (HRCT) and the number of AFB on sputum smears in patients with PTB. It was also shown that existence of cavities and airspace consolidation might be related to the degree of smear positivity in PTB patients.^[7]

The present study is an attempt to compare the HRCT findings of drug-sensitive and drug-resistant pulmonary tuberculosis patients.

Aims and Objectives

The aim of the study was as follows:

- To describe the HRCT findings of drug-resistant pulmonary tuberculosis.
- To describe the HRCT findings in drug-sensitive pulmonary tuberculosis patients.
- To compare the HRCT findings of drug-sensitive (DS) and drug-resistant (DR) pulmonary tuberculosis.

MATERIALS AND METHODS

Study Design

This was a cross-sectional analytical study

Study Center

This study was conducted at the Department of Radiodiagnosis Gandhi Medical College and associated Hamidia Hospital, Bhopal.

Duration of Study

The study duration was 18 months (September 1, 2017–June 31, 2019).

Adults patients referred to our department for HRCT who were sputum smear positive and drug susceptibility determined by Sputum culture sensitivity test and CBNAAT (cartridge-based nucleic acid amplification test) were included in our study.

All patients were subjected to:

- Detailed medical history taken.
- Symptom review about symptoms of pulmonary TB as cough, hemoptysis, constitutional symptoms as loss of weight, fever, or night sweating.
- General physical examination.

HRCT Chest

All chest MDCT studies were performed with MDCT scanner. Volumetric 1.25 mm slice thickness MDCT chest acquisition was done with the patient supine in the cranial-to-caudal direction during a single breath hold.

Inclusion Criteria

The following criteria were included in the study:

- Patients >18 years
- Sputum AFB examinations positive for tuberculosis
- Newly diagnosed case on treatment or defaulter, with or without positive chest radiograph finding.
- Drug-susceptibility testing (CB-NAAT or sputum culture and sensitivity) – to categorize the patients as drug sensitive or drug resistance.

Exclusion Criteria

The following criteria were excluded from the study:

- Patients < 18 years
- Patients with known malignancy
- Patients who are HIV positive
- Pregnant female
- Patients not ready to give consent

Sample Size

All patients were referred to our department for HRCT chest and fulfilled of the inclusion criteria ($n = 114$).

Investigation Details

On HRCT scans, the presence of each parenchymal abnormality, tree-in-bud signs, consolidation, ground-glass opacities and bronchial dilatation, cavities, presence of pleural effusion, pleural thickening, pericardial effusion, and lymphadenopathy were recorded.

Statistical Analysis

All the data analyses were performed using IBM SPSS ver. 20 software. Frequency distribution and cross-tabulation were used to prepare the tables. Data are expressed as number and percentage. PRISM and Microsoft Office were used to prepare the graphs. Chi-square test was used to compare the distribution. $P < 0.05$ is considered as statistically significant.

RESULTS

In the present study, majority of the drug-sensitive patient's had age between 31 and 40 years (33.8%), followed by 23.8% of patients who had age between 21 and 30 years, 15% had between 41 and 50 years, and 11.3% of patients had age between 61 and 70 years.

In the present study among the drug-sensitive patients, male preponderance was observed with 68.8% of males and 31.3% of females.

In the present study, the most common constitutional symptoms among drug-sensitive patients was cough which was present in all the patients (100%) followed by fever in 73.8%, weight loss in 57.5%, night sweat in 48.8%, and hemoptysis in 48.8% of patients.

In the present study, a history of smoking was reported in 72.5%, whereas 23.8% were defaulters among the drug-sensitive patients.

On HRCT examination of drug-sensitive patients, we found that 97.5% of patients were found positive for consolidation, 88.75 for ground-glass opacities, 86.25 for

cavities, 96.25% for tree-in-bud sign, 46.25% for nodules, 83.75% for pleural effusion, 35% for pleural thickening, 35% for pericardial effusion, 93.75% for lymphadenopathy, 25% for bronchiectasis, 41.25% for atelectasis, 17.5% for calcified granuloma, and 27.5% for peribronchial thickening. Out of that, consolidation (97.5%), tree-in-bud sign (96.25%), lymphadenopathy (93.75%), glass opacities (88.75%), and cavities (86.25%) were most common findings.

Among the drug resistance patients, majority of them had age between 21 and 30 years (44.1%) followed by 31 and 40 years (29.4%) and 41 and 50 years (14.7%).

Among the drug resistance patients, majority were male (61.8%) and 38.2% were female.

In the present study, the most common constitutional symptoms among drug resistance patients was cough which was present in all the patients (100%) followed by fever in 97.1%, weight loss in 88.2%, night sweat in 79.4%, and hemoptysis in 82.4% of patients.

In the present study, a history of smoking was reported in 70.5%, whereas 82.4% were defaulters among the drug resistance patients.

On HRCT examination of drug resistance patients, we found that all (100%) patients were found positive for consolidation, 91.2% for ground-glass opacities, all positive for (100%) cavities, all positive for (100%) tree-in-bud sign, 94.1% for nodules, 21.4% for pleural Effusion, 85.3% for pleural thickening, 61.8% for pericardial effusion, 88.2% for lymphadenopathy, 79.4% for bronchiectasis, 61.8% for atelectasis, 58.8% for calcified granuloma, and 76.4% for peribronchial thickening.

Patients divided which were categorized into six groups on the basis of their age.

In the present study, a history of smoking was reported in 72.5% of drug-sensitive patients, whereas 70.5% were defaulters among the drug-sensitive patients.

History of defaulters was reported in 23.8% of drug-sensitive patients, whereas 82.4% were defaulters among drug-resistant patients. Statistically significant correlation was found between defaulters and drug-resistant patients ($P < 0.001$)

On HRCT examination of drug-sensitive patients, we found that 97.5% of patients were found positive for consolidation, 88.75% for ground-glass opacities, 86.25% for cavities, 96.25% for tree-in-bud sign, 46.25% for nodules, 83.75% for pleural effusion, 35% for pleural

thickening, 35% for pericardial effusion, 93.75% for lymphadenopathy, 25% for bronchiectasis, 41.25% for atelectasis, 17.5% for calcified granuloma, and 27.5% for peribronchial thickening. Out of that, consolidation (97.5%), tree-in-bud sign (96.25%), lymphadenopathy (93.75%), glass opacities (88.75%), and cavities (86.25%) were most common findings.

On HRCT examination of drug resistance patients, we found that all (100%) patients were found positive for consolidation, 91.2% for ground-glass opacities, all positive for (100%) cavities, all positive for (100%) tree-in-bud sign, 94.1% for nodules, 91.2% for pleural effusion, 85.3% for pleural thickening, 61.8% for pericardial effusion, 88.2% for lymphadenopathy, 79.4% for bronchiectasis, 61.8% for atelectasis, 58.8% for calcified granuloma, and 41.2% for peribronchial thickening.

On HRCT examination of drug sensitive and resistance patients, we found that all (100%) patients were found positive for consolidation, tree in bud, and nodules among drug-sensitive patients compared to drug-resistant patients, in which the consolidation was positive in 97.5%, tree in bud positive in 96.2%, and cavities were present in 86.2% of patients [Tables 1-5, Figures 1-5, and Graphs 1-11].

DISCUSSION

Tuberculosis is one of the oldest ailments having an impact on humankind and is a noteworthy reason for mortality around the world. Drug-susceptible tuberculosis is curable in essentially all cases. In the event that it is left untreated, the malady may be deadly within a time span of 5 years in 50–65% of cases.^[8]

Age

In the present study, majority of the drug-sensitive patient's had age between 31 and 40 years (33.8%), followed by 23.8% of patients who had age between 21 and 30 years, 15% had between 41 and 50 years, and 11.3% of patients had age between 61 and 70 years. Similarly, in the study of Icksan *et al.*,^[9] a total of 183 drug-sensitive patient's, majority of them had age between <30 years 49 (27%) and 42 (23%) had age between 40 and 49 followed by 38 (21%) had age between 30 and 39 years and 16% had 50–59. In Li *et al.*,^[10] study, the mean age of the drug-sensitive patient's was 47.5 years and age range from 16 to 86 years ($P = 0.005$). In other study of Deesuan *et al.*,^[11] patients' age result was not much different. The WHO in 2013 stated that most TB patients are in their productive age. High level of mobility and social interaction in productive ages supports the higher prevalence of TB due to the increased risk of exposure.^[12] In the study of Cha *et al.*,^[13] of 141

patients of drug-sensitive tuberculosis, the mean age was 51 years and mean age range was 15–85 years.

In the present study, among the drug resistance patients, majority of them had age between 21 and 30 years (44.1%) followed by 31–40 years (29.4%) and 41–50 years (14.7%). Whereas in Icksan *et al.*,^[9] 183 patients from multidrug resistance TB group, majority of patients 31% were in the age group of 40–49 years, 30% were in the age of 30–39 followed by 19% of patients in the age group of <30 years, and 16% and 4% of patients had age 50–59 and >59, respectively. In Li *et al.*,^[10] study, the mean age of the drug resistance TB patients was 39.0 years and age range from 12 to 81 years. In other study of Deesuan *et al.*,^[11] patient's age result was not much different. The WHO in 2013 stated that most TB patients are in their productive age. High level of mobility and social interaction in productive ages supports the higher prevalence of TB due to the increased risk of exposure.^[12] In the study of Cha *et al.*,^[13] 53 patients of multidrug-resistant tuberculosis mean age were 38 years; age range was 15–74 years. On comparing the age distribution between both the groups, we found that majority of the drug-resistant patients were younger as compared to drug-sensitive patients.

Gender

In the present study among the drug-sensitive patients, male preponderance was observed with 68.8% of males and 31.3% of females. Similarly, in the study of Icksan *et al.*,^[10] majority of the drug-sensitive patients were male 127 (69%) and 56 (31%) females. In Li *et al.*,^[10] study, males were predominant 61 (68.5%) than females 28 (31.5%) in drug-sensitive patients group ($P = 0.63$). In the study of Cha *et al.*,^[13] of 141 patients of drug-sensitive tuberculosis, majority of males than females ratio 79:69.

In the present study among the drug resistance patients, majority were male (61.8%) and 38.2% were female. Similarly, in the study of Icksan *et al.*,^[9] genders of the drug resistance patients were mostly male 96 (52%) than female 87 (48%). Li *et al.*,^[9] observed majority of males 58 (65.2%) than females 31 (34.8%) in drug resistance patients ($P = 0.63$). In the study of Cha *et al.*,^[13] 53 patients of multidrug-resistant majority of males than female ratio (32:21). Male preponderance was observed in both drug-sensitive and drug-resistant patients.

Constitutional Symptoms

In the present study, the most common constitutional symptoms among drug-sensitive patients was cough which was present in all the patients (100%) followed by fever in 73.8%, weight loss in 57.5%, night sweat in 48.8%, and hemoptysis in 48.8% of patients. In the study of Tueller *et al.*,^[14] the most frequent symptom was cough (69%),

followed by weight loss (43%), night sweats (31%), fever (27%), dyspnea (12%), and hemoptysis (11%). Forty-seven (66%) patients had two or more symptoms. In the study of Sun *et al.*,^[15] cough was the most common symptom for the pulmonary tuberculosis patients, 38 of the 41 (92.7%) patients had cough. The less frequent manifestations were fever (26/41, 63.4%) and weight loss (28/41, 68.3%). The frequencies of hemoptysis, appetite loss, night sweats, and chest pain were even lower. In the study of Raghuvanshi *et al.*,^[16] between clinical findings chronic cough and night sweats were significantly linked to a greater possibility for PTB.

In the present study, the most common constitutional symptoms among drug resistance patients was cough which was present in all the patients (100%) followed by fever in 97.1%, weight loss in 88.2%, night sweat in 79.4%, and hemoptysis in 82.4% of patients. In the study of Tueller *et al.*,^[14] the most frequent symptom was cough (69%), followed by weight loss (43%), night sweats (31%), fever (27%), dyspnea (12%), and hemoptysis (11%). Forty-seven (66%) patients had two or more symptoms. In the study of Sun *et al.*,^[15] cough was the most common symptom for the multidrug-resistant pulmonary tuberculosis patients, 38 of the 41 (92.7%) patients had cough. The less frequent manifestations were fever (26/41, 63.4%) and weight loss (28/41, 68.3%). The frequencies of hemoptysis, appetite loss, night sweats, and chest pain were even lower. In the study of Raghuvanshi *et al.*,^[16] between clinical findings chronic cough and night sweats were significantly linked to a greater possibility for PTB. All the patients of Kulkarni *et al.*^[17] study, that is, 100% presented with fever, cough and weight loss followed by loss of appetite (i.e., 70%) and remaining presenting symptoms were breathlessness on exertion (40%) and hemoptysis (20%). This is comparable to the study findings carried out by Gupta *et al.*,^[18] showed fever, cough, and weight loss to be the most common symptom among these patients. Out of these constitutional symptoms, fever, weight loss, night sweat, and hemoptysis were more common in drug resistance patients as compared to drug-sensitive patients.

Smoking and Defaulter

In the present study, a history of smoking was reported in 70.5%, whereas 82.4% were defaulters among the drug resistance patients. Statistically significant correlation was found between history of defaulter and drug-resistant patients ($P < 0.05$). Similarly, in the study of Rao *et al.*,^[19] history of smoking was observed in 16 (5%) and 41 (7.5%) were non-smokers. A study by Gaude *et al.*^[20] from Karnataka showed a significant association of $P < 0.05$ for smoking in the development of drug resistance. Twenty-one patients (31.8%) had a history of smoking, while 32 patients (43.5%) had a history of alcohol consumption.

Another 14 patients had a history of smoking as well as alcohol consumption, thus predisposing them for the development of TB. A reasons may be due to high level of literacy (86%) and public awareness which has resulted in lesser percentage of population being addicted to alcoholism and smoking compared to other parts of Karnataka. The result of Shariff *et al.*^[21] study suggests that those patients who are passive smokers have 75% less chance of developing MDR-TB compared to non-passive smokers (OR 0.25, 95% CI 0.07–0.87). This means that defaulters were more in drug resistance cases as compared to drug sensitive ($P < 0.001$). However, smoking status was comparable between both the groups as revealed by the insignificant P value.

HRCT

On HRCT examination of drug-sensitive patients, we found that 97.5% of patients were found positive for consolidation, 88.75% for ground-glass opacities, 86.25% for cavities, 96.25% for tree-in-bud sign, 46.25% for nodules, 83.75% for pleural effusion, 35% for pleural thickening, 35% for pericardial effusion, 93.75% for lymphadenopathy, 25% for bronchiectasis, 41.25% for atelectasis, 17.5% for calcified granuloma, and 27.5% for peribronchial thickening. Out of that, consolidation (97.5%), tree-in-bud sign (96.25%), lymphadenopathy (93.75%), glass opacities (88.75%), and cavities (86.25%) were most common findings. Icksan *et al.*^[9] recorded that active lesion of lung parenchymal was found less in DS-TB and dominated by multiple consolidation and multiple cavities. Most of the lung parenchymal active lesions in DS-TB were also found in the upper right lung. Active lesions for DS-TB group were infiltrate (66.7%), consolidation (20.8%), the cavity (6%), and ground-glass opacity (2.7%). Deesuan *et al.*^[11] and Cha *et al.*^[13] stated that multiple reticulonodular infiltrate, ground-glass opacity, and multiple or solitary cavities are the dominant X-ray findings for DS-TB patients. Hashemian *et al.*^[22] observed that the most common finding in HRCT of these patients was ARDS-like radiologic manifestations (17.1%), followed by parenchymal nodular infiltration (13.6%) and cavitation (10.9%), consolidation (10.2%), interstitial involvement (9.5%), calcified parenchymal mass (8.3%), ground-glass opacities (7.5%), and pleural effusion or thickening (6.9%). Radiographic evidence of lymphadenopathy was seen in up to 43% of adults.

On HRCT examination of drug resistance patients, we found that all (100%) patients were found positive for consolidation, 91.2 for ground-glass opacities, all positive for (100%) cavities, all positive for 100% tree-in-bud sign, 94.1% for nodules, 21.4% for pleural effusion, 85.3% for pleural thickening, 61.8% for pericardial effusion, 88.2% for lymphadenopathy,

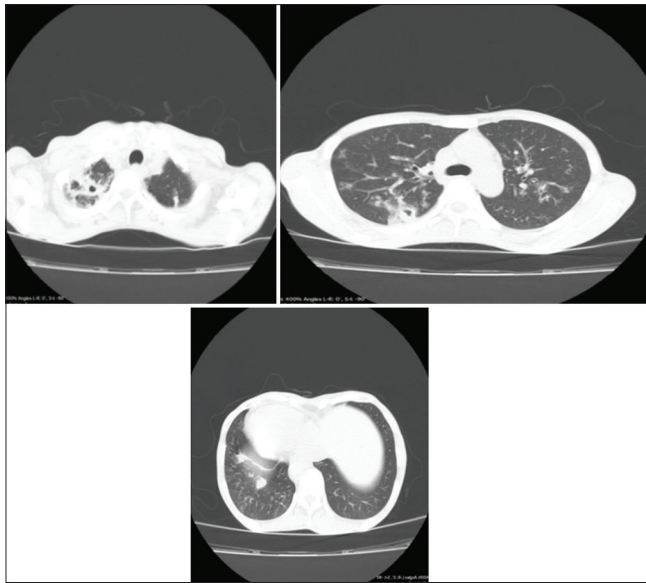


Figure 1: HRCT chest axial sections in a patient with drug-resistant tuberculosis showing multiple thick-walled cavities with centrilobular nodules arranged in branching pattern giving tree-in-bud appearance along with calcified granuloma

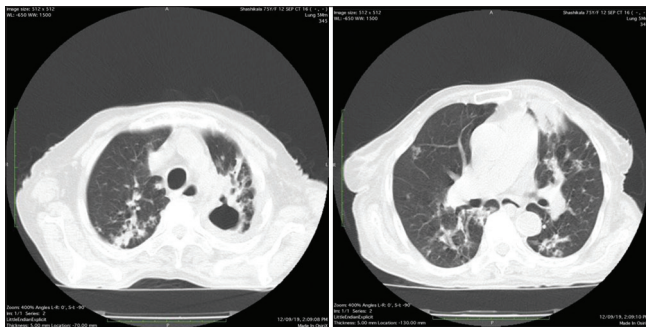


Figure 2: HRCT chest axial sections in a patient with drug-resistant tuberculosis showing large thick-walled cavity with adjacent apical pleural thickening and bronchiectasis changes in the left upper lobe. Small patch of consolidation noted in lingular segment

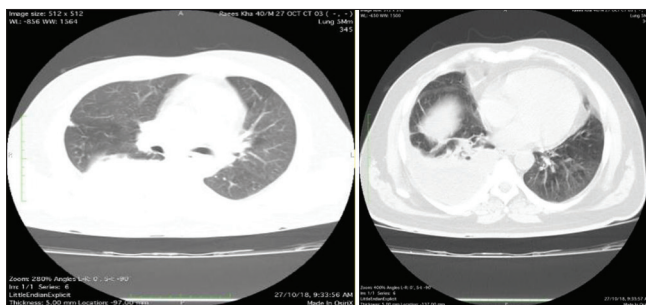


Figure 3: HRCT chest axial sections in a patient with drug-sensitive tuberculosis showing right-sided pleural effusion with areas of ground-glass haziness.

79.4% for bronchiectasis, 61.8% for atelectasis, 58.8% for calcified granuloma, and 76.4% for peribronchial thickening. In the study of Joshi *et al.*,^[23] out of 50 patients, nodules were present in 41 patients, cavities

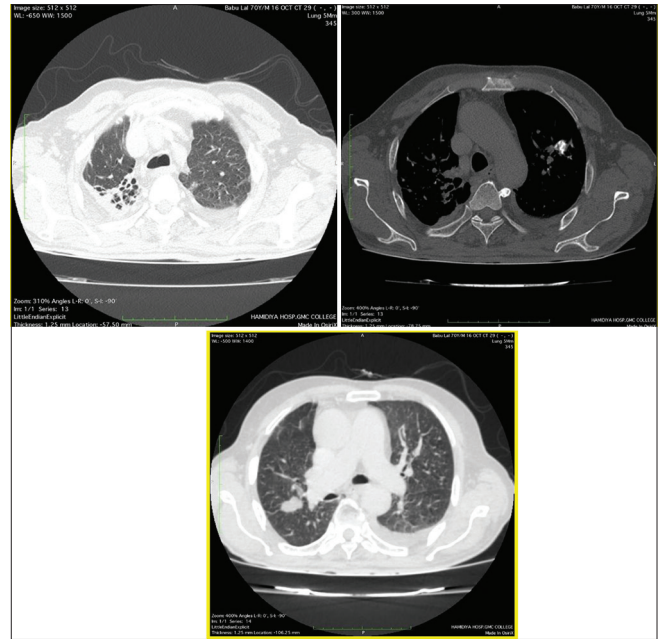


Figure 4: HRCT chest axial sections lung and mediastinal windows in a patients with drug-resistant tuberculosis patient showing fibrobronchiectatic changes in apical segment of the right upper lobe, calcified granuloma in anterior segment of the left upper lobe, and nodules in posterior segment of the right upper lobe along the oblique fissure

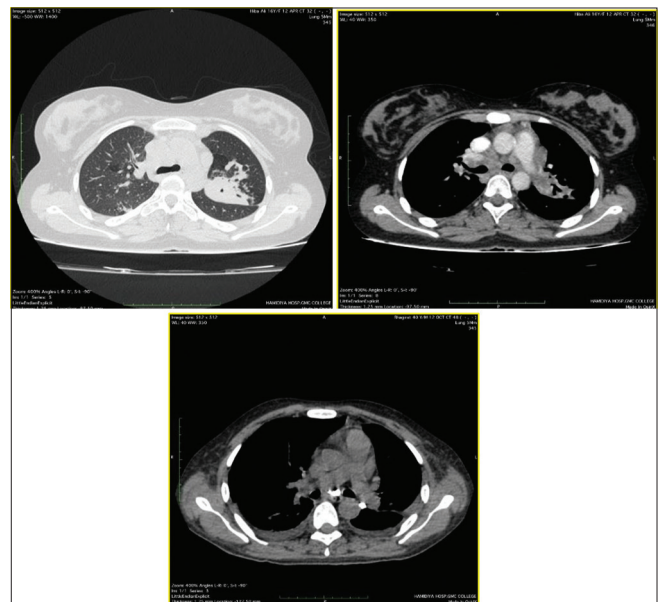
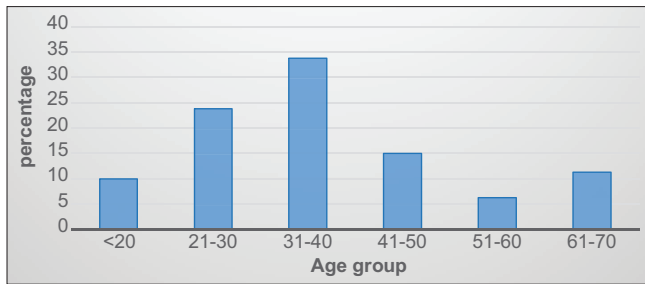
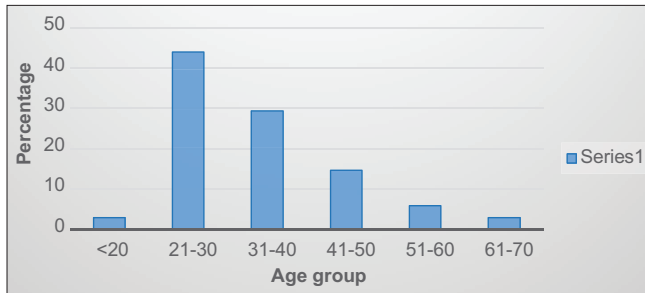


Figure 5: HRCT chest axial sections lung and mediastinal windows in a patient with drug-resistant tuberculosis patient showing consolidation in anterior segment of the right upper lobe, multiple conglomerated and calcified mediastinal lymph nodes

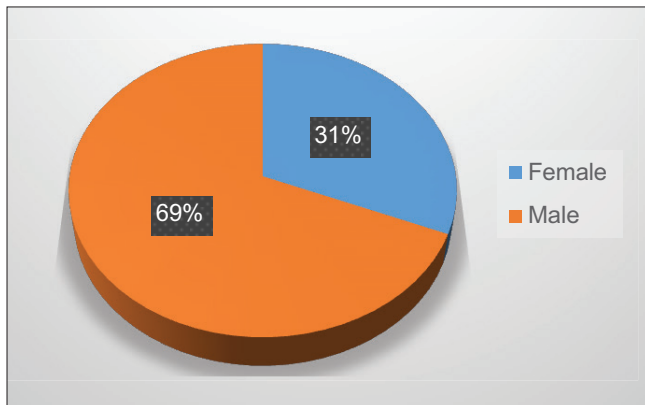
in 26 patients, consolidation in 25 patients, fibrosis in 25 patients, 22 patients had tree-in-bud/V-Y pattern of nodules, 21 patients had collapse, and 20 patients had bronchiectasis. Of the 26 patients who had cavities, 23 patients (88%) had multiple (>1) cavities and 3 patients



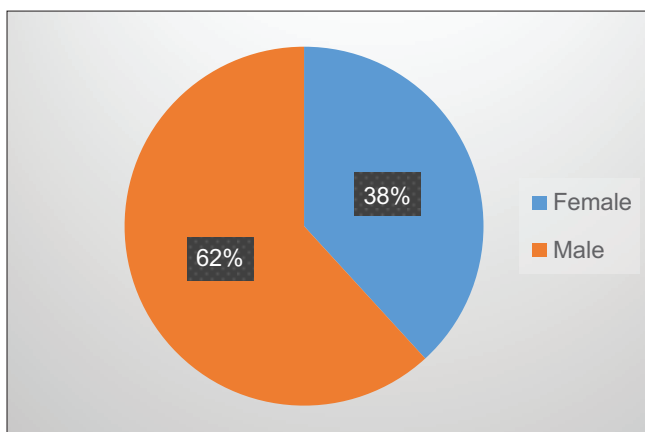
Graph 1: Age distribution of drug sensitive patients



Graph 2: Age distribution of drug resistant patients

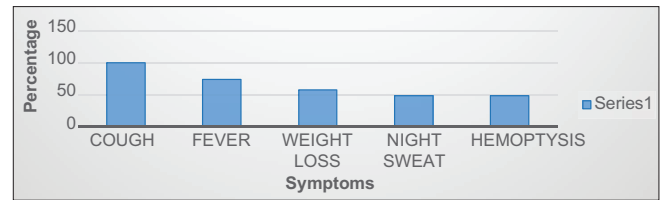


Graph 3: Gender distribution of drug sensitive patients

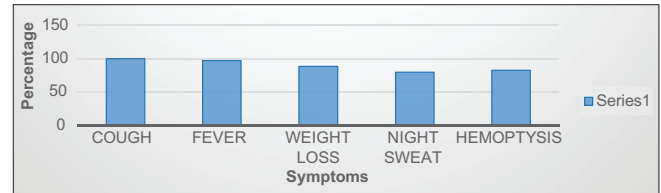


Graph 4: Gender distribution of drug resistant patients

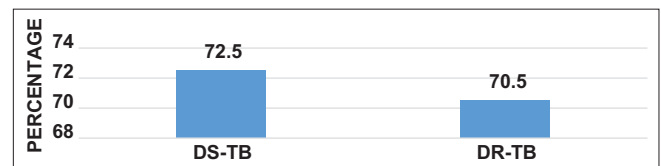
(12%) had single cavity, lymphadenopathy was present in 33 patients. Pleural involvement was seen in 25 patients,



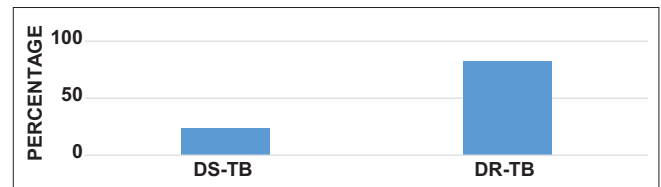
Graph 5: Constitutional symptoms of drug sensitive patients



Graph 6: Constitutional symptoms of drug resistant patients

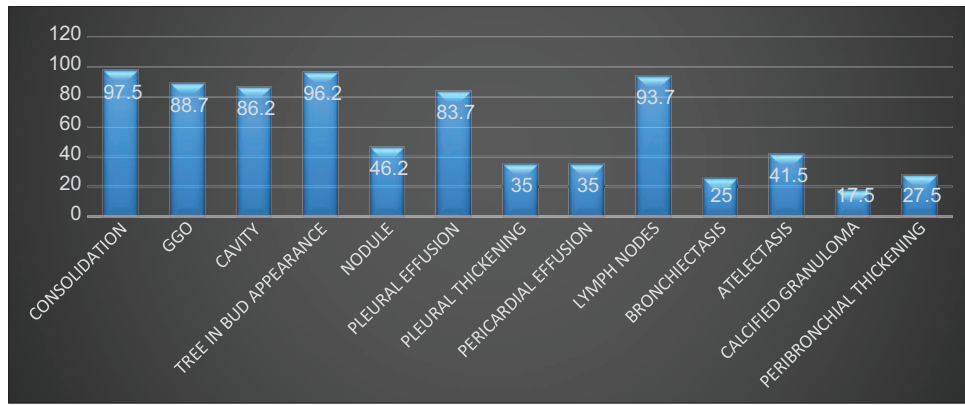


Graph 7: Distribution of history of smoking among DS-TB and DR-TB patients

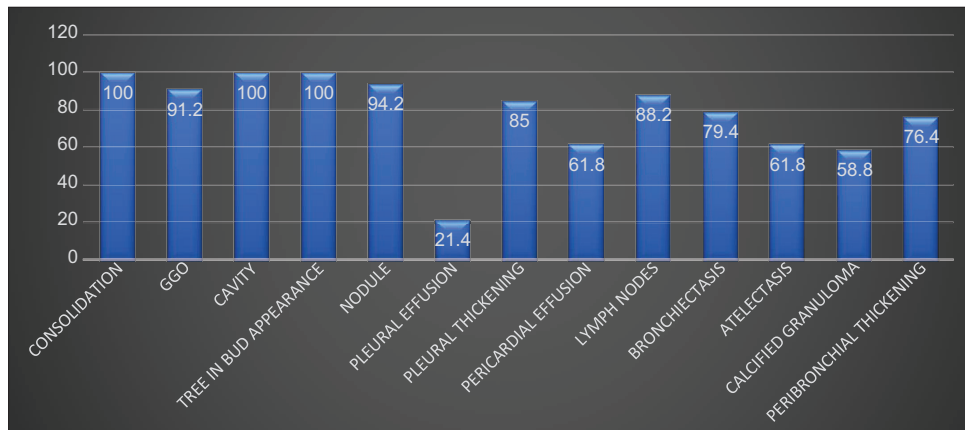


Graph 8: Distribution of history of defaulters among DS-TB and DR-TB patients

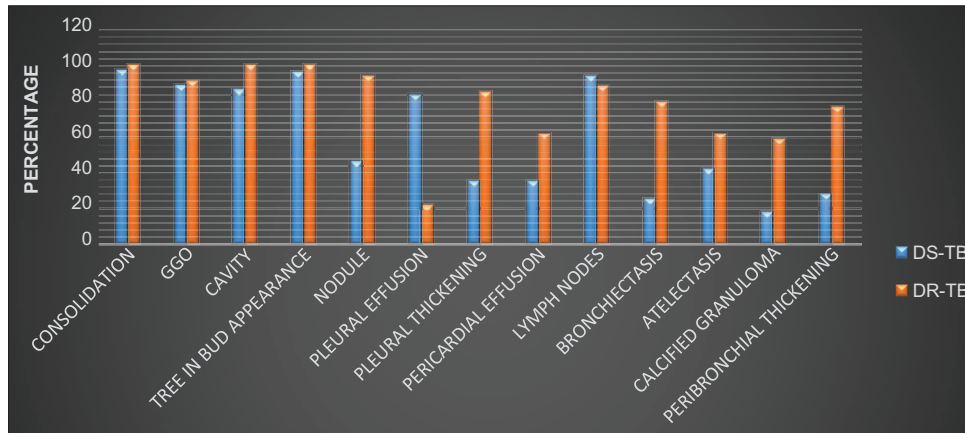
14 patients had pleural effusion, and 11 patients had pleural thickening. Kritski *et al.*^[24] performed a study among patients requiring retreatment and found that the presence of cavitary lesions was significantly associated with an unfavorable outcome. However, this finding was not associated with MDR-TB. Icksan *et al.*^[9] noted that active lesion morphologies in MDR-TB were consolidation (57.4%), cavity (57.9%), infiltrate (36.6%), and ground-glass opacity (1.1%). These active lesions were found mostly in the right upper lung. Cavity with ≤ 4 cm in MDR-TB was found most on upper right lung (66.1%) and had a significant difference compared to DS-TB (14.2%) group ($P < 0.005$). Multiple cavities were found on 68.3% MDR-TB group and had a significant difference compared to 14.2% of DS-TB group ($P < 0.005$). Deesuan *et al.*^[11] and Cha *et al.*^[13] stated that active lesions that were mostly found in thorax X-ray for MDR-TB patients are multiple consolidations and multiple cavities. These studies supported the hypothesis that the dominant characteristic lesions in MDR-TB are multiple consolidations and multiple cavities ($P < 0.005$).



Graph 9: HRCT Positive findings of DS-TB patients



Graph 10: HRCT Positive findings in DR-TB Patients



Graph 11: Comparing the HRCT Positive findings of DS and DR-TB patients

Table 1: Age distribution of drug-sensitive and drug-resistant patients

Age group	Frequency of drug-sensitive patients (n=80)	Percentage of drug-sensitive patients	Frequency of drug-resistant patients (n=34)	Percentage of drug-resistant patients
<20	8	10.0	1	2.9
21–30	19	23.8	15	44.1
31–40	27	33.8	10	29.4
41–50	12	15.0	5	14.7
51–60	5	6.3	2	5.9
61–70	9	11.3	1	2.9
Total	80	100.0	34	100.0

Table 2: Gender distribution of drug-sensitive and drug-resistant patients

Gender	Frequency of drug-sensitive patients (n=80)	Percentage of drug-sensitive patients	Frequency of drug-resistant patients (n=34)	Percentage of drug-resistant patients
Female	25	31.3	13	38.2
Male	55	68.8	21	61.8
Total	80	100.0	34	100.0

Table 3: Constitutional symptoms of drug-sensitive and drug-resistant patients

Symptoms	No. of drug-sensitive patients (n=80)	Percentage of drug-sensitive patients	No. of drug-resistant patients (n=34)	Percentage of drug-resistant patients
Cough	80	100	34	100.0
Fever	59	73.8	33	97.1
Weight loss	46	57.5	30	88.2
Night sweat	39	48.8	27	79.4
Hemoptysis	39	48.8	28	82.4

Table 4: History distribution of drug-sensitive and drug-resistant tuberculosis patients

History	No. of drug-sensitive patients (n=80)	Percentage of drug-sensitive patients	No. of drug-resistant patients (n=34)	Percentage of drug-resistant patients	P value
Defaulter	19	23.8	28	82.4	<0.001
Smoking	58	72.5	24	70.5	0.346

Table 5: HRCT findings of drug-sensitive and drug-resistant tuberculosis patients

Findings		No. of drug-sensitive patients (n=80)	Percentage of drug-sensitive patients	No. of drug-resistant patients (n=34)	Percentage of drug-resistant patients	P value
Consolidation	Negative	2	2.5	0	0.0	0.342
	Positive	78	97.5	34	100.0	
Ground-glass opacities	Negative	9	11.25	3	8.8	0.128
	Positive	71	88.75	31	91.2	
Cavities	Negative	11	13.75	00	0.0	<0.001
	Positive	69	86.25	34	100.0	
Tree-in-bud sign	Negative	3	3.75	00	0.0	0.255
	Positive	77	96.25	34	100.0	
Nodules	Negative	43	53.75	2	5.9	0.001
	Positive	37	46.25	32	94.1	
Pleural effusion	Negative	13	16.25	16	47.6	0.003
	Positive	67	83.75	18	52.4	
Pleural thickening	Negative	52	65	5	14.7	0.001
	Positive	28	35	29	85.3	
Pericardial effusion	Negative	52	65	13	38.2	0.021
	Positive	28	35	21	61.8	
Lymphadenopathy	Negative	5	6.25	4	11.8	0.678
	Positive	75	93.75	30	88.2	
Bronchiectasis	Negative	60	75	7	20.6	0.001
	Positive	20	25	27	79.4	
Atelectasis	Negative	47	58.75	13	38.2	0.212
	Positive	33	41.25	21	61.8	
Calcified granuloma	Negative	66	82.5	14	41.2	0.002
	Positive	14	17.5	20	58.8	
Peribronchial thickening	Negative	58	72.5	8	23.8	0.012
	Positive	22	27.5	26	76.4	

On comparing HCRT between both the groups, we found that pleural effusion (0.003) was more in drug-sensitive patients as compared to drug resistance patients. Cavities ($P < 0.001$), nodules ($P = 0.002$), pleural thickening ($P = 0.012$), pericardial effusion ($P = 0.021$), bronchiectasis ($P =$

0.002), calcified granuloma ($P = 0.002$), and peribronchial thickening (0.012) were more common in drug resistance patients as compared to drug-sensitive patients. While the distribution of consolidation, GGO, and tree-in-bud opacities was quite higher in both the groups.

In the present study, age distribution of drug-resistant TB patients was 21–30 (44.1%), 31–40 (29.4%), and 41–50 (14.7%) where age distribution of drug sensitive was 31–40 (33.8%), 21–30 (23.8%), 41–50 (15%), and 61–70 (11.3%). This shows that the drug-resistant patients were comparatively younger than the drug-sensitive patients. Similar results were recorded by Cha *et al.*^[13] where the mean ages were significantly different for the DS-TB group (mean age, 51 years; median age, 53 years; age range, 15–85 years, standard error, 1.61), the MDR TB group (mean age, 38 years; median age, 31 years; age range, 15–74 years, standard error, 2.41), or the XDR TB group (mean age, 36 years; median age, 30 years; age range, 19–75 years, standard error, 4.27). Patients with DS-TB were older as compared to patients with MDR TB or XDR TB.

In the present study, 82.4% of patients of multidrug-resistant TB were defaulters. Similar observation were made by Monadil *et al.*,^[25] where out of 76 TB patients, 34 had a history of TB of which 17 (23.9%) were defaulters and later developed MDR TB which 50% of the patients with a history of TB.

CONCLUSION

Results of the current study show that tuberculosis is a major health burden mainly affecting the working age group males. Drug-resistant TB patients were comparatively younger than the drug resistant TB patients. Common constitutional symptoms among drug-sensitive patients were cough, fever, weight loss, night sweat, and hemoptysis. Smoking and drug defaultation were the major causes of MDR TB. HRCT examination shows that consolidation, tree-in-bud sign, lymphadenopathy, ground-glass opacities, nodules, and cavities were most common findings in drug-resistant tuberculosis patients, while pleural effusion, tree-in-bud opacities, and consolidation were most common findings in drug-sensitive patients.

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Assessment of Acromiohumeral Interval in A-P Radiograph as an Indicator of Rotator Cuff Injury and Its Comparison with High-frequency USG in Bhopal, Central India

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Abstract

Introduction: Rotator cuff injuries are the most common cause of shoulder pain in people of all age groups. They represent a spectrum of disease, ranging from acute reversible tendinitis to massive tears involving the supraspinatus, infraspinatus, and subscapularis. The diagnosis of rotator cuff tears is based on clinical assessment and radiologic images, including plain radiographic, ultrasound, and MR images. Plain radiography is the most commonly used imaging modality in cases of shoulder pain.

Aims and Objectives: This study aims to assess acromiohumeral interval (AHI) in A-P radiograph in patients with rotator cuff injury and comparison of AHI with high-frequency USG to rule out rotator cuff injury.

Materials and Methods: In this cross-sectional prospective study, 100 patients of all age groups with clinically suspected cases all patients with h/o shoulder pain referred to the radiodiagnosis department over a period of 18 months was examined by plain A-P X-ray of the affected shoulder in standing neutral position. AHI was noted in excel sheet, then this interval was compared with high-frequency USG to rule out rotator cuff injury.

Results: In the present study, majority of the patients were males (63%) followed by 37% females, majority of the patients had acromiohumeral distance ≤ 7 mm (74%) followed by 26% patients who had acromiohumeral distance > 7 mm. On comparing the acromiohumeral distance (mm) with the USG findings, we found that majority of the patients were true positive cases (71%), 4% were false positive, 12% were false negative, and 13% were true negative cases.

Conclusion: This study concludes that the assessment of the AHI using standardized anteroposterior radiographs is a reliable and reproducible method of assessment of rotator cuff pathology. Early diagnosis and appropriate treatment are associated with a better outcome.

Key words: Acromiohumeral interval, High-frequency ultrasound, Rotator cuff diseases

INTRODUCTION

Shoulder pain is one of the most common complaints encountered in orthopedic practice and often leads to considerable disability. Rotator cuff injuries are the most

common cause of shoulder pain in people of all age groups, predominantly in the older age group. They represent a spectrum of disease, ranging from acute reversible tendinitis to massive tears involving the supraspinatus, infraspinatus, and subscapularis.^[1]

Rotator cuff disease is the most prevalent cause of shoulder pain, occurring in approximately 65–70% of patients. The prevalence full-thickness tears in the general population are about 20% and markedly increased after the age of 50: Patients in the seventh decade have a 50% prevalence of rotator cuff tears which increases to over 80% in patients in the eighth decade of life.^[2]

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The rotator cuff is a group of four muscles (the supraspinatus, infraspinatus, teres minor, and subscapularis) in the glenohumeral joint (GHJ). Rotator cuff tears can cause pain and weakness in the shoulder. It is an injury that plagues the public (4% of under 40's; 53% of over 60's) and athletes alike.^[3]

Rotator cuff tears are commonly classified topographically according to the location of the tear and by describing their geometric shape. Four main patterns have been described: Type 1 – crescent-shaped tears typically short in the medial to lateral direction and wide anteroposteriorly; Type 2 – longitudinal tears can have a “U” or “L” shape and are long and narrow; Type 3 – massive and contracted tears long in the medial to lateral direction and wide anteroposteriorly; and Type 4 – massive tears associated with significant glenohumeral arthritis and loss of the acromiohumeral interspace.^[4]

The diagnosis of rotator cuff tears is based on clinical assessment and radiologic images, including plain radiographic, ultrasound, and MR images. Among these modalities, plain radiography is the most commonly used imaging modality in cases of shoulder pain. However, the usefulness of radiographs for the diagnosis of rotator cuff tear is limited. Radiographic findings of patients with a documented rotator cuff tear include a decreased acromiohumeral distance, a hooked acromion, and degenerative changes of the greater tuberosity and acromioclavicular joint, and these findings are generally used to predict the presence of rotator cuff pathology.^[5]

In patients with chronic shoulder pain, an X-ray supplies important basic information. It allows for: Diagnosis of degenerative changes in the joint, visualization of an upward shift of the head of the humerus, which is a secondary sign of a large tear of the tendons of the rotator cuff; and also visualization of a downward shift of the head of the humerus in patients with bleeding inside the joint. In patients with chronic rotator cuff tendon tears, it allows visualization of changes in the head of the humerus, and sclerosis at the inferior portion of the acromion. X-ray also enables visualization of calcification inside the tendons and bony processes which take up space.

In patients with trauma to the shoulder, the first test to be performed should be radiography. Dislocation of the shoulder or fracture of the proximal humerus is first diagnosed using X-ray. X-ray is also recommended as the first step in patients with an acute rupture of a rotator cuff tendon, beyond the high position of the head of the humerus.^[6]

Acromiohumeral interval (AHI) defines as the distance between dense cortical bone at the inferior aspect of the

acromion and subchondral lamina of the humeral head. Normal AHI interval is about 7–14 mm. Knowledge of the AHI interval is important because the interval <7 mm has been considered to be pathologic condition and strongly suggests a large rotator cuff tear, which the likelihood of successful outcome after the repair is reduced.^[7]

Ultrasonography has increasingly been used as an imaging modality to diagnose rotator cuff tear because it is portable, radiation-free, non-invasive, and relatively cost-effective modality. A recent systematic review study also suggested that the radiographic measurement of AHI is closely aligned with the measurements using magnetic resonance imaging, and computed tomography.^[8]

The present study is an attempt to assess AHI in A-P radiograph as an indicator of rotator cuff injury and its comparison with high-frequency USG.

MATERIALS AND METHODS

Study Type

This study was a cross-sectional prospective study.

Study Place

The study was conducted at the Department of Radiodiagnosis Gandhi Medical College and Associated Hospital Bhopal.

Duration of Study

The study duration was 2017–2019.

Inclusion Criteria

The following criteria were included in the study:

1. All adult patients referred with a history of shoulder pain
2. Both sexes will be included
3. Patients with h/o trauma.

Exclusion Criteria

The following criteria were excluded from the study:

1. Patients not giving consent
2. Known case of arthritis
3. Inflammatory diseases/neoplastic etiology
4. Pregnant females.

Sample Size

100.

Procedure

- All patients with h/o shoulder pain referred to the radiodiagnosis department was examined by plain A-P X-ray of the affected shoulder in standing neutral position

- AHI was noted in excel sheet, then this interval was compared with high-frequency USG to rule out rotator cuff injury.

Investigation

1. Radiographic assessment included conventional anteroposterior radiographs with the arm in a neutral position
2. The beam was angled 20° craniocaudally
3. The humeral head was centered in the glenoid fossa, and the acromion was profiled
4. All radiographs were acquired with the patient in the upright position
5. The space between the acromion and the humerus was inspected
6. The width of the space between these two structures is normally 7–14 mm. A decrease in this distance may be an indicator of rotator cuff tears
7. Superior migration of the humeral head is quantified by acromiohumeral distance
8. Shoulder surgeons use acromiohumeral distance for evaluation of the rotator cuff and surgical decision making
9. An acromiohumeral distance ≤ 7 mm measured on an anteroposterior radiograph suggests a large rotator cuff tear
10. It is unknown whether tendon involvement (supraspinatus vs. infraspinatus), tear size, or muscle degeneration is the most important structural change in reduced acromiohumeral distance
11. The examination on the affected shoulder was carried out on USG machine available in our department, with a high-frequency linear transducer which has a frequency range of 5–13 MHz
12. The long head of biceps is used as the landmark and thereafter sequential scanning of subscapularis, supraspinatus followed by scanning of infraspinatus and teres minor was performed in both long and short axes (both axial and sagittal planes)
13. The acromioclavicular joint and the posterior aspect of the shoulder joint was also examined.

USG Technique

- There are various techniques for scanning the shoulder, some operators prefer to face the patient, and others prefer to stand behind, scanning over the patient's shoulder
- We preferred to scan standing behind the patient and recommends following a protocol that the user is comfortable with
- The probe was held at its end with the edge of the hand resting on the patient's shoulder, to reduce stress and allow fine motor control
- Good-quality ultrasound equipment and a high-frequency (12–15 MHz) linear-array (with a flat surface) probe was used
- The more the transducer frequency, which improves the resolution, the less is the depth penetration.
- Probe frequency was selected and it depends on the patient's build. Lower for the obese patient and higher for the thin patient.

Biceps Tendon

The tendon was identified in the intertubercular groove on the anterolateral aspect of the humerus with the arm in a neutral position and was examined in both transverse and longitudinal planes.

Subscapularis Tendon

While the arm is passively externally rotated, the subscapularis was examined in orthogonal planes from its insertion into the lesser tuberosity to the point at which it becomes hidden to ultrasound by the coracoid process medially. Diagnosing subscapularis injury is clinically difficult and assessment of subscapularis integrity may be limited during arthroscopy or open surgery. It is important to assess the superior portion of the tendon, close to the biceps tendon, on the transverse.

Supraspinatus Tendon (SST)

To visualize the SST, the patients were asked to place their hands on their back pocket. In the longitudinal plane, the tendon had a beak-shaped configuration.

Scanning protocol	Supplementary	Positioning
Long head of biceps tendon-short and long-axis		Hand resting on thigh and elbow flexed to 90°. Sliding the probe distally demonstrates the tendon down to its myotendinous junction
Subscapularis-long-and short-axis	Biceps tendon subluxation/dislocation	Patient externally rotates the arm with the elbow flexed at 90°. The subscapularis can be seen emerging inferior to the coracoid process and inserting on the lesser tuberosity
Supraspinatus-long and short-axis	Rotator interval	Patients are asked to put the palm of their hand on the back pocket, which abducts and internally rotates the shoulder and the supraspinatus tendon is assessed in long and short-axis. The injection into the subacromial subdeltoid bursa can be performed in this position
Infraspinatus-long-axis	Posterior joint space, spinoglenoid notch	Examined from behind the shoulder with the arm in neutral position or across the front of the chest. This is a good position to look at the posterior joint space and aspirate or inject into the joint
Acromioclavicular joint	Dynamic abduction for impingement	Assessed in the coronal plane with the arm in neutral position (hand on thigh). Dynamic abduction to assess for impingement can be done from a similar position and moving the transducer over the lateral edge of the acromion

Infraspinatus (IST) and Teres Minor Tendons

The IST and teres minor tendons lie more posteriorly and were well visualized with the arm in a flexed and adducted position. This was done by asking the patient to place their arm across the front of their body. The IST was demonstrated in a longitudinal section as a beak-shaped soft-tissue structure.

Data Collections

All patients with a history of shoulder pain and referred for an X-ray examination to the department of radiodiagnosis at Gandhi Medical College and Hamidia Hospital Bhopal.

Methods of Collecting Data

Complete evaluation of all patients was done, including detailed clinical history, X-ray shoulder joint AP view in standing neutral position, and AHI was compared with high-frequency USG to rule out rotator cuff injury.

RESULTS

1. Present cross-sectional prospective study was performed on 100 patients with shoulder pain at the Department of Radiodiagnosis Gandhi Medical College and Associated Hospital Bhopal from 2017 to 2019
2. In the present study, majority of the patients were in the age group of 51–60 years (27%) followed by 31–40 years (24%) and 41–50 years (23%)
3. In the present study, majority of the patients were males (63%) followed by 37% females
4. On A-P radiograph evaluation, it was revealed that fracture was seen in 31% patients, whereas dislocation was present in five patients. Fracture includes fracture of anatomical neck of humerus, hairline fracture of shaft of humerus, pathological fractures in the old age group. Dislocation mostly occurred as posteroinferiorly dislocation of the humeral head
5. Distribution of findings of high-frequency USG, it was found that supraspinatus tendon tear was present in 53%, infraspinatus tendon tear in 16%, subscapularis tendon tear in 20%, biceps tendon tear in 11%, and none of the patients in the present study had teres minor tendon tear
6. On comparing the findings of high-frequency USG with acromiohumeral distance, it was found that acromiohumeral distance was significantly less among the patients with supraspinatus tendon tear (8.95) as compared to those without it (7.08) ($P < 0.001$). However, acromiohumeral distance was similar among the patients with or without infraspinatus tendon tear, subscapularis tendon tear, biceps tendon tear, and teres minor tendon tear as revealed by the insignificant $P > 0.05$.
7. Although insignificant, acromiohumeral distance was more among the patients with (9.14) glenohumeral joint effusion as compared to those without it (7.80) ($P = 0.088$).
8. Though insignificant, acromiohumeral distance was more among the patients with (8.50) biceps tendon sheath effusion as compared to those without it (7.93) ($P = 0.633$).
9. Although insignificant, acromiohumeral distance was more among the patients with (8.22) soft tissue hematoma as compared to those without it (7.92) ($P = 0.680$).
10. Acromiohumeral distance was less among the patients with (6.72) infraspinatus bursa as compared to those without it (8.03) ($P = 0.680$).
11. Patients with supraspinatus tendon tear, majority had acromiohumeral distance < 7 (90.6%) and only 9.4% had acromiohumeral distance > 12 ($P < 0.001$). Majority of the patients with infraspinatus tendon tear had acromiohumeral distance < 7 (93.8%), but P -value was insignificant which indicates similar distribution ($P = 0.158$). Similarly, in subscapularis tendon tear majority had acromiohumeral distance < 7 (75%), but P -value was insignificant ($P = 0.297$). Distribution of acromiohumeral distance in biceps tendon tear was also similar ($P = 0.624$). Among A-P radiograph findings, dislocation was significantly high among the patients with acromiohumeral distance between > 12 mm (100%)
12. In the present study, majority of the patients had acromiohumeral distance ≤ 7 (74%) followed by 26% patients who had acromiohumeral distance > 7 .
13. On comparing the acromiohumeral distance (mm) with the USG findings, we found that majority of the patients were true positive cases (71%), 4% were false positive, 12% were false negative, and 13% were true negative cases
14. The sensitivity of USG in the present study was 85.5%, specificity was 76.5%, positive predictive value was 94.6%, and negative predictive value was 52%. The overall diagnostic accuracy in the present study was 84%
15. On Pearson correlation, supraspinatus tendon tear was positively correlated with the acromiohumeral distance ($r = 0.368$, $P < 0.001$). Other USG findings have not shown any significant correlation with acromiohumeral distance.
16. Based on all the results, it was found that tendon tears in the rotator cuff correlate with reduced acromiohumeral distance [Tables 1-14 and Figures 1-5].

DISCUSSION

In the present study, we compared the acromiohumeral distance in A-P radiograph with USG findings.

In 1970, Weiner and Macnab^[9] described the association between reduced acromiohumeral distance and rotator cuff tear. An arthrographic study showed that the average acromiohumeral distance in intact shoulders was 10.5 mm, whereas it was only 8.2 mm if a tear of the rotator cuff tendons was present.^[10] An acromiohumeral distance

≤ 7 mm was proof of full-thickness tear of the rotator cuff. Therefore, ≤ 7 mm is the cutoff value for abnormal acromiohumeral distance. Shoulder surgeons measure acromiohumeral distance on conventional radiographs to estimate the success of a rotator cuff repair. An acromiohumeral distance < 7 mm is considered a negative factor for rotator cuff repair.^[11]

In the present study, majority of the patients were in the age group of 51–60 years (27%) followed by 31–40 years (24%) and 41–50 years (23%). Singh *et al.* reported

Table 1: Age distribution of study subjects

Age group	Frequency	Percent
21–30	13	13.0
31–40	24	24.0
41–50	23	23.0
51–60	27	27.0
60–70	13	13.0
Total	100	100.0

In the present study, majority of the patients were in the age group of 51–60 years (27%) followed by 31–40 years (24%) and 41–50 years (23%).

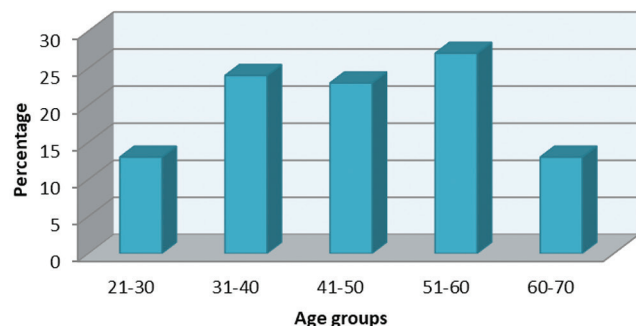


Table 2: Gender distribution

Gender	Frequency	Percent
Female	37	37.0
Male	63	63.0
Total	100	100.0

In the present study, majority of the patients were males (63%) followed by 37% females.

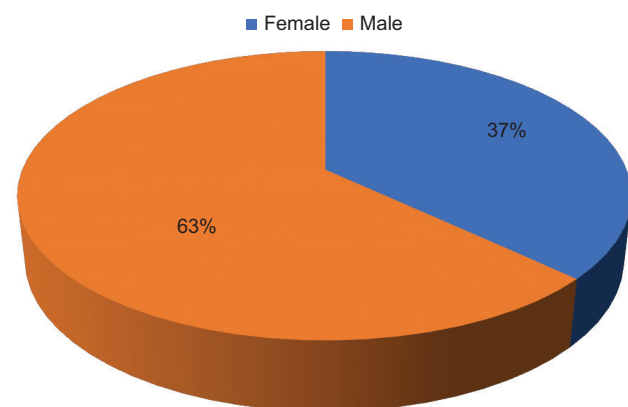


Table 3: AP radiograph findings

Findings	No of patients	Percentage
Fracture		
Absent	69	65
Present	31	31
Dislocation		
Absent	95	95
Present	5	5

On AP radiograph evaluation, it was revealed that fracture was seen in 31% patients whereas dislocation was present in 5 patients.

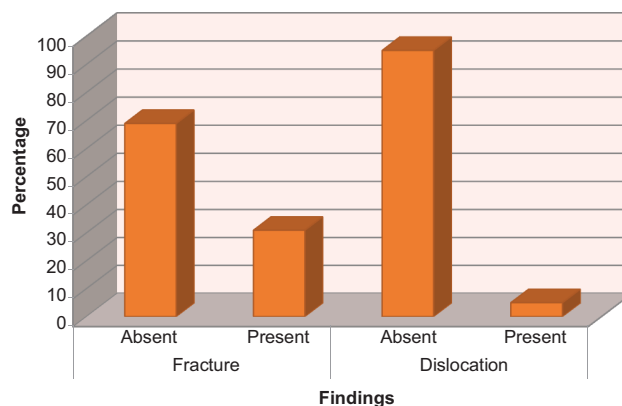
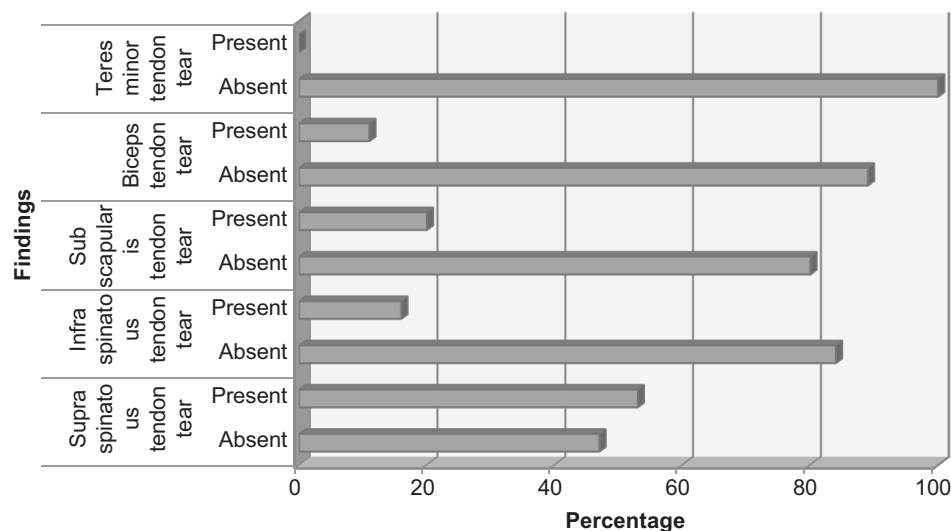


Table 4: High-frequency USG (rotator cuff tear)

Findings	No of patients	Percentage
Supraspinatus tendon tear		
Absent	47	47
Present	53	53
Infraspinatus tendon tear		
Absent	84	84
Present	16	16
Subscapularis tendon tear		
Absent	80	80
Present	20	20
Biceps tendon tear		
Absent	89	89
Present	11	11
Teres minor tendon tear		
Absent	100	100
Present	0	0

Distribution of findings of high-frequency USG, it was found that supraspinatus tendon tear was present in 53%, infraspinatus tendon tear in 16%, subscapularis tendon tear in 20%, biceps tendon tear in 11%, and none of the patients in the present study had teres minor tendon tear.



that majority of the patients were in the age group of 50–70 years with a mean age 56.67. Rotator cuff tears were seen in 31 (52%) patients in the age group of 50–70 years.^[12] The highest incidence of rotator cuff tears in our study was seen in fifth to sixth decade of life, similar to that observed by White *et al.*, 2014. This finding is in concordance with Milgrom *et al.*, who stated that the prevalence of rotator cuff disease increases with age.^[13] Anand *et al.* reported that most patients were in the age group of 41–50 years (30.0%) followed by 21–30 years (26.0%).^[14]

In the present study, majority of the patients were males (63%) followed by 37% females. Singh *et al.* in a similar study, including 60 patients where all patients underwent USG evaluation of the shoulder joint, reported that majority of the subjects were males ($n = 21$).^[12] In a similar study by Anand *et al.* showed that the involvement of males (56%) was more as compared to females (44%).^[14]

In our study, shoulder pain (either due to trauma or other cause) was found to be the commonest cause for referral to the department of radiodiagnosis for A-P radiograph and USG examination. Of which supraspinatus tendon tear was present in 53%, infraspinatus tendon tear in 16%, subscapularis tendon tear in 20%, biceps tendon tear in 11%, and none of the patients in the present study had teres minor tendon tear, which was found similar to study carried out by Mitchell *et al.*^[15] The present study findings are also comparable to the study by Zlatkin, wherein they found that SST involvement in around 80% of their cases.^[16] Supraspinatus involvement was followed by subscapularis tendon (24%) and infraspinatus tendon (14%) and least involved tendon was teres minor (4%). Of

Table 5: Comparing acromiohumeral distance with high-frequency USG (rotator cuff tear)

Findings	Mean	SD	P-value
Supraspinatus tendon tear			
Absent	8.95	2.86	<0.001
Present	7.08	1.84	
Infraspinatus tendon tear			
Absent	8.16	2.62	0.070
Present	6.91	1.77	
Subscapularis tendon tear			
Absent	7.85	2.42	0.360
Present	8.43	3.01	
Biceps tendon tear			
Absent	7.98	2.56	0.868
Present	7.84	2.50	
Teres minor tendon tear			
Absent	7.96	2.54	Na

On comparing the findings of high-frequency USG with acromiohumeral distance on AP Radiograph, it was found that acromiohumeral distance was significantly less among the patients with supraspinatus tendon tear (8.95) as compared to those without it (7.08) ($P < 0.001$). However, acromiohumeral distance was similar among the patients with or without infraspinatus tendon tear, subscapularis tendon tear, biceps tendon tear, and teres minor tendon tear as revealed by the insignificant $P > 0.05$

the 50 SST tears, there were 16 partial-thickness tears and 11 full-thickness tears.

In the present study on comparing the findings of high-frequency USG with acromiohumeral distance, it was found that acromiohumeral distance was significantly less among the patients with supraspinatus tendon tear (8.95) as compared to those without it (7.08) ($P < 0.001$). However, acromiohumeral distance was similar among the patients with or without infraspinatus tendon tear, subscapularis tendon tear, biceps tendon tear, and teres minor tendon tear as revealed by the insignificant $P > 0.05$.

Although insignificant, acromiohumeral distance was more among the patients with (9.14) glenohumeral joint

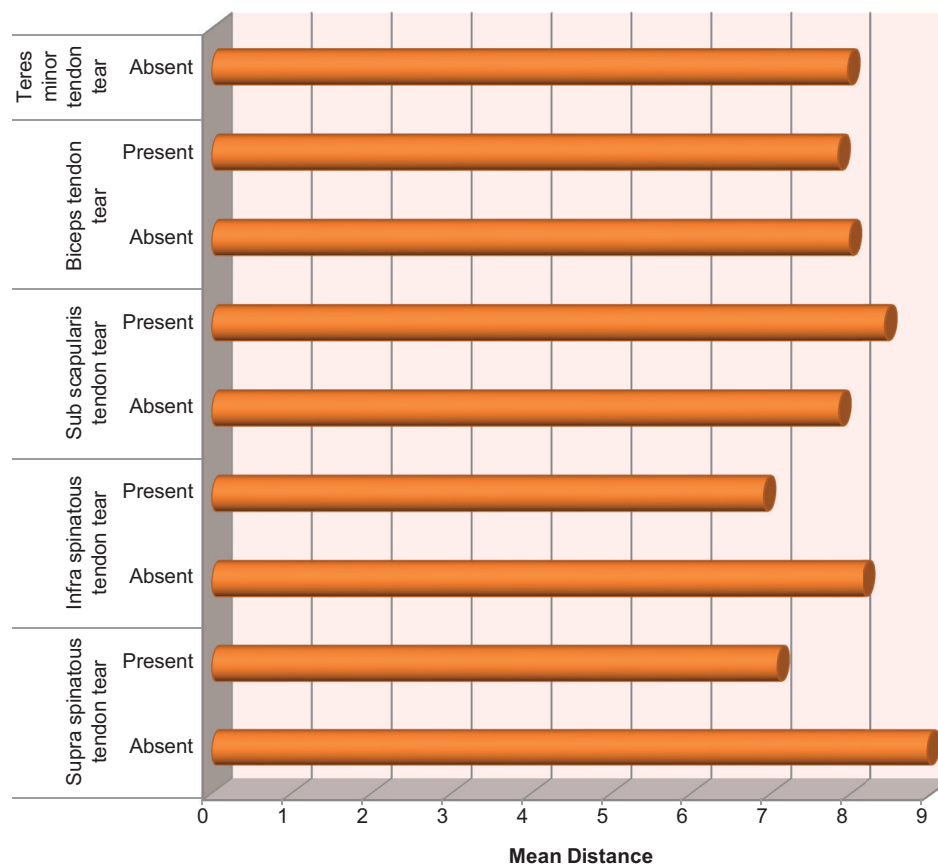
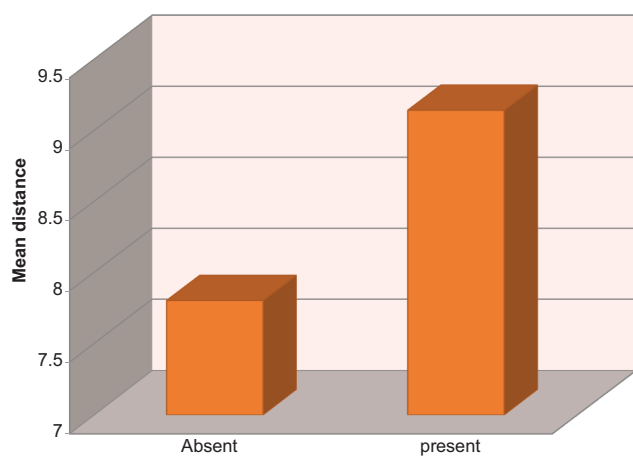


Table 6: Comparing acromiohumeral distance with glenohumeral joint effusion

Glenohumeral joint effusion	Mean	Std. Deviation	P-value
Absent	7.80	2.40	0.088
Present	9.14	3.31	

Although insignificant, acromiohumeral distance was more among the patients with (9.14) glenohumeral joint effusion as compared to those without it (7.80) ($P=0.088$)

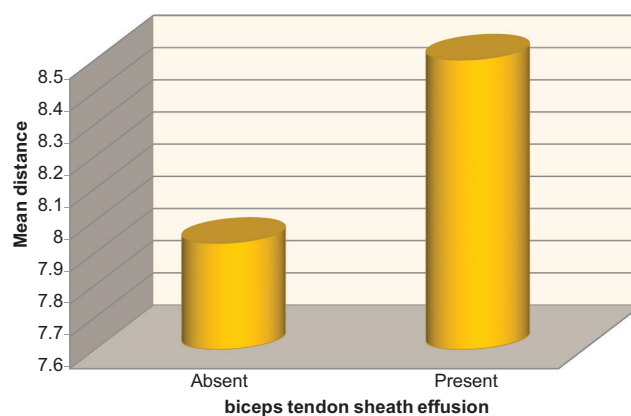


effusion as compared to those without it (7.80) ($P = 0.088$). Although insignificant, acromiohumeral distance was

Table 7: Comparing acromiohumeral distance with biceps tendon sheath effusion

Biceps tendon sheath effusion	Mean	Std. Deviation	P-value
Absent	7.93	2.44	0.633
Present	8.50	3.75	
Total	7.96	2.54	

Although insignificant, acromiohumeral distance was more among the patients with (8.50) biceps tendon sheath effusion as compared to those without it (7.93) ($P=0.633$)

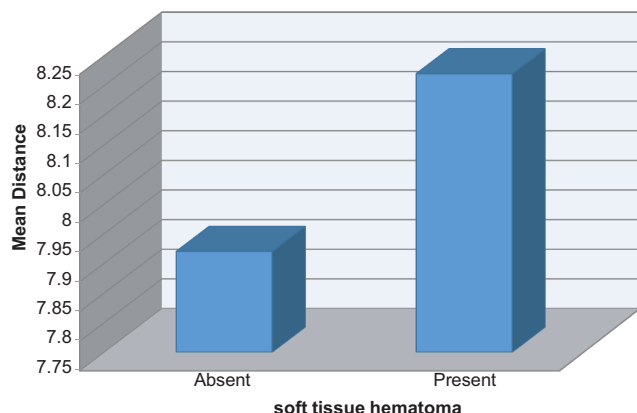


more among the patients with (8.50) biceps tendon sheath effusion as compared to those without it (7.93) ($P = 0.633$).

Table 8: Comparing acromiohumeral distance with soft tissue hematoma

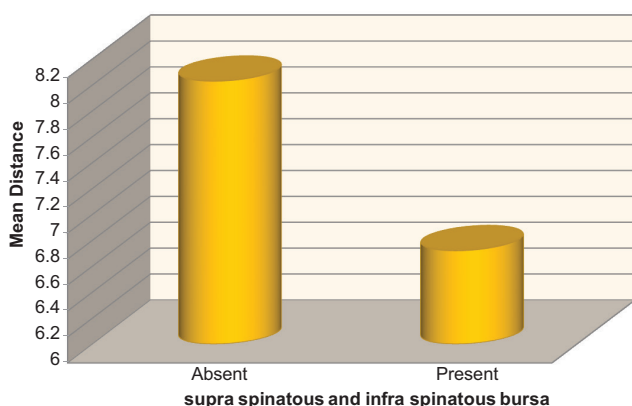
Soft tissue hematoma	Mean	Std. Deviation	P-value
Absent	7.92	2.59	0.680
Present	8.22	2.26	
Total	7.90	2.537	

Although insignificant, acromiohumeral distance was more among the patients with (8.22) soft tissue hematoma as compared to those without it (7.92) ($P=0.680$)

**Table 9: Comparing acromiohumeral distance with supraspinatus and infraspinatus bursa**

Supraspinatus and infraspinatus bursa	Mean	Std. Deviation	P-value
Absent	8.03	2.59	0.263
Present	6.72	0.19	
Total	7.90	2.537	

Acromiohumeral distance was less among the patients with (6.72) supraspinatus and infraspinatus bursa as compared to those without it (8.03) ($P=0.680$)



Although insignificant, acromiohumeral distance was more among the patients with (8.22) soft tissue hematoma as compared to those without it (7.92) ($P = 0.680$). Acromiohumeral distance was less among the patients with (6.72) infraspinatus bursa as compared to those without it (8.03) ($P = 0.680$).

Table 10: Comparing acromiohumeral distance (grouping) with AP radiograph and USG findings

	Acromiohumeral distance			P-value
	<7	7–12	>12	
USG				
Supraspinatus tendon tear	48 (90.6)	0(0)	5(9.4)	<0.001
Infraspinatus tendon tear	15 (93.8)	0 (0)	1 (6.2)	0.158
Subscapularis tendon tear	15 (75)	0(0)	5(25)	0.297
Biceps tendon tear	9 (81.3)	0 (0)	2(18.2)	0.624
Teres minor tendon tear	0 (0)	0 (0)	0 (0)	Na
X-ray				
Fracture	31 (88.6)	2 (5.7)	2 (5.7)	0.051
Dislocation	0 (0)	5 (100)	0 (0)	<0.001

Patients with supraspinatus tendon tear, majority had acromiohumeral distance <7 (90.6%) and only 9.4% had acromiohumeral distance >12 ($P<0.001$). Majority of the patients with infraspinatus tendon tear had acromiohumeral distance <7 (93.8%), but the p value was insignificant which indicates similar distribution ($P=0.158$). Similarly, in subscapularis tendon tear majority had acromiohumeral distance <7 (75%), but P-value was insignificant ($P=0.297$). Distribution of acromiohumeral distance in biceps tendon tear was also similar ($P=0.624$). Among X-ray findings, dislocation was significantly high among the patients with acromiohumeral distance between 7 and 12 (100%)

Superior migration of the humeral head with narrowing of the acromiohumeral distance is an important radiographic finding that is indicative of the presence of a large or massive rotator cuff tear that has disrupted the force couples of the GHJ. In the present study, majority of the patients had acromiohumeral distance ≤ 7 (74%) followed by 26% patients who had acromiohumeral distance >7. Goutallier *et al.*^[17] reported that an acromiohumeral distance of <6 mm was almost always associated with a full-thickness chronic infraspinatus tear and, therefore, surgical repair is not always amenable due to poor quality of the cuff and advanced fatty degeneration. Conversely, an acromiohumeral distance of 6 mm or more was of no diagnostic relevance.^[17] Other studies have also reported that the presence of cephalad migration of the humeral head is indicative of a chronic rotator cuff tear that cannot be surgically repaired.^[18] Other potential radiographic findings include os acromiale, fracture, osteoarthritis of the acromioclavicular or GHJ, and, less commonly, other bone abnormality such as malignancy.

In the present study on comparing the acromiohumeral distance (mm) with the USG findings, we found that majority of the patients were true positive cases (71%), 4% were false positive, 12% were false negative, and 13% were true negative cases. Another previous study reported that USG showed high accuracy of 96% in detecting supraspinatus atrophy. Another study by Viviane *et al.*^[18] reported that in the case of subscapularis tendon, there were three cases (6%) of partial-thickness tear and one

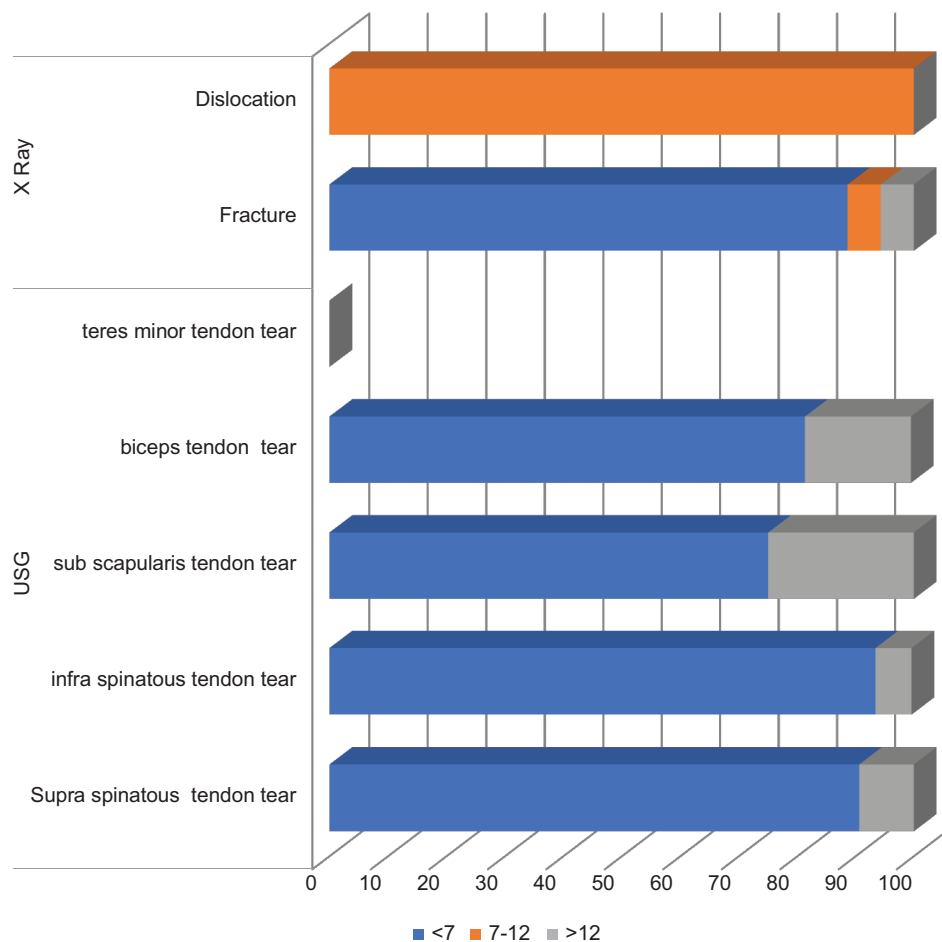
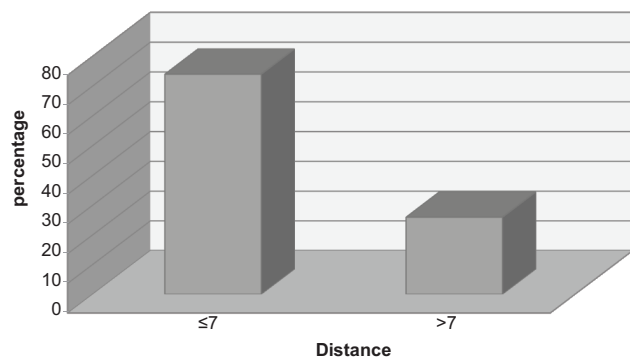


Table 11: Acromiohumeral distance (major group) distribution among patients

Acromiohumeral distance	No of patients	Percentage
≤7	74	74
>7	26	26

In the present study, majority of the patients had acromiohumeral distance ≤7 (74%) followed by 26% patients who had acromiohumeral distance >7

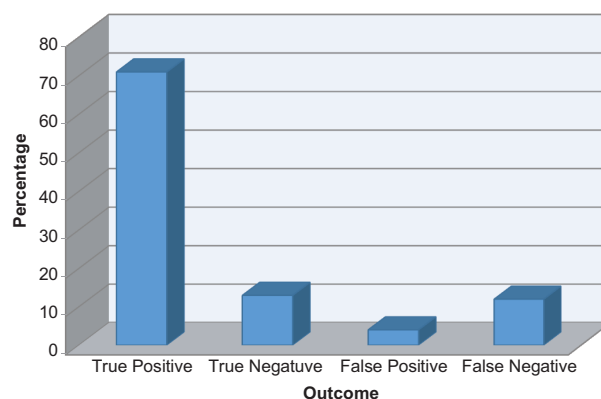


full-thickness tear (2%). Ultrasound detected five patients (10%) with partial-thickness tears, of which two cases (4%) were falsely positive and correctly detected one case

Table 12: Acromiohumeral distance with USG

Acromiohumeral distance (mm)	USG	
	Positive	Negative
≤7	71 (tp)	4 (fp)
>7	12 (fn)	13 (tn)

On comparing the acromiohumeral distance (mm) with the USG findings, we found that majority of the patients were true positive cases (71%), 4% were false positive, 12% were false negative, and 13% were true negative cases

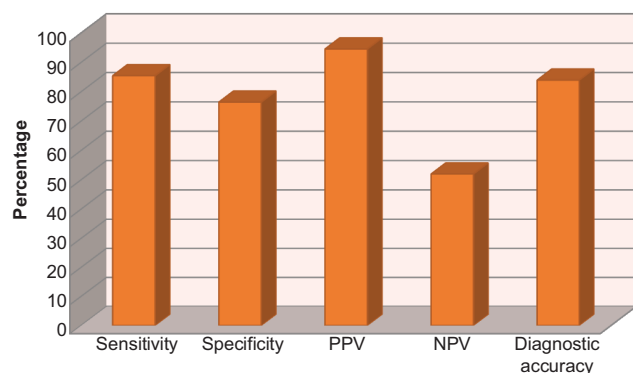


(2%) of full-thickness tear. Adams *et al.*^[19] reported that the false-positive results on ultrasound in supraspinatus and

Table 13: Sensitivity, specificity, PPV, and NPV

Parameters	Percentage
Sensitivity	85.5
Specificity	76.5
PPV	94.6
NPV	52.00
Diagnostic accuracy	84

The sensitivity of USG in the present study was 85.5%, specificity was 76.5%, positive predictive value was 94.6%, and negative predictive value was 52%. The overall diagnostic accuracy in the present study was 84%



subscapularis tendons can be explained due to scanning pitfall like anisotropy. Anisotropy has been described by Jacobson as the most common scanning pitfall where the normal hyperechoic tendon appears hypoechoic if tendon is not perpendicular to sound beam.^[20]

Radiography is used in the evaluation of the rotator cuff because imaging findings may indirectly suggest rotator cuff disease or provide additional information important to clinical management. For example, cortical irregularity of the greater tuberosity at the attachment site of the supraspinatus indirectly indicates the presence of a rotator cuff tear with a sensitivity of 90% and a negative predictive value of 96%.^[21]

Rotator cuff tears have been reported the most common rotator cuff pathology with USG showing high sensitivity and specificity for full-thickness tears, but less for partial-thickness tears. In the present study, we have compared the findings of ultrasound with X-rays, using it as a reference standard for the detection of the rotator cuff and related pathology in patients referred to our department. It was found that the sensitivity of USG in the present study was 85.5%, specificity was 76.5%, positive predictive value was 94.6%, and negative predictive value was 52%. The overall diagnostic accuracy in present study was 84%. Contrary to the present study, Martin Hervas, who concluded that USG has low sensitivity (67.9%) but high specificity (100%) for full-thickness tears of the rotator cuff.^[22] Moreover, the findings were also in concordance

Table 14: Pearson correlation between acromiohumeral distance and USG findings

	Acromiohumeral distance
Supraspinatus tendon tear	
Pearson correlation	0.368
Sig. (2-tailed)	<0.001
n	100
Infraspinatus tendon tear	
Pearson correlation	0.0182
Sig. (2-tailed)	0.070
n	100
Subscapularis tendon tear	
Pearson correlation	-0.092
Sig. (2-tailed)	0.360
n	100
Biceps tendon tear	
Pearson correlation	0.017
Sig. (2-tailed)	0.868
n	100
Glenohumeral joint effusion	
Pearson correlation	-0.171
Sig. (2-tailed)	0.088
n	100
Biceps tendon sheath effusion	
Pearson correlation	-0.048
Sig. (2-tailed)	0.633
n	100
Soft tissue hematoma	
Pearson correlation	-0.042
Sig. (2-tailed)	0.680
n	100
Supraspinatus and infraspinatus bursa	
Pearson correlation	0.113
Sig. (2-tailed)	0.263
n	100

On Pearson correlation, supraspinatus tendon tear was positively corrected with the acromiohumeral distance ($r=0.368$, $P<0.001$). Other USG findings have not shown any significant correction with acromiohumeral distance

with de Jesus *et al.* who concluded that USG and X-ray are not statistically different in sensitivity and specificity for detecting full-thickness tears.^[23] In another similar study by Singh *et al.* reported that USG had a sensitivity of 78.04%, specificity of 89.47%, PPV of 94.11%, and NPV of 65.38% in the detection of partial-thickness tears and a sensitivity of 88.89%, specificity of 100%, PPV of 100%, and NPV of 98.07% in the detection of full-thickness tears. The overall accuracy of USG in the detection of any tear was 82%.^[12] The US can also help diagnose rotator cuff muscle fatty degeneration and atrophy.^[24-26] Advantages of the US include portability, low cost, and lack of contraindications, whereas disadvantages relate to the limited assessment of the capsule, labrum, and cartilage as well as the inability to evaluate purely intraosseous abnormalities.

Cross-sectional nature and small sample size were the main limitations of the study, which limit the use of present study findings to a large population. There is a need of

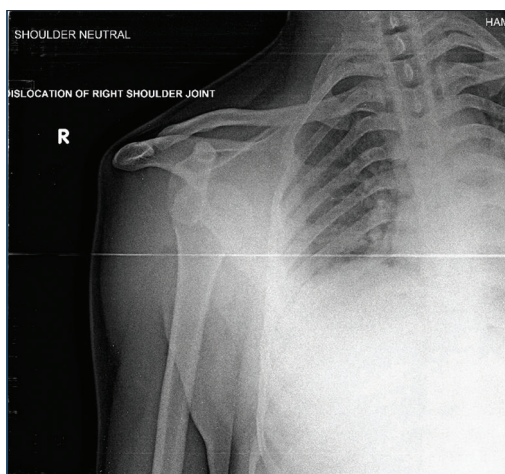


Figure 1: A-P radiograph right shoulder joint shows dislocation of humeral head posteriorly

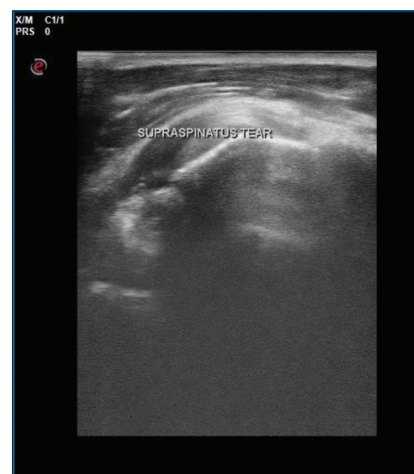


Figure 4: Patient in sitting position, long-axis view on high-frequency USG shows hypoechoic area at the insertion of supraspinatus tendon with loss of normal lamellar pattern (high-grade tear)

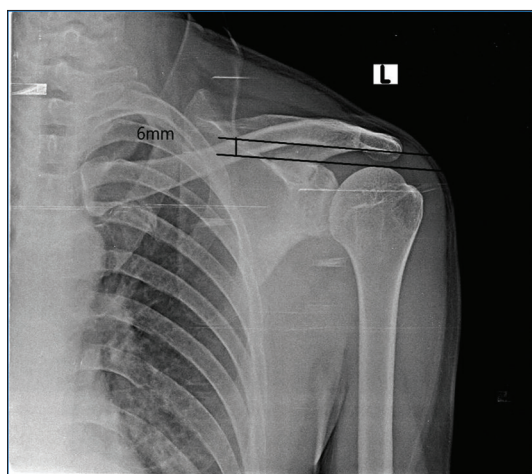


Figure 2: A-P radiograph left shoulder joint in neutral position shows reduced acromiohumeral interval (6 mm)

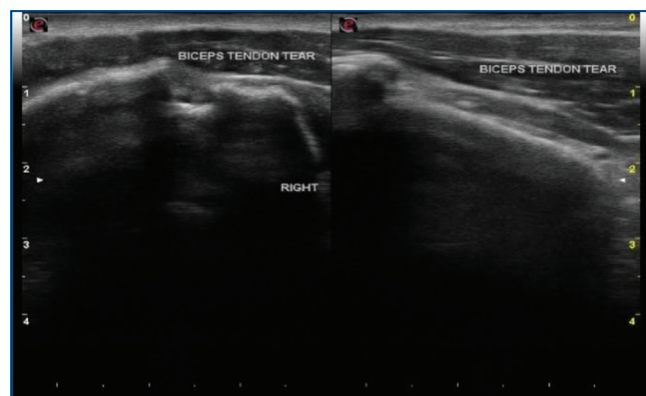


Figure 5: Patient in sitting position, short- and long-axis view shows biceps tendon tear

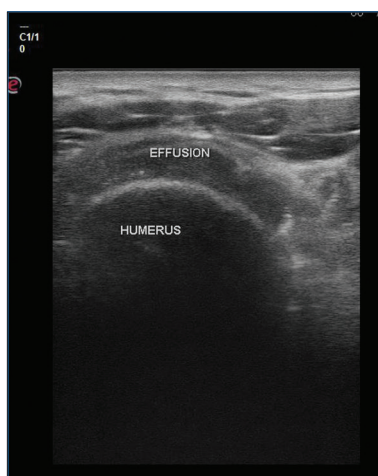


Figure 3: Patient is in sitting position, long-axis view on high-frequency USG shows effusion in glenohumeral joint

the large randomized clinical trial to provide strength to present study findings.

CONCLUSION

Rotator cuff pathology was more prevalent in patients who were in fifth to the sixth decade of their life; however, a small proportion of were young age group (athletics and who doing vigorous physical activity example gymming, labor, etc.) Rotator cuff pathology was more prevalent in males. A-P radiograph was able to reveal reduced acromiohumeral interval along with the fracture and dislocation associated with rotator cuff injury. A significant correlation was obtained between tendon tears in the rotator cuff with reduced acromiohumeral distance. A-P radiograph can be used as an initial line of investigation for evaluation of all patients with painful shoulder who are clinically suspected to have rotator cuff disorders. USG can provide additional advantages in the detection of rotator cuff pathology. Various techniques are used for evaluating patients with shoulder pain, including clinical examination. A-P radiograph of the shoulder joint is a cost-effective first-line investigation modality in the assessment of shoulder

pain. Dynamic examination and ability to compare findings with contralateral shoulder were added advantages.

A large randomized clinical trial will make the results more robust as it was a cross-sectional small study.

To conclude, the assessment of the acromiohumeral interval using standardized anteroposterior radiographs is a reliable and reproducible method of assessment of rotator cuff diseases.

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The Effect of Pulp and Paper Industry Effluent on the Biological and Bacteriological Parameters of River Hindon

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Abstract

The effluent from the industries may cause water pollution and result in the altered growth of zooplankton and phytoplankton. The identification and characterization of these species may help in determining the pollution caused by industrial effluent merging into the river. The pulp and paper mill (Star Paper Mill, Saharanpur) discharging effluents directly into the river Hindon were analyzed in the present study. The effluents from the pulp and paper mill were discharged through a canal into the Hindon river. The investigations were carried out from 2002 to 2003, in all the three seasons to assess the influence of effluent, on planktonic abundance and diversity in different seasons.

Key words: Bacteriological, Biological, Effluent, Pulp and paper mill and ETP, River Hindon

INTRODUCTION

In the western district of Uttar Pradesh, mainly Saharanpur, Muzaffarnagar, Meerut, and Bulandshar, a large number of lotic, lentic, and perennial water resources are present, which are used mainly for irrigation, fish catch, to procure fish seed, and fingerlings. The same water resources are also utilized for the disposal of the industrial wastes of about more than 20 different industries. The main water resources of this region are river Hindon, Kalinadi, Krishna, Ganga, and Jamuna with their respective tributaries and four canals. Since the rivers are an important natural source of water, maintaining water quality in them is indeed vital for all life because most of the rivers of the country suffer from pollution on one stretch or the other. According to the ministry of water resources, polluted and less polluted stretches of some major rivers have been identified.^[1] Hindon, a stretch between Saharanpur to the confluence

with the Yamuna has been identified as highly polluted and this stretch has been categorized in Class E (as per the primary water quality criteria of CPCB, 1984) with a critical situation of DO, BOD, and the toxic substances dissolved in it.^[2]

United States Public Health Service (USPHS) 1996 laid down that sample of water from approved areas shall not show the most probable number (MPN) of coliform in excess of 70 in 100 ml.^[3] More than this, the areas should be classified as grossly polluted.^[4] *Escherichia coli* and *Enterococci* are considered logical indicators of fecal pollution.^[4] Hindon water can be placed under the category of grossly polluted as these bacterial counts are very high up to 10,000/100 ml.^[5] Algae and ciliates have also been suggested as indicators of pollution.^[6,7] Changing patterns of plankton composition have also been proposed as an indicator of water pollution.^[8-11]

Many Indian rivers are studied in the last three decades on the algal taxonomy.^[12-14]

The determination of algal and other biological agents is a good indicator of the pollution level of the river. In the present study, the biological and bacteriological parameters have been studied under the stress of the pulp and paper

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industry (Star paper Mill, Saharanpur) effluent. The effect of this effluent has also been studied on the water quality of the river Hindan.

MATERIALS AND METHODS

Water samples were collected from five sites that comprise of pre-discharge point, discharge point, and post-discharge point of the effluent from the Star paper mill, Saharanpur. A total of five samples were collected from different locations. During sampling, all precautions were taken, as suggested according to the standard methods for the “examination of water and waste water sewage.” Samples were collected at five sites: Effluent treatment plant (EFT) (I), effluent at 1 km away EFT (II), pre-discharge point (III), discharge point (IV), and post-discharge point (V). Total coliform was determined by the multiple tube fermentation technique. Fecal coliform was detected by the fecal coliform membrane filter procedure. Plankton study was made by collecting 100 L of water and filtering it through a bolting silk net, and the concentrate was preserved in 5% formalin solution. Plankton count was made with Sedgwick-Rafter counting cell under a research binocular microscope. Effluent and water samples for bacteriological analysis were collected in sterile bottles of 500 ml capacity and were brought into the laboratory in an icebox, and incubation was made within 6 h of collection. Bacteriological examination for *E. coli* and Enterococci was done according to the method suggested by APHA.^[15]

RESULTS AND DISCUSSION

Bacteriological Characteristics

Biological characteristics happen to be the indicators of the water quality which also represents the extent of organic contamination. The total coliform ranged between 72 and 279/100 ml at ETP and 1 km away ETP, whereas, at Site III, it ranged between (16 and 49/100 ml), whereas, Sites – IV and V, it ranged between 89 and 324/100 ml. Based on these parameters, samples collected at the pre-discharge areas were not polluted and those collected at site III and site IV can be considered as moderately polluted. In the present investigation, the fecal coliforms have been found positive in all three seasons and at all the five sites. As the growing number of bacteria is indicative of a measure of organic pollution, it indicates that the water is polluted with organic matter. Two hundred meters downstream at site number five reflect that the self-purification process has begun. This process has been reported before in other studies.^[16,17] Table 1 summarizes the bacteriological characteristics of the river water at different sites of sample collection.

Table 1: Comparative bacteriological characteristics of the effluent of pulp and paper mill and Hindon river at effluent sites. The river water samples were collected in 2002–2003. Season is summer, rainy, and winter

Biological parameters	Site I	Site II	Site III	Site IV	Site V
Total coliform (MPN/100 ml)	203	244	29	270	188
	72	86	16	108	89
	231	279	49	324	192
Fecal coliform	+ve	+ve	+ve	+ve	+ve
	+ve	+ve	+ve	+ve	+ve
	+ve	+ve	+ve	+ve	+ve

Phytoplankton

The phytoplanktons in river Hindon have a diverse assemblage of major taxonomic groups. Many of these forms have different physiological and environmental requirements depending on the number, type, and distribution of these organisms present in any aquatic environmental factors interact to provide conditions for the growth of planktons, both specialty and seasonally. Table 2 summarizes the main phytoplankton observed in this study.

The group *Chlorophyceae* are indicative of progress in recovery and regeneration of polluted water, as most representatives of the group do not thrive in the deoxygenated waters. Many algal species grow nicely in the river water with a good amount of dissolved oxygen. *Chlorophyceae* were represented by genera *Cosmarium*, *Closterium*, *Scenedesmus*, *Pediastrum*, *Spirogyra*, *Volvox*, *Oedogonium*, and *Zygnema* in this study. Maximum genera (5) were observed at Site – III.

The periodicity of Myxophyceae has been well studied in various aquatic systems and there are mainly three factors that influence Myxophyceae populations. They include temperature, organic matter, and dissolved oxygen. In the present study, they were represented by the genera *Spirulina*, *Nostoc*, *Microcystis*, *Oscillatoria*, *Anabaena*, and *Phormidium*. The maximum of three genera was recorded at Site – III. The enrichment of water with high nitrogen and phosphorus is associated with high temperature which enhances the growth of *Microcystis*.

Zooplanktons

Like phytoplankton species, a few zooplankton species are also considered by many ecologists as indicators of organic pollution; thus, protozoans as an indicator of organic pollution have been described by few studies^[18–20]. Unlike phytoplankton, most of the zooplanktons show the reverse relationship with the pollution except protozoans and insects. In polluted stretch, the protozoans and insects occur in quite large numbers which indicate the polluted condition of the water [Table 3].

Table 2: Comparative phytoplankton's characteristics of the effluent of pulp and paper mill and Hindon river. Season is summer, rainy, and winter

Biological parameters	Season	Site I	Site II	Site III	Site IV	Site V
Chlorophyceae	S	Cosmarium-3	Cosmarium-2 Cosmarium-1	Pediastrum-2	Pediastrum-3	Pediastrum-3
				Closterium-2	Closterium-3	Spirogyra-1
				Spirogyra-2	Spirogyra-3	
	R		Scenedesmus-2	Spirogyra-3	Spirogyra-4	Spirogyra-6
				Volvox-4	Volvox-4	Volvox-5
				Oedogonium-1	Zygnema-2	Zygnema-2
	W	Cosmarium-2	Cosmarium-1 Closterium-3 Scenedesmus-2	Cosmarium-2		
				Zygnema-1		
				Volvox-5	Zygnema-2	Zygnema-3
Myxophyceae	S	Spirulina-2	Spirulina-3	Closterium-3	Scenedesmus-3	Scenedesmus-3
				Cosmarium-1	Cosmarium-1	Cosmarium-2
				Scenedesmus-1	Volvox-4	Volvox-4
	R		Nostoc-1	Spirulina-1	Microcystis-1	Microcystis-3
				Microcystis-2	Anabaena-1	Phormidium-2
				Oscillatoria-1	Phormidium-1	
	W			Oscillatoria-2	Anabaena-2	Phormidium-2
				Nostoc-2	Nostoc-13	Nostoc-6
				Microcystis-1		
				Nostoc-3	Nostoc-1	Nostoc-4
				Oscillatoria-3		
				Microcystis-4		

Table 3: Comparative biological zooplankton characteristics of effluent of pulp and paper mill and Hindon river at effluents. Season is summer(S), rainy (R), and winter (W)

Biological parameters	Season	Site I	Site II	Site III	Site IV	Site V
Protozoa	S		Euglena-3	Euglena 12	Euglena-6	Euglena-5
			Paramecium-2	Paramecium-5	Arcella-1	Arcella-1
				Diffugia-2	Centropyxis-2	Centropyxis-1
	R		paramecium-2	Nebela-1	Epistylis-1	
				paramecium-6	Nebela-1	paramecium-7
	W		Nebela-1	Epistylis-2	paramecium-7	Nebela-2
Rotifera	S		Euglena-3	Nebela-1	Phacus-2	Nebela-1
				Euglena-2	Diffugia-2	Euglena-4
					Euglena-5	
	R		Monostyla-1	Distyla-1	Distyla-1	Distyla-1
				Distyla-1	Rotaria-2	Rotaria-2
	W		Distyla-1	Rotaria-2	Monostyla-4	
					Brachionus-1	
					Euchlonis-6	Euchlonis-3
					Brachionus-4	Brachionus-1
					Distyla-1	
					Rotaria-6	Rotaria-2
					Distyla-4	Brachionus-3
					Brachionus-2	

The protozoan group was represented by *Englen*, *Paramecium*, *Nebela*, *Diffugia*, *Epistyls*, *Arcella*, *Centrophyis*, and *Phacus*. The total protozoan population was highest at Sites – III and IV, indicating water was polluted at these sites. Entomostraca group also shows an uneven distribution. At Sites – III and IV, around 3-4 genera were present, whereas, at Sites – I and II, they are absent, perhaps due to the intense pollution. *Copepoda*, *Cladocera*, and *Ostrocooda* are the main groups from the class Entomostraca, which are represented in the present investigation. In general,

the representatives of Entomostraca do not occur in polluted or toxic waters. It has been shown that the impact of pollutants in marine tropical coastal water the results indicate an increase in the nutrient levels of pulp wastewater (eutrophication), which causes an enhancement of the reproductive rate of copepods and a decrease in density of other zooplankton taxa and ichthyoplankton. The rotifers formed the most important group of zooplanktons. In the present study, the main genera observed were *Distyla*, *Monostyla*, *Euchlonis*, *Roteria*, and *Brachionus*. At Site – III,

(7) genera were recorded, and at Site – IV, (6) genera were recorded, whereas, at Site – V, (4) genera were present. At the site I, Rotifera are absent, however, at site II, they are represented by two genera.

CONCLUSION

The chemical substances resulting from pulp and paper mill effluent can cause long-term effects on zooplankton and phytoplankton. Among these chemicals, there are fibers and other settleable solids, substances that stimulate algal growth. These can also cause the eutrophication, and accumulation of these chemicals result in chronic-toxicity to the zooplankton and phytoplankton.

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Assessment of Impact of Nonsurgical Periodontal Therapy on Serum Homocysteine Levels in Patients with Chronic Periodontitis

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Abstract

Background: Periodontal diseases have a significant impact on oral health-related quality of life, especially with the worsening and extension of the disease in which it presents higher destructive consequences. Chronic inflammatory diseases enhance the systemic inflammatory load, which leads to inflammation-dependent vitamin depletion, thereby decreasing the availability of the essential nutritional cofactors responsible for the homocysteine conversion. Hence, the present study was conducted for assessing the impact of nonsurgical periodontal therapy on plasma homocysteine levels in patients with chronic periodontitis.

Materials and Methods: A total of 25 patients with a confirmed clinical and radiographic diagnosis of chronic periodontitis and 25 age and gender-matched healthy controls were enrolled. All the patients were recalled in the morning and blood samples were obtained. All the samples were sent to a laboratory where AutoAnalyzer was used for the assessment of serum homocysteine levels. Afterward, nonsurgical periodontal therapy was carried out in all the patients of the chronic periodontitis group. After finishing of nonsurgical periodontal therapy, again blood samples were taken and serum homocysteine levels were recorded.

Results: Mean serum homocysteine among the patients of the control group and the chronic periodontitis group (pre-treatment) was found to be 12.12 $\mu\text{mol/L}$ and 21.76 $\mu\text{mol/L}$, respectively. While comparing statistically, significant results were obtained. Mean serum homocysteine among the patients of the chronic periodontitis group before and after nonsurgical periodontal therapy was found to be 21.76 $\mu\text{mol/L}$ and 14.76 $\mu\text{mol/L}$, respectively. While comparing statistically, significant results were obtained.

Conclusion: Serum homocysteine levels are significantly raised in patients with chronic periodontitis. Furthermore, nonsurgical periodontal therapy leads to a significant reduction in serum homocysteine levels.

Key words: Impact, Nonsurgical, Serum

INTRODUCTION

Periodontal disease is an inflammatory process that affects the protective and supportive tissues around the tooth. Bacterial plaque accumulation on the tooth surface leads to marginal tissue inflammation, known as gingivitis. Gingivitis is a fairly common pathology. If left untreated, gingivitis may progress to periodontitis, which is characterized by

loss of periodontal attachment support (clinical attachment loss, [CAL]) and bone resorption, eventually resulting in tooth mobility and loss. Chronic periodontitis is a common disease characterized by a painless and slow progression.^[1-3]

Periodontal diseases have a significant impact on oral health-related quality of life, especially with the worsening and extension of the disease in which it presents higher destructive consequences. There are important risk factors/indicators for periodontal disease such as alcohol, overweight and obesity, smoking, and diabetes.^[4]

Homocysteine (Hcy) is a sulfur-containing, non-protein, thiol amino acid that is biosynthesized as an intermediate product during the metabolism of essential amino acid, methionine (Met). Physiologically, the re-conversion of

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Hcy to Met essentially requires certain co-enzymes such as Vitamin-B12 and folate, whose deficiency or systemic over-utilization may cause a disruption in the Hcy-Met cycle leading to a rise in plasma Hcy concentrations. Chronic inflammatory diseases enhance the systemic inflammatory load, which lead to inflammation-dependent vitamin depletion, thereby decreasing the availability of the essential nutritional cofactors responsible for the Hcy conversion.^[5-7] Hence, the present study was conducted for assessing the impact of nonsurgical periodontal therapy on serum homocysteine levels in patients with chronic periodontitis.

MATERIALS AND METHODS

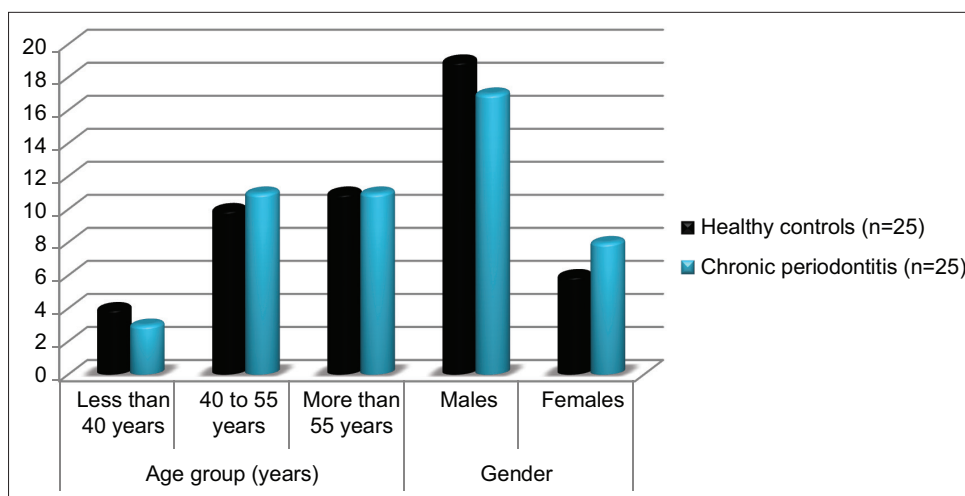
The present study was conducted for assessing the impact of nonsurgical periodontal therapy on serum homocysteine levels in patients with chronic periodontitis. A total of 25 patients with a confirmed clinical and radiographic diagnosis of chronic periodontitis and 25 age and gender-matched healthy controls were enrolled. All the patients <25 years and more than 65 years were excluded from the present study. Furthermore, patients with the presence of any systemic pathology were excluded from the study. Complete demographic details and clinical data of all the patients were recorded separately. All the patients were recalled in the morning and blood samples were obtained. All the samples were sent to a laboratory where AutoAnalyzer was used for the assessment of serum homocysteine levels. Afterward, nonsurgical periodontal therapy was carried out in all the patients of the chronic periodontitis group. After finishing of nonsurgical periodontal therapy, again, blood samples were taken and serum homocysteine levels were recorded. All the results were recorded in Microsoft excel sheet and were analyzed by SPSS software. Student's *t*-test was used for evaluation of the level of significance.

RESULTS

In the present study, 25 chronic periodontitis patients and 25 healthy controls were enrolled. Mean age of chronic periodontitis patients and healthy controls was found to be 56.8 years and 55.1 years, respectively. Majority of the patients of both the study groups belonged to the age group of more than 55 years. There were 19 males and six females in the control group and 17 males and eight females in the chronic periodontitis group. Mean serum homocysteine among the patients of the control group and the chronic periodontitis group (pre-treatment) was found to be 12.12 $\mu\text{mol/L}$ and 21.76 $\mu\text{mol/L}$, respectively. While comparing statistically, significant results were obtained. Mean serum homocysteine among the patients of the chronic periodontitis group before and after nonsurgical periodontal therapy was found to be 21.76 $\mu\text{mol/L}$ and 14.76 $\mu\text{mol/L}$, respectively. While comparing statistically, significant results were obtained [Tables 1,2 and Graph 1].

DISCUSSION

Periodontal disease and dental caries are the most common diseases in the oral cavity. Chronic periodontitis is one of the periodontal diseases. It is a long-lasting inflammatory disease affecting the soft and hard tissues around the teeth and it is common worldwide. This disease is related to common and preventable biological risk factors (e.g., high blood pressure, high blood cholesterol, diabetes, genetic factors, and obesity) and behavioral risk factors (e.g., an unhealthy diet, physical inactivity, and tobacco use). Chronic periodontitis is ideally diagnosed at the beginning of the disease.^[7,8] Thus, the conceivable etiologic mechanism linking periodontal disease and CVDs are the presence of chronic low-grade inflammation. Inflammation and CVD both are associated with elevated serum levels of CRP and



Graph 1: Demographic data

Table 1: Comparison of mean serum homocysteine ($\mu\text{mol/L}$) among the subjects of the control group and chronic periodontitis group (pre-treatment)

Number of patients	Healthy controls	Chronic periodontitis (Pre-treatment)	P-value
Mean	12.12	21.76	0.000 (Significant)
SD	2.86	4.12	

Table 2: Comparison of mean serum homocysteine ($\mu\text{mol/L}$) among chronic periodontitis patients before and after nonsurgical periodontal therapy

Number of patients	Chronic periodontitis (pre-treatment)	Chronic periodontitis (post-treatment)	P-value
Mean	21.76	14.76	0.010 (Significant)
SD	4.12	2.39	

homocysteine (Hcy). Hcy is a sulfur-containing amino acid that is a product of the methionine metabolic pathway and can get accumulated as a result of a deficiency or systemic overutilization of folate, Vitamin B12, or Vitamin B6. Elevated levels of plasma Hcy has been detected in patients with chronic periodontitis. Possible mechanisms include the sustained production of pro-inflammatory cytokines such as ILs and TNF- α from inflamed periodontal tissues. These mediators can initiate an inflammatory cascade that has the potential to disturb the Hcy homeostasis, thereby elevating plasma Hcy concentrations.^[7-9] Hence, the present study was conducted for assessing the impact of nonsurgical periodontal therapy on serum homocysteine levels in patients with chronic periodontitis.

In the present study, mean serum homocysteine among the patients of the control group and the chronic periodontitis group (pre-treatment) was found to be 12.12 $\mu\text{mol/L}$ and 21.76 $\mu\text{mol/L}$, respectively. While comparing statistically, significant results were obtained. Mallapragada *et al.* assessed the effect of nonsurgical periodontal therapy on circulating serum high-sensitivity capsule reactive protein (hs-CRP) and homocysteine (Hcy) levels in patients with chronic periodontitis. The study involved 50 participants. The test group included 25 systemically healthy controls (mean age 38.44 ± 3.27 years) with severe chronic periodontitis and the control group ($n = 25$) included age- and sex-matched systemically and periodontally healthy controls. Mean serum hs-CRP and Hcy concentration in patients with chronic periodontitis were 3.37 ± 0.54 mg/L and 21.47 ± 7.93 $\mu\text{mol/L}$, respectively, and was significantly higher than the controls (1.68 ± 0.71 mg/L and 13.93 ± 8.30 $\mu\text{mol/L}$, respectively) ($P < 0.05$). Post-treatment, the mean serum hs-CRP and Hcy concentration reduced significantly in both test and control groups ($P < 0.05$).

Chronic periodontitis leads to an increase in circulating levels of hs-CRP and Hcy in plasma and nonsurgical periodontal therapy decreases periodontal inflammation, which in turn reduces systemic inflammation and consequently decreases serum levels of hs-CRP and Hcy.^[10]

In the present study, mean serum homocysteine among the patients of the chronic periodontitis group before and after nonsurgical periodontal therapy was found to be 21.76 $\mu\text{mol/L}$ and 14.76 $\mu\text{mol/L}$, respectively. While comparing statistically, significant results were obtained. Dillon MC *et al.* investigated that if CRP and homocysteine could be routinely detected in the saliva of healthy adults and the relationship between salivary and blood levels. CRP and homocysteine concentrations were determined using ELISA and enzymatic assays, respectively. Homocysteine was detected in only two saliva samples. CRP was measurable in all saliva samples and plasma samples. Regression analysis demonstrated no relationship between CRP concentration in saliva and plasma. Generalized linear models, including variables such as saliva flow rate and time since eating or drinking, also did not pass a lack of fit testing. Therefore, a relationship between CRP concentration in saliva and blood could not be established in this group of subjects. More sensitive detection methods are needed to determine if a correlation between salivary and serum homocysteine levels exists.^[6] Agnihotram *et al.* 2010 and Joseph *et al.* 2011 demonstrated higher plasma Hcy concentrations in chronic periodontitis participants over the controls. As recognized in the preceding studies and the present study, there could be a biologically conceivable association between chronic periodontitis and serum Hcy levels with several possible underlying mechanisms explaining this link.^[7,11]

CONCLUSION

From the above results, the authors concluded that serum homocysteine levels are significantly raised in patients with chronic periodontitis. Furthermore, nonsurgical periodontal therapy leads to a significant reduction in serum homocysteine levels.

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Parity and Menarche as Factors Associated With Age at Natural Menopause

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Abstract

Introduction: “Menopause symptom” is defined when menstrual bleeding was not been observed for a full 12 months without a specific cause such as pregnancy or breastfeeding, according to the standards of the world health organization.

Objective of the Study: The objective of the study was to determine the effect of parity and menarche as risk factors in the time of menopause occurrence.

Materials and Methods: This study included 200 females in natural menopause. Each patient has undergone an interview based on the questionnaire, including demographic characteristics, other gynecological disorders, and clinical manifestations of menopause including vasomotor complaints, urogenital complaints, and psychosocial factors. Statistical analysis of data was carried out by the usual statistical methods of descriptive statistics.

Results: In the study group, there was no correlation between the age of menarche occurrence and the age of menopause occurrence. No correlation was found between parity and age of menopause.

Conclusion: There is no correlation between the age of menarche occurrence, parity, and age of the menopause.

Key words: Menarche, Menopause, Parity

INTRODUCTION

Menopause is a natural phenomenon signaling the reduction of ovarian function and onset of the last menstrual period and is generally diagnosed in retrospect since confirmation occurs only after a 12-month cessation of menstrual periods. Perimenopause is defined as the transition before the last menstrual cycle, when a woman may experience variable or irregular menstrual cycles and hormonal fluctuations, and the 12 months after the final menstrual period. Premenopause is the stage after menarche but before entering menopausal stages with normal fertility function during this phase.^[1] Postmenopause is defined

as the stage beginning 12 months after the last menstrual cycle.^[2] Menopause as complex process encompasses: Endocrine, genitourinary, cardiovascular, loco motor system, and leads to vasomotor and psychological symptoms. The first endocrine sign of announcement of menopause is the increase of level of FSH above 40 IU/L. The average age of menopause has not changed from 600 B.C.^[3] In a study conducted by the “National Health Centre,” it was seen that the average age of menopause among Iranian women was 49.6 years, while in U.S. women it was 51 ± 1 years.^[4]

The menopause transition is experienced by 1.5 million women each year and often involves troublesome symptoms, including vasomotor symptoms, vaginal dryness, decreased libido, insomnia, fatigue, and joint pain.^[5]

Due to lack of estrogen more than 80% of women experience decreases physical and mental well-being in the year approaching menopause.^[6] It is well-documented that

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menopausal symptoms experienced by women affect their quality-of-life.^[7] The beginning of menopause is subject to individual fluctuations and it cannot be encompassed exactly. Recent researches emphasize that marital status, parity, physical activity, education, and urban that is rural environment have enormous influence on age of menopause occurrence in the examined groups.^[8]

Aim and Objective

The objective of this study was to determine influence of parity and menarche as risk factors to time of menopause occurrence.

MATERIALS AND METHODS

The study included 200 women in the natural menopause who came for regular gynecological checkups in a tertiary care hospital in Jammu in the period from October 2018 to September 2019. The basic criterion for inclusion in the study was that the woman is in the natural menopause, that is, that it has been more than a year from the last menstruation. Each patient has undergone an interview based on the questionnaire. The parameters included in the questionnaire are chosen based on the date theoretical knowledge but also from the results of published studies. Each patient was verbally introduced to nature of the research and her verbal consent was obtained to take part in this research in line with the norms of the ethical medical research. We observed variables related to reproductive health: Age of menarche, the average age of menopause, and number of deliveries.

Statistical Analysis

Statistical analysis of data was carried out by the usual statistical methods of descriptive statistics. At the end of the study, all the data were compiled and analyzed with the help of computer software MS EXCEL and SPSS version 21.0 of Windows.

RESULTS

This study included 200 females from a tertiary hospital in Jammu who were in the natural menopause, age from 40 to 65 years, with an average age of years 51.59 ± 5.648 , with the maximum number of subjects between 46 and 50 years. In our study of 200 females, the mean age at menopause was 48.48 ± 2.29 years, as shown in Table 1.

In the examined group out of 200 females, 61 had three childbirths (parity), 48 had two, 35 had four, 24 had five, 17 had one, 9 had six, 4 had seven, and 2 had nine childbirths, as shown in Table 2.

Pearson correlation coefficient of 0.188 was observed between parity and age of menopause in our study population which was not significant.

In our study, age at menarche was seen to range from 12 to 15 years with mean age 13.08 ± 1.034 and maximum subjects had attained menarche at 12 years.

The correlation of age at menarche and age at menopause occurrence was analyzed but it could not be confirmed that there is linear correlation between them (Pearson correlation coefficient of 0.862), so there is no statistical importance, as depicted in Table 3.

DISCUSSION

The beginning of menopause is subject to individual variations and cannot be encompassed exactly. There are a number of studies in the world which give extensive

Table 1: Distribution of subjects according to the age at menopause

Age at menopause (years)	Number of subjects	Percent
<46	13	6.5
46 to <48	70	35
48 to <50	54	27
50 to <52	42	21
52 to <54	18	9
≥54	3	1.5
Total	200	100

Mean age at menopause \pm S.D = 48.48 ± 2.29

Table 2: Distribution of subjects according to their parity

Parity	Number of subjects	Percent
P 1	17	8.0
P 2	48	24.0
P 3	61	30.0
P 4	35	18.0
P 5	24	12.0
P 6	9	5.0
P 7	4	2.0
P 8	0	0.0
P 9	2	1.0
Total	200	100.0

Table 3: Correlation between menarche and age at menopause

Menarche (years)	Mean age at menopause (years)	Standard deviation
12	48.19	2.51
13	48.6	2.29
14	48.7	2.26
15	48.73	2.09

records on that the age at which the menopause occurs are not fixed, but that it varies from population to population. Our study was carried out on 200 females who had attained natural menopause. The mean age of subjects, in our study, was 51.59 years with minimum age of 40 years and maximum age of 65 years. The mean age of our subjects attaining menopause was 48.48 ± 2.29 years which is corresponding to studies conducted in India by Kaur *et al.*, 2019 (47.42 ± 3.64).^[9] In our study, no correlation was seen between parity and the age of menopause, with a correlation coefficient “ r ” = 0.188. Rizvanovic *et al.* (2013) did a study to determine the effect of parity and menarche as risk factors in the time of menopause occurrence and concluded that there was no correlation between the age of menarche occurrence, parity, and age of menopause.^[10] Our results are in accordance to the above-mentioned study. Parity as factor which influences years of age of menopause was taken into account in many researches. Results of British cohort research speak in favor of increased parity with statistical importance ($P < 0.001$) influencing delayed occurrence of menopause.^[11] Velez *et al.* with associates researching the connection of years of age of menopause and parity in the area of Latin America and the Caribbean in seven cities came to conclusion that null parity, and multiparity (women with five and more delivered children) earlier enter the menopause.^[12]

No correlation between age at menarche and age at menopause was observed in our study with a Pearson correlation coefficient of 0.862. A retrospective cohort study of 336788 women aged 48–71 years was carried out by Bjelland *et al.*, in Norway during the year 2006–2014 to determine the relation of age at menarche with age at natural menopause and it was concluded that their association was weak and non-linear and the duration of reproductive period was decreased by increasing age at menarche.^[13] In Pro-Saude study conducted by Brazilian authors statistical importance of connection was not proved between menarche and years of age at the menopause.^[14] Our results are consistent with these studies. As per Reynold’s and associates research, women who had the first menstruation (menarche) at the age of 11, enter menopause earlier than those who had menarche at 12 years of age and later.^[15] In the comparative study carried out by Bernis and associates in the region – Madrid got the results which indicated connection between menarche and years of age at menopause.^[16]

CONCLUSION

There is no correlation between age of menarche and age of menopause. Furthermore, no correlation is found between parity and age of menopause.

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