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Case Report

Interesting Internal Hernia: A Rare Case Report of Intestinal Obstruction

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Abstract

Internal hernias are a relatively uncommon condition and also a rare type of intestinal obstruction. Many types of internal hernias have been described, among which paraduodenal hernias are considered to be most common. Internal hernias are very challenging to diagnose clinically and may be missed in the emergency room because of their non-specific signs and symptoms. These hernias may present as a surgical emergency as they progress to intestinal strangulation and ischemia if their diagnosis is delayed. Hence, accurate preoperative diagnosis is crucial for appropriate management. Many a times these hernias are found intraoperatively as a surprise. Herein, we report a 43-year-old patient, who was preoperatively diagnosed with a left paraduodenal hernia with the help of contrast-enhanced computed tomography abdomen and pelvis and underwent a laparotomy in an emergency setting. The jejunum and ileum were entrapped (bowel was viable) and were seen herniating through the foramen of Landzert - left paraduodenal space. Once the hernial contents had been reduced, non-absorbable sutures were used to obliterate the defect. Post-operative period was uneventful and the patient was discharged on POD 3.

Key words: Foramen of landzert, Internal hernia, Multidetector computed tomography, Paraduodenal hernia

INTRODUCTION

Internal hernias are defined as protrusion of abdominal viscera through an opening within the peritoneal cavity, although all are not intraperitoneal. They can be congenital or acquired.[1] Paraduodenal hernias are one among many internal hernias. They are rare congenital hernias accounting for <2% of all intestinal obstructions, and most frequently involve the jejunum.[2] Left paraduodenal hernias are most common among them and result from abnormal rotation of midgut and failure of peritoneal fusion.[2] They usually present with acute abdominal pain, chronic digestive disorders, or variable symptoms; and can even remain silent. This non-specific presentation leads to delay in diagnosis often making internal hernias an incidental intraoperative finding.[3] Therefore, whenever the possibility of an internal hernia is considered, a rapid higher imaging is necessary to aid in early diagnosis and prompt intervention.

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Multidetector computed tomography (MDCT), with its wide availability, has become first-line imaging technique in such patients.[3] Timely surgical intervention minimizes the mortality and morbidity associated with this hernia.

CASE REPORT

A 43-year-old male presented to the emergency department with complaints of diffuse pain abdomen on and off for 1 month, aggravating with food intake. The pain was sudden in onset, of colicky type, gradually progressive in nature, and would relieve spontaneously. Occasionally, it was followed by non-bilious vomiting, containing food particles. Patient was admitted in a local hospital twice in the past 1 month for similar complaints where ultrasound and endoscopy were done and were normal. He had no history of previous surgeries and was not on any regular medications. On physical examination, the patient had tachycardia – 102 bpm and was dehydrated. Other vitals such as blood pressure and urine output were normal. There was no icterus. On examination, there was a diffuse mass noted in the left upper quadrant of the abdomen, not well defined, firm in consistency, tender, but there was no guarding. No hepatosplenomegaly. The rest of the abdomen was soft. Laboratory studies revealed total counts of 11,400, with other parameters

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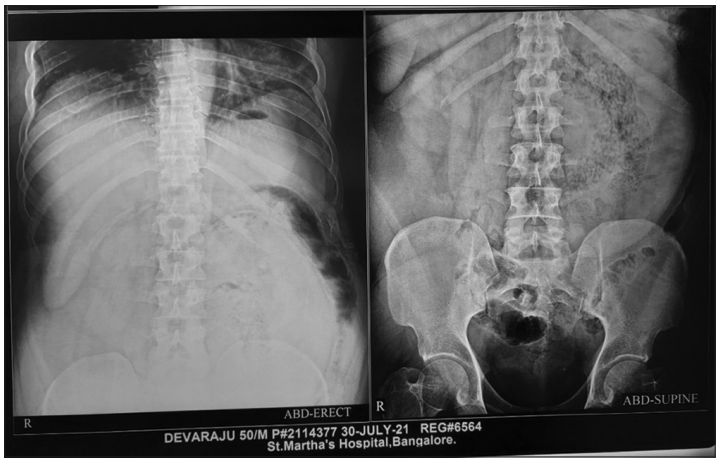

Figure 1: X-ray abdomen erect and supine done on admission

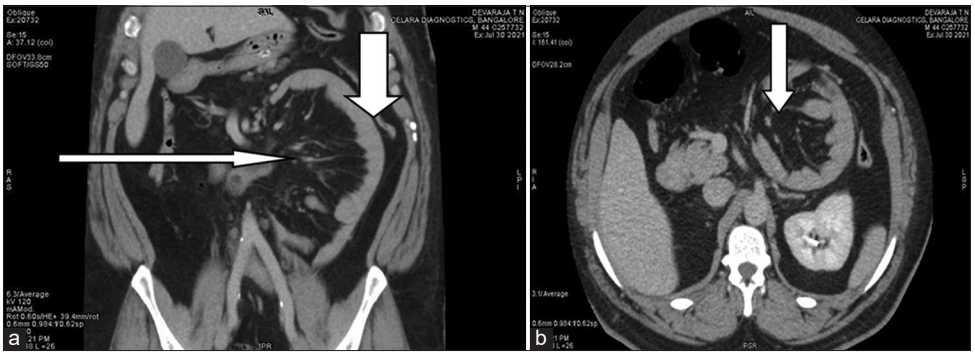

Figure 2: (a and b) Contrast-enhanced computed tomography images of abdomen showing bowel loops herniating through a defect in left paraduodenal region in left hyochondrium upto left lumbar region (arrow marks). Crowding of small bowel loops within the sac

being normal. X-ray of the abdomen erect and supine was normal [Figure 1]. Since the patient was hemodynamically stable, contrast-enhanced computed tomography (CECT) abdomen and pelvis were done [Figure 2] which revealed left paraduodenal hernia with entrapped small bowel loops and features suggestive of obstruction. Hence, patient was taken up for emergency exploratory laparotomy. Operative findings revealed a defect in the left paraduodenal space (foramen of landzert) with jejunal and ileal loops trapped in it [Figure 3]. Bowel appeared viable. After reducing the bowel from defect, the paraduodenal space was closed by approximating the mesocolon fold to the base of mesentery taking care not to injure the inferior mesenteric vein [Figure 4]. Pos-toperative period was uneventful. CECT repeated post-operatively showed normal bowel loops without any herniation [Figure 5]. The patient tolerated soft diet on POD 1, moved his bowel on POD 2, and was discharged on POD 3 in stable condition.

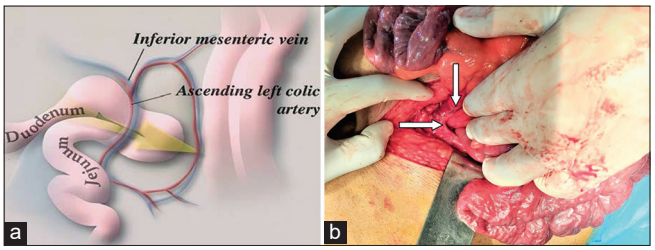

Figure 3: (a and b) Intraoperative photograph showing left paraduodenal hernia with small bowel loops herniating through foramen of Landzert. Contents being reduced. Bowel looks viable

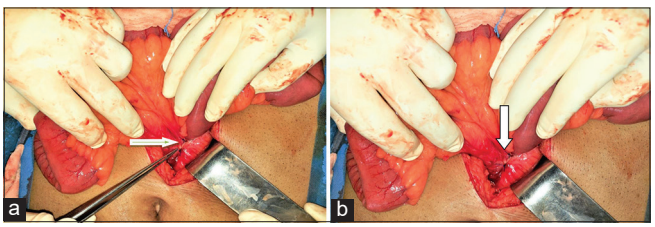

Figure 4: (a and b) Defect closed with non absorbable suture after reducing the contents

DISCUSSION

Internal hernias are either congenital or acquired, among which acquired are more common. Congenital internal hernias are classified by Gharemani into Paraduodenal (30–50%), Foramen of Winslow, pericaecal, intersigmoid, and paravesical.[2]

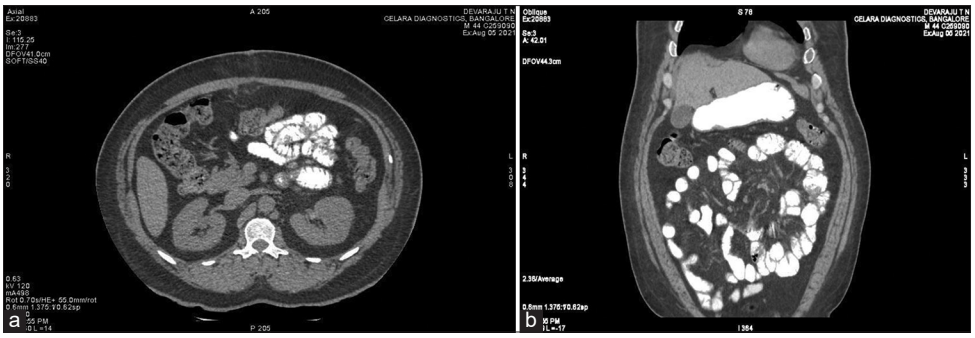

Figure 5: (a and b) Post operative computed tomography images showing no herniation

Paraduodenal hernia, also known as mesocolic hernia, was first described in an autopsy by Neubauer in 1786. Later, an accurate scientific description of the condition was provided by Treitz in 1857, who considered it a retroperitoneal protrusion of abdominal viscera. The classification of hernia into the distinct left and right types was made by Jonnesco in 1889.[4]

In 1923, Andrews postulated that paradudodenal hernias result from an embryological error during the midgut rotation. The mesentery fails to fuse with the parietal peritoneum of the posterior abdominal wall in the early weeks of development, that is, after the return of the herniated bowel loops into the abdominal cavity. This creates a potential space of herniation behind the mesocolon. Therefore, they are termed as mesocolic hernias.[4]

Left paraduodenal hernia, which arises from the fossa of Landzert, comprises <2% of all hernias and is about 3 times more common than its right counterpart (Waldeyer's hernia). It occurs through a defect in the left portion of the transverse mesocolon that gives way to retroperitoneal herniation of the small intestine (usually proximal jejunum). The fossa of Landzert is located to the left of the fourth part of the duodenum, posterior to the inferior mesenteric vein, and ascending branch of a left colic artery, where they form the congenital defect.[5]

Majority of presentations occur between the 4th or 5th decade with a mean age of 38.5 years.[6] Symptoms vary from being asymptomatic which are found incidentally during intraop or may present with symptoms such as diffuse pain abdomen, vomiting, and other features of obstruction and gangrenous bowel. Sometimes symptoms may mimic peptic ulcer disease or any biliary disease for which patient may be receiving unnecessary interventions.

MDCT has become the investigation of choice in detecting internal hernias.[5] Although ultrasonography of the abdomen, barium enhanced studies are other imaging modalities that can also be used.

The lifetime risk of incarceration or strangulation is over 50% with a mortality risk of 20–50%, if left untreated.[5] The principles of surgery in the treatment of paraduodenal hernia include reduction of the hernia content, resection of the necrotic intestinal segment if present and repair of the hernial orifice by the closure of the defect.

The treatment of the paraduodenal hernia is surgery. It may be carried out by either a conventional open approach or laparoscopic approach. In our case, we performed exploratory laparotomy, and contents were reduced. Many recent studies that have compared open to laparoscopic approach showed that the laparoscopic approach has better results in terms of less post-operative stay, pain, wound infections, and postop ileus.[6,7]

CONCLUSION

Paraduodenal hernia is a relatively rare cause of acute abdomen. Establishing a clinical diagnosis is challenging and is delayed owing to its variable signs and symptoms. Although it is a rare condition, it can cause high morbidity and mortality if left untreated. Internal hernia as the differential diagnosis has to be kept in mind, particularly in those who have not undergone previous abdominal surgery. With the advent of MDCT, early diagnosis of internal hernias has been made relatively easier. Early surgical intervention is necessary to avoid associated morbidity and mortality.

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Case Report

Management of Pseudomeningocele Associated with Failed Back Surgery Syndrome with Spinal Instability in an Elderly Female - A Rare Case Report

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Abstract

Lumbar canal stenosis causing low back ache is one of the most common health complaint with its prevalence in world population is calculated up to 12–38%. Failed back surgery syndrome (FBSS) is a term used when the result of lumbar spinal surgery fails to match the pre-operative expectations of the operating doctor and the patient. It has been best described by Dirks and Follet as surgical end stage after one or multiple interventions on lumbar neuroaxis indicated to manage low back ache, radicular pain, or combination of both without effect. Here, we present a rare case of 58-year-old female, a case of FBSS with progressive disabling symptoms of low back ache, radiculopathy, and claudication. She was managed with posterior instrumentation for spinal instability and pseudomeningocele was repaired with surgical durotomy and using bovine pericardial patch. Pseudomeningocele associated with FBSS is a very rare and surgically challenging case to manage due to distorted soft-tissue fibrosis from the previous surgery, with entrapment of intervening nerve roots. The progressive nature of disabling symptoms necessitated surgical management. Posterior instrumentation and fusion for spinal instability with decompression for lumbar canal stenosis and bovine pericardial patch for repair of pseudomeningocele were done with satisfactory improvement in neurology.

Key words: Bovine pericardial patch, Failed back surgery syndrome, Posterior instrumentation, Pseudomeningocele, Spinal instability

INTRODUCTION

Lumbar canal stenosis causing low back ache is one of the most common health complaint with its prevalence in world population is calculated up to 12–38%. Failed back surgery syndrome (FBSS) is a term used when the result of lumbar spinal surgery fails to match the pre-operative expectations of the operating doctor and the patient. It has been best described by Dirks and Follet as surgical end stage after one or multiple interventions on lumbar neuroaxis indicated to manage low back ache, radicular pain, or combination of both without effect.[1,2]

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In FBSS, Burton *et al.* in 1981 stated that 58% had lateral canal stenosis, 7–14% had central canal stenosis, 12–16% had recurrent (or residual) disc herniations, 6–16% had arachnoiditis, and 6–8% had epidural fibrosis.[1] There is soft-tissue fibrosis from the previous surgery and distorted spinal anatomy which along with causing nerve root compression makes the surgery technically difficult and challenging.

Hence, non-operative treatment with analgesics, anti-convulsants, psychiatric counseling, and adequate physical therapy forms the choice of management with surgical fusion in selected patients with disabling symptoms.[2] In 1946, Hyndman and Gerber first

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described post-laminectomy pseudomeningocele. There is extravasation of cerebrospinal fluid (CSF) forming an extradural cyst due to a ball valve phenomenon. This exerts a mass effect over surrounding neural structures and cause symptoms of low back ache and radiculopathy which aggravates by coughing and straining. Magnetic resonance imaging (MRI) has been gold standard for diagnosis. The standard treatment includes careful surgical extirpation of pseudomeningocele sac with dural repair.[3,4]

CASE REPORT

A 60-year-old female patient came to our outpatient department with complaints of low back ache with the right lower limb radiculopathy and tingling with claudication distance of 50 m. On examination, patient had the right SLRT positive at 45 degrees with the right lower limb power of four. She was operated by decompression at L4 level for lumbar canal stenosis 20 years back, with partial relief of symptoms. Since, then she had persistent low intensity low back ache for which she took analgesics and physiotherapy but the symptoms aggravated since past 6 months to the present condition.

Pre-operative X-rays are shown in Figure 1 suggestive of mild retrolisthesis of L3 over L4. MRI is shown in Figure 2 suggestive of pseudomeningocele at L3-L4 level with disc herniations at L3–L4 and L4–L5 levels. Patient was then taken up for surgery after proper pre-anesthetic fitness.

Patient was taken on operating table in prone position under general anesthesia and all aseptic precautions scrubbing, painting, and draping done. Midline skin incision was taken from L2 to L5 levels. Careful soft-tissue dissection was done with cobb elevator and electrocautery in view of gross fibrosis from the previous surgery which helped to free up the entrapped nerve roots. Reduction pedicle screws were inserted by free hand technique in L2, L3, and L5 vertebrae and retrolisthesis corrected. Decompression by laminectomy was done from L2 to L5 levels and discectomy at L3–L4 and L4–L5 levels. Pseudomeningocele was carefully incised and the surgical durotomy was repaired with bovine pericardial patch secured with prolene 5 sutures and fibrin sealant applied along the suture line as shown in Figure 3.

Post-operative X-rays and computed tomography (CT) scan are shown in Figure 4. Immediate post-operative there was symptomatic relief from radiculopathy and tingling with gradual recovery of power of the right lower limb to five. Dural tear protocol strictly followed for 7 days with gradual bedside mobilization started with lumbar corset belt. Suture removal done on day 14, found to be healthy in Figure 5.

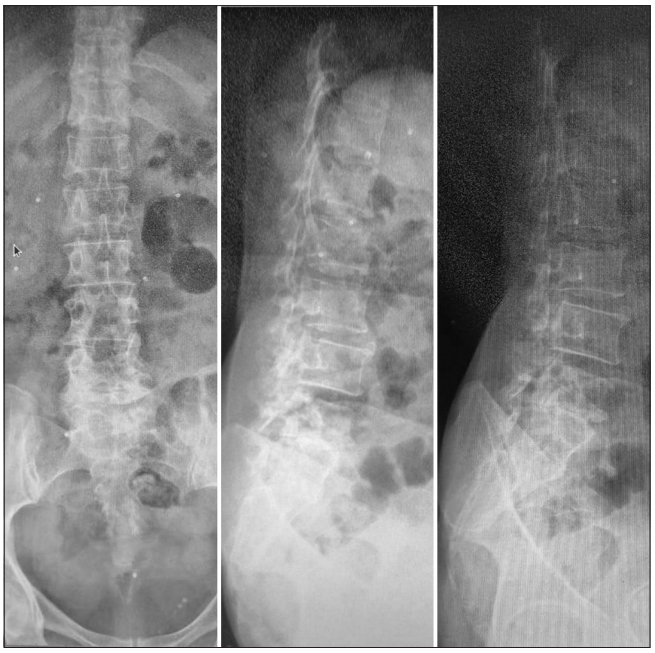

Figure 1: Pre-operative X-rays showing mild retrolisthesis of L3 over L4

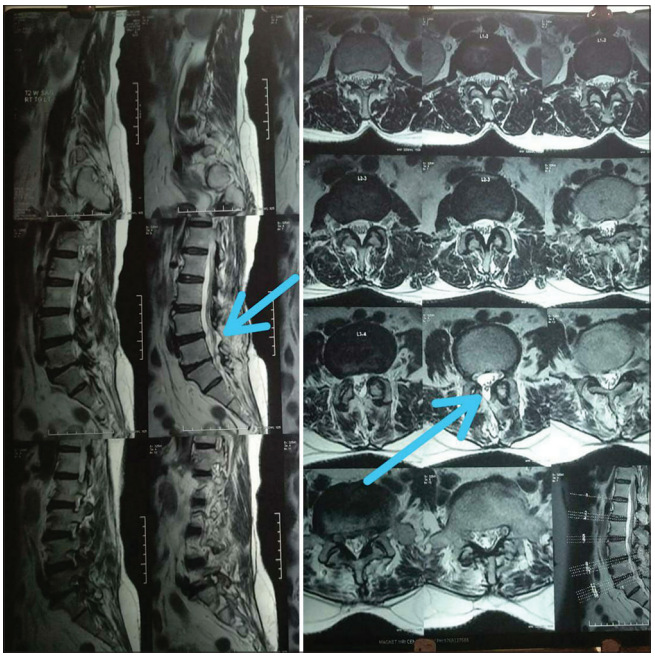

Figure 2: Pre-operative MAGNETIC resonance imaging scan showing pseudomeningocele (blue arrow) at L3–L4 level with disc herniations at L3-L4 and L4-L5 levels and sacralization of L5

DISCUSSION

FBSS is usually caused by poor patient selection, inaccurate diagnosis, incomplete decompression or decompression at wrong levels, recurring disc prolapses, vertebral instability, facet joint disease, epidural fibrosis, or arachnoiditis.[5] There is approximately 30% failure rate of lumbar spine surgeries and 20% eventually require secondary reoperation. The

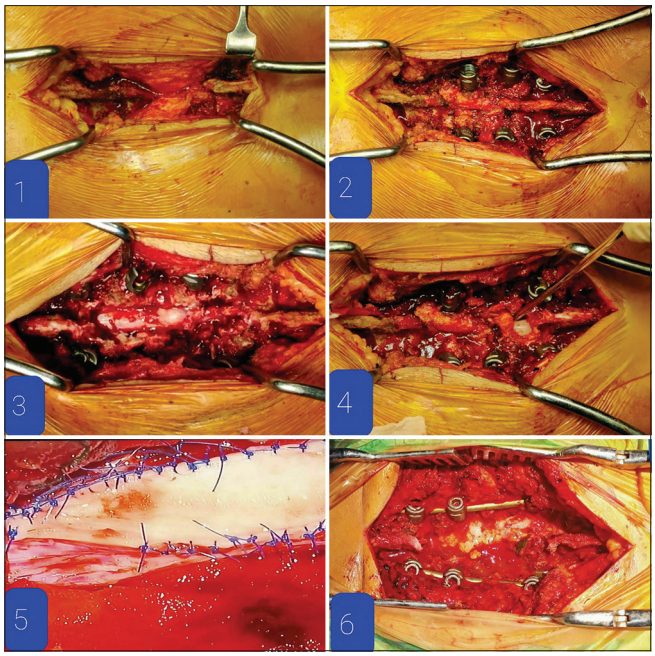

Figure 3: Surgical procedure illustrated. (1) Midline skin incision from L2 to L5 levels with careful soft-tissue dissection, (2) pedicle screws inserted at L2, L3, and L5 levels, (3) decompression by laminectomy done with exposure of pseudomeningocele at L4 level, (4) pseudomeningocele carefully excised, (5) dural repair done with bovine pericardial patch and secured with prolene five suture and application of fibrin sealant, and (6) retrolisthesis corrected with connecting rods fixed to pedicle screws and final tightening done

failure rates in reoperations of spine increase proportionally after repeated number of surgeries giving diminished outcomes. This leads to chronic disabling pain with poor quality of life and function for the patient.[2,6]

Carragee *et al.* associated increased rates of FBSS with psychosocial health of patients. It is correlated proportionally with predicting poor outcomes after spine surgery. Similar results are seen in chronic smokers, obese, anxiety, and depression patients. This stresses on importance of surgeon patient communication with psychiatric counseling, both pre and postoperatively.[2,7]

Failure rates are also majorly based on the choice and technique of operation. Errors while operating does not help the patient and also worsen the present condition of the patient triggering new complications.[2] The incidence of faulty screw insertion and implant breakage ranges up to 6.5–12% in patients undergoing lumbar spinal fusion using pedicle screws, with the risk of serious neurological damage and loss of sagittal balance when more than one level is fused.[2]

Conservative management with analgesics, anti-convulsant such as pregabalin and gabapentin, cognitive behavioral therapy, and physiotherapy is the first line of treatment.

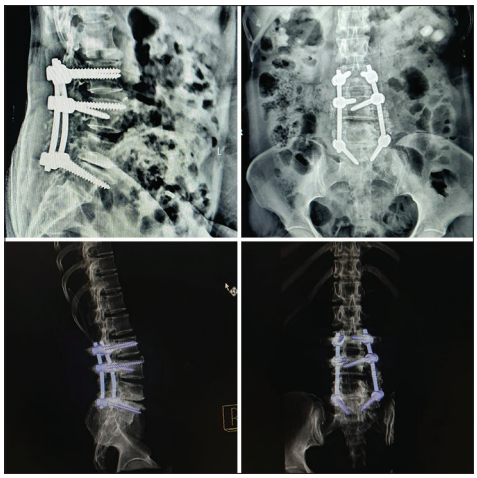

Figure 4: Post-operative X-rays and computed tomography cuts showing posterior instrumentation from L2 to L5 levels with correction of retrolisthesis of L3 over L4

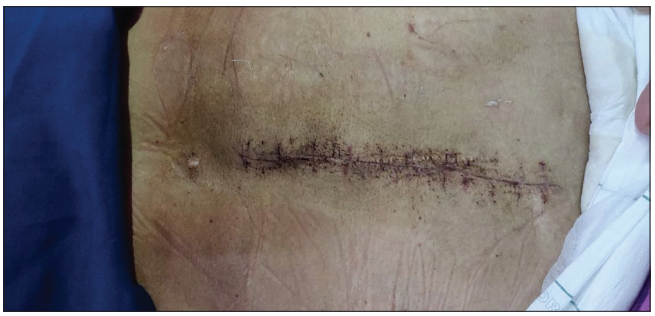

Figure 5: Suture removal at post-operative day 14 found to be healthy

Spinal cord stimulation is another modality of mini invasive treatment used preferably in patients with pain in neuropathic limb. The choice of surgical management depends largely on cause of pain which may be due to a single cause or confluence of more than one etiologies.[2,7] Foraminal stenosis is the most common structural cause of FBSS ranging from 25% to 29% causing disabling radiculopathy, followed by disc pain, pseudoarthrosis, neuropathic pain, recurrent disc herniations, iatrogenic instability, facet pain, and sacroiliac joint pain.[7]

Radiological assessment with X-rays, CT, and MRI scans helps to identify the cause of disability in FBSS. Axial cuts in MRI help in diagnosing foraminal stenosis while CT cuts can delineate pain due to pseudoarthrosis. Myelography is rarely indicated. Diagnostic anesthetic injections can diagnose pain due to nerve root compression and inflammation in sacroiliac joint and facet joint.[7]

Higher success rates after operating FBSS depend on proper diagnosis and adequate posterior instrumentation especially in cases of spinal instability. Although conservative management is considered gold standard, spinal fusion with posterior instrumentation has been successfully used

in selected patients of FBSS to relieve excessive pain and treat functional disability.[6,7]

Extradural cystic collection without any dural covering due to breach in dura arachnoid layer is called pseudomeningocele. It can be rarely traumatic and most commonly it is iatrogenic. It is a rare occurrence with 0.07–2% incidence and may lead to symptoms of FBSS.[3] In the literature, various techniques such as fascia lata, galea periosteal tissue, latissimus dorsi flap, trapezius flap, gluteus maximus flap, and dorsal intercostal artery perforator flap have been described for dural and neural placode repair. However, these techniques are challenging and time consuming with soft-tissue sacrifice.[8,9]

The bovine pericardial patch is a better solution for dural repair. It is a collagenous membrane which ensures reliable closure of tissue defects and provides scaffold for patient's own tissues. Fibrin sealants or glues are other alternatives which act as topical hemostatic agents and provide adequate adhesion for dura repair. It can be used along the sutures of bovine pericardial patch over durotomy. It prevents CSF leak and compressive scar tissue formation.[8]

CONCLUSION

Pseudomeningocele associated with FBSS is a very rare and surgically challenging case to manage due to distorted soft-tissue fibrosis from the previous surgery, with entrapment of intervening nerve roots. The progressive nature of disabling symptoms necessitated surgical management. Posterior instrumentation and fusion for spinal instability with decompression for lumbar canal stenosis and bovine pericardial patch for repair of pseudomeningocele were done with satisfactory improvement in neurology.

DECLARATION OF PATIENT CONSENT

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Case Series

Disability Due to Thromboembolism in Covid Recovered Patient

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Abstract

Peripheral arterial disease is mainly caused by atherosclerosis and thromboembolic disease. In coronavirus disease (COVID) era, we found there was an exponential increase in the cases of lower limb gangrene due to thrombus in the lower limb arterial system, resulting in the amputation. As COVID infection is hypercoagulable state this results in the thrombus. We want to report a case series of eight patients presented in M.G.M. Medical College and Maharaja Yashwant Rao Hospital, Indore. In all the following patients, on palpation, there was absent Dorsalis Pedal artery pulsation. For the routine imaging, Color Doppler and computed tomography angiography were done for the detection of the level of occlusion/cougulopathy. Hence, the only option left was amputation. The D-dimer has been shown to be frequently elevated in patients with COVID-19. Increased fibrinogen, fibrin degradation products, prothrombin time, activated partial thromboplastin time, and shortened thrombin time have been described in patients with COVID-19 compared to healthy controls. Clinicians are using prophylactic, intermediate, or therapeutic doses of anticoagulation, based on coagulation parameters and the clinical scenario. Although the optimal dosing remains unclear the benefit of anticoagulation with heparin products (mostly low-molecular-weight heparin at prophylactic doses) in COVID-19 patients.

Key words: Amputation, Anticoagulant, Coronavirus disease, Gangrene, Thromboembolism

INTRODUCTION

Peripheral arterial disease is mainly caused by atherosclerosis and thromboembolic disease. In coronavirus disease (COVID) era, we found there was an exponential increase in the cases of lower limb gangrene due to thrombus in the lower limb arterial system, resulting in amputation. As COVID infection is hypercoagulable state this results in thrombus. We want to report a case series of eight patients presented in M.G.M. Medical College and Maharaja Yashwant Rao Hospital, Indore. In all the following patients, on palpation, there was absent Dorsalis Pedal artry pulsation.

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Objective

The objective of the study is to present a series of cases with peripheral vessel thrombosis related to COVID-19. Unpredictable clinical presentation is emerging as a hallmark of severe acute respiratory syndrome coronavirus 2 (SARS-COV-2).

MATERIALS AND METHODS

Study was conducted in M.G.M. Medical College and M.Y Hospital, Indore, we, hereby, describing eight patients of the month of June 2021. All eight patients which we had studied were having a history of COVID and positive COVID antibodies. For the routine imaging, we have done Colour Doppler and computed tomography (CT) angiography for the detection of level

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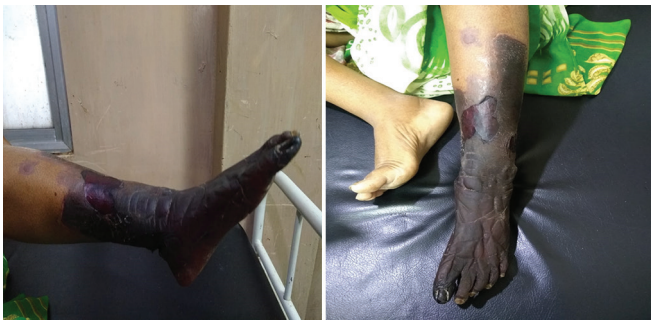
of occlusion/cougulopathy. Hence, the only option left was amputation.

CASE REPORT 1

A 65-year-old female, presented with a complaint of left lower limb gangrene for 2 months which was painful, started in the foot and rapidly progressive in nature, and up to mid-calf line of demarcation was present. Colour Doppler was suggestive of proximal poplial artry thrombosis. Finally, above-knee amputation was done.



CASE REPORT 2

A 60-year-old male, presented with complaint of the right lower limb gangrene, with impairment of right foot function, painful for 15 days. Line of demarcation was present at the level of just proximal to the right knee. Colour Doppler was suggestive of Right Superficial Femoral Artery (SFA) complete thrombus with no distal flow seen. At the end, the patient was managed with above-knee amputation.

CASE REPORT 3

A 80-year male, presented with right great toe gangrene for 6–7 days. Colour Doppler was s/o right Distal SFA Occlusion.

CASE REPORT 4

A 55-year male, presented with left great toe gangrene for 2 months. Color Doppler was s/o. left Distal SFA thrombosis.

CASE REPORT 5

A 65-year-male, presented with a chief complaint of pain in the abdomen for 1 month, patient was passing motion and flatus. From the last 5 days patient, I s passing black tarry stool. Contrast-Enhanced CT (CECT) (w+p) was suggestive of thrombus completely occluding aorta and bilateral common iliac vessels distal to the origin of renal arteries.

CASE REPORT 6

Channu More 5o year male presented with complaint of difficulty in walking with a tingling sensation in the right leg for 6 months. CT angiogram was suggestive of complete proximal SMA thrombus and with good distal collaterals. 60–70% Right common iliac thrombus artery occlusion. Right SFA complete thrombus occlusion.

CASE REPORT 7

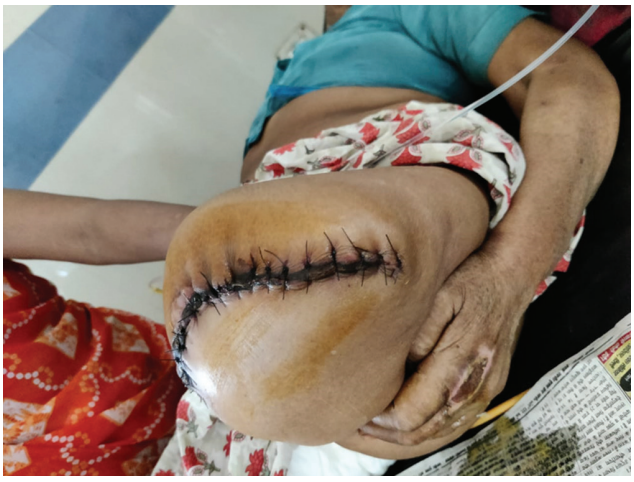
A 90-year–old female patient presented with a complaint of blackening of the left great toe for 45 days, associated with pain.

CASE REPORT 8

A 82-year-old male presented with blaceking of the right lower limb for 1 month and pain for 15 days. Color Doppler s/o thrombus occluding common femoral artery, SFA, deep femoral artery,and right popliteal artery.

CT Images (w/a+p): Thrombus completely occluding aorta and bilateral common iliac vessels distal to the origin of renal arteries.

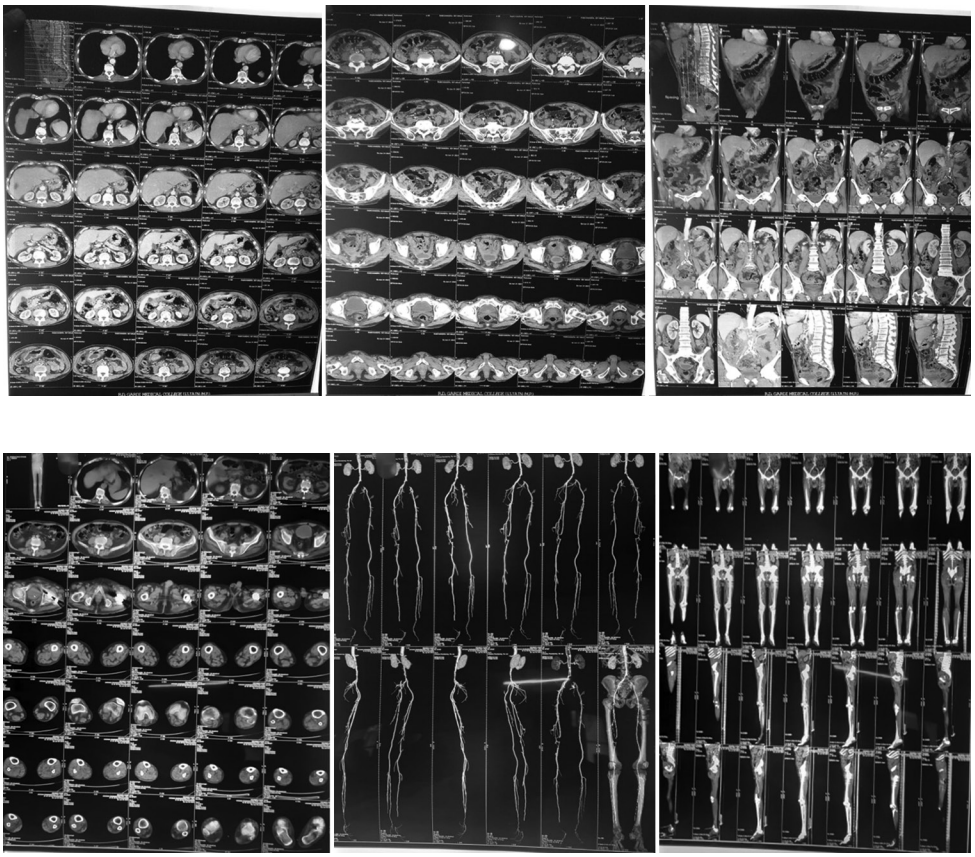
CT Angio S/O Left distal SFA artery thrombus.



Post-Operative Picture

DISCUSSION

COVID pandemic created havoc in the world. From underdeveloped to well-developed countries, each and



every country was severely effect and their were piles of dead bodies. Nobel Coronavirus affected >7 million people worldwide and claimed >400,000 lives as of June 2020.[1,2]

When COVID was started, everyone was thinking that it is mainly a medical disease and there will be no surgical role. However, after few months when the patient recovered from the COVID, they started having painful gangrenous limbs.

Coagulopathy, in the form of arterial and venous thromboembolism, is emerging as one of the most severe sequela of the disease, and has a poorer outcomes.[3-6] Reports of high incidences of thrombosis even after giving prophylactic and therapeutic doses of anticoagulation raise question about a pathophysiology unique to COVID-19.[7,8] Proposed hypotheses include a severe inflammatory response that leads to thrombo-inflammation, through mechanisms such as cytokine storm, complement activation, and endotheliitis.[4,5,9,10] It has also been suggested that the virus itself can activate the coagulation cascade.[11]

Pathophysiology of COVID-19 Coagulopathy: Inflammatory Thrombosis. The relationship between thrombosis and inflammation is well established.[12]

COVID-19 causes a profoundly pro-inflammatory state, as evident from multiple reports of high C-reactive protein, interleukin-6 (IL-6), ferritin, lactate dehydrogenase, and D-dimer levels.[13] fibrinogen and IL-6 levels are shown to relate with each other in COVID patients, providing the idea of inflammatory thrombosis.[14]

Localized Intravascular Coagulopathy

As per studies (Tang *et al.* and CICERI), initial viral damage occurring in the alveoli generates inflammation and local microvascular thrombosis. This is followed by more generalized endothelial dysfunction and thrombo-inflammation in the microvasculature of the kidneys, brain kidneys and other organs leading to a hypercoagulable state and multiple organ failure and finally death.[15-17]

Inflammatory Cytokines

The cytokine profiles in patients with severe COVID-19 show increased production of IL-6, IL-7, TNF alpha, and inflammatory chemokines such as CCL2, CCL3, and soluble IL-2 receptor. Excessive cytokine release contributes to thrombosis through multiple mechanisms, including activation of monocytes, neutrophils, and the endothelium, all of which generate a prothrombotic state and finally thrombus in a vessel causing obstruction.[18-20]

Endothelial Activation and Dysfunction

Endothelial activation or dysfunction with COVID-19 may occur through multiple mechanisms. This includes

inflammatory cytokines generated in the pulmonary interstitium, the activation of the complement components in blood, or possibly, as a direct result of SARS-CoV-2 infection of endothelial cells through the ACE2 receptor.[21] Endotheliitis later causes thrombosis.

Mononuclear Phagocytes

Activated monocytes rapidly upregulate tissue factor expression. This triggers the coagulation cascade resulting in the production of thrombin which, in turn, leads to thrombus generation, platelet activation, and amplification of pro-inflammatory pathways, primarily through PAR signaling.[22]

Complement-mediated Microangiopathy

Researchers in China observed complement hyper-activation in COVID-19 patients, as well as significantly increased plasma C5a levels in severe cases. Dysregulated complement system activation may be a major contributor to cytokine storm, particularly through the pro-inflammatory effects of anaphylatoxins C3a and C5a.[23]

Management

The first general rule in the management of coagulopathy is the treatment of the underlying cause. However, with COVID-19, treatments of the viral infection remain experimental at the current time. As such, until an effective treatment option is available, it is crucial to be able to appropriately manage the sequela of COVID-19-associated coagulopathy.

Monitoring of Laboratory Parameters

As a result of the crosstalk between inflammatory and thrombotic pathways, infections are almost always associated with a concomitant activation of the coagulation system, evidenced by elevation in the markers of an activated coagulation system. The D-dimer has been shown to be frequently elevated in patients with COVID-19. Increased fibrinogen, fibrin degradation products, prothrombin time, activated partial thromboplastin time, and shortened thrombin time have been described in patients with COVID-19 compared to healthy controls.

Anticoagulation

Use of prophylactic or therapeutic dose anticoagulants

As our understanding of the coagulopathy associated with COVID-19 evolves, the best approach to management continues to be explored. Given the paucity of data in the pathophysiology of this disorder, physicians globally are compelled to prepare guidelines for the management of this hypercoagulable state based on the established understanding of crosstalk between inflammation and thrombosis. Thus, clinicians are using prophylactic, intermediate, or therapeutic doses of anticoagulation, based on coagulation parameters and the clinical scenario. Although the optimal dosing remains unclear the benefit of anticoagulation with heparin products (mostly low-molecular-weight heparin [LMWH] at prophylactic doses) in COVID-19 patients was demonstrated by a study in China.[24]

Drug Interactions with anticoagulants and antiplatelets

The effect of direct oral anticoagulants appears to be potentiated by atazanavir, lopinavir/ritonavir, hydroxychloroquine and decreased by tocilizumab. Furthermore, apixaban may confer increased risk for QT prolongation when used with hydroxychloroquine. Atazanavir and lopinavir/ritonavir may decrease the active metabolite of clopidogrel and prasugrel. Among atazanavir, lopinavir/ritonavir, remdesivir, hydroxychloroquine, tocilizumab, and interferon beta, there has not been shown to be interactions with heparin products, fondaparinux, or argatroban.[25]

Duration of anticoagulation

The International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) venous thromboembolic event (VTE) risk score has been used as a tool to identify patients who would benefit from extended-use prophylaxis with LMWH.[26] Protocols suggest that patients hospitalized with COVID-19, especially those with an IMPROVE VTE score of >3, an elevated D-dimer level (>2× upper limit of normal), and 2 or more of the following characteristics: age >60, previous VTE, known thrombophilia, current cancer, should be strongly considered for extended thromboprophylaxis up to 39–45 days post-discharge either with prophylactic dose LMWH or rivaroxaban.[26-28] For patients who have been empirically started on therapeutic anticoagulation for suspected PE, the ASH panel recommends that they should remain anticoagulated for at least 3 months, regardless of results of future investigation studies. Furthermore, cases of confirmed VTE should be considered as "provoked" and treated for 3–6 months duration.[29]

Antifibrinolytics

The use of anti-fibrinolytics is not yet a strong recommendation due to major complications of bleeding. An alternative, safer approach that may confer benefit in COVID-19 induced acute respiratory distress syndrome (ARDS) is the use of nebulized fibrinolytics. In 2019, a study on 60 patients with ARDS showed that use of nebulized streptokinase in patients with severe ARDS resulted in improvements in oxygenation and lung mechanics more rapidly than nebulized heparin.[30] Another agent with fibrinolytic properties that has been considered is Nafamostat. Nafamostat is a synthetic serine protease inhibitor that has been used in Japan for the treatment of DIC in pancreatitis for decades. Nafamostat possesses both anti-fibrinolytic activities as well as anti-viral activity and has

thus generated interested in being repurposed as a potential therapeutic agent for COVID-19 in ongoing studies.[31]

Hence with the proper use of anticoagulant, we can prevent the gangrene of a limb and hence the amputation.

CONCLUSION

COVID-19 is a major risk factor of peripheral thromboembotic state that may endanger patient's life and may lead to amputation Despite therapeutic anticongoagulants, still all COVID-19 patients are at risk for thromboembolic phenomenon, high index of suspicion should be created and with minimal symptoms surgical consultation should be obtained as soon as possible.

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Review Article

Molecular Imaging of the Skeleton using Skeletal Scintigraphy from an Anatomist's Perspective

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Abstract

Imaging of the skeleton includes anatomical imaging modalities using radiographs, computed tomography (CT) scan or magnetic resonance (MR) imaging as well as functional imaging modalities like radionuclide imaging also known as molecular imaging. In the past few decades the concept of hybrid imaging using fusion of the two techniques such as single-photon emission CT/CT (using Gamma Camera) or positron emission tomography/CT (PET/CT) and recently PET/ MR. Understanding the concepts of imaging is of importance to the clinician as well as the anatomist for better utilization of the existing modalities as well as for development of better modalities for better patient management. We introduce the concept of molecular imaging of the skeleton with focus on skeletal scintigraphy known as the "bone scan" for the interest of the anatomist.

Key words: Anatomist, Bone scan, Molecular imaging, Single-photon emission computed tomography/computed tomography, Skeleton

INTRODUCTION TO THE SKELETON

Around 206–210 bones are present in adult human skeleton. At the time of birth, the young one is composed of 270 bones, but later it decreases to 70–80 bones. There are about 126 bones in axial skeleton and there are almost 20 major bones in appendicular skeleton.[1]

Bone tissue: Bone consists of collagen and non-collagenous tissue.[2] The rigid part of the bones helps to make the skeleton. The types of bone tissue are cortical bone tissue, cancellous bone tissue, and other types of bone tissue include bone marrow, endosteum, periosteum, nerves, blood vessels, and cartilage.[2]

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Bone cells are classified into four types:[Table 1][3]
Structure of bone: Bone consists of different parts: Diaphysis, epiphysis, metaphysis, articular cartilage, periosteum, medullary cavity, and endosteum. The central part of any long bone is diaphysis and the proximal and distal part of the bone is epiphysis and the region between diaphysis and epiphysis is metaphysis. Articular cartilage covers the epiphysis part where bone makes an articulation with other bone. Periosteum covers the outer surface of bone which is not covered by articular cartilage. It helps in growth of bone in thickness but not in length. Medullary cavity is an empty space within the diaphysis which contains yellow bone marrow. The spongy part of bone of epiphysis and metaphysis contains red marrow (having red blood cells). Endosteum lines the internal bone surface.[4-6]

Bone comprises about 80% compact bone and 20% spongy bone. Compact bone is the strongest part of bone. It is also known as cortical or dense bone. It does not have any hollow space. It contains blood vessels, lymphatic vessels and nerves. Spongy bone is also known as cancellous bone which contains red bone marrow (having red blood cells).[1]

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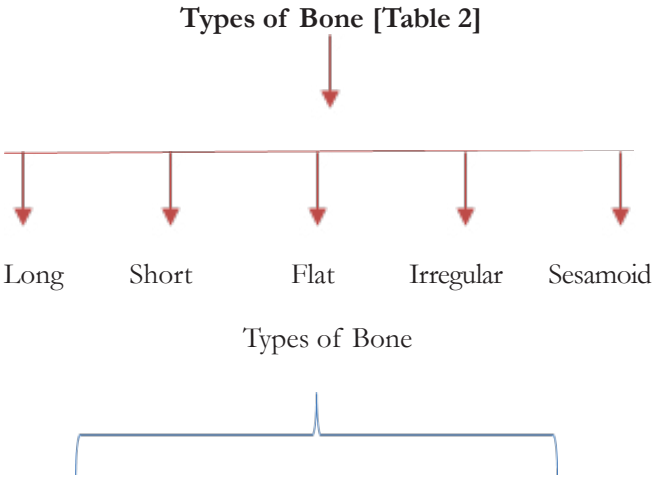
BONE IS CLASSIFIED INTO DIFFERENT TYPES



Axial skeleton	
Cranial bones	• Parietal (2) • Temporal (2) • Frontal (1) • Occipital (1) • Ethmoid (1) • Sphenoid (1)
Facial bones	• Maxilla (2) • Zygomatic (2) • Mandible (1) • Nasal (2) • Platine (2) • Inferior nasal concha (2) • Lacrimal (2) • Vomer (1)
Auditory Ossicles*	• Malleus (2) • Incus (2) • Stapes (2)
Hyoid	
Vertebral column	• Cervical vertebrae (7) • Thoracic vertebrae (12) • Lumbar vertebrae (5) • Sacrum (1) • Coccyx (1)
Thoracic cage	• Sternum (1) • Ribs (24)
Appendicular	
Pectoral girdles	• Clavicle (2) • Scapula (2)
Upper extremity	• Humerus (2) • Radius (2) • Ulna (2) • Carpals (16) • Metacarpals (10) • Phalanges (28)
Pelvic girdle	• Sacrum • Hip bones (2)
Lower extremity	• Femur (2) • Tibia (2) • Fibula (2) • Patella (2) • Tarsals (14) • Metatarsals (10) • Phalanges (28)

HISTOLOGY

<u>Tissue Preparation for Transmission Electron Microscopy</u>

Animal is sacrificed & bone sample is taken out

↓

Place sample in formalin (primary fixative)

↓

Place sample in Osmium Tetroxide (Secondary fixative)

↓

Place sample in different concentration of ethanol (30% → 50% → 70% → 90% → 100%) for 1hr each

↓

Place 1:1 mixture of alcohol with propylene oxide

↓

Place sample in propylene oxide

↓

Place sample in 1:1 mixture of propylene oxide with resin

↓

Place sample in pure resin (for Plasticization process)

↓

Slice sample with ultramicrotome & collect the tissue sections

↓

Place tissue in Grid (meshwork of copper wires)

↓

Bombardment of electrons on the tissue to get image on the screen

<u>Tissue Preparation for Scanning Electron Microscopy</u>

Animal is sacrificed & bone was taken out

↓

Place sample in formalin (primary fixative)

↓

Place sample in Osmium Tetroxide (Secondary fixative)

↓

Place sample in different concentration of ethanol (30% → 50% → 70% → 90% → 100%) for 1hr each

↓

Physical drying is achieved by critical point drying (Remove solvent from the sample with no latent heat of vaporization)

↓

Acetone is replaced from the tissue with liquefied carbon dioxide in critical point drying unit (By critical point drying technique)

↓

Tissue is fractured by freeze fracture technique (For internal structure visualization)

↓

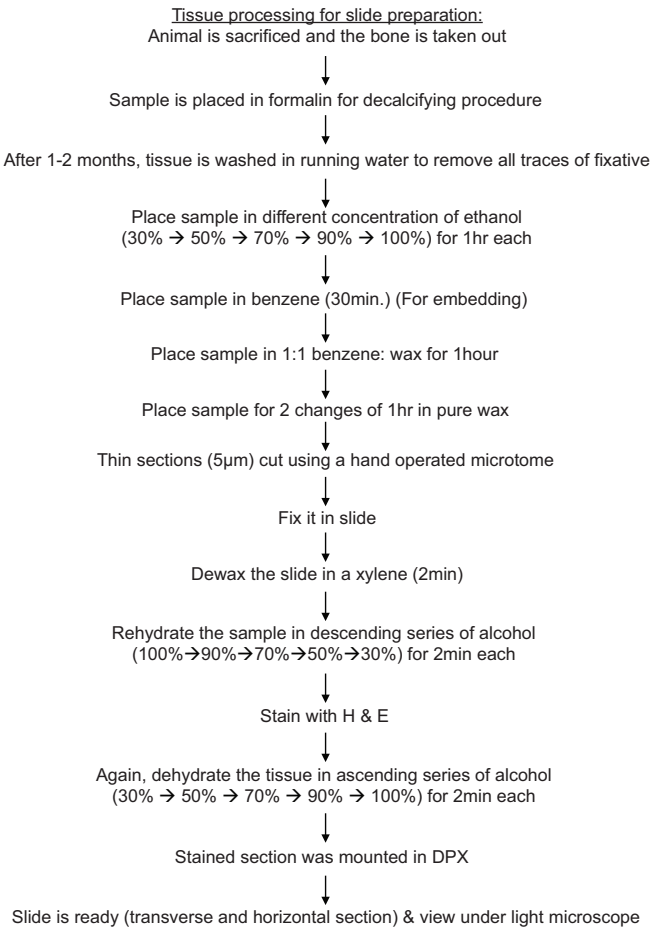
Tissue is coated with a thick layer of metal such as gold, platinum and palladium in <u>Sputter coating machine</u>

↓

Electrons are bombarded on the metal coated tissue which produces lines on the screen

↓

Scan the tissue for getting scanning image of the tissue



Bone is studied histologically by transverse and horizontal section of bone tissue. In transverse section, the central canal, concentric lamellae, osteon in Figure 1.

Skeletal scintigraphy is one of the most sensitive studies for imaging of the skeletal disorders. It finds application in detection of bone disease like metastasis which may be located anywhere in the body and whether the patient has symptoms or not. It is cost effective and easily available at reasonable cost; however, one of the major limitations is low specificity. This may lead to false positive studies and clinical as well as radiological correlation is required. An abnormal or positive bone scintigraphy shows an ongoing osteoblastic process which may represent bone disease. It is most useful in evaluation of skeleton for metastasis especially in tumors such as prostate, breast, and lung carcinoma which have common metastasis to the bones. It is useful in assessment of bone involvement in other conditions such as renal cell carcinoma, primary tumors such as multiple myeloma and leukemia, metabolic bone disease - hyperparathyroidism, Osteoporosis, and Paget's disease and benign bone tumors such as osteoid osteoma. In addition, three phase bone scan differentiates Soft Tissue infection/inflammation from skeletal lesions, painful joint prosthesis, skeletal trauma - fracture detection, complex regional pain syndrome, stress fracture, and bone grafting. It also shows uptake in bone scan in evaluation of cases suspected in battered baby syndrome or child abuse - detects recent fractures which is not detected in radiography (3–5 days) and detect old fractures in patients with burns and other findings suggesting child abuse.

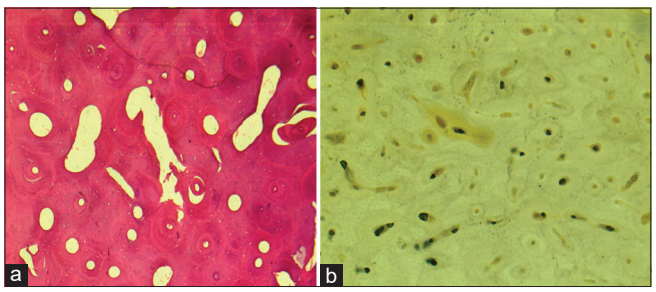


Figure 1: Transverse bone tissue section at ×5: (a) with H and E stain (b) Unstained section 99mTc MDP whole body bone scan

The uptake mechanism of bone seeking radiopharmaceuticals like 99mTc Methylene diphosphonate (MDP), 99mTc HMDP and 99mTc HEDP occur by chemo-adsorption on hydroxyapatite crystals. The radiotracers readily distribute into the extracellular fluid and after that, it resides into the bone. Its accumulation depends upon the osteogenic activity of cells and amount of blood flow.[7] The tracer used in positron emission tomography (PET) for bone imaging-Na18F in which there is an exchange mechanism of the 18F ions with hydroxyl ions (OH^-) on the surface of the hydroxyapatite to form fluoroapatite. This is cleared fast from the blood which leads to high bone to background ratio.[8]

Different technologies such as single-photon emission computed tomography (SPECT) and PET are available for bone imaging. In SPECT, 99mTc diphosphonate such as 99mTc HEDP, 99mTc HDP, and 99mTc MDP are commonly used. Radiopharmaceuticals - 47Ca, 85Sr, and 87mSr were used earlier but due to their drawbacks, these are not used nowadays. In case of lymphoma, 67Ga is used in detecting bony lesions in addition to soft-tissue masses. It is also used in assessing the response to therapy. 99mTc-Sulphur colloid is used for evaluating bone marrow metastases.[1] In PET, Na18F is used in benign bone disorders - Paget's disease which is superior for the assessment of bone formation. In combination with dynamic PET acquisition, ^{18}F-NaF allows for quantitative kinetic modeling of bone blood flow and metabolism.[9,10] ^{18}F-FDG PET is used for imaging of osteomyelitis which has excellent sensitivity and specificity for bone infection, with higher accuracy than ^{99m}Tc-hexamethylpropyleneamine oxime or ^{111}in-labeled white blood cell scintigraphy [Table 3].[11]

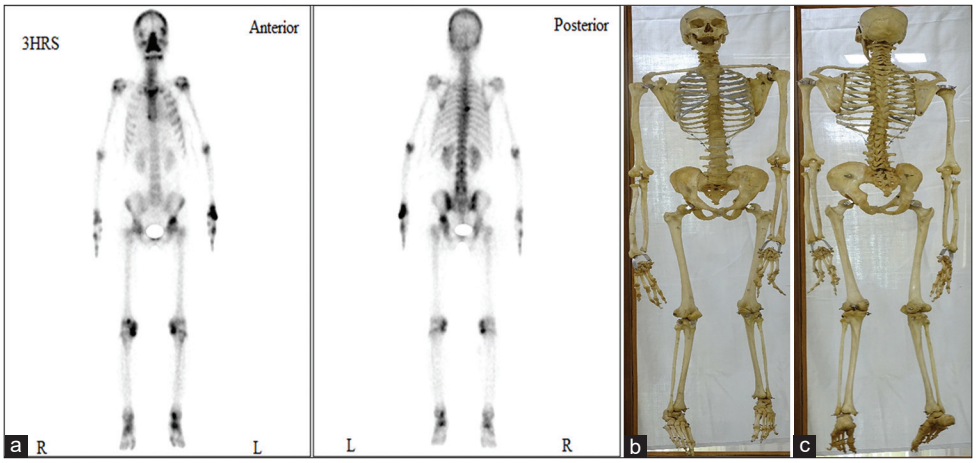


Figure 2: (a) Anterior and posterior whole body bone scan views with (b and c) corresponding anatomical skeleton images

Comparison of skeletal views with bone scan (gamma camera images)

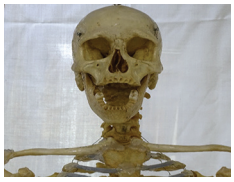
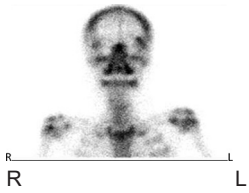
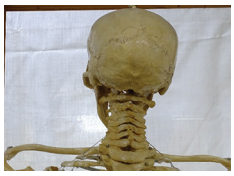
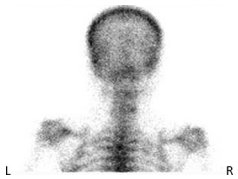
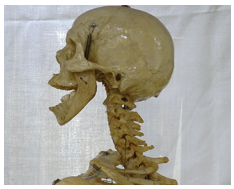
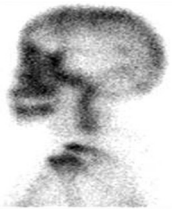
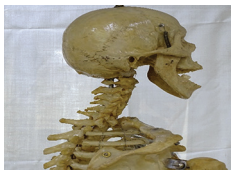
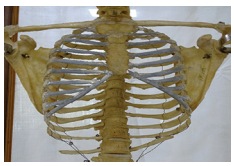
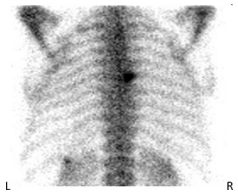
S. No	Region	Anatomical image (a)	Gamma camera images (b)
1	Skull Anterior		 R L
	Skull Posterior		 L R
	Skull Left Lateral		
	Skull Right lateral		
2	Thorax Anterior		 R L

Figure 3: Understanding various standard views of a bone scan (1a-g): Compared with corresponding images of anatomical skeleton 1

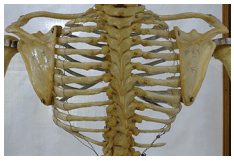
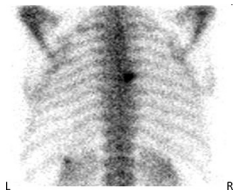
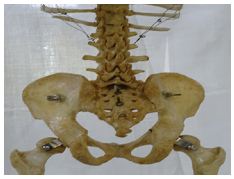
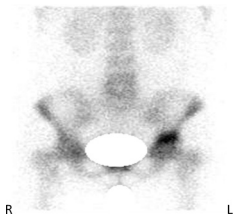
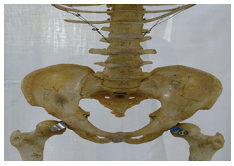
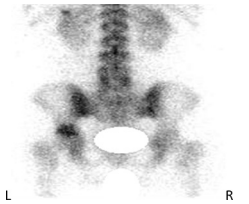
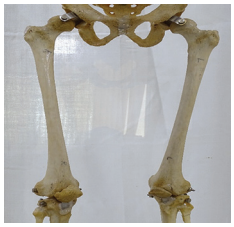
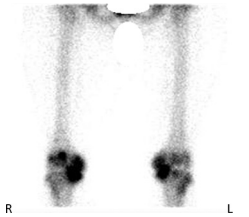
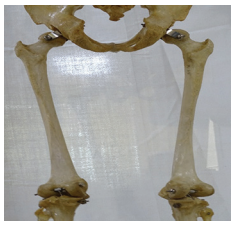
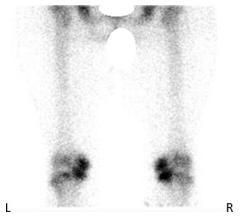
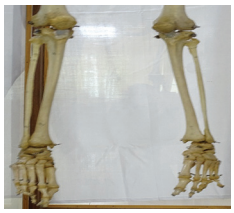
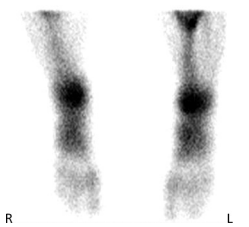
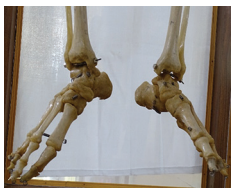
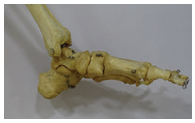
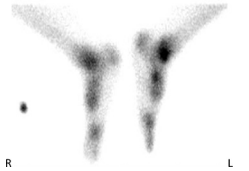
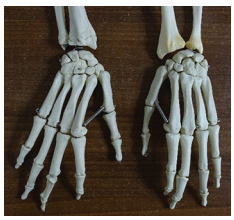
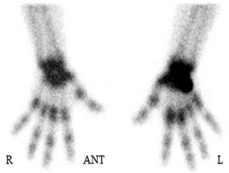
	Thorax Posterior		 L R
3	Lumber-pelvis Anterior		 R L
	Lumber-pelvis Posterior		 L R
4	Thighs Anterior		 R L
	Thigh Posterior		 L R
5	Feet Anterior		 R L
	Feet Lateral	 	 R L

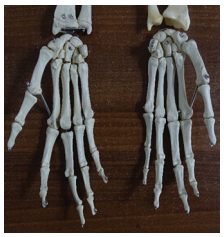
Figure 3 : ***(Continued)***

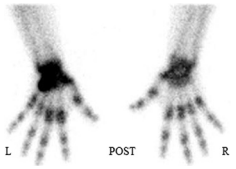
6 Hands





Anterior





Posterior

Figure 3: ***(Continued)***

Table 1: Type of cells in bone

Bone cells	Function
Osteoblasts	New bone or bone-forming cell
Osteocytes	Maintain bone metabolism
Osteoclasts	Repair and remodeling of bones
Osteogenic cells	Stem cell

Table 2: Classification

Long bones	Short bones	Flat bones	Irregular bones	Sesamoid bones
Lower limbs • Femora • Tibiae • Fibula	Foot • Tarsals	Skull • Occipital • Parietal • Frontal	Vertebra	Patella
Upper limbs • Humerus • Radius • Ulna	Hands • Carpals	Nasal	Sacrum	Pisiform (smallest of the carpals)
Hands • Metacarpals		Lacrimal	Mandible	2 small bones at the base of the 1st metatarsal
Feet • Metatarsals		Vomer		
Fingers and toes • Phalanges		Scapula		
Clavicles		Ilium (hip bone) Sternum Ribs		

PROCEDURE OF BONE SCINTIGRAPHY WITH 99MTC MDP

Radiopharmaceutical: 99mTc MDP is used for whole body bone imaging.

Dosage

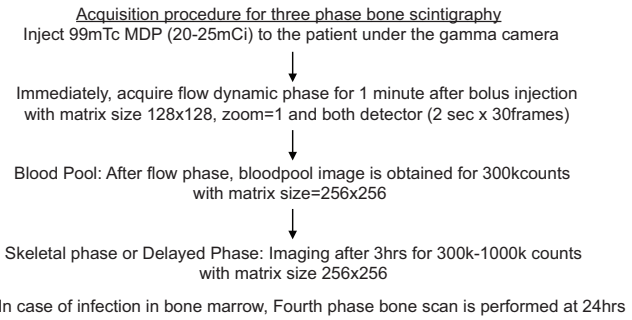
The usual administered activity for adult patients is 740–1.110 MBq (20–30 mCi) injected intravenously. For pediatric patients, the administered activity is 9–11 MBq/ kg (250–300 μCi/kg), with a minimum of 20–40 MBq (0.5–1.0 mCi).

Acquisition

Delayed images are usually obtained from 2 to 4 h after injection. Whole-body bone scintigraphy is accomplished with multiple overlapping images (i.e., spot images) [Figure 3] or with continuous images (i.e., whole-body scan) [Figure 2] obtained in anterior and posterior views with a

Table 3: Overall impact of molecular imaging for bone: Bone scan

Major advantages	Limitations
Non-invasive imaging, cost effective technique	• Radiation exposure – however radiation exposure is lesser than that received for a diagnostic contrast-enhanced computed tomography scan
Highly sensitive	• Time consuming - one bone scan may take 20–30 min compared to few seconds for computed tomography scan
Whole body Imaging vis –a- vis regional for most anatomical imaging modalities	• Does not provide soft tissue details like magnetic resonance imaging – may be partly overcome with positron emission tomography /magnetic resonance imaging
Hybrid Imaging – single-photon emission computed tomography/computed tomography, positron emission tomography/ computed tomography - One stop shop for anatomical and functional information	–
Non-claustrophobic unlike magnetic resonance imaging	–
Most useful in conditions: Metastasis, stress fractures, osteomyelitis, and avascular necrosis	• Limited use in conditions: Diagnosis of primary bone tumors (may help in assessment of extent of involvement), osteolytic lesions like those of multiple myeloma



high-resolution low energy collimator dual head gamma camera. Whole-body views are obtained in a 256 × 1024 matrix. In case of pediatric patients, spot views are taken as the primary method of acquiring bone images, the areas of bony skeleton covered by the spot views are made to over-lap to avoid missing regions of the skeleton. Spot views are acquired for approximately 500,000–1 million counts using 256 × 256 matrix. In addition, SPECT/CT is acquired for more clarification [Figure 3].[1]

CONCLUSION

Molecular imaging with radioisotopes has its use in management of various diseases. For skeletal imaging, the most commonly use modality is the bone scan. It is imperative to understand the anatomy of the skeleton to correctly understand the images of bone scan and it may also be of interest for an anatomist to be introduced to the various basics of this technique. This is important for application of the techniques to their fullest as well as for future development of newer techniques for better clinical outcomes.

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Original Article

Febrile Seizure: A Study among Children Admitted in Pediatric Ward

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Abstract

Background: Febrile Seizure is one of the most common pediatric emergencies seizure disorders that occur in children aged 6–60 months. The objective of the study was to assess the demographic features and etiological factors for a febrile seizure.

Materials and Methods: This was a hospital-based descriptive cross-sectional study conducted in the Department of Pediatrics, JNIMS, Imphal among children presenting with febrile seizure admitted in pediatric ward from January 2019 to December 2019. The scientifically calculated sample size of 160 was included as study subjects. Children between 6 months and 5 years were included in the study. Children not meeting the age criteria were excluded from the study. The demographic and clinical data were collected from inpatient records and analyzed.

Results: A total of 160 children which constituted 6.1% of total pediatric admissions were included in the study. Mean age of children was 21.46 ± 12.98 months. Maximum cases 65 (40.6%) were in the age group 12–24 months. About 117 (73.1%) were male and 43 (26.87%) were female. Majority 28 (17.5%) of cases occur in the monsoon season (June). Simple febrile seizure and complex febrile were seen in 119 (74.4%) and 41 (25.6%), respectively. Children who developed first episode of febrile seizure (100%) were below 24 months of age. Generalized tonic-clonic seizures were the most common presentation. About 53 (33.1%) of affected children had positive family history of febrile seizure. Most common precipitating factors were upper respiratory infection 138 (86.3%), gastroenteritis 22 (13.8%). First episode of complex febrile seizure after 12 months (P = 0.000), higher prevalence of complex febrile seizure duration >15 min (P = 0.000) and complex febrile seizure had longer hospital stay (P = 0.000).

Conclusions: Febrile seizure is a common pediatric problem in male child observed predominantly in children below the age of 2 years. Simple febrile seizure was the commonest presentation. Most of the children had a positive family history and the most common causative factors were upper respiratory infection, gastroenteritis. Risk of febrile seizure decreased with age.

Keywords: Complex febrile seizure, Febrile seizure, Simple febrile seizure

INTRODUCTION

Febrile seizures are that occur between the age of 6 and 60 months with a temperature of 38°C (100.40°F) or higher, that are not the result of central nervous system infection or any metabolic imbalance and that occur in the absence of a history of prior afebrile seizures, occurring in 2–5% of children. Most commonly affected age is between 12 and 18 months.[1] Febrile seizures are classified as simple and complex types. Approximately 60–90% of febrile seizures are simple type.[2] Simple febrile seizures are generalized seizures, lasting <15 min, not recurring within 24 h or associated with postictal neurological abnormalities. Complex febrile seizures are focal, prolonged, or recurrent within 24 h or associated with postictal neurological abnormalities including Todd paresis.[3] Febrile convulsions appear to occur in families and both parents may transmit this genetic susceptibility. Family history of febrile convulsions and reported frequency ranges from 9% to 22% in their siblings.[4] Viral infection (80%) is the most common cause of fever in febrile seizures.[5] Viral upper respiratory tract infection, pharyngitis, otitis media, and gastroenteritis are other important causes of fever in febrile seizures.[6,7] Western European and US epidemiological reports indicate that

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febrile convulsions are associated with upper respiratory infections and other infectious diseases.[8] Seasonal variation with regard to seizure incidence has not yet been fully understood. Studies have shown that febrile seizure tends to occur more in the winter months and common in the evening.[9] Hence, the objective of the study was to assess the demographic features and etiological factors for febrile seizure among the children admitted in the ward.

MATERIALS AND METHODS

This was a hospital-based descriptive cross-sectional study conducted at the Department of Pediatrics, JNIMS, Imphal from January 2019 to December 2019 among children admitted with febrile seizures from records of children during the study period.

Inclusion Criteria

Based on the standard definition of febrile seizure records of all children with the diagnosis of febrile seizure were included.

Exclusion Criteria

Children with previous episodes of afebrile seizures, neurodevelopmental disorders, age below 6 months and above 5 years were excluded from the study.

Sample Size

A sample size of 160 was calculated at 95% confidence interval at 5.8% acceptable margin of error by epi info software version 7.2. All children between 6 months and 5 years of age who were diagnosed as febrile seizure were included in the present study. Children's demographic, clinical data regarding type of seizures, duration, number of episodes of seizures, family history of febrile seizures, causes of fever, and duration of hospital stay were obtained from hospital medical records.

Statistical Analysis

All the data were recorded on Microsoft excel spreadsheet and data analysis was done at 5% alpha and 95% confidence interval using SPSS v22 software. Descriptive statistics such as Mean, SD, Percentage were used and analytical analysis was done using Chi-square test. $P < 0.05$ was considered as statistically significant.

RESULTS

A total of 160 children which constituted 6.4% of pediatric admission with febrile seizure who fulfilled the selection criteria were included in our study. Among the study groups, the youngest child was 6 months and the oldest 60 months of age. The mean age of children was 21.46 ± 12.98. The age ranged from 6 months to 60 months. Our study revealed that out of 160 children in the study group, febrile seizures were most common in the age group 12–24 months 40.6% (65) followed by 32.5% (52) between 6 and 12 months of age group. Study of result showed 117 (73.1%) were male and 43 (26.9%) were female. Most of the children in the study group were males. 53 (33.1%) children had positive history of febrile seizure in the family, out of which three had a family history of febrile seizure in both the parent and 5 had a history of febrile seizure in older siblings [Table 1].

According to seizure characteristics, the most common presentation was simple febrile seizure 119 (74.4%) and complex febrile seizure in 41 (25.6%) cases. Seizures were more common in males as compared to females with male-to-female ratio of 2.7:1. Generalized tonic-clonic seizure was the most frequent type of seizure presentation [Table 2].

Month wise seasonal variations in the incidence of febrile seizure were observed with the maximum number of cases in the month of June 28 (17.5%) and the lowest in February 4 (2.5%) [Figure 1].

Majority of children 103(64.5%) had single episode of seizure and 57 (35.6%) had >2 episodes of febrile seizure. The first episode of febrile seizure was more common in children >12 months of age group 97 (60.6%) followed by 63 (39.4%) in children <12 months. Most

Table 1: Age, Sex, and Family history distribution data of patients presenting with seizures

Demographic history	No of cases	Percentages
Age		
6–12 months	52	32.5
12–24 months	65	40.6
24–60 months	43	26.9
Total	160	100
Sex		
Male	117	73.1
Female	43	26.9
Total	160	100
Family history		
Present	53	33.1
No	107	66.9
Total	160	100

Table 2: Distribution of seizure type of patients presenting with seizures

Type of seizure	No of cases	Percentages
Simple	119	74.4
Complex	41	25.6
Total	160	100

common precipitating factor for febrile seizures was upper respiratory tract infection in 138 (86.3%) children followed by gastroenteritis 22 (13.8%). In 138 (86.3%) children the duration of seizure was <than 15 min followed by 28 (13.8%) children with seizure >15 min. The length of hospitalization in 124 (77.5%) was 1 to 2 days and 26 (16.3%) children the hospitalization period was 3 to 7 days and in 10 (6.3%) children the period of hospitalization was >7days [Table 3].

Mean (SD) duration of hospitalization was found to be 1.29 ± 0.576 days.

Table 4 showed the prevalence of complex febrile seizure was 71.9% (41 out of 57) in children with first episode of seizure at an age >12 months whereas the prevalence of complex febrile seizure was zero in children with first episode of febrile seizure at an age <12 months ($P = 0.000$). Children who had seizure episodes lasting >15 min complex febrile seizure 100% (22 out of 22) whereas in children with seizure episodes lasting <15 min the prevalence of complex febrile seizure was 13.8% (19 out of 138) with ($P = 0.000$). Table also showed that with the increased in length of hospital stay the prevalence of complex febrile also increased (10.5% in 1–2 days and 90% in >7 days $P = 0.000$). However, no statistically significant results were found in age, sex, family history, and etiology of febrile seizure.

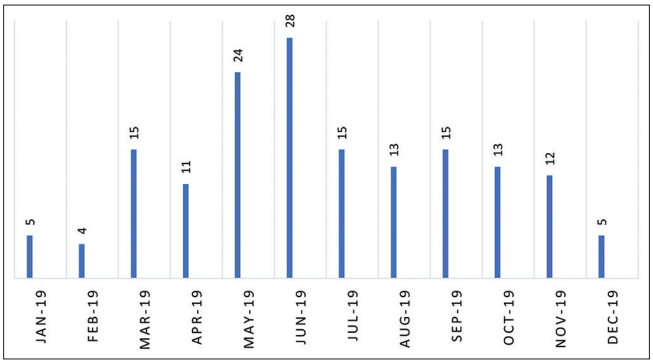

Figure 1: Month-wise prevalence of febrile fever

DISCUSSION

Febrile seizure is one of the most common seizures in childhood.[10] In the present study, febrile seizures represent 6.1% of total pediatric admissions which was comparable to study that showed the proportion in 6.1% of among 325 total admissions.[11] The majority of febrile seizure predominantly occurred in children below 24 months of age and this was in agreement with other studies.[12-14] The febrile seizure is age-dependent this should be considered as critical for developing febrile seizure. The incidence of febrile seizures decreased as age increased. Our study showed children in the age group of 12–24 months are more commonly affected. Peak incidence at 18 months of age had been observed in children between 6 months and 5 years in another study which was comparable to present study.[15] Mean age of children with febrile seizure was 21.46 ± 12.98 months which was comparable to other studies.[16,21] Male-to-female ratio was 2.7:1 in the present study. Another study had shown ratio of 2.9:1 in total 150 study population which was comparable to our study.[30]

Table 3: Distribution of causative factors during seizure among the patients

Causative factors	No of Cases	Percentages
Seizure frequency		
1	103	64.4
>2	57	35.6
Total	160	100
Age at first episode		
<12 months	63	39.4
>12 months	97	60.6
Total	160	100
Etiology of fever		
URTI	138	86.3
AGE	22	13.8
Total	160	100
Duration of seizure		
<15 min	138	86.3
>15 min	22	13.8
Total	160	100
Duration of hospitalization		
1–2 days	124	77.5
3–7 days	26	16.3
>7 days	10	6.3
Total	160	100

Table 4: Distribution of demographic profile and causative factors of patients in febrile seizure according to seizure type

Characters	Age of patients	Seizure type		Total	*P*-value
		Complex%	Simple%		
Age	6–12 months	14 (26.9)	38 (73.1)	52	0.913
	12–24 months	17 (26.2)	48 (73.8)	65	
	24–60 months	10 (23.3)	33 (76.7)	43	
Sex	Male	31 (26.5)	86 (73.5)	117	0.677
	Female	10 (23.3)	33 (76.7)	43	
Family history	Present	16 (30.2)	37 (69.8)	53	0.352
	No	25 (23.4)	82 (76.6)	107	
Age at first seizure	<12 months	0	103 (100)	103	0.000*
	>12 months	41 (71.9)	16 (28.1)	57	
Seizure frequency	1	20 (31.7)	43 (68.3)	63	0.153
	>2	21 (21.6)	76 (78.4)	97	
Etiology of fever	URTI	35 (25.4)	103 (74.6)	138	0.849
	AGE	6 (27.3)	16 (72.7)	22	
Duration of seizure	<15 min	19 (13.8)	119 (86.2)	138	0.000*
	>15 min	22 (100)	0	22	
Duration of hospital stay	1–2 days	13 (10.5)	111 (89.5)	124	0.000*
	3–7 days	19 (73.1)	7 (26.9)	26	
	>7 days	9 (90.0)	1 (10.0)	10	

*$P<0.05$, significant

Sex distribution of the children in our study showed a definite male predominance 73.12% which was comparable to a study that had shown 74% of study population were male.[17] Such male predominance had been shown in other literatures.[23-26] The present study also reemphasized male predominance in febrile seizure. No satisfactory explanation for male sex predominant was found in any published literature.

In the present study majority of cases, 74.4% had simple febrile seizure, and remaining 25.6% had complex febrile seizure. Different studies had observed simple febrile seizure and complex febrile seizure in 76.7%, 23.3%, and 80%, 20%, respectively, which was comparable to our study.[26,27] Most of convulsions occur within 24 h of onset of fever. The present study showed high incidence of seizure in younger children with a decreasing trend in older children which is in agreement with other studies.[20,21] Previous studies have also described generalized seizure as the most common seizure. Our study showed that majority of children had generalized tonic-clonic seizure as the most frequent presenting seizure. In this study, 64.4% of children had single episode of seizure which was comparable to the result of 72.8% of children in a study.[26] Previous studies had also reported single episode of seizure in their studies.[12,16,21,22]

Different studies had shown that causes of fever vary depending on geographical region. The most common causes of fever in our study were upper respiratory tract infection 86.3% and gastroenteritis 13.8%. The study population showed upper respiratory infection as the most frequent cause of febrile convulsion. Upper respiratory infection 74.29% and gastroenteritis (11.68%) were the commonest cause of fever in one study which was comparable to our study.[20] Similar other studies also reported upper respiratory infection as the major infective etiology of febrile seizure.[12,13,18,21,29] The important viral or bacterial infection causes of febrile seizures in various studies in Iran were upper respiratory infection 42.3%, gastroenteritis 21.5%, otitis media infections 15.2%, pneumonia 8.7%, urinary tract infections 3.2%, roseola 2.0%, and other infections 12.8%.[28]

There are two seasonal peaks in FS incidence: November – January, corresponding to the peak of viral upper respiratory infection, and June- August, when common viral gastrointestinal illnesses occur.[24] Variation in prevalence is related to differences in case definitions, ascertainment methods, geography, and cultural factors.[25] In this study population number of febrile seizures was more prevalent in the month of June 17.5%. Other studies conducted in Finland and Iran showed that seizures were more prevalent in winter.[18,19]

Family history of seizures varied from 0.4% to as high as 20.6% of children with febrile seizure as reported in previous studies.[20-22] In the present study 33.1% of children had family history of febrile seizure which was similar to a study that had shown family history in 30% of cases.[31] Complex febrile seizure was more common in children who had first episode of seizure after 12 months of age ($P = 0.000$). Children with seizure duration lasting more than 15 min had higher prevalence of complex febrile seizure ($P = 0.000$). Our study also revealed that complex febrile seizure was more in children who stayed longer at the hospital following seizure episodes ($P = 0.000$). The patients stayed on an average of 3.1 days in the ward with the minimum stay being 1 day and the maximum 18 days.[16] This finding was comparable to the present study with a minimum hospital stay of 1–2 days.

Being a cross-sectional study, we had few limitations while collecting the detailed history of seizure characteristics in few cases as there were missing records and also a small sample group with short duration of study.

CONCLUSIONS

We concluded from the present study that febrile seizure was one of the most common causes of pediatric hospital admissions. The most common type of seizure was simple febrile seizure predominantly affecting male child below 2 years of age. Incidence of febrile seizure decreased with age. Generalized tonic-clonic seizure was the most common presentation of febrile seizure. Majority of first episode of febrile seizure occurred in the age group of 12–24 months. The most common precipitating factors for febrile seizures were upper respiratory infection and gastroenteritis. Despite our limitations, the study provided an insight in identifying the cause of fever and the need for parental education and counseling for the prevention of febrile seizure.

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Original Article

Calculation of Ki-67 Proliferation Index in Lymph Node Excision Biopsy of Non-Hodgkin's Lymphoma: Comparative Analysis of Four Methodologies

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Abstract

Background: Ki67 antigen, identified by Scholzer and Gerdes in 1983. In Non Hodgkin lymphoma, found to be in high concentrations in rapidly multiplying cells. Due to this property the Ki-67 proliferation index is used in numerous malignancies for grading and staging. Its prognostic value is well studied and documented. Many methods can be used to count the Ki67 proliferation index - Eyeballing, Manual counting with microscope, Manual counting in printed image of slide & Automated counting to name a few. In this study we will evaluate all the above mentioned methods of counting Ki67 proliferation index and correlate one another.

Design: 50 ki-67 proliferation index done on lymph node excision biopsy of Non Hodgkin's lymphoma collected & calculated by Eyeballing, Manual counting with microscope, Manual counting in printed image of slide & Automated counting (Qupath - 0.2.3) in the same slide. Eyeballing and Manual counting with microscope is done using Olympus BX43 microscope. Whole slide image (WSI) is captured using Morphle Optimus 6T, printed image is taken and used for manual counting and the WSI of Ki67 is analyzed using QuPath - 0.2.3

Results: Ki67 proliferation index calculated using the above 4 methodologies and analysed using Epi Info™ - 7.2. Pearson correlation coefficient was obtained for each methodologies and correlated with each other.

Conclusion: Our study demonstrated that all the 4 methodologies were correlating with each other statistically. Hence any of the above methods can be used to calculate the Ki67 proliferation index. While in comparison with Manual counting with microscope, Manual counting in printed image of slide correlates more than other methods used in this study..

Key words: Digital pathology, Ki-67, MIB1, Morphle, Non-Hodgkin's lymphoma, Qupath

INTRODUCTION

Ki-67 antigen was discovered by Scholzen and Gerdes in 1983.[1] This antigen expression is a strong indicator of mitotic activity, hence cellular proliferation, during the event of cellular mitosis, in the interface these isoforms are detected in high concentration on the nucleus.[2] Thus used in numerous malignancies for staging and grading including breast, prostate, neuroendocrine, and non-hodgkin's lymphoma (NHL).[3-5] Higher Ki-67 labeling index correlates with bad prognosis in some variants of lymphoma, while other variants particularly diffuse large B-cell lymphoma show no association or the reverse results.[6-10] Many counting methods are used to count the Ki-67 including, eyeballing, manual counting with microscope, manual counting with printed image, and Automated (Qupath).[11] There are discrepancies in the Ki-67 proliferation index counting among the observers and also among the method used to count them. Therefore with this background, we

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compared the four different methodologies for counting Ki-67 in various types of NHL. Thus in this study, we studied the Ki-67 proliferation index using four independent methods and correlated them with each other.

MATERIALS AND METHODS

Ki-67 (MiB-1) immunohistochemistry stained slides (5 micrometer sections of Formalin-Fixed Paraffin-Embedded blocks - MiB-1 clone, Prediluted; Biogenex (Fremont, California, USA). Antigen retrieval was conducted in Tris buffer at pH 8 by heat retrieval method. Diaminobenzidine as the chromogen and Hematoxylin as the counterstain) of 50 cases of NHL were taken from departmental archives. Nuclear brown labeling is taken as positive staining. The Ki-67 index was counted using four methodologies [Figure 1].

"Eye-balling" The most widely used method is estimating the Ki-67 proliferation index. An estimate of the Ki-67 proliferation index is made by scanning the slide in the hotspot without counting the individual positive and negative cells. The scanning of the entire slide is made in Low power (100× magnification). European Neuroendocrine Tumor Society and the North American Neuroendocrine Tumor Society recommend this method in routine reporting.[12,13] "Automated counting" The Ki-67 labeling index of all the slides was counted using Qupath - 0.2.3 (Open source software for digital pathology and whole slide image analysis) [Figure 2]. The slides were scanned using Morphle Optimus 6T (Whole slide scanner) Hotspots were selected and Ki-67 quantification was calculated by the Qupath - 0.2.3.[11] Positive cell detection and percentage calculation are done after stain vector calibration. "Manual counting with microscope" Hotspot area is identified in 100× magnification (Low power) and individual cells are counted for positive and negative at 400x magnification (High power). Hand counter is used for counting the individual cells (Differential counter used to count in peripheral smear). This method was used as the standard method to correlate and evaluate the other methodologies. "Manual counting with printed image" Hot spot was selected in 100× magnification. The static color image of the hot spot was captured via microscope mounted camera (Q imaging, British Columbia) at 400× magnification then it is color printed on photographic paper. Ki-67 - Negative and Positive stained cells were then counted and immediately marked off once counted with circling of the Ki67 - positive and - negative tumor cells. Pale-stained and equivocal nuclei were ignored during counting.

Analysis of the above-mentioned methods will be assessed based on these parameters:

1. The practicality, as well as cost of performing each method, were recorded
2. Pearson's correlation (R) for comparative analysis of the results from individual methods.

RESULTS

The Ki-67 index calculated by different methods were correlated by Pearson's correlation, which revealed that all the methods are statistically correlating with each other and hence can be used for reporting but the manual counting with printed image of the slide was found to have the highest Pearson's correlation index, hence has the highest agreeability factor when compared with manual counting of the slide [Figures 3 and 4].

"Eye-balling" method appears to be the most practical, the speed of this method comes with the price of lack

S. No.	Specimen ID	Eyeballing	Qupath	Microscope	Print
41	H-92/2020	10	12.32	13.67	13.87
42	H-89/2017	40	37.27	42.13	41.29
43	H-86/2020	95	92.12	96.72	95.02
44	H-80/2020	40	35.23	43.3	40.87
45	H-733/2019	70	90.24	86.87	84.24
46	H-700/2019	80	76.25	78.98	75.03
47	H-67/2020	70	79.67	75.9	77.12
48	H-662/2019	50	55.78	53.87	52.34
49	H-640/2019	60	64.68	70.21	67.12
50	H-63/2020	95	98.63	97.19	96.23

Figure 1: Table containing Ki-67 value from 4 different methodologies

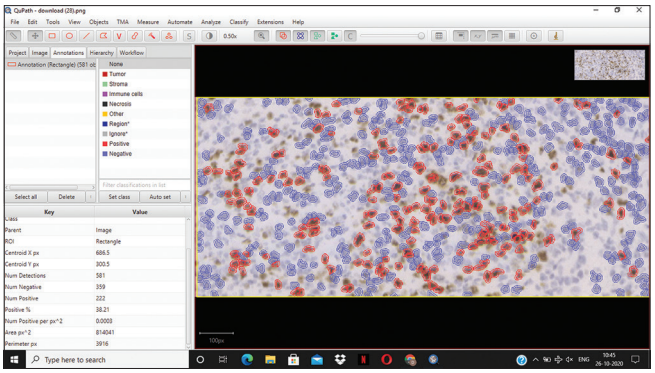

Figure 2: Screenshot of Qupath while performing Ki-67 automated counting

		eyeballing	qupath	microscope	print
eyeballing	Pearson Correlation	1	.950**	.984**	.985**
	Sig. (2-tailed)		.000	.000	.000
	N	50	50	50	50
qupath	Pearson Correlation	.950**	1	.982**	.983**
	Sig. (2-tailed)	.000		.000	.000
	N	50	50	50	50
microscope	Pearson Correlation	.984**	.982**	1	.996**
	Sig. (2-tailed)	.000	.000		.000
	N	50	50	50	50
print	Pearson Correlation	.985**	.983**	.996**	1
	Sig. (2-tailed)	.000	.000	.000	
	N	50	50	50	50

**. Correlation is significant at the 0.01 level (2-tailed).

Figure 3: Table showing Pearson correlation between each different method

of accuracy. Manual counting of printed images is time-consuming and exhausting. It has the upper hand by keeping a permanent record of the labeling index. The manual counting with the light microscope by an expert pathologist is considered as standard but it also is exhausting and time-consuming. Automated method has the undue advantage of repeatability; it is moderate in terms of time consumption factor as the time taken to slide is 40 min. It is non-exhaustive and does not require a pathologist at all times. Although the automated method cannot differentiate the tumor cells from tumor-infiltrating lymphocytes and endothelial cells. Considering the balance of practicality, speed, and accuracy, this study concludes that all four methods are equally effective and correlates with each other. Manual counting of printed images stands above the rest in all the terms plus it has an undue advantage of permanent storage for documentation of counted printed images for future references. In monetary terms, "Eye-balling" and "manual counting" methodologies do not have any additional cost as they were performed by routine microscopic methods. Automated slide scanner costs about US$20,000. However, the digital slide analyzing software was free (Open source). The Printed image method, which was found to be the most desirable, commercially affordable, estimated to be US$6000 for the camera mounted on Olympus microscope. With the arrival of cell phone microscope adapters, this cost will be significantly lower and be restricted only to the purchase of an adapter (which on average costs US$50). Color printers printing images in photographic papers were used (average cost US$10) as an operating cost.

DISCUSSION

The prognostic capabilities of the Ki-67 index in NHL is well documented and studied.[6-10,14] In this study, we focused on the assessment of four of the most widely used Ki-67 index counting methodologies and assessed their practicality and applicability, and the following conclusions were reached. Eye-Balling: College of American Pathologists stated that Ki-67 index estimation is acceptable.[15] In a recent study, showed similar pitfalls in the "eye-balling" method as evidenced by poor interobserver agreement when grading well-differentiated neuroendocrine tumors.[16] The eyeballing method has poor repeatability and interpersonal acceptance. This method depends on stain factors, section thickness, and tumor cell overlapping for better results. The fact that this is the least time-consuming and method with no additional equipment or cost cannot be neglected, but this comes with a hefty price. Manual Counting: The most tiresome and exhaustive method when compared with the rest, not to mention difficult to employ.[17] Even with handheld differential counters it is highly cumbersome and time-consuming to use in routine practice based on workload and other operational factors. We have found that after 2-3 slides of continuous counting it becomes dizzy and puts a lot of strain on the already strained eyes of a pathologist. Manual counting of printed image: This method has an additional cost of US$6000 as an initial investment of microscope mounted camera and color printer. The cost is expected to come down considering the arrival of mobile camera adapters and high-quality mobile cameras. This method also has an undue advantage of keeping a permanent record of the counted photographic sheet for future reference.[18] This method has the highest correlation factor when compared with the so-called standard method of manual counting by an expert pathologist. Automated Counting: This method proved to be an effective alternative to the other routine methods, but it comes with its unique sets of disadvantages, cost factor, time taken to train the laboratory personnels and its false-positive counting (lymphocytes and endothelial cells).[11] This method still requires a pathologist to identify the hotspot for the software to calculate the index. Although the calculation software is an open-source, the need for a whole slide scanner, its operation factors have to be weighed in before opting for this method for routine reporting. The findings of our study were found to be in correlation with various similar studies correlating Ki-67 counting with different methodologies, including manual and automated techniques, where values of manual counting and automated counting methodologies are in agreeable correlation [Figure 5].

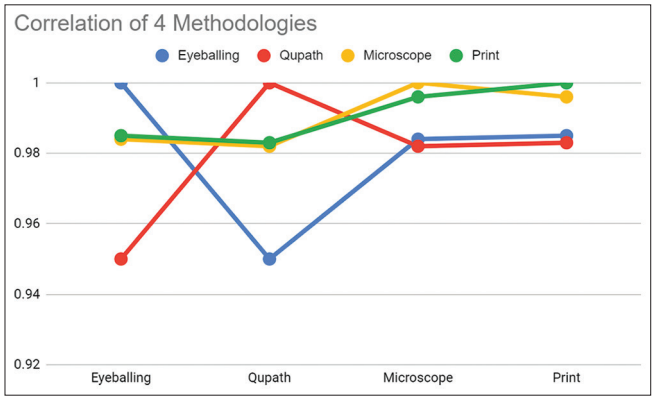

Figure 4: Correlation of Pearson correlation coefficient between four methods

Study	Manual Versus Machine correlation
Reid *et al.*[19]	Pearson's correlation (R = 81.7%)
González-González *et al.*[20]	*P*<0.05
Kinra and Malik[21]	Accuracy and reproducibility (99.9%)
Koopman *et al.*[22]	*P*<0.001

Figure 5: Reference table

CONCLUSION

After analyzing the four different methodologies to calculate the Ki-67 labeling index on the same slide the most practical, accurate, and documentable method is the manual counting of printed images of the slide. Though the manual counting by an expert pathologist is considered as standard it is not employable in routine practice where the caseload and burden placed on pathologists are high. Manual counting of printed images of the slide is not the one without disadvantages, but considering the overall factor, this method is recommended for routine practice with the fact that with the arrival of handheld camera adapters, the time and cost factor will be considerably reduced in the near foreseeable future.

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Original Article

Evaluation of Color Stability and Shear Bond Strength of Gingival Colored Composite Resin to Heat Cure Denture Base Resin using Compression Moulded Technique and Injection Moulded Technique

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Abstract

Statement of Problem: Acrylic resins are the materials of choice for Complete Denture fabrication but, the color of acrylic resin often fails to give a desired esthetic outcome.

Purpose: To triumph over this, gingival color composite resins were used for dentures which provide the gain of improving the esthetics. This study was done to comparatively evaluate and determine the color stability and shear bond strength of gingival colored composite resin when applied over heat cure denture base resin, fabricated by Injection molding technique and compression molding technique.

Materials and Methods: For color stability and shear bond strength testing, 40 acrylic blocks (n = 40) were fabricated. Twenty were compression molded and other 20 were injection molded. Out of 20 of each molding technique, 10 each were tested for color stability and shear bond strength. For color stability testing, a spectrophotometer was used. For shear bond strength testing, universal testing machine was used. The data obtained were statistically analyzed by independent sample $t$test.

Results: No statistical significance was observed in the color stability. However, when injection molded denture base resin was layered with gingival composite resin, the bond strength significantly was higher than when compared with compression molded denture base resin.

Conclusion: The bond strength of injection molded denture base layered with gingival colored composite resin was high and clinically acceptable. This adds to the clinical relevance for acceptability of this technique for the fabrication of dentures with superior esthetics.

Clinical Implication: This technique helps in the fabrication of dentures with superior esthetics and gives more characterization to the denture and a realistic appearance.

Key words: Compression molded denture base resin, Crealign, Gingival composite resin, Injection molded denture base resin

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INTRODUCTION

Esthetics has become increasingly important in dentistry and is related to a natural and harmonious appearance. A smile can enhance the personality of a person and can command social acceptance easily.[1] The dentist must visualize aesthetics in relation to the patient and then

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translate that visualization into a suitable aesthetic result. For a healthy gingiva, esthetics is also an important key factor. It's challenging to settle on acceptable, restorative treatment for teeth with gingival recession within the esthetic zone.[2] The esthetics of a dental prosthesis should blend seamlessly with the soft tissues that surround the dentition, especially within the anterior smile zone. Zalkind and Hochman introduced the usage of pink composite resin as a man-made gingival tissue for the management of a cervical defect.[3] The composites are more resistant to wear and are color stable. Fabrication of complete dentures not only replaces the missing teeth but also restores the esthetics and phonetics. Complete denture characterization is necessary to bring a life-like appearance to the dentures.[4] Every denture should be characterized consistent with a private patient, instead of doing a pearl-like arrangement of teeth with a twinkling acrylic denture base which reveals it to be false. Our aim was to fabricate dentures with anatomic characterization that were present before the loss of teeth. A natural-looking prosthesis is often achieved by applying artistic principles with reference to the key elements of the face. Every patient being unique requires more detailed and customized approach for proper esthetics, by incorporating the patient's characteristics in the denture, a natural-looking prosthesis can be fabricated. Inspite of all ongoing efforts to maximize esthetics with acrylic resins, there seems to be a shortfall. In completely edentulous patient gingival colored porcelain can also be used to enhance the esthetics and improve the look of the patient.[5] A new material gingival colored composite now can be used. Although studies have been published comparing the flexural strength of acrylic resin denture base materials; there are fewer studies comparing the bond strengths of homogenous denture base materials with denture base layered with gingival colored composite. The range and frequency of the use of the gingival-colored composites are expected to increase with time. The understanding and evaluation of the color stability and bond strength of these materials to the denture base resin is important to decide the relevance of the gingiva colored composite. The addition of gingiva shade composite resin to enhance the esthetics of denture base resin can be used if a thin layer of 1.5 mm is applied to the fabricated denture acrylic resin.

The purpose why the present study was chosen was to evaluate the influence of the fabrication process of the denture base resin on the shear bond strength and color stability of the removable prosthesis.

MATERIALS AND METHODS

Forty acrylic blocks of dimensions 8 mm*4 mm were fabricated. Vernier caliper was used to measure the dimension of the blocks. Twenty acrylic blocks were fabricated by each molding technique (20 compression molding, 20 injection molding) which were randomly divided into two groups of 10 samples each to evaluate the color stability and bond strength respectively.

Fabrication of acrylic block by compression molding was carried out on gypsum models in gypsum compression forms, which were received after burning out of wax. A mix of type II gypsum plaster was placed in the base of the bottom half (lower half) of the flask, the metal block (8 mm*4 mm) was centered in the lower half and pushed downward into plaster until the bottom of the block touched the base of the flask and nearly leveled with the top edge of the flask. After the final setting of plaster had occurred, it was coated with a separating medium. The upper lid of flask was placed and a mix of type III dental stone was poured and allowed to set. The lid was placed on the flask and was tapped firmly to place. Excess stone extruded through the holes in the lid and around the edges.

The flask was placed in boiling water for 5 min, separated following which the wax was flushed out. The flask was then placed aside to drain the water and allowed to dry. A heat cure acrylic resin (SR TripleX, Dental Products Ltd., India)was proportionally mixed according to manufacturer instructions. After the consistency was at dough stage, Bench curing of the flask was done under pressure for 30–60 min. The flask and clamp were placed in a curing unit. The block was processed for 9 h in water held at a constant temperature of (60–70°C). Deflasking was done.

According to the manufacturer instructions, wax was duplicated, flasked, and invested for injection molded specimens. The flask was heated in a hot water at 65°C for 5 min and separated, and wax was flushed by hot and clean water. After that, it was allowed to chill to room temperature. The Ivoclar Vivadent Separating Fluid was used while the plaster surfaces were moist and allowed to dry. For about 5 min, premeasured capsules of resin and monomer (SR Ivocap High Impact; Ivoclar Vivadent AG) were united in a commercial mixer (Cap Vibrator; Ivoclar Vivadent AG).In a hydraulic press (corresponding to about 80 bar/1133 psi hydraulic pressure), 3 tons/6000 lbs., pressure was applied to the clamping frame with the flask. The substance of the mixed capsule was embedded into the flask, and the pressure injection apparatus (SR Ivocap System; Ivoclar Vivadent AG) was connected. The pressure apparatus was connected to a compressed air supply (6 bar/85 psi) to allow the plunger to descend and inject material into the mold. The assembly was then immersed and polymerized in boiling water for 35 min as per the manufacturer guidelines. The assembly was then removed out and quickly placed in cold water while

maintaining the pressure, for around 15–25 min, after which the specimens were deflasked.[6]

After fabrication of compression and injection molded acrylic blocks, the blocks were Sandblasted with aluminum particles (110 μm) and then Gingiva colored composite resin was layered using Crealign, Bredent for 2.5 mm thickness [Figures 1 and 2]. The material has a gel-like consistency and the homogeneity of the material allows for the adaption of elasticity and hardness of the composite to various substructure materials [Figure 3]. Composite matrix combination (i.e. Opalescent ceramic and crack-resistant) transforms the properties of a liquid ceramic to Crealign. Using this procedure, restorations perfectly matching natural teeth can be produced with shade stability and plaque resistance within the laboratory. Chairside veneering can be done. Crealign can be used crowns and bridges and also for the "additional veneer technique". The Crealign was layered on the block using the Incremental Horizontal Layering technique. Small brush was used to apply material.

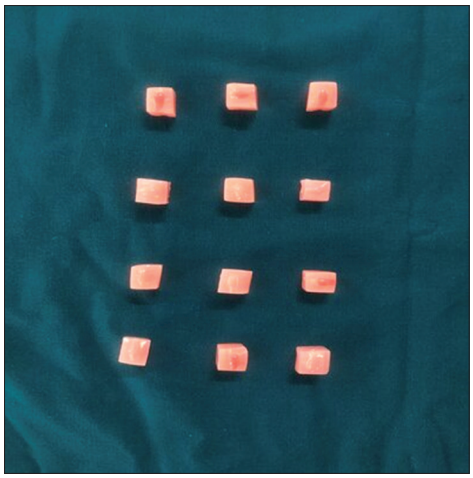


Figure 1: Compression molded denture base resin layered with gingiva colored composite resin

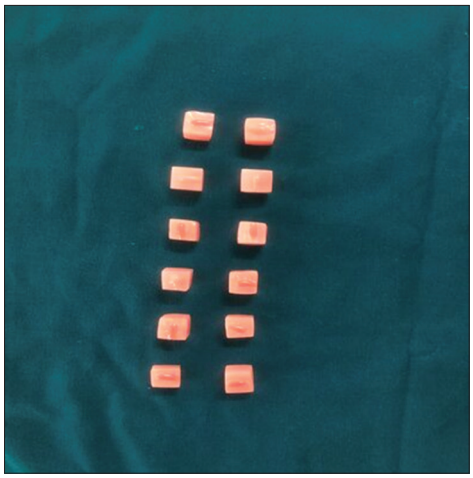


Figure 2: Injection molded denture base resin layered with gingiva colored composite resin

Pre-curing for 2–3 s was done with the Bre.Lux hand lamp with a suitable light source [Figure 4]. The thickness was measured using the Caliper and was standardized, and thus it was polymerized for 180 s in the Bre. Lux Power Unit Curing device and the final polymerization was done for 360 s. The dispersion layer was removed using surface cleaner and a toothbrush.

Specimens were stored in distilled water at 37°C for 24 h and thermocycled between 5°C and 55°C for 1000 cycles, with a dwell time of 30 s [Figures 5 and 6]. After thermocycling, they were stored in 37°C distilled water for an additional 15 h before subjecting to color stability and shear load testing. All color stability samples were tested under Spectrophotometer [Figure 7]. VITA Easyshade was adjusted by setting a probe tip on the calibration port aperture before measuring every specimen. The targets were measured by holding the probe tip at 90 degrees on the surface of the teeth. The CIE color space represents a uniform color space, with equal distances corresponding to equal perceived color differences.

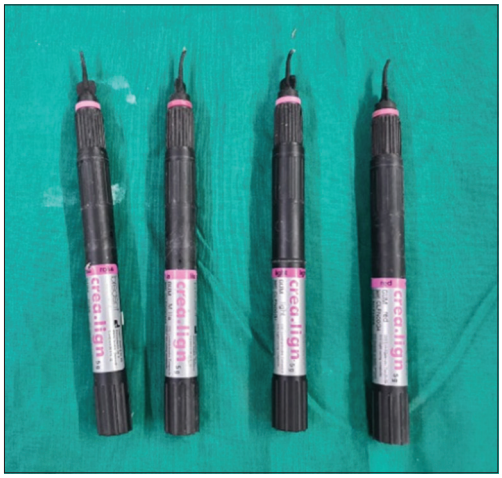


Figure 3: Gingival colored composite resin (Crealign)

Figure 4: The Bre.Lux curing unit

Figure 5: Thermocycling: Samples kept in cold chamber

Figure 6: Thermocycling: Samples kept in hot chamber

Figure 7: Equipment used for color stability

Figure 8: Equipment used for testing of shear bond strength (Universal Testing Machine)

The three axes in this three-dimensional color space were L*, a*, and b*. The L* value was a metric for item lightness that was measured on a scale with a perfect black having a L* value of 100. The a* value represented the proportion of redness (positive a*) or greenness (negative a*) in the image. The b* number represented a percentage of yellowness (positive b*) or blueness (negative b*) in the image. For natural colors, the a* and b* coordinates were close to zero but grew in magnitude for more saturated or strong hues. The CIE Laboratory approach had the advantage of expressing color contrasts in units that could be linked to visual perception and clinical relevance. The measurement was accepted when two consecutive, indistinguishable readings were produced for each region, as per the manufacturer's instructions. The data for continuous variables were presented as mean ± standard deviation (SD).

All the samples of the shear bond strength were measured on computerized, software-based Universal Testing Machine (Acme Engineers, India, Model: UNITEST 10) with a crosshead speed of 5 mm/min at a 50 mm distance. Each specimen was positioned on the lower part of the machine [Figure 8]. The jigs had a diameter of 10 mm and the span length was 50 mm. The upper part of the testing machine had a steel pointer which was placed in between of the specimen. Shear forced values required to separate the block (N) were recorded by machine's software. The data on continuous variables were shown as mean ± SD.

Statistical Analysis

The inter-group statistical significance of difference was tested using independent sample *t*-test. The data on continuous variables were shown as mean ± SD. The inter-group statistical significance of difference was tested using independent sample *t*-test. The underlying normality assumption of study variables was tested before subjecting the study variables to *t*-test. All results were displayed in tabular and graphical configuration to envision the factually significant difference precisely.

In the whole study, the *P*-values under 0.05 were viewed as statistically significant. Using two-tailed alternatives, all the

hypothesis were formulated against every null hypothesis (hypothesis of no distinction). The data were measurably analyzed utilizing Statistical Package for Social Sciences (SPSS ver 21.0, IBM Corporation, USA) for MS Windows.

RESULTS

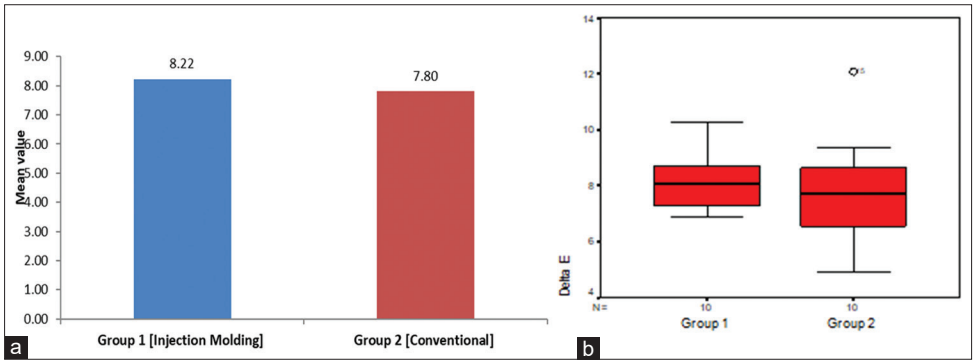
From the study conducted, the following results were observed:

1. The inter-group comparison of mean color stability (Delta E) between the groups was shown in [Graph 1] The inter-group comparison of mean shear bond strength between the groups was shown in [Graph 2]
2. The mean ± SD of color stability (delta E) in Group 1 (Injection Molding) and Group 2 (Conventional) was 8.22 ± 1.03 and 7.80 ± 2.09 respectively. The minimum-maximum range of color stability (delta E) in Group 1 and Group 2 was 6.92–10.24 and 4.94–12.07 respectively
3. The distribution of mean color stability (delta E) in Group 1 (Injection Molding) did not differ significantly compared to Group 2 (Conventional) ($P > 0.05$)
4. The mean ± SD of shear bond strength in Group 1 (Injection Molding) and Group 2 (Conventional) was 3.68 ± 1.81 MPa and 1.95 ± 0.58 MPa respectively. The minimum-maximum range of shear bond strength in Group 1 and Group 2 was 2.08–7.46 MPa and 1.05–2.82 MPa respectively
5. The distribution of mean shear bond strength was significantly higher in Group 1 (Injection Molding) compared to Group 2 (Conventional) ($P < 0.05$).

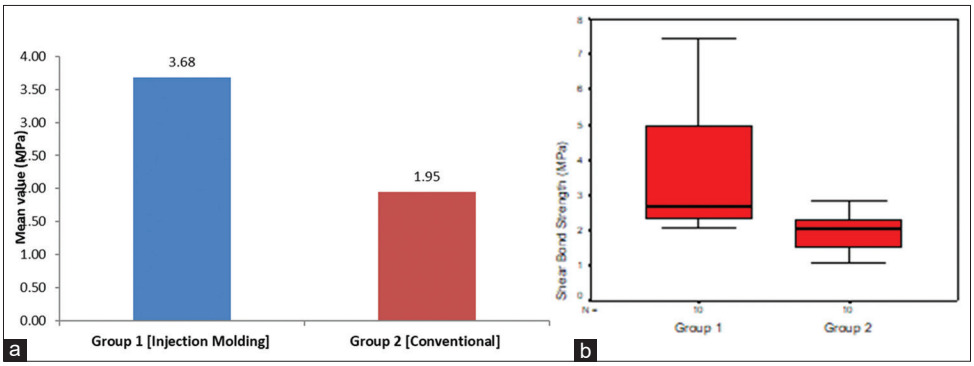
DISCUSSION

The objective of the present study was to evaluate and compare the Color Stability and Bond Strength of Gingival Colored Composite Resin to Denture Base Resin processed by two Different Techniques: Compression Moulding Technique (SR Triplex Hot by Ivoclar Vivadent), and Injection Moulding Technique SR Ivocap system-BPS-Ivoclar Vivadent. Polymethyl methacrylate is a successful denture base material for removable dentures. However, because it does not portray the natural appearance of the gingiva, traditional acrylic denture base resin has restricted aesthetics. Therefore, efforts have been made to modify or veneer these resins to enhance their appearance either with gingival color porcelain or gingival colored composite resin. But these materials have had limitations in their color stability and their bond strength to resins.

Color stability is the capacity of any dental material to have the option to hold its unique color. The resin matrix, depth of polymerization, filler particle measures, and coloring agents all affect the color stability of a resin composite. The oral cavity has a dynamic environment.



Graph 1: (a and b) Bar-graph and Box-Whisker Plot showing inter-group distribution of mean color stability (Delta E)



Graph 2: (a and b) Bar-graph and Box-Whisker Plot showing inter-group distribution of mean shear bond strength

With the persistent presence of microflora, salivation, and successive admission of colored food (chromatogens), the color stability of material may get bargained aesthetically.

Da Silva *et al.* compared the Easyshade spectrophotometer to three other optical shade guidance systems in 2008. The crowns were made using a spectrophotometer in their study, which resulted in a substantially better color match and a reduced percentage of rejection owing to shade mismatching. There are a number of other studies that support instrumental procedures above visual ones. Hence, Easyshade Spectrophotometer was used for the color stability.[7] Crea.lign consists of nano particles and no ground glass filler. It consists of 50% opalescent ceramic filler and a high-strength oligomer matrix. The absence of strong glass fillers improves plaque and abrasion resistance and keeps the material from being embrittled.

Even after the thermocycling of gingival colored composite resin (Crealign), there was no change in the color of the specimen when bonded with two differently processed denture base resins. This indicates that the properties of the material are highly unaffected by and useful as an esthetic material for characterization of the denture.

Injection molding, which was first used in 1942, has the property through which it reduces the resin flash and compensates for shrinkage by pushing additional resin into the flask during the polymerization process. According to recent studies, full dentures made with an injection method have a much smaller incisal pinhole than dentures made with the compression moulding approach. Injection molding allows directional control of the polymerization process through the flask design.[8] A constant flow of new material from the sprue compensates for the polymerization shrinkage. This method permitted the utilization of new thermoplastic resins as a choice to the heat-cured PMMA, without the requirement for synthetic added substances or catalysts that might be unfavorably susceptible for patients. The chemical properties may cause some porosity and can increase the contact surface area; therefore, greater forces are needed for fracture. This could have increased the bond strength between the gingival-colored composite resin and injection molded denture base resin.

In this *in-vitro* study, the bond strength of gingival colored composite resin to injection molded denture base resin showed maximum shear bond strength when compared with compression molded denture base resin while the color stability did not differ significantly.

The results of this study could be used to fulfill the following clinically relevant objectives:

1. Help the clinician decide which fabrication procedure of the denture base resin would provide better bond strength to gingival colored composite resin
2. Help the clinician get an idea about the errors that can be minimized using different techniques for the fabrication of denture base resin
3. Help the clinician get an idea about the gingival color composite resin and its color stability with the denture base resin.

CONCLUSION

Within the limits of this *in-vitro* study, the following conclusions were drawn:

1. When layered with gingival colored composite resin, compression molded denture base resin showed higher color changes after thermocycling as compared to the injection molded denture base resin
2. Injection Molding technique and Compression Molding technique layered with Gingival Colored Composite Resin did not show statistical difference, in the Color Stability test
3. Injection Molding technique of fabrication showed significantly higher bond strength as compared to the Compression Molding technique with gingival composite resin.

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Original Article

A Cephalometric Evaluation of Dentoskeletal and Soft Tissue Changes with Mini-Implants versus Conventional Methods of Anchorage Reinforcement for En-masse Retraction of Anterior Teeth in Bialveolar Dental Protrusion Cases

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Abstract

Aims: The purpose of this study was to investigate and compare the dentoskeletal and soft-tissue treatment effects with mini-implants as anchor units in bialveolar dental protrusion patients requiring extraction of four first premolars and maximum retraction of anterior teeth with patients treated by conventional methods of anchorage reinforcement. In addition, the anchorage loss and the time taken for space closure were recorded.

Materials and Methods: A total of 20 patients were assigned to two groups each containing 10 patients - group 1 (G1) - anterior space closure was done with mini-implants as anchorage and group 2 (G2) - anterior space closure was done with conventional methods of anchorage. Skeletal, dental, and soft-tissue changes were analyzed in both groups on lateral cephalograms taken before retraction (T1) and after space closure (T2).

Statistical Analysis Used: Student *t*-test was done to analyze the treatment changes in the 2 groups.

Results: For the skeletal parameters, a statistically significant decrease in the facial vertical dimensions was seen in G1 ($P < 0.01$), but the variables in G2 showed a significant increase ($P < 0.01$). Anchorage loss, in both the horizontal and vertical directions, was noted in G2, whereas G1 showed distalization (anchorage gain) and intrusion of molars. Although the soft-tissue response was variable, facial convexity angle, nasolabial angle, and lower lip protrusion had greater changes in G1.

Conclusion: Mini-implants are more efficient for intra-oral anchorage reinforcement for en-masse retraction than conventional methods of anchorage reinforcement. The skeletal, dental, and soft tissue treatment changes were favorable. However, no differences in the mean retraction time were noted between the two groups.

Key words: Anchorage, Mini-implant, Space closure

INTRODUCTION

Bialveolar dental protrusion is one of the most common problems seen today around the globe. Dentoalveolar flaring of the anterior teeth with resultant protrusion of lips and convexity of the face are unique features of bimaxillary protrusion. Protrusive lips and a convex facial profile usually result in poor facial esthetics.[1]

The current treatment modality followed by most orthodontists to treat bialveolar protrusion is the extraction of the four first premolars. It was also observed that retraction of maxillary incisors causes upper lip retraction, increases the length of the lower lip and the nasolabial angle, whereas mandibular incisor position determines lower lip position

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and shape. The magnitude of anterior dental reduction and the resulting change in lip position is determined not merely by the extraction of teeth but by how anchorage is managed. Anchorage loss is the reciprocal reaction of the anchor unit that can obstruct the success of orthodontic treatment by complicating anteroposterior correction.[2]

Minimizing anchorage loss during the treatment of such cases is of paramount importance. To address this problem, many appliances and techniques have been devised; Nance holding arch, transpalatal bars, extraoral traction, multiple teeth at the anchorage segment, and differential moments are the commonly used ones.[3]

The advent of temporary skeletal anchorage devices (TSADs) such as mini-implants and mini-screws has, however, significantly simplified orthodontic biomechanics by providing independent absolute anchorage.[4] With its help, it is now possible to obtain absolute anchorage of the posterior teeth and close the extraction spaces completely by anterior teeth retraction. Their primary advantages are easy placement and removal, immediate loading, placement at various anatomic locations including the alveolar bone between the roots of teeth, and low cost.[3] Consequently, TSADs are quickly becoming the preferred method of skeletal anchorage. Despite all the above advantages, what is of primary importance is to know whether the TSAD's are efficient enough to hold the anchorage units intact during en-masse retraction.

The aims and objectives of this study were:
1. To compare the dentoskeletal changes in bialveolar dental protrusion patients requiring extraction of four first premolars with mini implants as anchor units when compared with conventional methods of anchorage reinforcement for en-masse retraction of anterior teeth
2. To compare soft tissue changes between the two groups
3. To compare the amount of anchorage loss between the two groups
4. To compare the time taken for space closure in both the groups.

Thus, the null hypothesis in the study is that mini-implants are more efficient for intra-oral anchorage reinforcement for en-masse retraction than conventional methods of anchorage reinforcement.

MATERIALS AND METHODS

The study included 20 Class I bialveolar protrusion patients between the age group of 15–25 years in the permanent dentition. The sample was randomly divided into two groups of 10 each: the study group (G1) [Figure 1] and the control group (G2). For all the 20 patients, consent was taken regarding the extraction of four first premolars. In the study group G1, consent was also taken from the patients regarding the placement and removal of implants under local anesthesia.

The inclusion criteria were:
1. Minimum age of 14 years at the beginning of treatment, to minimize confounding results due to growth
2. Class I molar relationship (±1 mm) and overjet not exceeding 5 mm (measured on the study models with a digital caliper)
3. Well-aligned maxillary and mandibular incisors with minimum crowding (<3.5 mm).

The exclusion criteria were:
1. Previous history of mouth breathing, thumb sucking, tongue thrusting, or orthodontic treatment
2. Congenitally missing teeth except for third molars.

In both the groups, only the first molars were banded and all the remaining teeth mesial to the first molars were bonded. All patients were treated with the pre-adjusted edgewise appliance system (MBT prescription, slot size 0.022 × 0.028 in). After the initial leveling and aligning 0.017 × 0.025-in stainless steel archwires with crimpable hooks were placed distal to the lateral incisors in both arches. To ensure that the wires remained passive, they were left in place for at least 4 weeks before starting the en-masse retraction procedure.

In G1 subjects, titanium mini-implants (1.3 mm in diameter, 5–9 mm in length, self-drilling, S.K. Surgicals, Pune) [Figure 2] were used as anchorage units in both the arches. Implants were placed in the alveolar bone between the roots of the first molar and second premolar at the mucogingival junction. The implants were then immediately loaded with pre-calibrated nickel-titanium closed-coil springs (150 g, Dentos India Pvt. Ltd., Mumbai) extending from the implant head to the crimpable hooks for en-masse retraction of maxillary and mandibular anterior teeth [Figures 3 and 4].

In G2 subjects, conventional methods of anchorage reinforcement were used according to the need of space closure, such as transpalatal arches, banding of the second molars, and application of differential moments. After initial leveling and aligning, 0.017 × 0.025-in stainless steel archwires with hooks were placed in a passive state for 4 weeks, and then conventional sliding mechanics were employed for en-masse anterior retraction.

To estimate treatment changes primarily due to retraction of anterior teeth, lateral cephalograms were taken at the end of alignment (T1) and after space closure (T2) in both the

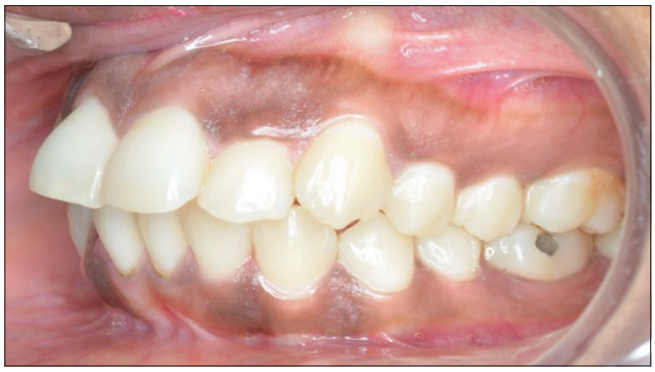

Figure 1: Pretreatment intraoral photos of G1 subject

Figure 2: Titanium mini-implants (1.3 mm in diameter, 5-9 mm in length, self drilling, S.K. Surgicals, Pune)

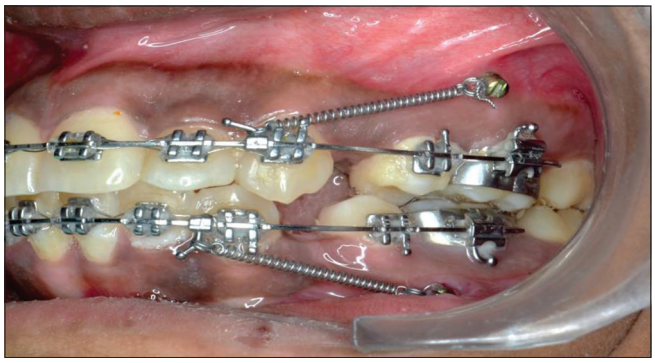

Figure 3: Nickel titanium closed coil springs extending from the implant head to the crimpable hooks in G1 subject

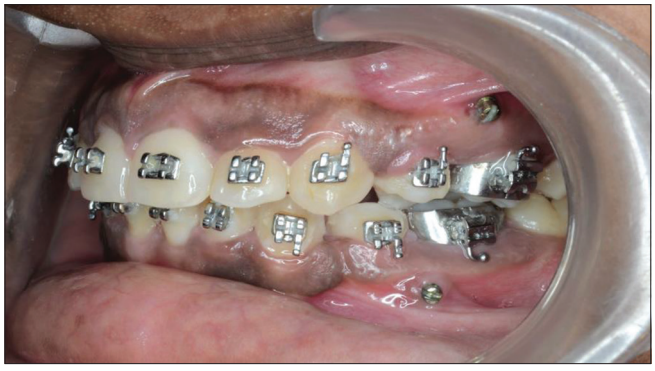

Figure 4: End of space closure intraoral photos of G1 subject

groups. All the 40 cephalograms were traced and analyzed to assess the skeletal, dental, and soft tissue changes.

The cephalometric parameters used in this study were as follows:

Landmarks

Hard tissue [Figure 5]

(1) Nasion (N), (2) Sella (S), (3) Pogonion (Pog), (4) Gnathion (Gn), (5) Gonion (Go), (6) Point A, (7) Point B, (8) Mesial cusp tip of maxillary first molar (U6), (9) Mesial cusp tip of mandibular first molar (L6), (10) Incisal tip of maxillary central incisor (U1), (11) Incisal tip of mandibular central incisor (L1).

Soft tissue [Figure 5]

(12) Nasal tip (Nt), (13) Subnasale (Sn), (14) Sulcus superior (Ss), (15) Labrale superior (Ls), (16) Labrale

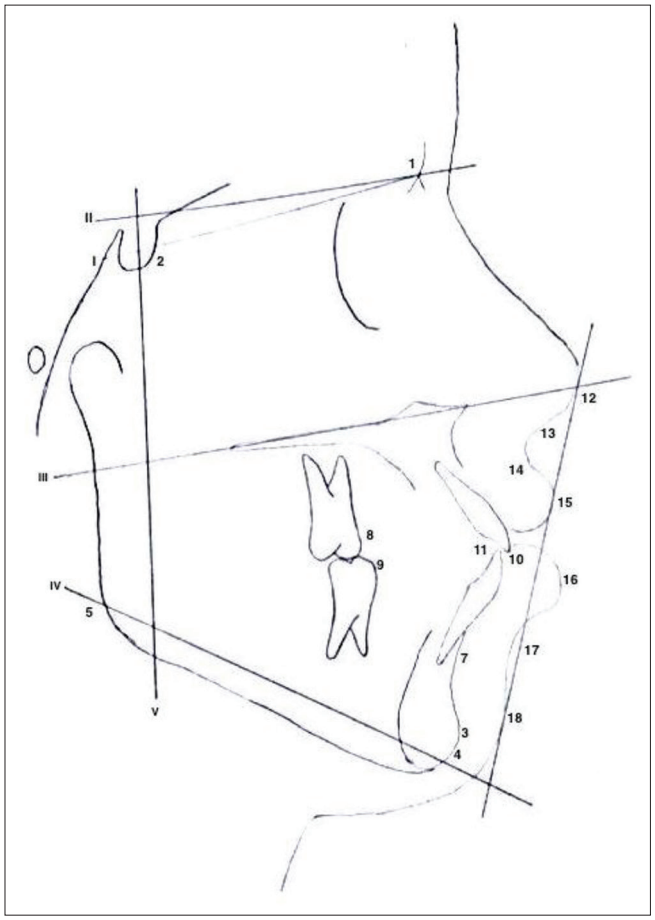

Figure 5: Cephalometric landmarks (hard tissue, soft tissue) and cephalometric planes (Cephalometric landmarks [hard tissue]: (1) nasion [N]; (2) sella [S]; (3) pogonion [Pog]; (4) gnathion [Gn]; (5) gonion [Go]; (6) Point A; (7) Point B; (8) U6; (9) L6; (10) U1; (11) L1. Cephalometric landmarks [soft tissue]: (12) Nt; (13) Sn; (14) Ss; (15) Ls; (16) Li; (17) Si; (18) Pg. Cephalometric planes: (I) S-N plane; (II) constructed Frankfort horizontal plane [x-axis]; (III) palatal plane [anterior nasal spine [ANS]-posterior nasal spine [PNS]); (IV) mandibular plane [Go-Gn); (V) sella vertical [Sv or y-axis); (VI) Ricketts' E-plane [Nt-Pg])

inferior (Li), (17) Sulcus inferior (Si), (18) Soft-tissue Pog (Pg).

Cephalometric planes [Figure 5]

(I) S-N plane, (II) Constructed Frankfort horizontal plane (X-axis), (III) Palatal plane (anterior nasal spine [ANS] - posterior nasal spine [PNS]) (IV) Mandibular plane (Go-Gn), (V) Sella vertical (Sv or Y-axis), (VI) Ricketts' E-plane (Nt-Pg).

Skeletal angular measurements [Figure 6]

(1) SNA angle, (2) SNB angle, (3) ANB angle, (4) SN-Go-Gn.

Skeletal linear measurements [Figure 6]

(5) Upper facial height (UFH) (N-ANS), (6) lower facial height (LFH) (ANS-Me), (7) posterior facial height (PFH) (S-Go), (8) total anterior facial height (TAFH) (N-Me), (9) Sv-Pog.

Dental angular measurements [Figure 7]

(1) U1-SN Plane, (2) IMPA, (3) Interincisal angle (U1-L1).

Dental linear measurements [Figure 7]

(4) Vertical position of maxillary first molar (U6-PP), (5) Sagittal position of maxillary first molar (U6-Sv), (6) Sagittal position of mandibular first molar (L6-Sv), (7) Vertical position of mandibular first molar (L6-MP), (8) Sagittal position of maxillary incisor edge (U1-Sv), (9) Sagittal position of mandibular incisal edge (L1-Sv).

Soft tissue angular measurements [Figure 8]

(1) Facial convexity angle (G-Sn-Pg), (2) Nasolabial angle (Sn tangent and Sn-Ls), (3) Labiomental angle (Li-Si and Si-Pg).

Soft tissue linear measurements [Figure 8]

(4) Sv-Nt; (5) E-line – Ss; (6) E-line – Ls; (7) E-line – Li; (8) E-line – Si.

RESULTS

The data obtained from this study was evaluated and comparisons were made within the group and between the study group (G1) and the control group (G2). Means, standard deviations, correlation coefficients, and level of

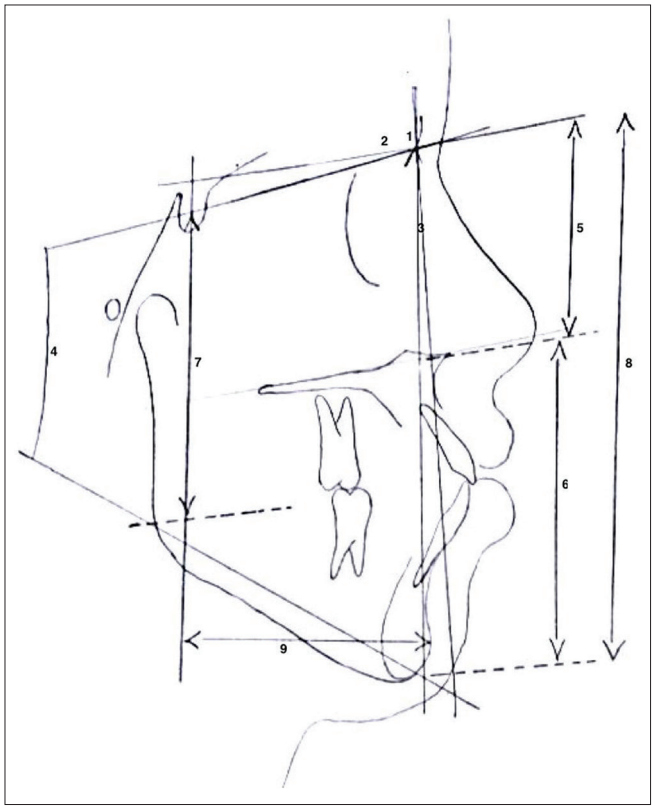

Figure 6: Skeletal angular and linear measurements (Skeletal angular measurements: (1) SNA angle; (2) SNB angle; (3) ANB angle; (4) SN-Go-Gn. Skeletal linear measurements: (5) Upper facial height [N-ANS]; (6) Lower facial height [ANS- Me]; (7) Posterior facial height [S-Go]; (8) Total anterior facial height [N-Me]; (9) Sella vertical-Pogonion)

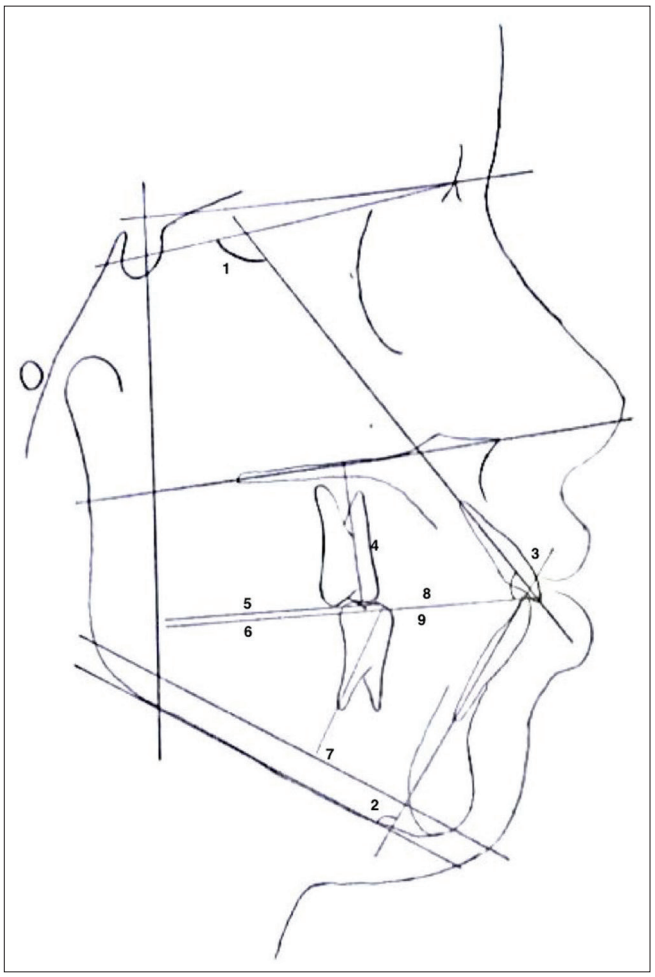

Figure 7: Dental angular and linear measurements (Dental angular measurements: (1) U1-SN plane; (2) IMPA; (3) U1-L1 [interincisal angle]. Dental linear measurements: (4) U6-PP; (5) U6-Sv; (6) L6-Sv; (7) L6-MP; (8) U1-Sv; (9) L1-Sv)

significance were determined. Student t-test was done to find the significance of study parameters within each group. $P < 0.01$ indicated strong significance. *P*-value between 0.01 and 0.05 ($0.01<P<0.05$) indicated moderate significance.

(* Moderately significant [*P*-value: $0.01<P\leq0.05$], ** Strongly significant [*P*-value: $P \leq 0.01$]).

Age and duration of time taken for retraction:
Although mean retraction time for G1 (8.55 ± 0.55 months) was less than that of G2 (9.05 ± 0.72 months), the differences were not significant ($P > 0.01$) [Table 1].

Skeletal Changes

Both the implant group and conventional group had a significant reduction in the SNA angle ($P \leq 0.01$), moderate reduction in the ANB angle ($0.01<P\leq0.05$), and no significant change in SNB. Forward displacement of the chin (Sv-Pg) was noted for the implant group. The implant group showed significant increase in the UFH, PFH, and reduction in the SN-MP angle ($P \leq 0.01$). In the conventional group, there was only a moderate increase in the UFH ($0.01<P\leq0.05$) and significant increase in the LFH ($P \leq 0.01$). However, there was a significant increase in the SN-MP angle ($P \leq 0.01$). The differences between G1 and G2 were statistically significant ($P < 0.05$) [Tables 2 and 3].

Dental Changes

No anchor loss was observed in the horizontal direction in the implant group. Instead a net distal movement was recorded, which was clinically and statistically significant ($P \leq 0.001$). On the other hand, in the control group the molars showed clinically and statistically significant levels of molar mesialization ($P \leq 0.001$). Significant vertical changes were also observed in both the groups. In the implant group, there was significant intrusion of the molars whereas in the conventional group there was extrusion of the molars ($P \leq 0.001$). The incisors in both the groups showed significant intrusion but more so in the implant group ($P < 0.05$) [Tables 4 and 5].

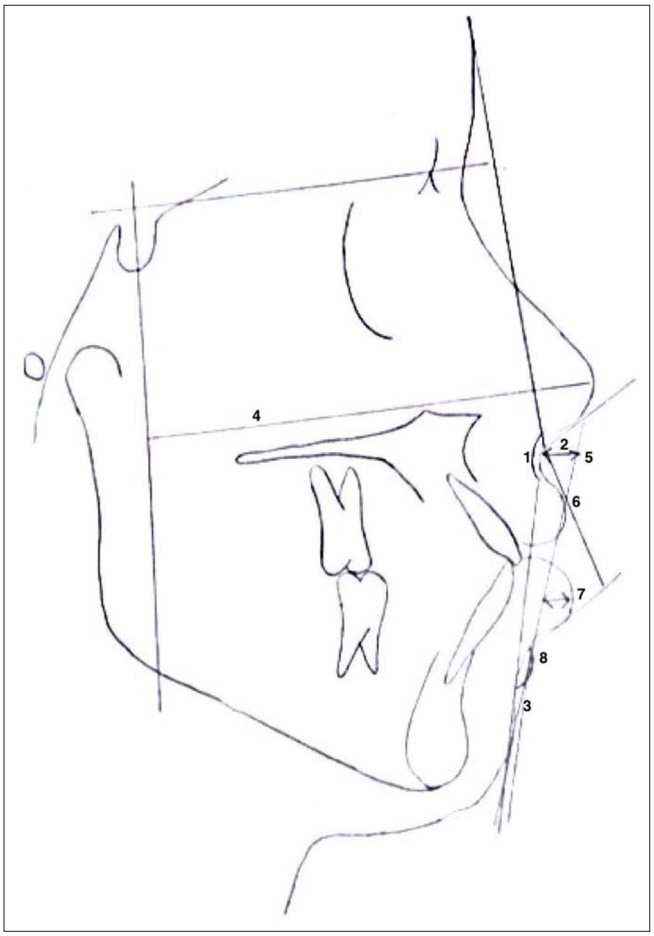

Figure 8: Soft-tissue angular and linear measurements (Soft-tissue angular measurements: (1) G-Sn-Pg; (2) nasolabial angle; (3) labiomental angle. Soft-tissue linear measurements: (4) Sv-Nt; (5) E-line–Ss: distance from sulcus superior to E-line; (6) E-line–Ls; (7) E-line–Li; (8) E-line– Si)`

Table 1: Age and duration of retraction

	Group G1	Group G2	*P*-value
Age in years	20.50±3.78	24.30±4.24	0.049*
Duration of retraction	8.55±0.55	9.05±0.72	0.099+

Table 2: A comparison of skeletal effects in G1 group AT T1 and T2

Skeletal effects in G1	T1	T2	*P*-value
SNA Angle (degree)	82.70±1.49	81.30±1.42	0.003**
SNB Angle (degree)	79.10±1.73	79.30±1.49	0.555
ANB Angle (degree)	3.20±1.14	2.20±0.92	0.042*
SN-GO-GN	31.50±1.96	30.00±2.11	0.009**
UFH (N-ANS) (mm)	50.60±7.12	52.30±7.17	0.001**
LFH (ANS-Me)(mm)	68.00±2.94	67.40±2.50	0.217
PFH (S-Go)(mm)	78.10±6.31	78.80±6.27	0.010**
TAFH (N-Me)(mm)	116.90±9.02	117.20±8.94	0.627
SV-Pog(mm)	58.40±4.53	59.80±5.27	0.013*

UFH: Upper facial height, LFH: Lower facial height, PFH: Posterior facial height, TAFH: Total anterior facial height, SV-Pog: Sella vertical-Pogonion

Table 3: A comparison of skeletal effects in G2 group at T1 and T2

Skeletal effects in G2	T1	T2	*P*-value
SNA Angle (degree)	83.30±1.83	82.10±2.08	<0.001**
SNB Angle (degree)	78.80±1.62	78.70±1.83	0.811
ANB Angle (degree)	4.50±1.58	3.40±1.26	0.024*
SN-GO-GN	32.70±3.09	34.50±2.32	0.001**
UFH (N-ANS) (mm)	51.10±3.81	51.80±3.43	0.025*
LFH (ANS-Me)(mm)	70.00±5.81	71.90±5.26	0.001**
PFH (S-Go)(mm)	80.50±6.72	81.00±6.86	0.096+
TAFH (N-Me)(mm)	119.80±8.77	123.10±8.84	<0.001**
SV-Pog(mm)	58.30±4.08	57.70±3.71	0.111

UFH: Upper facial height, LFH: Lower facial height, PFH: Posterior facial height, TAFH: Total anterior facial height, SV-Pog: Sella vertical-Pogonion

Soft Tissue Changes

Profile changes (labiomental angle, nasiolabial angle, and facial convexity angle) showed significant changes in both the groups ($P \leq 0.01$), but changes were more pronounced in the implant group ($P < 0.05$). There were statistically significant levels of lip retraction seen in both groups ($P \leq 0.01$) but the intergroup difference was not statistically significant ($P > 0.05$) [Tables 6 and 7].

DISCUSSION

Preserving anchorage has always been a humongous task for the orthodontist. Conventional methods of anchorage control included both intraoral and extraoral means. With the advent of preadjusted edge-wise appliance systems, sliding mechanics has become a commonly practiced technique. During the past 5 years, anchorage control with self-tapping screws or mini-implants has gained enormous credibility in the clinical management of space closure.

Upadhyay *et al.* conducted a study to determine the efficiency of mini-implants as intraoral anchorage units for en-masse retraction of the 6 maxillary anterior teeth when the first premolars were extracted compared with conventional methods of anchorage reinforcement. Thirty patients requiring high anchorage after extraction of the maxillary first premolars were selected for this study. They were divided into two groups of 15 each. In the first group (G1), mini-implants were used for en-masse retraction; in the second group (G2), conventional methods of anchorage preservation were followed. Horizontal, vertical, and angular positions of the maxillary first molar and central incisor were evaluated cephalometrically before and after orthodontic retraction. The maxillary first molars in the G1 patients showed net distal movement of 0.55 mm, and mesial movement of 1.95 mm was found in G2. The differences were statistically significant In G1 patients; net intrusive

Table 4: A comparison of dental effects In G1 group at T1 and T2

Dental Effects in G1	T1	T2	*P*-value
U1-SN Plane (Degree)	112.00±2.67	99.90±1.66	<0.001**
IMPA (Degree)	99.00±4.59	88.30±3.09	<0.001**
Interincisal angle (U1-L1) (Degree)	114.20±5.22	134.20±4.61	<0.001**
Vertical position of maxillary first molar (U6-PP) (mm)	24.20±1.99	22.90±1.91	0.001**
Sagittal position of maxillary first molar (U6-Sv) (mm)	42.70±2.31	41.60±3.06	0.048*
Sagittal position of mandibular first molar (L6-Sv) (mm)	45.70±2.11	44.40±2.80	0.004**
Vertical position of mandibular first molar (L6-MP) (mm)	31.70±3.23	30.10±3.11	<0.001**
Sagittal position of maxillary incisor edge (U1-Sv) (mm)	70.80±3.91	64.20±3.88	<0.001**
Sagittal position of mandibular incisal edge (L1-Sv) (mm)	67.50±3.84	62.50±3.44	<0.001**

Table 5: A comparison of dental effects in G2 group at T1 and T2

Dental Effects in G2	T1	T2	*P*-value
U1-SN Plane (Degree)	112.50±2.12	105.80±7.16	0.008**
IMPA (Degree)	99.10±2.73	92.20±1.99	<0.001**
Interincisal angle (U1-L1)(Degree)	115.00±4.06	128.60±2.72	<0.001**
Vertical position of maxillary first molar (U6-PP) (mm)	24.80±2.25	27.00±2.31	<0.001**
Sagittal position of maxillary first molar (U6-Sv) (mm)	42.80±4.87	45.00±4.78	<0.001**
Sagittal position of mandibular first molar (L6-Sv) (mm)	46.00±5.60	48.40±6.15	<0.001**
Vertical position of mandibular first molar (L6-MP) (mm)	34.90±3.21	36.90±3.35	<0.001**
Sagittal position of maxillary incisor edge (U1-Sv) (mm)	71.70±6.46	67.50±6.24	<0.001**
Sagittal position of mandibular incisal edge (L1-Sv) (mm)	68.70±5.98	65.30±5.64	<0.001**

Table 6: A comparison of soft tissue changes in G1 group at T1 and T2

Soft tissue changes in G1	T1	T2	*P*-value
Facial convexity angle (G-Sn-Pg) (Degree)	162.70±9.27	159.70±8.91	<0.001**
Nasolabial angle (Sn tangent and Sn-Ls) (Degree)	94.20±4.83	106.30±3.92	<0.001**
Labiomental angle (Li-Si and Si-Pg) (Degree)	122.80±5.69	127.60±5.82	<0.001**
SV-Nt (mm)	93.00±5.52	94.10±5.28	<0.001**
E-line–Ss (mm)	–4.30±3.92	–6.60±2.87	0.001**
E-line–Ls (mm)	2.30±1.95	1.30±1.89	<0.001**
E-line–Li (mm)	4.60±1.43	0.90±0.88	<0.001**
E-line–Si (mm)	–3.00±0.94	–5.70±0.95	<0.001**

Table 7: A comparison of soft tissue changes in G2 group at T1 and T2

Soft tissue changes in G2	T1	T2	*P*-value
Facial convexity angle (G-Sn-Pg) (Degree)	160.90±3.48	159.40±3.92	0.048*
Nasolabial angle (Sn tangent and Sn-Ls) (Degree)	96.60±2.63	103.00±3.02	<0.001**
Labiomental angle (Li-Si and Si-Pg) (Degree)	122.30±13.47	127.20±13.64	<0.001**
SV-Nt (mm)	95.50±7.09	95.50±6.50	1.000
E-line–Ss (mm)	–5.60±1.96	–7.15±1.67	<0.001**
E-line–Ls (mm)	1.40±1.43	0.60±1.07	<0.001**
E-line–Li (mm)	4.30±1.77	1.00±1.49	<0.001**
E-line–Si (mm)	–3.70±1.30	–5.65±1.38	<0.001**

effect on the molars was recorded though not statistically significant. No significant differences were found in the rates of incisor retraction between the two groups. However, G1 showed more than 2 mm of incisor intrusion, which was statistically significant. The average time required for space closure was 9.2 months in G1 and 10.6 months in G2.[2]

The findings in our study corroborated the above study. It was seen that time required for space closure was less in G1 (8.55 ± 0.55 months) than G2 (9.05 ± 0.72 months) subjects, the differences were however not significant. G1 patients showed distal movement of the maxillary first molars along with intrusion of the same whereas G2 subjects showed mesial movement and extrusion of the maxillary first molars. There was significant incisor retraction in both the groups, however greater retraction was found in G1 subjects ($P \leq 0.01$). Thus, the above study supports our study.

Thiruvenkatachari *et al.*, conducted a study to compare and measure the amount of anchorage loss with titanium microimplants and conventional molar anchorage during canine retraction. Subjects for this study comprised ten orthodontic patients (seven women, three men) with a mean age of 19.6 years (range, 18–25 years), who had therapeutic extraction of all first premolars. After leveling and aligning, titanium microimplants 1.3 mm in diameter and 9 mm in length were placed between the roots of the second premolars and the first molars. Implants were placed in the maxillary and mandibular arches on 1 side in 8 patients and in the maxilla only in two patients. A brass wire guide and an intraoral periapical radiograph were used to determine the implant positions. After 15 days, the implants and the molars were loaded with closed-coil springs for canine retraction. Lateral cephalograms were taken before and after retraction, and the tracings were superimposed to assess anchorage loss. The amount of molar anchorage loss was measured from the pterygoid vertical in the maxilla and sella-nasion perpendicular in the mandible. The superimpositions showed that anchorage loss occurred on the nonimplant side, which was evident with the mesial migration of that molar; anchorage loss did not occur on the implant side, and no mesial movement was noted there. Anchorage loss was <20% on the molar-anchored side which was acceptable for the subjects selected. Anchorage loss in this study ranged from 1 to 2 mm with means of 1.6 mm in the maxilla and 1.7 mm in the mandible. Statistical analyses showed a significant anchorage loss in both the maxilla and the mandible.[5]

In our study too, we saw that there was significant anchor loss of the first molars in both maxilla and mandible in the conventional anchorage group. There was mesial migration of the maxillary and mandibular first molars in the sagittal plane and the differences were statistically significant ($P \leq 0.01$), when compared with the implant group. Thus, the above study affirms our study.

Rajni *et al.* did a study where three sets of profile cephalograms- pre-treatment, pre retraction and post retraction cephalograms of 20 skeletal Class I dentoalveolar bimaxillary protrusion patients, half of which were treated with conventional enmasse sliding mechanics and other half by enmasse sliding mechanics using micro-implants were obtained. Seven parameters were used to evaluate anchorage loss, quality of retraction, and treatment duration. It was seen that the control group showed an anchorage loss of 1.72 mm whereas implant-supported group showed an anchorage loss of only 0.09 mm. The quality of retraction of upper incisors obtained by retracting with help of implants was superior to that obtained by conventional enmasse sliding mechanics. Control group showed mean retraction of upper incisors by 2.5 mm during space closure and experimental group showed mean retraction of 3.79 mm. Both were highly significant. There was no significant difference in the treatment duration between the two groups.[6]

When compared with the above study, our study too showed similar findings. There was anchor loss in the sagittal and vertical direction of the maxillary first molars in the conventional group whereas there was little or no anchor loss in the mini-implant group. There was significant retraction of the upper incisors in both the groups but more so in the mini-implant group ($P \leq 0.01$). Although treatment time was slightly shorter in the mini-implant group, it was not significant. Thus, the above study supports our study.

CONCLUSION

The quality of retraction obtained by retracting with the help of implants was superior to that obtained by conventional enmasse sliding mechanics.

Thus, the following conclusions were made:

1. Mini implants were efficient sources of intraoral anchorage and remained stable all throughout the retraction phase. The advantages of the treatment approach were - elimination of compliance-depended intraoral and extraoral anchorage aids, favorable esthetics, immediate force application, and relatively predictable outcomes
2. The screw insertion and retrieval procedures were quick, simple, and painless
3. Although mean retraction time for implant group was less than that of the conventional one, the differences were not significant ($P > 0.01$)

4. Both the implant group and conventional group had a significant reduction in the SNA angle ($P \leq 0.01$), moderate reduction in the ANB angle ($0.01<P\leq0.05$), and no significant change in SNB. Forward displacement of the chin (Sv-Pg) was noted for the implant group
5. The implant group showed significant increase in the UFH, PFH and reduction in the SN-MP angle ($P \leq 0.01$). In the conventional group, there was only a moderate increase in the UFH ($0.01<P\leq0.05$) and significant increase in the LFH ($P \leq 0.01$). However, there was a significant increase in the SN-MP angle ($P \leq 0.01$). The differences between G1 and G2 were statistically significant ($P < 0.05$)
6. No anchor loss was observed in the horizontal direction in the implant group. Instead, a net distal movement was recorded, which was clinically and statistically significant ($P \leq 0.001$). On the other hand, in the control group the molars showed clinically and statistically significant levels of molar mesialization ($P \leq 0.001$)
7. Significant vertical changes were also observed in both the groups. In the implant group, there was significant intrusion of the molars whereas in the conventional group there was extrusion of the molars ($P \leq 0.001$)
8. The incisors in both the groups showed significant intrusion but more so in the implant group ($P < 0.05$)
9. Profile changes (labiomental angle, nasiolabial angle, and facial convexity angle) showed significant changes in both the groups ($P \leq 0.01$) but changes were more pronounced in the implant group ($P < 0.05$)
10. There was statistically significant levels of lip retraction seen in both groups ($P \leq 0.01$) but the intergroup differences were not statistically significant ($P > 0.05$).

Thus, the null hypothesis in the study that mini-implants are efficient for intra-oral anchorage reinforcement for en-masse retraction than conventional methods of anchorage reinforcement is acceptable.

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Original Article

Effect of Resin-based and Bioceramic Based Root Canal Sealers on Post-operative Pain After Single Visit Endodontics: A Randomized Controlled Clinical Trial

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Abstract

Aim: The aim of the present study was to compare the postoperative pain after single visit root canal treatment using AH plus and mineral trioxide aggregate (MTA) fillapex root canal sealers.

Methods: Forty patients with single-rooted tooth requiring endodontic therapy were included in the present study. In every patient, pre-operative pain was recorded. Local anesthesia was administered and rubber dam was applied. Then, endodontic access cavities were prepared. Working length was established and was instrumented upto #25.6%. Then, the samples were randomly divided into two groups: Group 1-AH plus and Group 2-MTA fillapex. Then, the root canal was dried with paper points and obturated with cold lateral compaction technique using gutta-percha cones and AH plus sealer/MTA fillapex. Post-operative pain was recorded by visual analog scale score after 24 h and 48 h after obturation.

Results: Results showed that all the patients in Group A experienced pain and 65% of patients in Group B experienced pain after 24 h. In total 20 patients, 45% of patients in Group A experienced pain, and 25% in Group B after 48 h. There was no significant difference between groups in the incidence of postoperative pain after 48 h.

Conclusion: Post-operative pain associated with MTA fillapex sealer reduced after 24 h as compared to AH plus sealer and there was no difference in post-operative pain after 48 h.

Key words: AH plus, Mineral trioxide aggregate fillapex, Post-operative pain, Root canal sealers, Visual analog scale scores

INTRODUCTION

The goal of endodontic treatment after cleaning and shaping is three-dimensional filling and sealing of root canal system and to prevent microorganisms and promote periradicular tissue repair.[1] Pain management during and after root canal treatment is one of the most important concern of endodontic practice.[2] According to I.A.S.P "pain is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".[3] Pain after root canal treatment is a common sensation, which may initiate a few hours to days postoperatively.[4] It is reported with high incidence rate ranging between 3% and 58%. Pain can be aggravated by -mechanical, chemical, or microbiological injuries to periodontal tissues.[5] There are various factors that may influence postoperative pain after single visit root canal treatment include pulp status, preoperative pain level, the number of root canals present, the choice of instrumentation, the choice of root canal sealer, obturation technique.[4] Sealers placed in the root canal may interfere with periodontal tissues through the apical foramen, lateral canals and can possibly affect the healing process in the periodontium. Thus, the local inflammation produced by root canal obturating

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materials may result in post-operative pain. The severity of inflammatory reactions is influenced by a variety of factors including the root canal sealers composition. It has been suggested that bioceramic materials improve the treatment outcome by promoting the differentiation of odontoblasts and by releasing biologically active substances. The bioceramic materials have been shown to be less cytotoxic compared with resin-based sealer (AH Plus) *in vitro*.[6-9] The aim of the present study was to compare the postoperative pain after single visit root canal treatment using AH plus and mineral trioxide aggregate (MTA) fillapex root canal sealers.

MATERIALS AND METHODS

In this study, a total of 40 patients with single-rooted tooth requiring endodontic therapy were included. Maxillary or mandibular single-rooted teeth diagnosed with symptomatic irreversible pulpitis with either normal apical tissues or symptomatic apical periodontitis were included in the study. Patients with immature apices or root resorption were excluded from the study. Medically compromised patients, pregnant females, patients using medications such as analgesic or anti-inflammatory drugs, patients who refused to participate in the study were also excluded from the study. Patients were randomly divided into two groups Group A = AH plus and Group B = MTA Fillapex. Prior to treatment the patients were instructed how to complete a visual analog scale (VAS) [Figure 1] to determine their pain score. The VAS included a 10 cm straight horizontal line numbered at each centimeter with the following criteria.

Local anesthetic with 2% lignocaine containing 1:80000 epinephrine (Lignox, Indoco Remedies, India) was administered to each patient after preoperative pain levels were recorded [Table 1]. A rubber dam was applied. The endodontic access cavities were prepared with endo access burs (Dentsply Maillefer, Ballaigues, Switzerland). Working length was established with #10 K file and the root canal was instrumented with one shape rotary system up to #25.6% under copious irrigation with 3% sodium hypochlorite and normal saline. Before obturation root canals were final rinse with 5 ml of 17% EDTA solution.

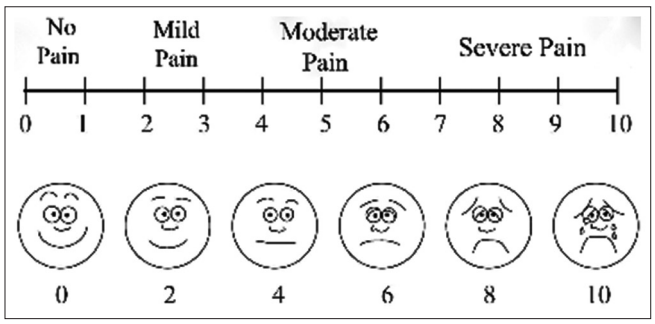

Figure 1: Visual analog scale

In both groups, the root canal was dried with paper points and obturated with cold lateral compaction technique using gutta-percha cones and AH plus sealer/MTA fillapex. Coronal access cavities were restored with direct composite restorations using dentinal adhesives and universal composite resin (Kerr, United States). Postoperative VAS scores were recorded after 24 h and 48 h to determine their post-operative pain [Table 1]. Data were analyzed by student *t*-test using SPSS software.

RESULTS

After 24 h all the patients in Group A experienced pain and 65% of patients in Group B experienced pain. After 48 h in total 20 patients, 45% of patients in Group A experienced pain and 25% in group B [Table 2].

After 24 h, mean VAS score was significantly better for MTA fillapex than AH plus ($P = 0.000166$). However after 48 h, there was no significant difference in mean VAS score between MTA fillapex and AH plus [Figure 2 and Table 3].

DISCUSSION

Postoperative pain in endodontics represents activation of the local inflammatory response in the periapical tissues, which is known to be associated with release of biochemical mediators such as reactive oxygen species (ROS), root canal sealer composition, and obturation methods. ROS have been shown to be associated with inflammatory pain *in vivo* and the production of ROS increased 4–7 times when the human pulp had been treated with the root canal sealers *in vitro*.[4,5]

AH Plus (Dentsply, Konstanz, Germany) is an epoxy resin-based root canal sealer that has the ability to improve the wettability of the dentine and gutta-percha surfaces. Resin-based root canal sealers are preferred as a material

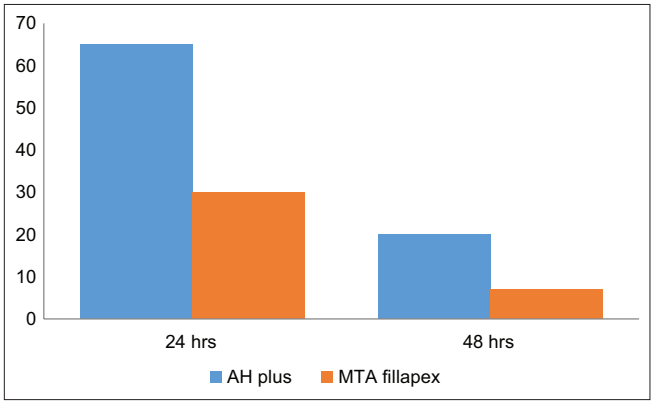

Figure 2: Graphic representation of the post-operative pain intensity after 24 h and 48

Table 1: Pre-operative and post-operative vas score were recorded

Groups					
AH Plus			MTA Fillapex		
Pre-operative	24 h	48 h	Pre-operative	24 h	48 h
7	5	3	6	4	2
4	2	0	8	4	2
6	3	0	7	3	1
5	3	0	5	3	1
4	2	0	6	2	0
5	4	2	5	2	0
4	1	0	4	0	0
8	6	3	5	1	0
7	4	2	4	0	0
5	2	0	5	2	0
3	1	0	4	0	0
4	2	0	5	1	0
4	3	1	5	2	0
6	5	3	3	0	0
6	4	2	3	0	0
5	2	0	6	3	1
8	5	2	4	0	0
4	3	0	4	0	0
5	4	0	4	1	0
6	4	2	6	2	0

MTA: Mineral trioxide aggregate

Table 2: No. (percentage) of patients in the groups

Intensity	AH plus group (%)		MTA fillapex group (%)	
	24 h	48 h	24 h	48 h
No pain	0 (0)	11 (55)	7 (35)	15 (75)
pain	20 (100)	9 (45)	13 (65)	5 (25)

MTA: Mineral trioxide aggregate

Table 3: Pre-operative, 24 h and 48 h mean VAS score in two group

Groups	Pre-operative (total score)	24 h (total score)	48 h (total score)
AH plus	106	65	20
MTA Fillapex	99	30	7
t	0.82047	3.9457	2.09586
	P=0.2085	*P*=0.000166	0.021405

MTA: Mineral trioxide aggregate, VAS: Visual analog scale

of choice due to their ability to penetrate into dentinal tubule and the possibility of creating monoblocks between the root canal filling material and intraarticular dentin.[10]

MTA Fillapex (Angelus, Londrina, Brazil) is a MTA-based, salicylate resin root canal sealer. It contains 13% MTA and salicylate resin. It has high radiopacity, low solubility, low expansion during setting, bactericidal property, biocompatibility, cementum regeneration with good sealing property. MTA Fillapex root canal sealer releases free calcium ions (Ca^{2+}) which help in the healing process by stimulating tissue regeneration.[10]

For the past 30 years, bioceramic-based sealers have only been available for use in endodontics, their rise to popularity in the fields of medicine and dentistry leading to the increased use of bioceramic technology. Bioceramics are ceramic materials which are designed specifically for medical and dental use. Bioceramics are ceramic materials that have been specifically developed for medical and dental use. They include alumina, zirconia, bioactive glass, glass ceramics, hydroxyapatite, and calcium phosphates.[10] In *in vitro*, bioceramic materials have been shown to be less cytotoxic compared with resin-based AH plus. However, AH plus exhibited stronger bonding capacity and higher radioopacity compared bioceramic sealers. The clinical relevance of these features is still uncertain.[5]

Resin-based AH Plus was mildly cytotoxic and released toxic monomers such as bisphenol A diglicidyl ether. Zhou *et al.* concluded that AH Plus was cytotoxic only as freshly mixed sealer and allowed growth of gingival fibroblasts on the surface of the set material.[11] Benetti *et al.* conducted a study on cytotoxicity and biocompatibility on Sealer Plus BC, AH Plus, and MTA Fillapex. Based on the result of this study, MTA fillapex and AH plus caused minor cytotoxic effects toward L929 cells.[12]

Graunaite *et al.* revealed that AH Plus sealer and Total Fill sealer have similar effect on the occurrence and intensity of postoperative pain in teeth after 24 h and 48 h.[5] In the present study, after 48 h there was no significant difference in mean VAS score between MTA fillapex and AH plus. After 24 h, MTA fillapex was significantly better than AH plus. This may occur due to the release of biochemical mediators such as ROS.

Many clinician focus on drugs for pain management such as NSAID's along with antibiotics to prevent post-endodontic pain.[13] Ates *et al.* in 2018 compared the postoperative pain after root canal treatment using a carrier-based obturation system and two different sealers. Based on the result of this study, they concluded that iRoot SP sealer(Bioceramic based sealer) was associated with less analgesic intake compared to AH Plus sealer (Resin based sealer).[4]

Acc. To Paz (2018), single cone with Bioceramic root canal sealer referred post-endodontic pain more frequently than continuous wave with resin root canal sealer or Lateral condensation with resin root canal sealer. Single cone with Bioceramic root canal sealer also showed the highest percentage of moderate post-endodontic pain intensity felt during the 7 day evaluation period. Obturation technique may influence postoperative pain after single-visit root canal. This could be the probable reason for pain after 7 days.[14]

There has been no study reported till date comparing the effect of AH plus sealer and MTA fillapex sealer

on post-operative pain after single-visit endodontics. Therefore furthermore studies are required in this field.

CONCLUSION

Within the limitation of this study, it can be concluded that post-operative pain associated with MTA fillapex sealer reduced after 24 h as compared to AH plus sealer. There was no difference in post-operative pain after 48 h.

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Original Article

Comparative Study of Serum Creatinine Level in Normotensive and Hypertensive Individuals

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Abstract

Background: Hypertension is a major contributor to the global disease burden. Persistent hypertension is a leading cause of chronic renal failure. One of the simple and most commonly performed renal function tests to determine the functioning state of the kidney is the determination of serum creatinine level.

Aims and Objectives: To evaluate and compare serum creatinine levels in hypertensive and normotensive individuals.

Materials and Methods: The study was conducted in tertiary care hospital. The study was done in 50 hypertensive patients and 50 normotensive subjects between the age group of 40 and 60 years. Blood pressure was measured using sphygmomanometer and serum creatinine was estimated by the alkaline picrate method.

Results: The serum creatinine was higher in hypertensive cases than normotensive controls, i.e., 2.15 ± 0.47 mg/dl versus 0.86 ± 0.14 mg/dl, $P < 0.0001$. Serum creatinine level is higher in Stage-1 ($P < 0.01$) and Stage-2 hypertensive subjects ($P < 0.01$) than normal.

Conclusion: From this study, it can be concluded that serum creatinine is an important indicator for the determination of functional state of the kidneys, so routine monitoring of serum creatinine level is required in hypertensive patients to prevent end-stage renal disease.

Key words: Blood pressure, End-stage renal disease, Hypertension, Serum creatinine

INTRODUCTION

Hypertension is a major contributor to the global disease burden. It poses an important public health challenge to both economically developing and developed countries, including India.[1] Persistent hypertension is a leading cause of chronic renal failure (CRF).[2]

One of the simple and most commonly performed renal function tests to determine the functioning state of the kidney is the determination of serum creatinine level.

Creatinine is a breakdown product of creatine phosphate. Creatine is synthesized in the liver, transported to the muscles for storage as creatine phosphate, and then catabolized in the muscle to form creatinine. Creatinine is removed from the body entirely by the kidneys. If kidney function is abnormal, creatinine level will increase in the blood.[3-5]

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Aims and Objectives

To evaluate and compare serum creatinine levels in hypertensive and normotensive individuals.

MATERIALS AND METHODS

This study was carried out in a tertiary care hospital. The study was done in 50 hypertensive patients and 50 normotensive subjects between the age group of 40 and 60 years, which included both males and females.

Inclusion Criteria

The criteria of considering patient hypertensive was blood pressure (BP) >140/90 mm of Hg based on the average of two readings with a duration of <5 years on

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medication. The controls were healthy volunteers with BP <120/80 mm of Hg.[6]

Exclusion Criteria

The subjects with any associated diseases such as diabetes, peripheral vascular diseases, pregnancy, alcohol, tobacco, smoking, terminally ill hypertensive patients, leprosy, or other conditions, which are known to cause peripheral neuropathy were excluded from the study.

Estimation of Serum Creatinine Level[7-9]

- Fresh sample of serum with no evidence of hemolysis was specimen of choice.
- Serum creatinine level was estimated by the alkaline picrate method.

Measurement of BP[10-11]

- BP was measured by an indirect method using a sphygmomanometer.
- Current clinical criteria for defining hypertension are generally based on the average of two or more BP readings during each or more outpatient visits.

RESULTS

Statistical Analysis

All the data would be selected randomly and tabulated, and then analyzed with appropriate statistical tools "MedCalc". Data will be presented as mean with standard deviation or proportions as appropriate. Mean, median, standard deviation, and variance would be calculated and the following statistical significance tests would be applied.

1. Student's paired *t*-test will be used as the statistical tool to test for significance of observed mean differences.

Finally, the calculated value should be compared with the tabulated value at particular degree of freedom and finds the level of significance.

A "*P*-value" should be considered to be non-significant if >0.05 and significant if <0.05.

For Test of Significance, Here we use

"Test of significance difference between two means {| t | –Test}"

| t | cal=12.68 {at 95% confidence limit,with degree of freedom =58, | t | tab = 1.96}

| t | cal > | t | tab {12.68 >1.96} at 5% level of significance.

Hence, the hypertensive group is statistically significant than the Normotensive group, according to their Systolic BP, in hypertensive group mean was much more than Normotensive group, with *P* – value {$P < 0.0001$}.

For Test of Significance, Here we use

"Test of significance difference between two means {| t | –Test}"

| t |cal=14.714 {at 95% confidence limit,with degree of freedom =58, | t | tab = 1.96}

| t | cal > | t | tab { 14.714 >1.96} at 5% level of significance

Hence, Hypertensive group is Statistically significant than Normotensive group, according to their Diastolic BP, in Hypertensive group mean was much more than Normotensive group, with *P* – value{$P < 0.0001$}.

For Test of Significance, Here we use

"Test of significance difference between two means {| t | –Test}"

| t |cal=14.408 {at 95% confidence limit,with degree of freedom =58, | t | tab = 1.96}

| t | cal >| t | tab { 14.408 >1.96} at 5% level of significance.

Hence, the hypertensive group is Statistically significant than the Normotensive group, according to their serum creatinine, in hypertensive group mean was much less than Normotensive group, with *P* – value{$P < 0.0001$}.

For Test of Significance, Here we use

"Test of significance difference between two means {| t | –Test}"

At 95% confidence limit,with degree of freedom 58, | t | tab = 1.96

In all the above cases | t | cal > | t | tab {at 5% level of significance}.

Hence, the hypertensive group is statistically significant than the Normotensive group, according to their Systolic BP, Diastolic BP, serum creatinine in hypertensive group means are much less than Normotensive group, with *P* – value {$P < 0.05$}.

DISCUSSION

Several studies worldwide have been done on serum creatinine in relation to the risk of chronic kidney disease such as CRF and end-stage renal disease (ESRD), but a few studies are in relation to hypertension have been found yet. The observations of our study are discussed as below:

In our study serum creatinine was higher in hypertensive cases than normotensive controls, i.e., 2.15 ± 0.47 mg/dl versus 0.86 ± 0.14 mg/dl, $P < 0.0001$ [Tables 1-4 and Graphs 1-4]. The creatinine difference was found statistically significant. Similar findings were obtained in multiple risk factor intervention trial, which showed that no relationship was seen between BP at baseline and serum creatinine levels, but in hypertensive patients showed greatest increase in serum creatinine over 6 years follow up.[12]

Similarly, findings of study by Nagah *et al.* in Sudan have shown that mean values of serum creatinine was higher in hypertensive cases than normotensive controls, i.e., 141.3 ± 39.0 μ mol/L versus 52.4 ± 18.0 μ mol/L and the difference was statistically significant. They found elevated serum creatinine and protein, in addition to the presence of protein in urine might to be direct effect of hypertension and its related complication on renal function.[13] A 9 years follow-up study on 897 subjects in hypertension conducted by Rosanky *et al.*, has shown that essential hypertensive subjects had a considerably high rate of turndown in renal function compared with normotensive subjects.[14]

The results of National Health and Nutrition Examination Survey third have shown that serum creatinine level is an indicator of chronic renal disease and was found common and strongly related to inadequate treatment of hypertension.[15]

A study done in Japan by Ishida *et al.*, to know the effect of high BP on renal function by estimating serum creatinine as a marker of kidney functioning and shown that high serum creatinine levels are accelerated in hypertensive subjects and in those with proteinuria and especially in those in whom both are present.[16]

In contrast, study by Kadri *et al.*, showed that serum creatinine was higher in hypertensive subjects than normotensive subjects but the differences were not statistically significant.[17] A study done by Wannamethee *et al.*, have shown that elevated serum creatinine was found in 13.8% of hypertensive cases and in 8.6% of normotensive subjects (test of difference, $P < 0.001$). The serum creatinine levels in male hypertensive cases was higher than male normotensive control, i.e., 0.95 ± 0.05 mg/dl versus 0.89 ± 0.05 mg/dl ($P = 0.396$). The difference was not found statistically insignificant.[18] Another study done by Sarkar *et al.* has shown that serum creatinine was higher in hypertensive cases than normotensive control group i.e., 0.86 ± 3.20 mg/dl versus

Table 1: Comparison of systolic blood pressure

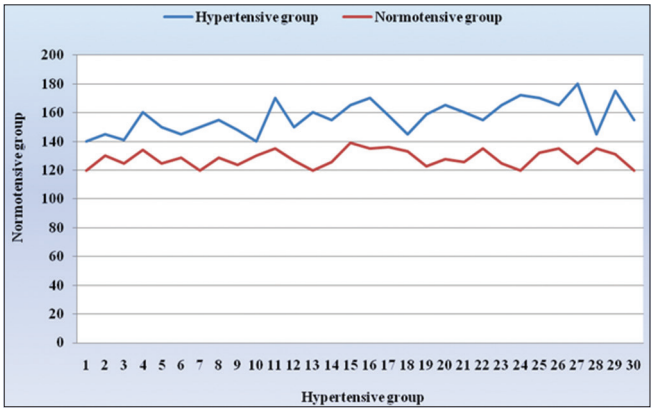
Parameter	Hypertensive (*n*=30)	Normotensive (*n*=30)
Mean	157.10	128.40
Standard deviation	11.03	5.65

Table 2: Comparison of diastolic blood pressure

Parameter	Hypertensive (*n*=30)	Normotensive (*n*=30)
Mean	96.87	82.27
Standard deviation	4.67	2.78

Table 3: Comparison of serum creatinine

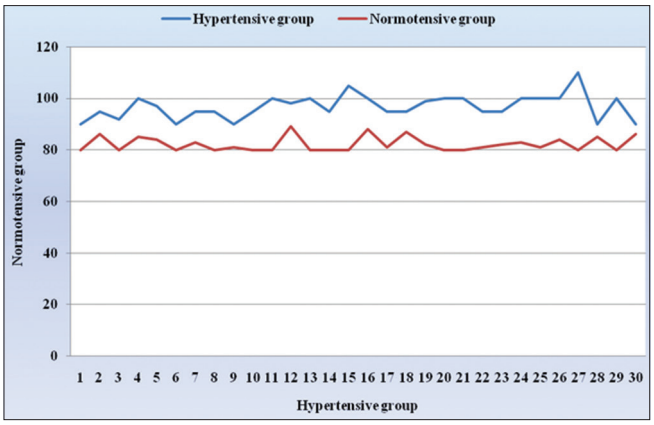
Parameter	Hypertensive (*n*=30)	Normotensive (*n*=30)
Mean	2.15	0.86
Standard deviation	0.47	0.14



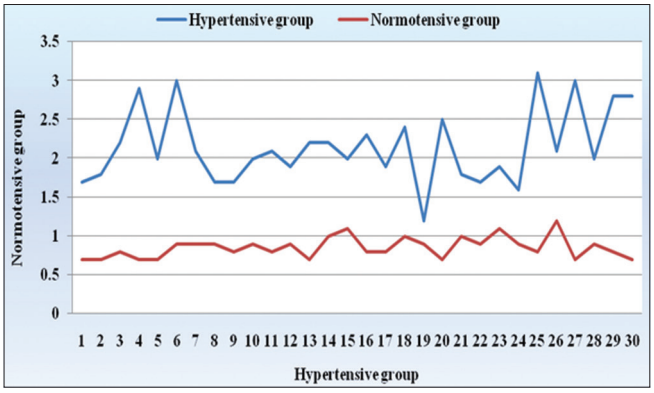
Graph 1: Comparison of systolic blood pressure between the two groups

Table 4: Comparison of different parameters

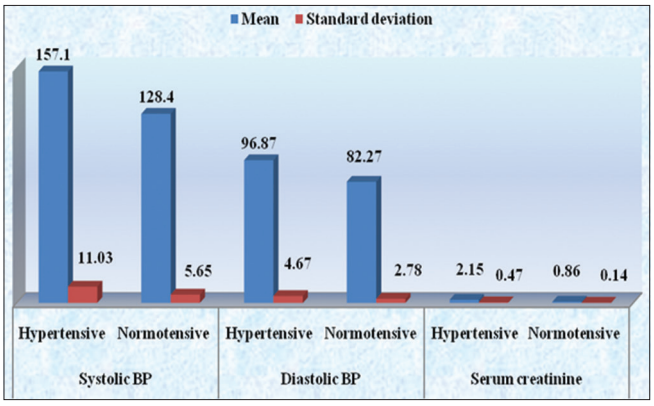
Parameter	Hypertensive (*n*=30) Mean±s.d.	Normotensive (*n*=30) Mean±s.d.	|t|cal	d.f	*P*-value	Conclusion
Systolic BP	157.1±11.03	128.4±5.65	12.68	58	*P*<0.0001	Significant
Diastolic BP	96.87±4.67	82.27±2.78	14.714	58	*P*<0.0001	Significant
Serum creatinine	2.15±0.47	0.86±0.14	14.408	58	*P*<0.0001	Significant



Graph 2: Comparison of diastolic blood pressure between two groups



Graph 3: Comparison of serum creatinine between two groups



Graph 4: Comparison of different parameters

0.79 ± 4.01 mg/dl, $P = 0.990$, but the difference was not statistically significant.[19]

The present study shows that serum creatinine level was higher in hypertensive cases than in normal healthy controls. Hence, it is concluded that hypertensive patients are more prone to develop elevated serum creatinine levels and chronic kidney diseases. Hence to prevent the chronic kidney disease and other consequences in hypertension, it is needed to plan the estimation of serum creatinine in daily clinical practice.

CONCLUSION

- The following conclusion can be drawn from this study serum creatinine is higher in hypertensive subjects than non-hypertensive subjects.
- As serum creatinine is an important indicator for the determination of the functional state of the kidneys, so routine monitoring of serum creatinine level is required in hypertensive patients to prevent ESRD.

DATA AVAILABILITY

The data used to support the findings of this study are included within this article.

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Original Article

Prospective Study of Incision Characteristics for Surgically Induced Astigmatism in Small Incision Cataract Surgery at Tertiary Rural Centre

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Abstract

Introduction: Cataract is a major cause of blindness in developing countries. The developing countries cannot afford expensive modern technologies to treat these poor patients. Therefore a cost effective, fast, machine independent procedure is necessary. Manual sutureless small incision cataract surgery is comparable to other relative new techniques and has been increased in popularity.

Materials and Methods:
- This prospective, non comparative, observational hospital based study enrolled 350 eyes of 329 cases over 4 years and 6 months from August 2011 to March 2016
- It was carried out at the department of Ophthalmology, R.D Gardi Medical College, Ujjain, (M.P.)
- All the patients of cataract where manual, sutureless, small incision cataract surgery was possible, were included
- The pre-operative refraction, keratometry, autoref Keratometer (Nidek), A-scan (Sonomed) and intraocular lens calculation was done accordingly
- Post-operative results recorded on second and seventh post-operative day and 4 and 8 weeks from surgery.

Results: Correlation of surgically induced astigmatism (SIA) and wound size: Mean (SD) was 0.76 (0.44) for 7 mm and 0.48 (0.41) for 6mm group. S.I.A. of 6 and 7 mm groups was significantly different (P = 0.0002) (95% C.I. = −0.50–−0.25). Correlation of SIA and wound shape: Mean (SD) was 0.95 (0.39) for straight and 0.46 (0.39) for frown group. S.I.A. of straight and frown incision groups was significantly different (P < 0.0001) (95% C.I. = −0.75–−0.5). S.I.A: 79.42% had S.I.A. <1.00 D, 12.85% had S.I.A. 1.25 D–2.00 D, 7.73% had nil.

Conclusions: Manual small incision cataract surgery is a safe and effective procedure with good overall outcomes resulting in rapid visual rehabilitation. Post-operative astigmatism was significantly more in straight (P < 0.0001) and 7 mm incision (P= 0.0002) as compared to frown and 6 mm incision.

Key words: Incision, Small incision cataract surgery, Surgically induced astigmatism

INTRODUCTION

Cataract, a major cause of blindness in developing countries, contributing to over 90% of the total disability adjusted life years[1] and is a big health morbidity. Although cataract surgery is the most cost effective intervention, its delivery in developing country has many issues and challenges.[2] The developing countries cannot afford expensive modern technologies to treat these poor patients. Therefore, a cost effective, fast, machine independent procedure is necessary.

This prospective, non-comparative, and observational hospital-based study enrolled 350 eyes of 329 cases over 4 years and 6 months in central part of Indian, Ujjain.

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MATERIALS AND METHODS

Study Site and Setting

- This prospective, non-comparative, observational hospital-based study enrolled 350 eyes of 329 cases over 4 years and 6 months from August 2011 to March 2016
- It was carried out at the Department of Ophthalmology, R.D Gardi Medical College, Ujjain, (M.P.) a tertiary, referral and teaching hospital, receiving patients from semi-urban and rural populations.

Inclusion Criteria

All the patients of cataract where manual, sutureless, and small incision cataract surgery (MSICS) was possible were included in the study. Same surgeon was operator in all.

Exclusion Criteria

Any other ocular co-morbidities as pterygium, corneal degeneration and dystrophy, ocular injuries, uveitis, retinal detachment and vitreous hemorrhage, congenital cataract, high myopia, and lens induced glaucoma were excluded from the study.

Data Collection Techniques

All datum was entered in pro forma (Excel) and was analyzed statistically with GraphPad Prism 6 version 6.02. Demographic particulars, presenting complaint, general, systemic, and detailed ocular examination (visual acuity, anterior segment torch light, and slit lamp) were performed and intraocular pressure (applanation tonometry); ophthalmoscopy direct and indirect were done.

The pre-operative refraction, keratometry, axial length of eye was recorded with the help of autoref Keratometer (Nidek), A-scan (Sonomed). IOL calculation was done accordingly. B-scan was done whenever indicated.

The operative procedures were recorded with specific reference to the type of procedure done, size and shape of wound and any intra-operative complication noted. The post-operative results were recorded on 2nd and 7th post-operative day and 4 and 8 weeks from surgery.

The post-operative results were recorded next which included the visual acuity, slit lamp examination, refraction, post-operative keratometry using same keratometer, intra-ocular pressure measurement, fundus examination. Special attention was given to the amount of astigmatism induced postoperatively, which was calculated by simple subtraction method. Detailed analysis of all datum was done.

Statistical Analysis

Unpaired *t*-test was applied using GraphPad Prism 6 version 6.02. $P < 0.05$ is considered statistically significant.

Ethical Consideration

- Project proposal was submitted and approved by the college Research and Ethics Committees. The decision to admit and treat was based on clinical grounds/investigations and not for the sake of the study. Informed consent was obtained from patients after explaining the objectives and protocol of the study.

RESULTS

Correlation of SIA and Wound Size (6 mm and 7 mm) (Figure 1)

147 and 203 cases had wounds of 7 & 6 mm; respectively. The Mean (SD) was 0.76 (0.44) for 7mm and 0.48 (0.41) for 6mm group, their respective medians being 0.75 & 0.50. S.I.A. was not normally distributed and unpaired t test (two tailed) was applied. S.I.A. of 6 & 7 mm groups was significantly different (*p=0.0002*) {95% C.I. = -0.50 to -0.25}. So, it can be concluded that there is a *strong association between the size of the wound and the S.I.A.*

Correlation of SIA and Wound Shape (Straight and Frown) (Figure 2)

95 and 255 cases had straight & frown incisions; respectively. The Mean (SD) was 0.95 (0.39) for straight and 0.46 (0.39) for the frown group, their respective medians being 0.1 & 0.5. S.I.A. was not normally distributed and unpaired t test (two tailed) was applied. S.I.A. of straight & frown incision groups was significantly different (*p< 0.0001*) {95% C.I. = -0.75 to -0.5}. Thus, there is a *strong association between shape of the wound and the S.I.A.*

Comparative assessment of Pre and post operative amount of astigmatism: (n=350) (Table 1)

Pre-operatively 191 cases had astigmatism upto 1 D, while post operatively 221 were having it. Pre-operatively 25 cases had more than 2 D, while postoperatively only 3 cases had more than 2D ($P < 0.01$, Unpaired T test).

Comparative assessment of Pre and post operative type of astigmatism: (n=350) (Table 2)

Pre-operatively 112 cases had against the rule astigmatism, while post operatively 206 were having it. Pre-operatively 66 cases had no astigmatism, while postoperatively only 7 had it ($P < 0.05$, Chi square test).

S.I.A. {Surgically Induced Astigmatism} : (Table 3) (Figure 3)

79.42% had S.I.A. < 1.00D, 12.85% had S.I.A. 1.25D to 2.00D and none > 2.00D. 7.73% cases had nil.

Post-op unaided Visual acuity at 8 week: (Table 4)

92% had unaided visual acuity better than 6/18, with only 8% less than 6/18.

Operative Procedures

All the incisions were superiorly placed and around 2.5mm away from limbus.

In our study, size of incision was 7mm in 42% eyes and 6mm in 58% (Table 5).

Shape of incision was frown in 72.85% and remaining had straight incision (Table 6).

DISCUSSION

Modern cataract surgery, aims to achieve a better unaided visual acuity with rapid post-surgical recovery and minimal surgery related complications. Early visual rehabilitation, better unaided visual acuity and surgical safety can be achieved in a great measure by reducing the incision size. Incision size depends on the mode of nucleus delivery and the type of intraocular lens used.

In this study, we have tried to assess the surgical outcome in terms of visual recovery, induced astigmatism in eyes undergoing cataract surgery by the technique of MSICS. Post-operative astigmatism plays an important role in the evaluation of final outcome of surgery. Astigmatic outcomes (amount and type) were studied in detail as primary outcome of interest of sutureless small incision cataract surgery (SICS).

SICS in Different Types of Cataract

There were no major appreciable differences in type of cataract with predominance of nuclear cataract (38%), combined (cortical, nuclear, and posterior subcapsular cataract) being 31%, cortical 22%, and posterior subcapsular cataract 9%. We found that MSICS can be done in almost all types of cataract with good visual outcome. Thomas *et al.*[3] also found that manual small incision technique is utilized to achieve the desired outcome as often as possible and for all types of cataracts.

Singh *et al.*[4] did a prospective randomized controlled trial, involving 93 patients and concluded that SICS with implantation of rigid PMMA lens is a suitable surgical technique for immature cataract in developing countries. A study of 100 eyes where, 16 had intumescent, 67 mature, and 17 hypermature cataract concluded that MSICS proves to be safe and efficacious alternative for white cataracts.[5]

Pre-operative Astigmatism

Type of astigmatism

In our study, against the rule astigmatism was seen in 32%, with-the-rule in 25%, oblique in 24%, and nil in 19%. We observed that pre-operative assessment plays important role in determining the amount of astigmatism postoperatively. Ernest *et al.* in a multifactorial, multivariate study of 426 patients analyzing factors influencing axis of the induced astigmatism, most important for a postoperative astigmatism against the rule is using the no-stitch-technique and a pre-operative astigmatism against the rule.[6]

Nielsen in 1995 did prospective evaluation of SIA and astigmatic keratotomy effects of various self-sealing small incisions. He concluded that if pre-operative astigmatism is considered in selecting incision type and location for SICS, one can minimize post-operative keratometric astigmatism.[7]

Operative Procedures

Wound construction

In cataract surgery, incision size determines various factors such as wound stability, corneal curvature changes, post-operative induced astigmatism, and visual rehabilitation.[8]

In our study, size of incision was 7 mm in 42% eyes and 6 mm in 58%; while shape of incision was frown in 73% and remaining had straight incision. All the incisions were superiorly placed and around 2.5 mm away from limbus. We found that frown incision induces less astigmatism and smaller the incision; less will be the induced astigmatism, this being in accordance with the literature.

Singer developed frown incision in 1991 and a series of 62 eyes with 6 mm and 7 mm incisions were prospectively evaluated for induced astigmatism. They propounded that frown incision provided many benefits.[9]

Huang and Tseng in 1997 did the corneal topographic analysis of small incision and concluded that smaller produces less astigmatism, faster post-operative recovery and more stable refraction.[10]

Anwar[11] in 1999 studied the changes in SIA after Extra-capsular Cataract Extraction. Post-operative astigmatism was more when extraction is done through the incision and more anterior incision having greater induced astigmatism.

Burgansky *et al.* (2002) found that the 7.0 mm group had statistically significantly greater induced astigmatism than the 5.0 mm group ($P = 0.01$, simple subtraction; $P = 0.002$, vector analysis).[12]

Haldipurkar *et al.*[13] suggested that the basis of MSICS is the tunnel construction for entry to the anterior chamber. The parameters important for the structural integrity of the tunnel are the self-sealing property of the tunnel, location with respect to the limbus and shape of the wound.

POST-OPERATIVE RESULTS

Post-operative type of astigmatism

In our study, postoperatively, 59% had against-the-rule astigmatism, 29% had oblique, 20% had with-the-rule, and 2% had no astigmatism, as we had superiorly placed incisions ($P < 0.05$). Our results are in accordance with Nielsen[14] who did astigmatic keratometric evaluation of the incisions and found temporal resulted in with-the-rule induced change and superior ones against-the-rule.

Oshika *et al.* found superior incision had slight against-the-rule astigmatic changes, whereas slight with-the-rule astigmatism in the temporal incision. Amount of irregular astigmatism 1 day after surgery being significantly greater than pre-operative ($P < 0.001$), but not thereafter.[15]

Post-operative amount of astigmatism

In this study, postoperatively, majority of patients (63%) had amount of astigmatism <1.00D, while 34% patients had astigmatism in between 1.25D and 2.00D and only 1% had being more than 2.00D. The mean post-operative corneal astigmatism was 0.92 ($P < 0.01$) at the end of 8 weeks which was comparable to Ang *et al.*[16] in whom the mean post-operative astigmatism was significantly higher than preoperatively (1.40D vs. 0.99D, $P = 0.02$).

Gogate *et al.* (2003) found that the corneal astigmatism was (1.01 ± 0.97) D ($n = 95$) 1 week postoperatively and (0.62 ± 0.53) D ($n = 90$) at 1 month ($P < 0.01$).[17]

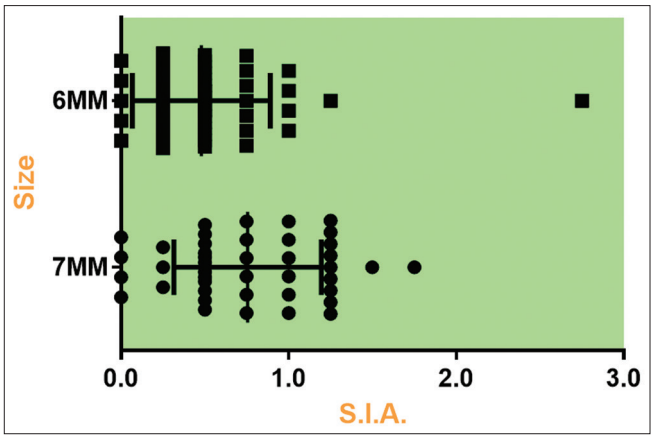
Gokhale and Sawhney (2005) propounded mean astigmatism induced by surgery was 1.28 D × 2.9 degrees for superior incision.[18]

In a non-randomized interventional case series of 102 patients with BBC undergoing cataract extraction by MSICS, superior scleral tunnel was employed in 30.4%, and had post-operative astigmatism of –1.08 D.[19]

SIA

In our study, 79% had SIA <1.00D with only 14% patients had SIA in between 1.25D and 2.00D and no one more than 2.00D. About 7% patients had no SIA. The mean (SD) was 0.76 (0.44) for 7 mm group and 0.48 (0.41) for the 6 mm group. The mean (SD) was 0.95 (0.39) for straight group and 0.46 (0.39) for the frown group.

The results were encouraging and in accordance with the world literature, as discussed below.



Figures 1: Unpaired test data of the surgically induced astigmatism of the two wound sizes

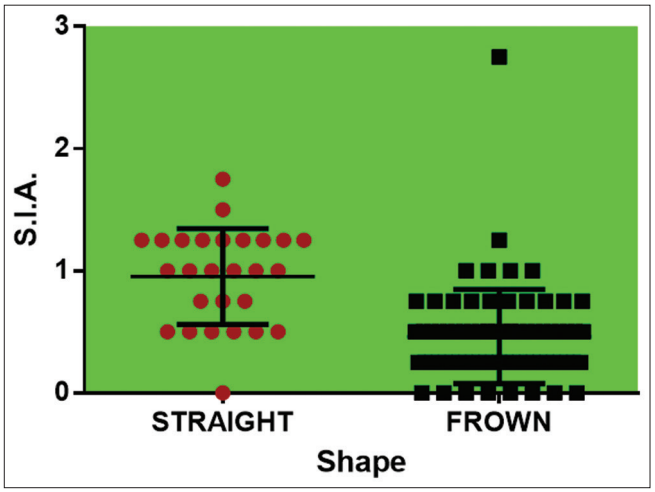


Figure 2: Unpaired test data of the surgically induced astigmatism of the two wound shapes

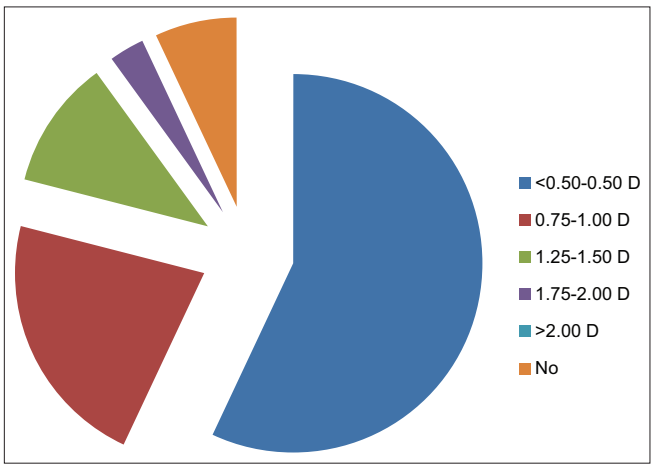


Figure 3: Surgically Induced Astigmatism encountered in the study

Singer did vector analysis calculations of diopters (D) of mean induced keratometric astigmatism for the frown incision versus the scleral pocket incision groups were 0.80 D versus 1.19 D ($P = 0.0263$) at 1 day; 0.74 D versus 1.03 D

Table 1: Comparative assessment of pre- and post-operative amount of astigmatism: (*n*=350)

Amount of astigmatism	Pre-operative	Post-operative
Nil	66	7
0.25–1.00 D	191	221
1.25–2.00 D	68	119
>2.00 D	25	3

Table 2: Comparative assessment of pre- and post-operative type of astigmatism: (*n*=350)

Type of astigmatism	Pre-operative	Post-operative
With the rule	88	70
Against the rule	112	206
Oblique	84	67
No	66	7

Table 3: SIA found in the study (*n*=350)

SIA (at 8 week)	No. of Eyes	Percentage
0.25–0.50 D	201	57.42
0.75–1.00 D	77	22
1.25–1.50 D	37	10.57
1.75–2.00 D	8	2.28
>2.00 D	0	0
No	27	7.73
Total	350	100

SIA: Surgically induced astigmatism

Table 4: The post-operative unaided visual acuity at 8th weeks (*n*=350)

Post-operative visual acuity	No. of eyes	Percentage
6/9 or better	147	42
6/12–6/18	175	50
6/24–6/36	28	8
Total	350	100

Table 5: Size of incision (*n*=350)

Size of wound	No. of Eyes	Percentage
7 mm	147	42
6 mm	203	58
Total	350	100

Table 6: Shape of incision (*n*=350)

Shape of wound	No. of Eyes	Percentage
Straight	95	27.14
Frown	254	72.85
Total	350	100

($P = 0.0547$) at 1 week; 0.71 D versus 1.07 D ($P = 0.0057$) at 4 weeks; 0.84 D versus 1.15 D ($P = 0.0072$) at 6 months; and 0.82 D versus 1.30 D ($P = 0.0144$) at 1 year.[9]

Steinert *et al.*[20] evaluated induced astigmatism and postoperative wound stability in a randomized prospective study of 130 patients. Vector analysis calculations of prism D of mean post-operative-induced keratometric astigmatism for the small incision versus conventional incision groups were, at day 1, 1.54 D versus 3.07 D ($P < 0.0001$); at weeks 1 to 2, 1.00 D versus 2.43 D ($P < 0.0001$); at 1 month, 0.98 D versus 1.44 D ($P = 0.004$); and at 3 months, 0.82 D versus 1.03 D ($P = 0.089$).

Uusitalo *et al.*[21] in 1993 studied the outcomes of SICS. Less initial induced astigmatism was demonstrated at day 7 with a 4.0-mm incision (0.1 ± 0.53 D) compared with a 7.5-mm incision (1.90 ± 1.97). The low amount of induced cylinder, rapid stabilization of the wound, and faster visual rehabilitation confirms the advantage of small-incision cataract surgery to large-incision surgery.

Uusitalo and Tarkkanen found that mean SIA in all eyes was 0.2 D ± 0.7 (SD); 91.2% were within ±1.0 D of preoperative values. Improvement after first-eye surgery was: Snellen visual acuity (95.0%), VF-14 score (89.4%), satisfaction with vision (80.1%), self-reported trouble with vision (75.8%), and cataract symptoms (75.1%).[22]

Archana *et al.* observed that SIA was 1.85 ± 0.62 D, 1.56 ± 0.54 D, 1.35 ± 0.49 D, and 1.34 ± 0.45 D at 1 week, 2 weeks, 4 weeks, and 8 weeks postoperatively. Surgically-induced astigmatism is significantly higher in clear corneal MSICS than in sclero-corneal. Thus, the study confirmed the safety and improvement in acuity after small-incision cataract surgery using sclero-corneal tunnel incision.[23]

Thus, our results are in accordance with the world literature.

Post-operative Unaided Visual Acuity

In our study, majority of the patients (91%) had unaided visual acuity better than 6/18, with only 9% of patients <6/18. Our results are comparable with the world literature, as mentioned below. Wright *et al.* where 56% and 70% of patients had unaided visual acuities of 6/12 or better at 3 weeks and 3 months, respectively.[24] Mpyet *et al.* found that on 5th day and 6 weeks uncorrected visual acuity (UCVA) was good in 43.7% and 69.0%, respectively.[25] Venkatesh *et al.* found that on the 40th post-operative day, 78.4% achieved UCVA of 6/18 or better and 97.1% best-corrected visual acuity of 6/18 or better.[19]

Singh *et al.* in 2009 did a study where in SICS group ($n = 89$), more than three quarters of the patients had good visual outcome (6/6-6/18) on 1st post-operative day ($P = 0.065$).[4]

Trivedy[26] in 2011 carried out a retrospective interventional study. Out of 368 subjects, 81.8% of the patients achieved post-operative UCVA of 6/18 and better by the 4th week. Fifteen patients were found to have posterior capsular

opacification and had the UCVA between 6/24 and 6/60. The study results show that high quality cataract surgery can be attained in a high volume setting.

Sherwin *et al.* found that without correction (uncorrected VA), nearly 80% (78.7%) achieved a "good" outcome (VA 6/6-6/18), 19.8% were "borderline" (VA <6/18-6/60), and 1.5% had a poor (VA <6/60) outcome. With pinhole-correction, the proportion of good outcomes increased to 89.4%, and poor outcomes decreased to 0.9%. Poor outcomes were most commonly due to ocular co-morbidities (54.5%) and refractive error (36.4%). Older age and pre-operative blindness were strongly associated with borderline or poor visual outcomes.[27]

Some studies like Sadiq *et al.* got UCVA of 6/6, on 1st post-operative week in 8.3% cases. By the end of 12th post-operative weeks, 34.5% had the same. About 66.7%, 75%, and 83.3% eyes had best correctable visual acuity of 6/6 after 4 weeks, 8 weeks, and 12 weeks, respectively.[28]

Murthy *et al.*[29] found among cataract-operated eyes, 18.7% presented with VA > or = 20/32 and 18.0% were <20/200. With best-corrected acuity, the corresponding percentages were 55.7% and 11.0%.

CONCLUSIONS

MSICS is a safe and effective procedure with good overall outcomes and results in rapid visual rehabilitation and can be done in almost all types of cataract with good visual outcomes.

The amount of post-operative astigmatism was significantly more in straight incision ($P < 0.0001$) and in 7 mm (longer) incision ($P = 0.0002$) as compared to frown incision and 6 mm incision.

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Original Article

Prophylactic Antibiotics in Various Surgeries: A Prospective Study

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Abstract

Background: In recent years, there is an improvement of our clinician's approach to the appropriate and proper use of prophylactic antibiotics in surgical patients. The present study was done to evaluate the effect of Prophylactic antibiotics before operative procedures versus postoperative antibiotic.

Materials and Methods: This prospective, observational, and comparative study was conducted on 130 adult patients who underwent surgical procedures in the Gynecology and Surgery departments of Autonomous State Medical College and Hospital, Shahjahanpur, Uttar Pradesh, India from 1st January to 31st May 2021.

Results: Among 130 study subjects, 33 (25.38%) had Cesarean section, 25 (19.23%) patients had laparotomy, 20 (15.38%) patients had operative laparoscopy, 8 (6.15%) patients had abdominal hysterectomy, 12 (9.23%) patients had vaginal hysterectomy, 10 (7.69%) patients had diagnostic laparoscopy, while 22 (16.92%) patients had hydrocele/hernia repair. Majority, i.e. 78 (60%) patients had clean wound while 52 (40%) patients had a clean-contaminated wound. In 105 (80.76%) patients, the surgery lasted for 1–2 h while 25 (19.23%) had surgery for >2 h. Prophylactic antibiotic was not given for >24 h even if duration was more or blood loss was more. There was no infection in clean wounds. The prevalence of superficial surgical site infections (SSI) was 3.84% while the prevalence of deep SSI in the clean-contaminated wound was 1.53%. Organ-specific infection was not seen in any of the patient.

Conclusion: In the present study, prevalence of SSI was very low. This might be because proper and appropriate prophylactic antibiotic was given in all cases in tertiary care hospitals. Furthermore, proper skin preparation and strict asepsis and antisepsis was followed.

Key words: Surgical site infection, Surgical antibiotic prophylaxis, Timing, Dosage, Duration of surgery

INTRODUCTION

A surgical site infection (SSI) is defined as an infection that occurs at or near a surgical incision within 30 days of the procedure. It is within 1 year if an implant is left in place.[1]

Table 1 shows classification of surgical wounds.[1] SSI is one of the major complications of operative procedures. It is among the most common nosocomial infections.[2]

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SSI causes significant morbidity and mortality. It increases the healthcare costs.[3]

Patients who develop SSIs are 5 times more likely to be readmitted to the hospital. 60%of them are more likely to spend time in the intensive care unit. They are 2 times likely to die compared with surgical patients without the infections.[4]

The most common organisms causing SSIs are.[5]

- *Staphylococcus aureus*
- *Staphylococcus epidermidis*
- *Aerobic streptococci*
- *Anaerobic cocci*

Surgical antibiotic prophylaxis (SAP) is a very brief course of antibiotics initiated closely before the start of operative

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Table 1: CDC Classification of surgical wounds[1]

Class	Description
Class I-Clean	An uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or uninfected urinary tract is not entered. In addition, clean wounds are primarily closed and, if necessary, drained with closed drainage.
Class II- Clean contaminated	An operative wound in which the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions and without unusual contamination. Specifically, operations involving the biliary tract, appendix, vagina, and oropharynx are included in this category
Class III- Contaminated	Open, fresh, accidental wounds. In addition, operations with major breaks in sterile technique (e.g., open cardiac massage) or gross spillage from the gastrointestinal tract, and incisions in which acute, no purulent inflammation is encountered
Class IV- Dirty	Old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera means that the organisms causing postoperative infection were present in the operative field before the operation

procedures. The aim of this is to reduce postoperative SSI.[6]

Surgical Care Improvement Project performance measures to reduce postoperative SSI include (the first three comprise the core infection prevention measures).[7]

- Prophylactic antibiotics should be started within 1 h before giving surgical incision, or within 2 h if the patient is receiving vancomycin or fluoroquinolones.
- Prophylactic antibiotics should be appropriate for their specific procedure.
- Prophylactic antibiotics should be discontinued within 24 h of surgery completion.
- Postoperative 6 a.m. blood glucose levels should be controlled.
- Surgical site hair removal should be appropriate for the location and procedure.

Antimicrobial prophylaxis may be considered primary if it is given for prevention of an initial infection. It is considered secondary if given for prevention of the recurrence or reactivation of an infection. It may also be administered to prevent infection by eliminating a colonizing organism.[8]

At least 30 min, but no >60 min before the skin incision is made is the optimal timing for the pre-operative administration of most commonly used antibiotics.[9]

A single antibiotic dose, given immediately before the start of surgery is just as effective in preventing infection and reducing the risk of drug side effects.[10]

Cefazolin is the most often used drug for surgical prophylaxis in patients with no history of beta-lactam allergy, a history of MRSA infection [Tables 2 and 3].[11]

Aims and Objectives

- To evaluate the selection, timing and duration of prophylactic antibiotic in Gynecological and Surgical patients.

Table 2: FOGSI recommendations for prophylactic antibiotics for obstetrical procedures[17]

Procedure	Antibiotic	Dosage
Emergency or elective cesarean section	Cefazolin IV 15–60 min prior to skin incision	1–2 g IV
If penicillin allergic	Clindamycin or Erythromycin	600 mg IV 500 mg IV
PPROM without chorioamnionitis	Amoxy/ampicillin, antibiotics for latency e.g., erythromycin or erythromycin	2 g IV. 6 hourly for 48 h, 250 mg orally, 6 hourly for 10 days (400 mg orally, 6 hourly for 10 days)

Table 3: FOGSI recommendations for prophylactic antibiotics for gynecological procedures[17]

Procedure	Antibiotic	Dosage
Hysterectomy	Cefazolin (single dose)	1–2 g IV
Laparohysteroscopy	None	
Laparotomy	None	

- Follow-up monitoring to determine the success of antibiotic prophylaxis.

MATERIALS AND METHODS

This prospective, observational and comparative study was conducted on 130 adult patients who underwent surgical procedures in the Gynecology and Surgery departments of Autonomous State Medical College and Hospital, Shahjahanpur, Uttar Pradesh, India from 1st January to 31st May 2021, for five consecutive months.

Inclusion Criteria

- Adult surgical and gynecology patients
- Clean, clean-contaminated procedures
- Prophylactic antibiotic use.

Exclusion Criteria

- Pediatric patient (<18 years)
- Dirty, contaminated procedures
- Therapeutic and other non-surgical prophylaxis uses.

For group A, we administered 2 g of cefuroxime 30–60 min before scheduled incision in the anesthesia room for elective surgeries or in the operating room 0–30 min before scheduled incision for emergency surgeries to 75 patients.

For group B, Same antibiotic was administered to randomly selected 75 patients postoperatively after 2 h of surgery. These were followed for a 30-day duration.

For group A, repeat dose was given only if surgery was prolonged for more than 2 h or if blood loss was excessive before shifting from operation room. No patient received antibiotic for more than 24 h.

The following variables were recorded in a pre-designed proforma.

- Patient demographics (Age, Sex)
- Date of operation
- Type of operation performed
- Time at start and end of operation
- Classification of operation (clean, clean-contaminated, or contaminated)
- Status of operation (elective or emergency)
- Primary diagnosis
- Previous adverse reactions or allergies to antibiotics.

Duration of prophylaxis was considered "APPROPRIATE" if it was a single preoperative dose given for a duration not exceeding 24-h, based on recommendations.

Data was collected and analyzed in MS excel. Descriptive statistics was used for summarizing frequencies and proportions.

RESULTS

In present study, 25 (19.23%) of subjects were between 21 and 30 years, 27 (20.76%) of subjects were between 31 and 40 years, 40 (30.76%) of subjects were between 41 and 50 years while 38 (29.23%) of subjects were between 51 and 60 years.

In present study, males were 57 (43.84%) while females were 73 (56.15%).

Thus, majority were females.

In present study, in group A, average hospital stay for 45 (69.23%) patients was 1 day, for 18 (27.69%) patients, it was 4 days while 02 (3.07%) patients required readmission & stay for 10 days.

In present study, in group B, average hospital stay for 28 (43.07%) patients was 1 day, for 17 (26.15%) patients, it was 4 days while 20 (30.76%) patients required readmission & stay for 10 days [Table 4].

In present study, majority i.e., 33 (35.38%) (18.2–33.8%, 95% CI) had Cesarean section followed by 25 (19.23%) (12.8–27.1%, 95% CI) patients had laparotomy, 20 (15.38%) (9.7–22.8%, 95% CI) patients had operative laparoscopy, 8 (6.15%) (2.7–11.8%, 95% CI) patients had abdominal hysterectomy, 12 (9.23%) (4.9–15.6%, 95% CI) patients had vaginal hysterectomy, 10 (7.69%) (3.7–13.7%, 95% CI) patients had diagnostic laparoscopy while 22 (16.92%) (10.9–24.5%, 95% CI) patients had hydrocele/hernia repair [Table 5].

In present study, majority of subjects i.e., 78 (60%) (51.0–68.5%, 95% CI) patients had clean wound while 52 (40%) (31.5–48.9%, 95% CI) patients had clean-contaminated wound [Table 6].

In present study, 85 (65.38%) (56.5–73.5%, 95% CI) patients had elective surgery while 45 (34.61%) (26.5–43.5%, 95% CI) patients had emergency surgery.

Table 4: Demographic features

Age groups	No. of subjects (*n*=130)	Percentage
21–30 years	25	19.23
31–40 years	27	20.76
41–50 years	40	30.76
51–60 years	38	29.23
Sex distribution	**No. of subjects**	**Percentage**
Males	57	43.84
Females	73	56.15
Median hospital stay	**No. of subjects**	
	Group A (*n*=65)	**Group B (*n*=65)**
1 day	45 (69.23%)	28 (43.07%)
4 days	18 (27.69%)	17 (26.15%)
10 days (Readmission)	02 (3.07%)	20 (30.76%)

Table 5: Operations performed

Name of Operation	No. of subjects *n*=130	Percentage (95%CI)
Caesarean section	33	25.38 (18.2–33.8)
Laparotomy	25	19.23 (12.8–27.1)
Operative laparoscopy	20	15.38 (9.7–22.8)
Abdominal hysterectomy	8	6.15 (2.7–11.8)
Vaginal hysterectomy	12	9.23 (4.9–15.6)
Diagnostic laparoscopy	10	7.69 (3.7–13.7)
Hydrocele/ Hernia repair	22	16.92 (10.9–24.5)

In 105(80.76%) (72.9–87.2%, 95% CI) patients, surgery lasted for 1–2 h while 25(19.23%) (12.8–27.1% 95% CI) had surgery for >2 h.

Prophylactic antibiotic was not given for >24 h even if duration was more or blood loss was more. Thus, majority were elective surgeries lasting for 1–2 h [Table 7].

In present study, there was no infection in clean wounds. Prevalence of superficial SSI was 3.84% (1.3–8.7%, 95% CI) while prevalence of deep SSI in clean-contaminated wound was 1.53% (0.2–5.4%, 95% CI). Organ specific infection was not seen in any of the patient.

Thus, prevalence of SSI was very low in our study [Table 8].

DISCUSSION

In present study, in group A, average hospital stay for 45 (69.23%) patients was 1 day, for 18 (27.69%) patients, it was 4 days while 02 (3.07%) patients required readmission & stay for 10 days.

In present study, in group B, average hospital stay for 28 (43.07%) patients was 1 day, for 17 (26.15%) patients, it was 4 days while 20 (30.76%) patients required readmission & stay for 10 days [Table 4].

In present study, average hospital stay for 55 (42.30%) patients was 1 day, for 73 (56.15%) patients, it was 4 days while 2 (15.38%) patients required readmission and stay for 10 days [Table 4].

Alemkere *et al.* found that the median age of the study participants was 35.0 (Interquartile range [IQR]: 25–50) years. There were 58.8% of male patients. The median hospitalization period was 8.0 (IQR: 5–11) days.[12]

In present study, majority i.e., 33 (35.38%) (18.2–33.8%, 95% CI) had Cesarean section, followed by 25 (19.23%) (12.8–27.1%, 95% CI) patients had laparotomy, 20 (15.38%) (9.7–22.8%, 95% CI) patients had operative laparoscopy, 8 (6.15%) (2.7–11.8%, 95% CI) patients had abdominal hysterectomy, 12 (9.23%) (4.9–15.6%, 95% CI) patients had vaginal hysterectomy, 10 (7.69%) (3.7–13.7%, 95% CI) patients had diagnostic laparoscopy while 22 (16.92%) (10.9–24.5%, 95% CI) patients had hydrocele/hernia repair [Table 5].

Alemkere *et al.* found that most of the participants were from the general surgical ward (60.1%). Majority of the surgical cases were gastrointestinal (39.2%) followed by gynecology and obstetrics (15.7%).[12]

Tolba *et al.* found that the most common operations performed were plastic surgeries (22.7%), followed by general surgery (16%), breast and endocrine (11.3%), urology (10.7%), orthopedic (10%), and neurosurgery (9.33%) departments. Other departments comprised the remaining 20%.[13]

In present study, majority of subjects i.e. 78 (60%) (51.0–68.5%, 95% CI) patients had clean wound while 52 (40%) (31.5–48.9%, 95% CI) patients had clean-contaminated wound [Table 6].

Tolba *et al.* found that 74 (49.3%) operations were classified as clean, 74 9.3%) were clean-contaminated, while two (1.3%) surgeries were contaminated.[13]

In present study, majority i.e., 85 (65.38%) (56.5–73.5%, 95% CI) patients had elective surgery while 45 (34.61%) (26.5–43.5%, 95% CI) patients had emergency surgery.

In 105 (80.76%) (72.9–87.2%, 95% CI) patients, surgery lasted for 1–2 h while 25(19.23%) (12.8–27.1%, 95% CI) had surgery for >2 h.

Prophylactic antibiotic was not given for >24 h even if duration was more or blood loss was more [Table 7].

Table 6: Type of operation

Type of operation	No. of subjects *n*=130	Percentage (95%CI)
Clean	78	60 (51.0–68.5)
Clean-contaminated	52	40 (31.5–48.9)
Contaminated	Nil	Nil
Dirty	Nil	Nil

Table 7: Type of procedure and duration

Type of procedure	No. of subjects *n*=130	Percentage
Elective	85	65.38 (56.5–73.5)
Emergency	45	34.6 (26.5–43.5)
Duration of surgery		
1–2 h	105	80.76 (72.9–87.2)
>2 h	25	19.23 (12.8–27.1)

Table 8: Prevalence of SSI

Prevalence of SSI	No, of subjects	Percentage (95% CI)
Clean wound	Nil	Nil
Clean-contaminated wound	**No. of subjects**	**Percentage (95 CI)**
Superficial	5	3.84 (1.3–8.7)
Deep	2	1.53 (0.2–5.4)
Organ site	Nil 3	

Tolba *et al.* found that out of 150 operations of patients, 137 (91.3%) were elective while the remaining 13 (8.7%) operations were emergency cases.[13]

Tolba *et al.* found that Ninety-eight (65.3%) cases lasted <2 h while 52 (34.7%) exceeded the 2-h duration.[13]

Singh *et al.* found that the mean timing of administration of antibiotics was 3.22 ± 1.03 h prior to surgery. Patients received post operative antibiotics for a mean duration of 5 days while in hospital.[14]

Kefale *et al.* found that 53.4% of these surgical procedures were elective. Clean contaminated and contaminated wounds constituted 26.3%. 23.5% of surgical procedures respectively.[15]

Kefale *et al.* found that all procedures (62.6%) were performed between 1 h and 3 h.[15]

In present study, there was no infection in clean wounds. Prevalence of superficial SSI was 3.84% (1.3–8.7%, 95% CI) while prevalence of deep SSI in clean-contaminated wound was 1.53% (0.2–5.4%, 95% CI). Organ specific infection was not seen in any of the patient.

Thus, prevalence of SSI was very low in our study [Table 8].

Kefale *et al.* found that 19.6% (95% CI: 18–21.1) of patients developed SSIs. 14.5%, 3% and 3% involved superficial, deep, and organ structures, respectively.[15]

Weber *et al.* found that the rate of SSI was 5.1%. It did not significantly differ in the early group and the late group. This finding was confirmed in each population: surgical division, wound class, immunosuppressive drugs, body mass index, diabetes and age.[16]

CONCLUSION

In present study, prevalence of SSIs was very low. This might be because study setting was a tertiary care center where proper and appropriate prophylactic antibiotic was given in all cases. Also, proper skin preparation and strict asepsis was followed.

This study will help to improve future utilization of surgical antimicrobial prophylaxis.

Limitations of the Study

- This study is an observational study in a tertiary care setting. Hence the study finding is only generalized to the patient population of similar setting.
- This was a single group descriptive study but an analytical study with comparison group could only provide idea about possible role of other factors.
- Randomized clinical trials would be the best design.

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Original Article

Ultrasonographic Study of Foetal Craniometry in the First Trimester of Pregnancy to Rule out Any Congenital Anomalies in East Singhbhum

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Abstract

Aim: The aim of the study is to review the first trimester normal anatomy of the fetal skull and diagnosis of cranial defects.

Material and Method: A total no. of 50 cases were studied in the department of anatomy, Mahatma Gandhi Memorial (M.G.M.) Medical college Jamshedpur. All cases were selected in the gestational age group of 10–14 weeks referred to Radiology department for Ultrasonographic evaluation of fetal wellbeing from the department of Obstetrics and Gynecology, M.G.M. Medical College and Hospital Jamshedpur.

Result: Out of 50 cases, 41 (82% of cases) had normal Biometric parameters, while 6 (12% of cases) had small for gestational age and 3 (6% of cases) had large for gestational age.

Key words: Biparietal diameter, Cephalic index, Foetal skull, Ultrasonography, Congenital anomalies

INTRODUCTION

Ultrasound can demonstrate fetal head by the 8th week of Gestation, but intracranial anatomy becomes visible only after the 12th week. The fetal head is the most prominent part of the Foetus and as such it is easily accessible for examination during the first trimester anatomy scan. Examination of the fetal head should include the skull shape and the membranous gap between the cranial bones such as Fontanelles and sutures for the assessment of Intracranial development and also various parameter and indices such as Biparietal diameter (B.P.D), Fronto-occipital diameter (F.O.D), Head Circumference (H.C), Cephalic index (C.I) and Head: Body ratio for the assessment of gestational age of and monitoring of normal growth of the fetus. Conventionally, most of congenital anomalies have been diagnosed in the second trimester of pregnancy. However, with the increasing incorporation of the 10th–14th week scan into clinical practice, this examination is progressively used for performing an early anatomy scan.[1-10]

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The Foetal Craniometry

The B.P.D is the distance between the parietal eminences on either side of the skull and is, therefore, the widest diameter of the skull from side to side. Measurements of B.P.D made from the outer table of the proximal skull (the part nearest to the transducer) to the inner table of the distal skull (the part farthest away from the transducer).

The Biparietal diameter of the Head was the first measurement of Foetus growth described (Willocks *et al.*, 1967). Among all the parameters B.P.D remains the simplest. As the fetus grows, the B.P.D of the fetal head also increases throughout pregnancy. Fetal skull is well defined ultrasonically from 11 to 12 weeks onwards the B.P.D is the most discussed and documented Obstetric ultrasound measurement.

The FOD is measured along the longest axis of the skull at the level of the BPD from outer edge to outer edge.

CI is the ratio of B.P.D to FOD which is reported as percentage.

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Normal range (±2 standard deviations) of CI = 70–86. Head: body ratio is calculated by dividing the HC by the abdominal circumference. With normal anatomy, the head: body ratio can be considered normal if it lies between the 57th and 95th percentiles for the gestational age.[10-17]

Congential Anomalies of Foetal Head, that May be Diagnose During the 1st Trimester Ultrasonographic Scan

Acrania/Anencephaly

Open neural tube defects are severe congenital anomalies occurring with a prevalence of one in 1000–2000 pregnancy. Among them, the anencephaly sequence is the most severe central nervous system (CNS) malformation, which is characterized by complete absence of the calvarium.

Microcephaly

An abnormally small head can be diagnosed when BPD is more than 3 standard deviations below the normal.

Cephalocele

Cephalocele is serious CNS malformation characterized by partial protrusion of the brain through a cranial defect.

Hydrocephalus

Although it can be recognized by the 18th week of gestation when there will be dilatation of the lateral ventricles, however, it can be suspected in the 1st trimester scan when biometric diameter and HC are more than of its normal range, showing abnormally large head size.[17-25]

MATERIAL AND METHOD

This work "Ultrasonographic study of fetal craniometry in the first trimester of pregnancy to rule out any congenital anomalies in East Singhbhum" was carried out in the department of Anatomy, M.G.M Medical College, Jamshedpur, and ultrasonic examination was done in the ultrasound unit of the department of Radiology, M.G.M Medical College, Jamshedpur.

Cases were selected from the patient referred to the radiology department from the department of obstetrics and Gynecology for ultrasonic evaluation of fetal well being within 10-14 weeks of pregnancy or confirmation of pregnancy.

A total no. of 50 cases were studied.

Method of Study

1. History was taken with her consent.
2. Clinical study of the cases.
3. Determination of different parameter of coriometry.

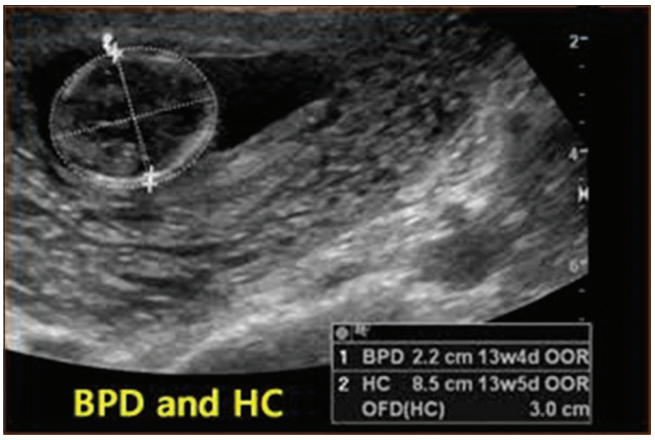

Figure 1: Normal biometric measurement

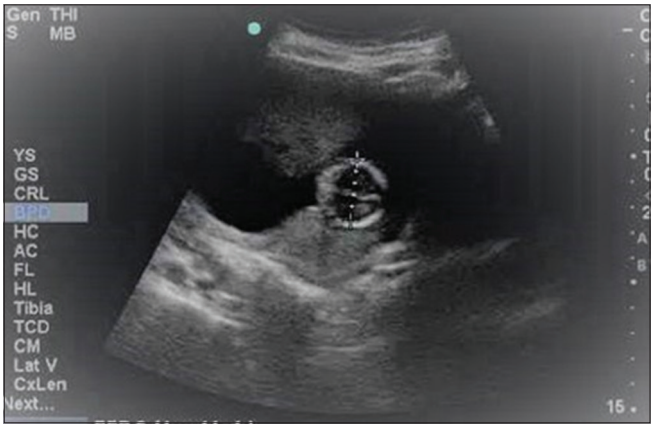

Figure 2: Lesser biometric measurement

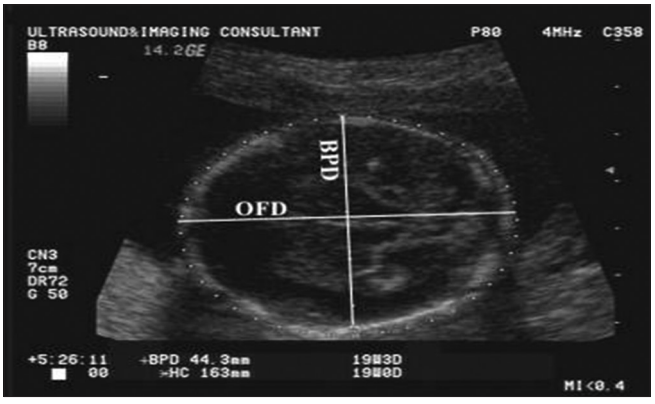

Figure 3: Greater biometric measurement

Table 1: Showing distribution of cases according to gestation period in weeks

Gestation period in week	No. of cases	Percentage
10–11.5	5	10
11.6–13	15	30
13.1–14	30	60

Table 2: Showing biometric findings against different gestational age group

Gestational period in week	Mean HC (cm)	Mean BPD (cm)	Mean FOD (cm)	Mean C.I (%)
10–11.5 weeks	8.1 cm	2.1 cm	2.4 cm	87.5%
11.6–13 weeks	8.6 cm	2.4 cm	3.0 cm	80%
13.1–14 weeks	9.5 cm	2.8 cm	3.5 cm	80%

Table 3: Showing variation in the biometric finding

No. of cases	Percentage	Biometric parameter
41	82%	Normal range
6	12%	Below the normal range (small for Gestational age)
3	6%	Above the normal range (large for Gestational age)

That is BPD, HC, FOD, CI, Abdominal circumference (AC), and femur length.

4. The Gestational age was computed using L.M.P
5. Determination of fetal age from ultrasonic measurements mark.
6. Any abnormalities or variation taken into account.

RESULTS AND DISCUSSION

The present study was designed to study the various aspect of the significance of fetal craniometry regarding fetal well-being. Fetal Biometric finding (HC, BPD, FOD, and CI) is observed and compared with a normal level of these biometric parameters and any variation taken into account – to exclude any cranial defect.

About 60% of cases were examined of Gestation period in between 13 and 14 weeks, 30% in between 11.6 and 13 weeks and rest 10% in between 10 and 11.5 weeks at Gestation.

In the Gestational age group 10–11.5 weeks, Mean HC 8.1 cm, Mean BPD 2.1 cm, mean FOD 2.4 cm, and C.I 87.5%.

In the gestational age group 11.6–13.0 weeks, mean HC 8.6 cm. Mean BPD 2.4 cm, mean FOD 3.0 cm, and Cephal index 80%.

In the gestational age group 13.1–14 weeks, Mean HC 9.5 cm, Mean B.PD 2.8 cm, Mean FOD 3.5 cm, and Cepatic index 80%.

About 82% of cases had normal biometric parameters, while 12% had small for gestational age and 6% had large for gestational age [Tables 1-3].

CONCLUSION

- BPD is a measurement that can be obtained with great consistency and accuracy.
- It has proved its efficacy in the estimation of gestational age of fetus and is expected to help the obstetrician in making obstetric decision and with refinement in technique and using other biometric parameters with BPD is likely to reduce iatrogenic prematurity which, in turn, would reduce prenalal mortality.
- The transition between first and second trimester is also the appropriate time to make the transition from CRL to BPD, FOD, HC, AC, and F.L.
- Growth rate of fetal BPD decreases gradually as the fetus increases in size.
- For better results, one should also take serial measurements of BPD to evaluate the continuous fetal growth and ideal time of intervention should be guided by clinical judgment along with ultrasonographic findings, because BPD alone is not reliable in the case of IUGR, especially in symmetrical variety.
- The use of multiple parameters reduces to effect of outliers caused by biologic phenomena (i.e. congenital anomalies or growth variation) or technical error in the measurement of a single structure.

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Original Article

Stone Formation Around Foleys Balloon in Neglected Suprapubic Catheter an Impact of Coronavirus Disease-19 Lockdown

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Abstract

Suprapubic catheterization (SPC) is an alternative for urethral catheterization. SPC is not free of complications such as bacteriuria, leakage, and stone formation. Bacteria attach to the foleys surface forming a biofilm and secrete an extracellular polysaccharide matrix of bacterial glycocalices. The host urinary protein and salts complex with this matrix, leading to encrustation of foleys. Good catheter hygiene, including aseptic catheter insertion, is necessary to reduce the entry of microorganism into the urinary bladder.

Key words: Suprapubic catheterization, Bacteriuria, Stone formation

INTRODUCTION

Suprapubic catheterization (SPC) of the urinary bladder is alternative to urethral catheterization in cases of bladder neck contracture, complete urethral stenosis, neurogenic urinary bladder, in patients who fails to do clean intermittent catheterization. Surapubic catheterization can also be indicated in cases where urinary diversion is required for urinary bladder and urethral healing.[1] SPC is not free of complications such as bacteriuria, leakage, stone formation. A foreign body within the bladder will initially encrust with calcium oxalate, as a result of the normal stasis that occurs with the storage of urine. Should infection supersede, rapid coalescence of the stone may occur as struvite is deposited on the nascent stone.[2,3]

We report a case series of two cases where stone formed around foleys balloon catheter.

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CASE REPORT

Case 1

A 32-year-old male patient underwent SPC 3 years back for post-traumatic urethral stricture. The patient came with a complaint of passing urine from opening on the ventral aspect of penis and blockage of suprapubic catheter. Patient was lost to follow-up during Coronavirus Disease (COVID-19) lockdown and did not get his SPC changed for about last 1 year. On examination, patient SPC was draining urine and patient was passsing urine from urethrocutaneous fistula on the ventral aspect of the penis. We tried to deflat the SPC balloon but could not be deflated. Patient Ultrasonography and X-ray Kidney, Ureter, and Bladder (KUB) was done shown in [Figure 1] which shows opacification around foleys. Patient underwent open suprapubic cystolithotomy with repair of urethrocutaneous fistula which reveals stone formed around SPC foleys catheter shown in [Figure 2].

Case 2

A 30-year-old patient presented with a complaint of SPC blockage and passing urine from the ventral aspect of base of the penis for 6 months. Patient underwent urethroplasty for urethral stricture 1 year back. On examination, patient had urethrocutaneous fistula with blocked SPC. Patient lost to follow-up and did not get his SPC change during Covid

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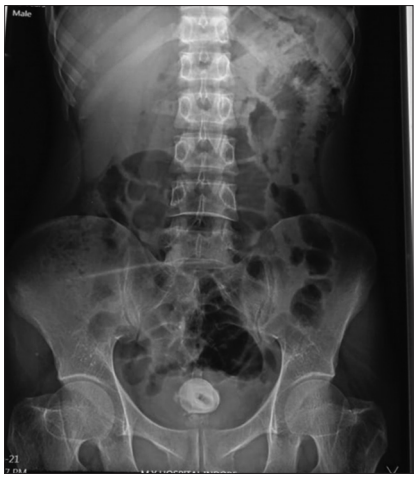

Figure 1: X- ray KUB is showing bladder caliculi around the foleys bulb of case 1

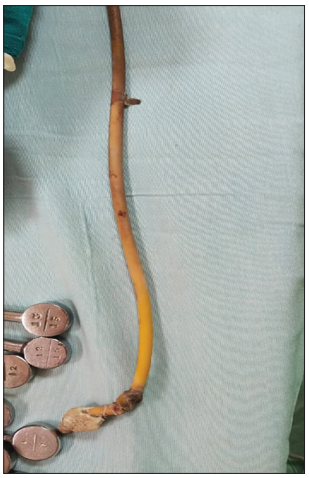

Figure 3: Intra operative image showing multiple caliculi removed from bladder of case 2

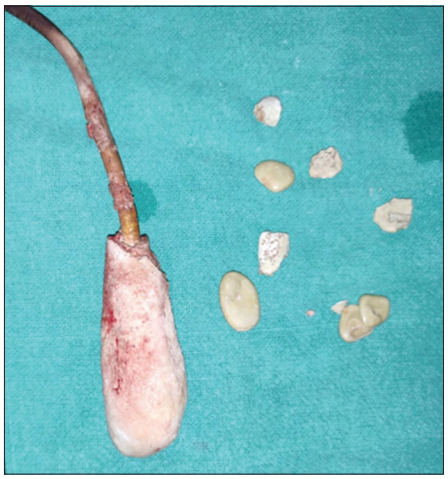

Figure 2: Intra operative image showing multiple caliculi removed from bladder of case 1

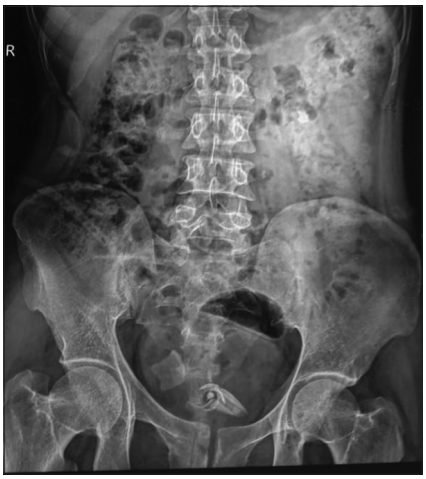

Figure 4: X- ray KUB is showing bladder caliculi around the foleys bulb of case 2

19 lockdown. Patient ultrasonography and X-ray KUB [Figure 3] get done and reveal stone formation around foleys balloon [Figure 4]. Patient underwent lay open stage I urethroplasty and Open cystolithotomy.

DISCUSSION

Bacteriuria in presence of indwelling catheter is inevitable and the duration of catheterization is the most important risk factor for the development of bacteriuria which occurs at an incidence of approximately 10% per day of catheterization.[4] There are two types of the bacterial population (a) Planktonic growth (b) Biofilm growth(layers of organisms on infected indwelling catheters).[5] Bacteria attach to the foleys surface forming a biofilm and secrete an extracellular polysaccharide matrix of bacterial glycocalices. The host urinary protein and salts complex with this matrix, leading to encrustation of foleys lumen. Colonization with urease-producing microorganisms increases urinary pH which promotes precipitation of struvite and apatite crystals resulting in catheter encrustation and stone formation. Long-term bladder drainage may also result in bladder lithiasis, with a reported incidence of 0.07–2.2% in patients with chronic indwelling catheters.[6]

Good catheter hygiene, including aseptic catheter insertion, is necessary to reduce the entry of microorganisms into the urinary bladder. A three weekly catheter change is advised by some to minimize encrustation.

CONCLUSION

It is concluded that in patients of suprapubic catheter proper instruction should be given about foleys care and regular change of SPC to reduce the incidence of stone formation. In our cases, patient did not comply proper follow-up due to covid 19 lockdown. These cases required open surgery for stone removal.

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Original Article

Prevalence and Determinants of Mortality among Preterm Infants in Jos University Teaching Hospital, Jos, Nigeria

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Abstract

Background: Prematurity is a leading cause of child death globally, a burden that is higher in Sub-Saharan Africa. There is paucity of data on outcomes and trends in prematurity in North-Central Nigeria. This study aimed at determining the mortality rate and factors associated with mortality among preterm infants admitted in a tertiary hospital in Jos, North-Central Nigeria.

Materials and Methods: This was a retrospective cross-sectional study of neonatal admissions in Jos University Teaching Hospital, Jos over a 5 year period. Socio-demographic, obstetric, and neonatal variables were extracted from Unit records. Data analysis was done using SPSS version 21.

Results: A total of 646 (32.8%) preterms out of 1961 admitted neonates were studied. The gestational age ranged from 24 to 36 weeks at birth with 34 (5.6%) aged <28 weeks. The overall mortality rate among preterm was 18.7% (121/646). Sepsis (28.9%), respiratory distress syndrome (20.7%), congenital anomalies (13.2%), and asphyxia (9.9%) were the commonest cause of death. Being delivered at a gestational age <28 weeks (AOR 17.8, 95% confidence interval [CI] 4.7–67.8), 28–31 weeks (AOR 5.19, 1.7–15.9), 5 min APGAR score <7 (AOR=2.59, 95% CI=1.4–4.7), and birth weight <1000g (AOR 3.35, 95% CI=1.4–7.9) were associated with increased risk of mortality.

Conclusion: Prematurity is a major cause of neonatal mortality in our health facility. These deaths are associated with being delivered very premature. Measures aimed at improved infection control, respiratory support and effective neonatal resuscitation could reduce preterm deaths significantly.

Key words: Asphyxia, Birth weight, Cause of death, Infant, Newborn, Prematurity, Sepsis

INTRODUCTION

Globally, each year, an estimated 15 million preterm births (before 37 completed weeks) occur with 1.1 million deaths as a result of complications from prematurity.[1] Sub-Saharan Africa and Asia account for 60% of preterm births and 80% of preterm deaths.[2] The incidence of preterm births appears to be increasing and prematurity is now the leading cause of child death globally.[1] In spite of progress toward achieving global targets of reducing child mortality, prematurity significantly contributed to the non-actualization of the fourth millennial development goal and threatens success of the sustainable development goal. Common causes of mortality in preterm include: Respiratory distress syndrome (RDS), sepsis (including pneumonia), apnea, hypothermia, and jaundice.[3,4]

There exist high inequalities in preterm mortality rates between countries with about half of infants born before 32 weeks in low-income countries dying while half of infants delivered at 24 weeks in high-income countries survive, reflecting weak health systems.[5] Preterm infants born in Sub-Saharan Africa and South-east Asia are 12 times more likely to die than does in developed countries.[5]

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With an estimated 871,000 preterm births and 98,000 mortalities as a direct result of prematurity annually, Nigeria ranks 3rd as country with the highest number of preterm births globally.[6] Prematurity is the third leading cause of child death in Nigeria, after malaria and pneumonia.[6] There is a wide range (5.4–34%) of hospital-based preterm-related deaths in Nigeria which largely represents the method of calculation.[4,7-9] Studies reporting cumulative incidence reported lower values compared to point prevalence. Some studies included stillbirths, those who were discharged against medical advice, or calculated perinatal mortality while others excluded a significant proportion of the target population.[4,7,10] Other factors that may contribute to these differences include: Tier of health care facility, skills of healthcare workers, and availability of specialized facilities and interventions to manage complications such as continuous positive airway pressure (CPAP) machines, surfactants, and incubators for very preterm infants.

There is paucity of data on prematurity in North-Central Nigeria. The available reports included a small number of preterm limiting generalizability.[4] Therefore, this study aims at bridging this gap by determining the prevalence of mortality and evaluating factors associated with mortality amongst preterm in a tertiary hospital in Jos, North-Central, Nigeria.

MATERIALS AND METHODS

This was a retrospective cross-sectional study of all preterm neonates admitted into the Special Care Baby Unit (SCBU) of Jos University Teaching Hospital, Jos, Plateau state, Nigeria, over a 5 year period (between January 1, 2016, and May 31, 2021). During that period, there was a 5-month cumulative period of no neonatal admissions due to industrial actions by health workers. Therefore, 60 months were included in this analysis.

Jos University Teaching Hospital is a 600 bed spaces tertiary hospital located in Jos, Plateau State and serves as the foremost referral center in Plateau State. The hospital receives referral from neighboring states of Bauchi, Nasarawa, Taraba, Benue, and Southern Kaduna, and States with combined human populations of over 20 million (National population Commission). It has a 30 bed SCBU which is manned by three consultant pediatricians, one senior registrar and two pediatric resident. It also has 16 nurses with a minimum of two nurses per shift. The unit has five incubators and introduced improvised CPAP in 2016 for managing neonates with respiratory distress. Other facilities include ten low emission diode phototherapy devices that all provide intensive phototherapy and an irradiance meter.

Data extraction was done by trained research assistant. Data were entered into pre-coded Microsoft Excel spreadsheet. Variables of interest include socio-demographic variables such as maternal age, age, sex, obstetric variables (parity and place of birth), and other characteristics (type of gestation, gestational age, duration of admission, outcome of admission, and diagnosis at outcome). Outcome of admission was either discharge or died (mortality). Patients whose parents signed against medical advice and patients with no information about outcome were excluded from the study. Gestational age was determined by past menstrual period, early ultrasound scan or modified Ballard score. Prematurity was defined as a gestational age <37 completed weeks.

The minimum sample size was calculated using the prevalence formula for proportions of death. Assuming 29% of preterm deaths are due to one of the likely causes of preterm mortality, with a 5% precision and 95% level of confidence, power set at 80% and 15% for incomplete data, 364 preterm were required.[3]

Ethical approval was obtained from the institutional ethics review board of JUTH with ref JUTH/DCS/REC/127/XXX/2239. Dataset was de-identified before data analysis.

Statistical Analysis

Collected data were cleaned and checked for completeness. Data analysis was carried out using IBM's SPSS statistical software version 25 (2017). Baseline characteristics of the sampled population and causes of mortality were presented in frequency tables. Bivariate and multivariate logistic regression was used to determine factors associated with mortality. Independent variables with $P < 0.2$ following bivariate logistic regression were included in the multivariate logistic regression. Crudes odds ratio and adjusted odds ratio situated within 95% confidence interval (95% CI) were used to estimate effect size for bivariate and multivariate logistic regression, respectively. $P < 0.05$ was considered statistically significant.

RESULTS

A total of 1961 admitted neonates were studied of whom 646/1967 (32.8%) were preterm. (Figure 1) Of the 646 preterms hospitalized and treated for various medical and surgical conditions, 302 (50.9%) were male and 490 (75.9) were admitted within 24 h of birth. The gestational age ranged from 24 to 36 weeks with 34 (5.6%) with a gestational age <28 weeks. The modal gestational age was 32–33 weeks (274/603, 45.4%). The mean maternal age was 29.4 ± 6.5 years with 424 (71.3%) being aged 20–34 years. Table 1 describes the characteristics of the studied preterm babies.

Table 1: Characteristics of preterm neonates admitted in JUTH between 2016 and 2020

Variable	*n*	Frequency	Percentage
Age (day)	646		
<1		490	75.9
1–2		72	11.1
≥3		84	13.0
Gestational age (weeks)	603		
<28		34	5.6
28–31		167	27.7
32–33		274	45.4
34–36		128	21.2
Sex	593		
Male		302	50.9
Female		291	49.1
Birth weight (g)	620		
<1000		38	6.1
1000–1499		153	24.7
1500–2499		377	60.8
≥2500		52	8.4
Maternal age (years)	595		
<20		28	4.7
20–34		424	71.3
≥35		143	24.0
Maternal parity	613		
1		221	36.1
1–4		292	47.6
≥5		100	16.3
Type of gestation	639		
Singleton		521	81.5
Multiple		118	18.5
APGAR score at 5 min	412		
<7		108	26.2
≥7		304	73.8
Outcome	646		
Discharge		525	81.3
Death		121	18.7

The all-cause mortality rate in preterm infants was 121/646 (18.7%) and in term infants 114/1321 (8.6%). Complications of prematurity accounted for 51.5% of all neonatal deaths in studied infants. Causes of death were unrecorded in 15(12.4%) infants. Sepsis accounted for 35 (28.9%) deaths, excluding 5 (4.2%) deaths from congenital pneumonia. Other causes of mortality were RDS, asphyxia, and congenital anomalies with 25 (20.7%), 112 (9.9%), and 16 (13.2%), respectively [Table 2].

Bivariate analysis of factors associated with mortality [Table 3] showed that gestational age ($P \leq 0.001$), birth weight ($P \leq 0.001$), maternal parity ($P = 0.031$), and APGAR score at 5 min ($P = 0.001$) were significantly associated with mortality, respectively. There were 22 (64.7%) and 29 (76.3%) deaths in infants delivered at gestational age <28 weeks and 28–31 weeks, respectively. Being delivered at a gestational age of <28 weeks and 28–31 weeks was significantly associated with increased risk of death when compared to those delivered at 34–36 weeks (COR=16.22, 95%CI=6.5–40.2 and COR=2.7, 95% CI=1.4–5.3, respectively). Death was recorded in

Table 2: Causes of mortality in preterm infants in JUTH between 2016 and 2020

Causes of death	Number (*n*=121)	Percentage
Sepsis	35	28.9
Respiratory distress syndrome	25	20.7
Asphyxia	12	9.9
Congenital pneumonia	5	4.2
Congenital anomalies	16	13.2
Neonatal jaundice	3	2.5
Apnea	4	3.2
Anemia	2	1.6
Necrotizing enterocolitis	2	1.6
Disseminated intravascular coagulopathy	1	0.8
Hypoglycemia	1	0.8
Unrecorded	15	12.4

29 (76.3%) and 34 (22.2) infants delivered with a birth weight of <1000 g and 1000–1499 g, respectively. The risk of death was significantly higher in infants with a birth weight of <1000 g (COR=52.6 and 95%CI=13.2–210.2) and 1000–1499 g (COR=4.67 and 95%CI=1.4–15.9) when compared with those with a birth weight ≥2500 g. Infants delivered to multiparous mothers (1–4 deliveries) had a lower risk of death (COR=0.48 and 95%CI=0.3–0.8) when compared with grand multiparous mothers (≥5 deliveries). Infants delivered with an APGAR score of <7 at 5 min had a higher risk of death (COR=2.47 and 95%CI=1.4–4.2) when compared to those with APGAR score ≥7 at 5 min. Age, sex, maternal age, and type of gestation were not associated with mortality.

Multivariate logistic regression of factors with $P < 0.2$ in the bivariate analysis was done in two models [Tables 4A and B] ensuring that both gestational age and birth weight were not included in the same model. This is because gestational age had a high correlation with birth weight. Following multivariate logistic regression, being delivered at a gestational age <28 weeks (AOR 17.8 and 95%CI 4.7–67.8), 28–31 weeks (AOR 5.19 and 1.7–15.9), 5 min APGAR score <7 (AOR=2.59 and 95%CI=1.4–4.7), and birth weight <1000 g (AOR 3.35 and 95%CI=1.4–7.9) were associated with increased risk of mortality. Having a birth weight between 1500 and 2499 g was associated with the lower risk of mortality (AOR 0.71 and 95%CI=0.5–0.9).

DISCUSSION

Findings from our study suggest that prematurity contributes significantly to the burden of neonatal admissions and deaths. Prematurity accounted for nearly a third of neonatal admissions which is similar to reports from tertiary hospitals in India (28.5%), Cameroun (36.6%), Southern Nigeria (24%), and North-Eastern Nigeria (32.9%).[8,11-13] These values are generally higher than those

Table 3: Bivariate analysis of factors associated with mortality among preterm infants admitted in JUTH between 2016 and 2020

Variable	Discharge (%)	Death (%)	Crude odds ratio	95% Confidence interval	*P* value
Age (day)					0.232
<1	399 (81.4)	81 (18.6)	1.37	0.7–2.6	0.346
1–2	54 (75.0)	18 (25.0)	2.00	0.9–4.5	0.094
≥3	72 (85.7)	12 (14.3)	1.00 (Ref)		
Gestational age (weeks)					<0.001*
<28	12 (35.3)	22 (64.7)	16.22	6.5–40.2	<0.001
28–31	128 (76.6)	39 (23.4)	2.70	1.4–5.3	0.004
32–33	231 (84.3)	43 (15.7)	1.65	0.8–3.2	0.138
34–36	115 (89.8)	13 (10.2)	1.00 (Ref)		
Sex					
Male	247 (81.8)	55 (18.2)	1.17	0.8–1.8	0.459
Female	231 (79.4)	60 (20.6)	1.00 (Ref)		
Birth weight (g)					<0.001*
<1000	9 (23.7)	29 (76.3)	52.63	13.2–210.2	<0.001
1000–1499	119 (77.8)	34 (22.2)	4.67	1.4–15.9	0.014
1500–2499	333 (88.3)	44 (11.7)	2.16	0.6–7.2	0.212
≥2500	49 (94.2)	3 (5.8)	1.00 (Ref)		
Maternal age (years)					0.336
<20	24 (85.7))	4 (14.3)	0.97	0.3–3.1	0.956
20–34	340 (80.2)	84 (19.8)	1.44	0.9–2.4	0.174
≥35	122 (85.3)	21 (14.7)	1.00 (Ref)		
Maternal parity					0.031*
1	180 (81.4)	41 (18.6)	0.62	0.4–1.1	0.088
2–4	248 (84.9)	44 (15.1)	0.48	0.3–0.8	0.008
≥5	73 (73.0)	27 (27.0)	1.00 (Ref)		
Type of gestation					
Singleton	425 (81.6)	96 (18.4)	0.89	0.5–1.5	0.631
Multiple	94 (79.7)	24 (20.3)	1.00 (Ref)		
APGAR score at 5 min					
<7	78 (72.2)	30 (27.8)	2.47	1.4–4.2	0.001*
≥7	263 (86.5)	41 (13.5)	1.00 (Ref)		

Ref – reference category, * significant factor ($P < 0.02$)

reporting the cumulative incidence of preterm births which describe the burden of prematurity as a proportion of preterm births, not neonatal admissions.[7,14]

Our study observed a preterm mortality rate of 18.7% giving a survival rate of 81.3% at discharge. The survival rate is similar to 79.4% and 81.3% reported from studies in India and Cameroun but higher than figures from Nepal.[12,15,16] The major difference with the study from Nepal is that they included discharge against medical advice as an outcome which invariably reduced the percentage of infants that survived. Studies that report survival rate as a proportion of all preterm birth generally report higher survival rates.[17] This could be as a result of improved survival among late preterm infants who constitute about 70% of preterm births as a higher proportion of late preterm are expected to have normal extra-uterine transition and are usually discharged from nurseries without being admitted in NICUs or SCBUs.[18,19]

Sepsis, RDS, congenital anomalies, and asphyxia were the commonest identified causes of death in preterm infants studied. While respiratory problems and sepsis have been identified as major causes of mortality in preterm in most studies, fewer studies report asphyxia as a common cause.[8,12,15,16] Congenital anomalies were a common cause of mortality in our study which probably reflects the nature of our facility being a major referral center for Pediatric surgery in North-Central Nigeria. Infants delivered with major congenital anomalies are at higher risk of neonatal death with the risk being even higher if they are delivered premature.[20-22] In a recent study, having a major birth defect increased the risk of mortality ten-fold among very low birth weight infants.[20] Necrotizing enterocolitis (NEC) was identified as the cause of death in 2 (1.6%) of mortalities in our study. This is rather low compared to another study estimating about a quarter of deaths in preterm as a result of NEC.[16] This may be a reflection of a low incidence of NEC in this cohort of preterm infants because NEC has been reported to have one of the highest case fatality rates (up to 66%) in preterm infants.[8] The low incidence of NEC observed in this study may also be limited by the data extraction which underestimated incidence using reported causes of death.

In our study, mortality was significantly higher with decreasing gestational age, being extreme low birth weight and with a

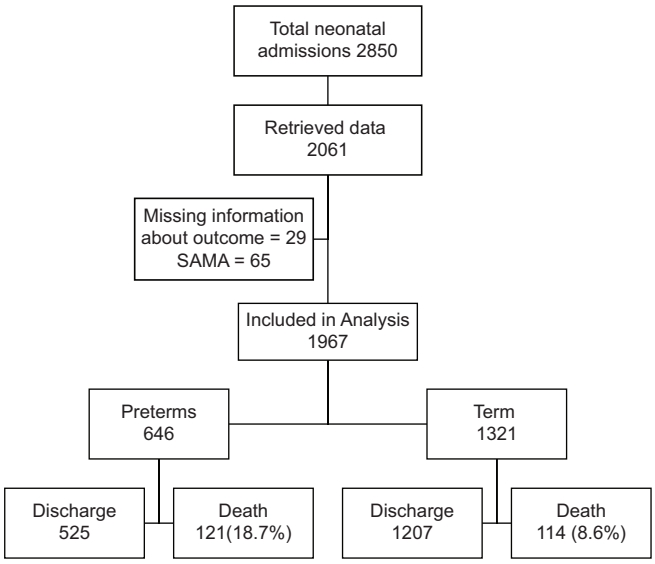

Figure 1: Flow chart of neonates in the study. SAMA: Signed against medical advice

Table 4: Multivariate logistic regression of factors associated with preterm mortality in JUTH between 2016 and 2020

A. (analysis without birth weight)			
Variable	**Adjusted odds ratio**	**95% Confidence Interval**	***P* value**
Gestational age (weeks)			<0.001*
<28	17.80	4.7–67.8	<0.001*
28–31	5.19	1.7–15.91	0.004*
32–33	2.44	0.8–7.5	0.119
34–36	1.00 (Ref)		
Maternal parity			0.021*
1	0.67	0.3–1.5	0.321
2–4	0.35	0.2–0.8	0.008*
≥5	1.00 (Ref)		
APGAR score at 5 min			
<7	2.59	1.4–4.7	0.002*
≥7	1.00 (Ref)		
B. (analysis without gestational age)			
Variable	**Crude odds ratio**	**95% Confidence Interval**	***P* value**
Birth weight (g)			<0.001*
<1000	3.35	1.4–7.9	0.005*
1000–1499	0.90	0.6–1.3	0.590
1500–2499	0.71	0.5–0.9	0.011*
≥2500	1.00 (Ref)		
Maternal parity			0.024*
1	0.71	0.3–1.6	0.390
2-4	0.37	0.2–0.8	0.010*
≥5	1.00 (Ref)		
APGAR score at 5 min			
<7	1.95	1.0–3.7	0.039*
≥7	1.00 (Ref)		

#Due to the strong correlation between birth weight and gestational age, two models (A and B) had to be produced to prevent the reducing effect of either on risk of mortality

5 min APGAR score <7. This is consistent with findings from different studies globally.[15,23-25] A study in East Africa reported that birth asphyxia was 3 times more likely to lead to mortality than RDS.[26] Low APGAR score at five minutes <5 has been used as a proxy for asphyxia and was a significant predictor of death in our study and in keeping with the previous reports.[13,25] Blundell and Chakraborty reported that low 1st and 5th min APGAR scores (<7) were significant predictors of mortality in infants delivered between 28 and 32 weeks but had limited prognostic value in those aged <28 weeks, possibly due to the high mortality in this group.[27] A multicenter study in Nigeria and Kenya identified being delivered very preterm and extreme low birth weight as independent predictors of neonatal mortality.[28] The 76.3% mortality rate reported among ELBW preterm infants was comparable to 80% reported previously among ELBW infants by Shrestha *et al.*[16] However, the mortality rate in extreme preterm infants of 65% obtained in our study was much higher than 28% obtained in South Wales.[29] Thus, reflecting the general observation that mortality in extreme preterm infants may be similar in different setting in LMICs but much higher than reported in high income countries.

Maternal parity of 2–4 was significantly associated with the lower risk of death when compared to being grand multiparous. Being primiparous was not significantly associated with increased mortality. The reason for our findings about parity is not immediate but seems not to differ from a previous report that found no significant association of mortality with sex, maternal age, and parity.[25]

The study was limited by its retrospective nature; therefore, data about certain possible factors such as place of birth, socio-demographic details of parents, and important obstetric history were not analyzed because they were largely unavailable. Furthermore, attributing only one cause of death is rather simplistic than often experienced in clinical practice.

CONCLUSION

Prematurity is a major cause of neonatal admissions and deaths in our facility. Neonatal infections, RDS, and asphyxia account for about half of deaths in the studied preterm infants. Decreasing gestational age, extreme low birth weight, low APGAR, and low APGAR scores are associated with mortality in studied preterm infants. Interventions targeted at preventing extreme prematurity and intrapartum complications are recommended to meet global targets in neonatal mortality.

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Original Article

Expression of Microbial Isolates, Sensitivity Profile, and Clinical Aspects in Maxillofacial Infections with or without Diabetes Mellitus

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Abstract

Aim: The aim of the study was to assess and compare the clinical presentation, microbial profile, antibiotic susceptibility of maxillofacial infections, and in diabetic and non-diabetic patients.

Materials and Methods: All patients presenting with maxillofacial infection were initially screened through a complete case history including any known medical comorbidities patients with either a known history of diabetes or sustained hyperglycemia were assigned to Group I and other to Group II. Clinical presentation and laboratory profile were monitored for patient in both the groups. Exudates obtained either through sterile close aspiration technique or during incision and drainage were subjected to Gram staining microbial culture and antibiotic sensitivity.

Results: There was a significant difference between the clinical presentation, age, and antibiotic susceptibility in both the groups although there was no significant deference in the microbial expression in both the groups.

Conclusion: Because of the ever-changing nature of microorganisms due to contentious adaptation, reassessment to improve our knowledge, we have performed a prospective study. After the evaluation of the results of the study, we were able to state that; diabetic males are at higher risk of getting infections. Diabetic patients are at a higher risk of bacteremia, the spread of infection is higher in diabetic patients. The response to empirical antibiotic therapy (clindamycin) in both the groups provides satisfactory results. There were no significant differences in organism isolated and antibiotic susceptibility between the groups. *Kleibsiella* (facultative anaerobe) isolated in higher numbers in diabetic population.

Key words: Culture Sensitivity, Maxillofacial Infections, Microbial Isolates

INTRODUCTION

Evidence of maxillofacial infections troubling mankind has been found in the remains of early Egyptians with signs of dental abscess and osteomyelitis.[1] Establishment of any infection is a consequence of disturbed equation between pathogenicity of the microorganism and host defense mechanisms. Factors which govern the spread of infection are, the mode of entry of the organism, production of toxins, virulence, physical and chemical barriers of host resistance, and immune defense mechanisms of the host.[2]

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Infections can be autogenous, caused by body's resident flora that becomes pathogenic due to some reason as in case of odontogenic infection or may be the result of cross infection. Cross infection leading to sepsis may be a responsible factor if unsterile injections and contaminated needles have been used.

Odontogenic infections are the most common type of orofacial infections oral and maxillofacial surgeons come across.[3] It has been suggested that immunocompromised patients are more susceptible to these infections, in whom their course is often unpredictable.[4] Outcome depends on the host defense, anatomic location and abnormality, virulence of micro-organisms, as well as the timing and choice of anti-microbial treatment.[5]

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Diabetes mellitus (DM) is becoming much more prevalent with advancement of civilization and elongation of lifespan. Angiopathy and susceptibility to infection constitute two major problems in DM. Correlations have been shown between mean plasma glucose levels and the frequency of acute bacterial infections.[6] The coexistence of DM may complicate orofacial infections, and treatment in these cases may be difficult. Suppression of neutrophil functions has also been stated to contribute to the tendency for infection in diabetes. In diabetics, impairment of other bactericidal functions may exist, such as those of chemotaxis, phagocytosis, and reactive oxygen generation. Investigations have indicated that suppression of neutrophil function in diabetes allows microbial invasion and multiplication.[7]

Investigation of the pathogenic potential of individual species of micro-organisms is fraught with difficulties[8] as the micro-organisms are indigenous, their profile changes during an individual's life span and varies depending on anatomic location, environmental factors, and host defenses. These dynamics may influence our ability to isolate organisms.[9]

MATERIALS AND METHODS

A prospective study design was employed for comparison of the cohorts. All patients presenting with signs and symptoms suggestive of maxillofacial infection were thoroughly screened with a complete case history and detailed local and systemic examination. Relevant radiographs and hematological investigations were performed. For the cases diagnosed as having maxillofacial infection (odontogenic/non-odontogenic), initial segregation into two groups, that is, diabetics in Group I and non-diabetics in Group II was carried out taking into account a known history of DM. Those patients who did not give a history of DM but had a Random Blood Glucose value >130 mg/dl were also assigned to the diabetic group (Group I). Patients presenting with wound sepsis, history of anti-cancer chemotherapy or any other additional comorbidity such as chronic renal failure, severe anemia, etc., were excluded from the study.

Collection of Pus Samples

Sample collection was done preferentially by closed aspiration using an 18-gauge needle and 10 ml disposable syringe. Site of aspiration was chosen after careful examination and site was cleansed with isopropyl alcohol. Intra-oral site was prepared using 0.2% chlorhexidine mouth rinse. Subsequently sterile dry gauze was used to wipe the area clean. Maximum sample was aspirated in a single attempt to avoid contamination of the aspirate. In cases, where significant aspirate was not available, sterile culture swabs were introduced into the wound after incision and drainage. A few drops of sterile water were used to keep the swabs hydrated during transport.

Immediately on aspiration residual air was evacuated from the syringe and the needle was capped with a serial rubber cork. The sample was transported to laboratory avoiding any delay.

Monitoring of Clinical Progress

Patients were monitored through a process of daily clinical evaluation and periodic change of dressings as required by the quantum of soakage. Patients were examined for reduction in magnitude of swelling and cessation of pus discharge. The period of recovery was recorded by determining the number of days required for complete cessation of discharge and that required for at least 70% reduction in swelling. The latter was assessed subjectively by two independent observers blinded to the cohorts.

Antibiotic administration was continued for 72 h after cessation of discharge in full therapeutic dose.

Assessment of Microbial Profile

Pus samples were processed and smear studies by Gram staining were done and reported. All samples were subjected to aerobic, anaerobic, and fungal cultures. All the culture media used in the study were prepared by reconstituting the commercially available dehydrated media from HiMedia, India. For aerobic culture, samples were inoculated on blood agar, MacConkey's agar, and in Peptone water/Nutrient broth. For anaerobic culture, sample was transferred to Robertson's Cooked Meat medium and after a delay of 24 h, inoculation was done on Vancomycin/Kanamycin blood agar. The third part of the sample was inoculated on Sabouraud Dextrose Agar for fungal growth.

Incubation was done at 37°C for 18–24 h. If there was no growth, new plates were streaked and were re-incubated along with old plates at 37°C for 18–24 h. Plates for anaerobic cultures were incubated in anaerobic jar at 37°C in an anaerobic workstation (Don Whitley, India) using Gaspak.

If any of the plates showed, growth then smear was prepared after describing colony characteristics. Smear was stained by Gram's Method for assessment of morphologic characteristics. Thereafter, for Gram-positive cocci, the Catalase Backtracking sensitivity, Op tchin sensitivity, Coagulase test, and growth in 6.5% sodium chloride were used, whereas, for gram negative bacilli; oxidase test, catalase test, indole test, urease test, citrate test, and

triple sugar iron test were used. In addition, growth on any media was reconfirmed by taking a pure culture. To identify fungal growth, one plate was incubated at 25°C in a cooling incubator (Remi, India) and the other at 37°C. After positive growth, direct microscopy was done to identify the gross characteristics of the fungi.

Before concluding negative growth, anaerobic plates and fungal plates were incubated for to 14 days and 1 month, respectively. For plates incubated under aerobic conditions, negative cultures were concluded if no growth was observable 72 h post incubation.

Antibiotic Susceptibility Testing

Samples from plates exhibiting positive growth were re-inoculated on Muller-Hinton Agar for rapidly growing non-fastidious organisms. For fastidious organisms, the agar was supplemented with 5% sterile, defibrinated blood. Antibiotic sensitivity studies for the microbial isolates were done by the standard Kirby-Bauer Disk Diffusion technique.

Interpretations were carried out based on the diameter of the zone of inhibition as, Sensitive, Moderately Sensitive or Resistant, using the manual provided by HiMedia Pvt Ltd, India. Antibiotic used were Amoxicillin-Clavulanic acid, Ampicillin, Ampicillin-Sulbactam, Cefadroxil, Clarithromycin, Clindamycin, Linezolid, Norfloxacin, Azithromycin, Vancomycin, Amikacin, Cefoperazone-Sulbactam, Cefotaxime, Ceftazidime, Ceftriaxone, Cefuroxime, Ciprofloxacin, Erythromycin, Gentamycin, Imipenem, Levofloxacin, Penicillin G, Metronidazole, Ornidazole, and Ofloxacin.

Statistical Analysis

The clinical and laboratory data so obtained were analyzed statistically to meet the objectives of the study using the SPSS V.19 (IBM, Chicago, USA). Chi-squire (χ^2) test was applied for the comparison between the groups. The statistical significance was kept at $P \leq 0.05$.

RESULTS

A total of 56 patients with maxillofacial infection fulfilling the inclusion and exclusion criteria were enrolled in the study, 26 patients in Group I (diabetic group), and 30 patients in Group II (non-diabetic group).

Age and Gender

The age of the patients ranged from 15 to 75 years with a mean age of 51.84 years in Group I and 31.16 years in Group II. A majority of the patients (38.5%) within Group I were within the age group of 56–65 years whereas 43% of the Group II patients were in the age range of 15–25 years. Those in Group I were thus significantly older, and this difference was found to be statistically significant [Table 1 and Graph 1].

Table 2 shows the gender distribution of the subjects, and it was observed that a statistically significant difference existed with respect to this parameter between the two cohorts. A reversal of sex ratio was observed when the gender characteristics of the two cohorts was analyzed [Graph 2], with males dominating in Group I and females in Group II.

Table 1: Age distribution of the patient

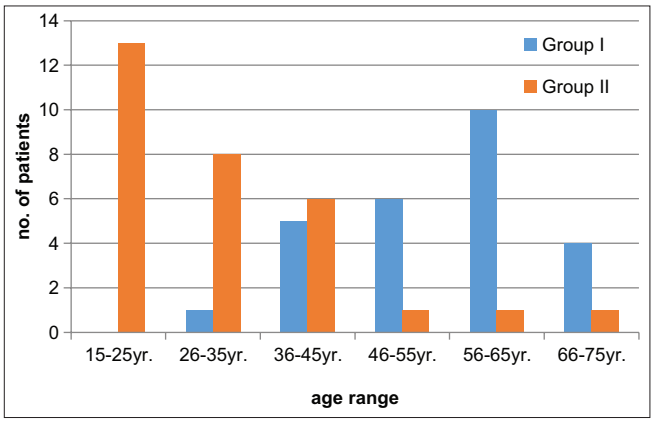
Age	Group I (%)	Group II (%)	*P*-value
15–25 years	0 (0)	13 (43)	0.000 (S)
26–35 years	1 (3.8)	8 (26.7)	
36–45 years	5 (19.2)	6 (20)	
46–55 years	6 (23.1)	1 (3.3)	
56–65 years	10 (38.5)	1 (3.3)	
66–75 years	4 (15.4)	1 (3.3)	

S: Significant, NS: Non significant

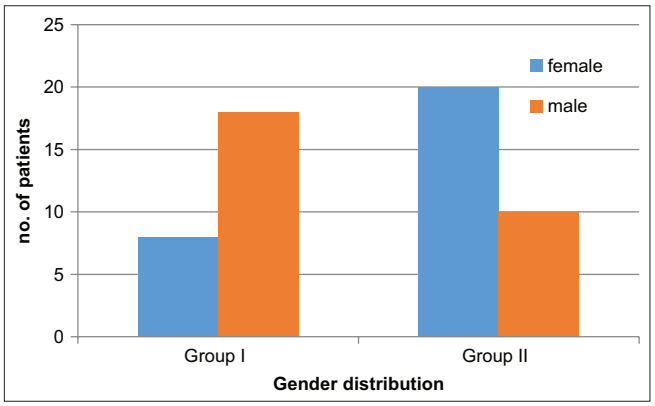
Table 2: Gender distribution of patient

Gender	Group I (%)	Group II (%)	*P*-value
Female	8 (30.8)	20 (66.7)	0.007 (S)
Male	18 (69.2)	10 (33.3)	

S: Significant, NS: Non significant



Graph 1: Age distribution of the patients



Graph 2: Gender distribution of patients

Presentation

The extensiveness of infection in the two groups was evaluated through assessment of the number of facial compartments involved (characterized dichotomously as single or multiple), fever and total white blood cell (WBC) counts.

Number of Spaces Involved

Majority of patients in the diabetic cohort (57.7%) had multiple space involvement as opposed to the non-diabetic group where 60% of the patient had a single space involvement. A statistically significant difference was thus observed with respect to this parameter [Table 3 and Graph 3].

Fever

Significantly higher proportion of patients in the non-diabetic group is presented in an afebrile state as opposed to the diabetic group. The majority of patient in diabetic group were noted to have mild fever on presentation [Table 4 and Graph 4].

Total WBC Count

The leukocyte response was considered under four heads; normal, mild, moderate, and high. The reference range for the same is indicated in Table 5. Analysis of this parameter showed that the counts were significantly raised in the diabetic cohort as compared to non-diabetic patients as in the latter group significantly higher no. About 73.3% of patients had normal counts. These differences were noted to be statistically significant [Table 5 and Graph 5].

Table 3: Number of space involved

No. of space	Group I (%)	Group II (%)	*P*-value
No space	4 (15.4)	7 (23.3)	0.005 (S)
Single	7 (26.9)	18 (60.0)	
Multiple	15 (57.7)	5 (16.7)	

S: Significant, NS: Non significant

Table 4: Fever

Fever	Group I (%)	Group II (%)	*P*-value
No fever	7 (26.9)	19 (63.3)	0.013 (S)
Mild 99–100°F	14 (53.8)	10 (33.3)	
Moderate 101–102°F	5 (19.2)	1 (3.3)	
High >102°	0	0	

S: Significant, NS: Non significant

Table 5: Total leukocyte counts

TLC (cells/mm³)	Group I (%)	Group II (%)	*P*-value
Normal (4500–10000)	5 (19.2)	22 (73.3)	0.000 (S)
Mild (>10000–15000)	16 (61.5)	6 (20.0)	
Moderate(>15000–20000)	5 (19.2)	2 (6.7)	
High (>20000)	0	0	

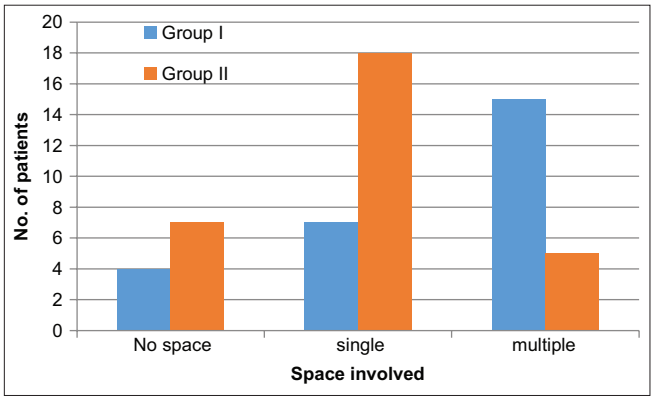
S: Significant, NS: Non significant, TLC: Total leukocyte counts

Comparison of Isolates

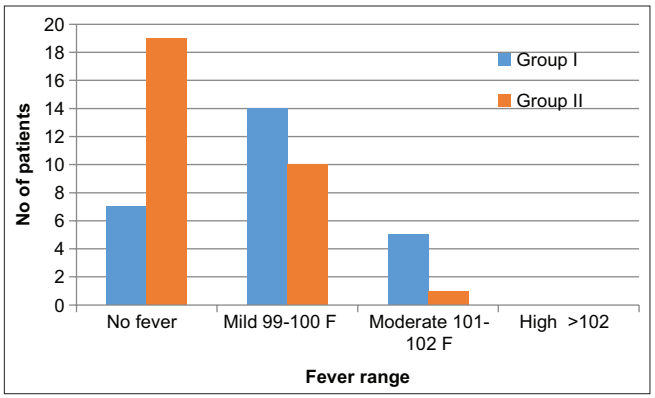
Microbial profile of the infections was determined through Gram staining characteristics, and isolation in culture.

Gram's Stain

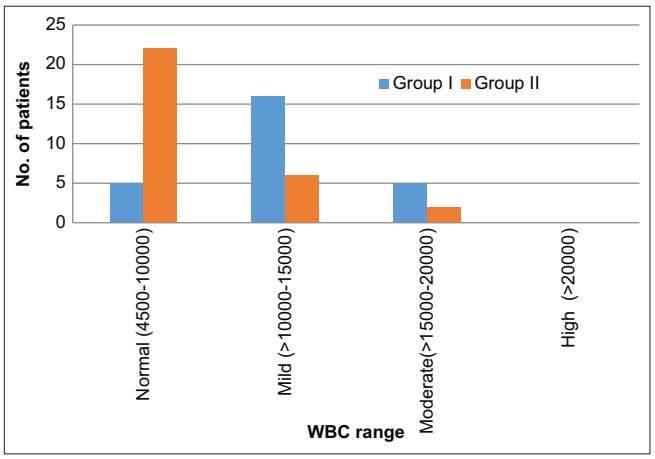
The organisms identified on the basis of staining characteristics were categorized as purely gram positive, mixed population of Gram positive and Gram negative and purely Gram negative. No organisms were identifiable in one patient belonging to diabetic cohort. Comparison of



Graph 3: Number of space involved



Graph 4: Fever



Graph 5: White blood cell count at presentation

the two groups on the basis of Gram staining characteristics showed no statistically significant differences. Majority of infections in both groups (69.2% and 83.3% in Groups I and II, respectively) were caused by purely Gram-positive organisms [Table 6 and Graph 6].

Bacterial Isolates

35 isolates in each group accounting for 11 different organisms were identified from 51 patients (24 in Group I and 27 in Group II). 2/26 and 3/30 patients in Groups I and II, respectively, had sterile cultures. Overall, *Staphylococcus aureus* was the most frequently isolated organism collectively as well as independently in both cohorts. Comparison of microbial isolates between the two groups did not how ever reveal any significant statistical differences [Table 7 and Graph 7].

Antibiotic Susceptibility Profile

In vitro susceptibility to different antibiotics was assessed and compared between the groups for the purpose of evaluation; moderate sensitivity was also regarded as susceptibility. Susceptibility pattern to 26 antibiotics tested for each isolate was compared between the two groups. Analysis for *in vitro* susceptibility showed statistically significant differences between the two groups for ceftazidime, erythromycin, and levofloxacin. The resistance to levofloxacin was significantly higher in diabetic cohort whereas resistance to erythromycin and ceftazidime was found to be significantly higher in the non-diabetic cohort. Overall, excellent responses were evident for clindamycin, linezolid, and metronidazole in both the groups [Table 8 and Graph 8].

Table 6: Gram stain

Gram stain	Group I (%)	Group II (%)	*P*-value
No stain	1 (3.8)	0 (0)	0.333 (NS)
Gram-positive	18 (69.2)	25 (83.3)	
Mixed	7 (26.9)	5 (16.7)	

S: Significant, NS: Non significant

Table 7: Bacterial isolates

Isolates	Group I (%)	Group II (%)	*P*-value
Staphylococcus aureus	13 (50)	10 (43.5)	0.161 (NS)
Streptococcus mutans	3 (11.5)	8 (26.7)	0.139 (NS)
Pseudomonas aeruginosa	3 (11.5)	2 (6.7)	0.431 (NS)
Klebsiella pneumoniae	5 (19.2)	1 (3.3)	0.068 (NS)
Streptococcus viridans	2 (7.7)	4 (13.3)	0.407 (NS)
Actinomyces	0 (0)	1 (3.3)	0.536 (NS)
Streptococcus salivarius	1 (3.8)	2 (6.7)	0.554 (NS)
Streptococcus sanguinis	4 (15.4)	3 (10)	0.418 (NS)
Staphylococcus epidermidis	2 (8.0)	2 (6.7)	0.622 (NS)
Streptococcus milleri	1 (3.8)	2 (6.7)	0.554 (NS)
β hemolytic streptococcus	1 (3.85)	0 (0)	0.464 (NS)

S: Significant, NS: Non significant

DISCUSSION

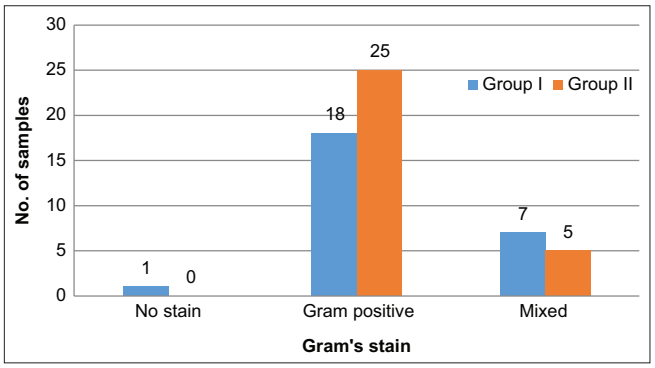
Treatment of maxillofacial infections is a routine practice in oral and maxillofacial surgery. Most of the times the origin is odontogenic.[5] Primary etiology may be carious tooth or a periodontal pocket and sometimes may be a partially erupted tooth.

Infections usually spread into a potential anatomical space present in maxillofacial region following the path of least resistance. Host defense plays the most important role, it may be compromised due to multiple factors.[5] Diabetes has been considered as one of the major factors adversely affecting the host defense.[10] Diabetes represents a major public health problem worldwide. India leads the world in so far as diabetic population is concerned and the same is expected to touch 69.9 million by 2025 (Mohan and Sandeep 2007).[11]

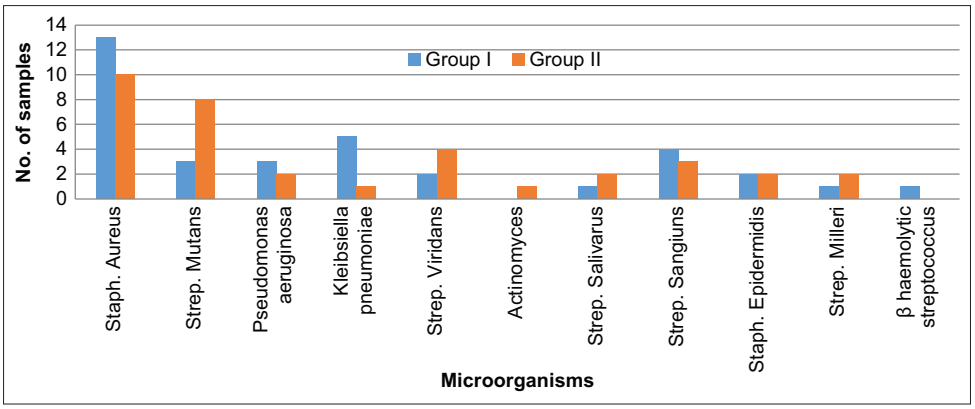
The mechanisms by which diabetes predisposes the infections are stated to be hyperglycemia, disturbed neutrophil function, depressed cellular immunity, abnormalities in compliment activation along with the vascular abnormality, all of which predisposes the patients to a higher risk of infections.[13] In a retrospective cohort study Shah and Hux (2003)[10] concluded that infection should be considered as a complication of diabetes.

It is known today that more than 500 different strains of microorganisms inhabit the oral cavity in a normal healthy adult.[12] Various studies have reported that usually harmless commensals of oral cavity turn pathogenic in certain conditions. Sharma *et al.* (2011)[13] also reported that the increased occurrence of oral infection in diabetic patients can be attributed to the changed environment of oral cavity which enhances the growth of bacteria.

Earlier there was a debate over the microbial aspect of odontogenic infections. In 1970, it was thought that odontogenic infections had a predominance of aerobic and microaerophilic organisms, mainly staphylococci



Graph 6: Gram stain



Graph 7: Bacterial isolates

Table 8: Antibiotic sensitivity pattern

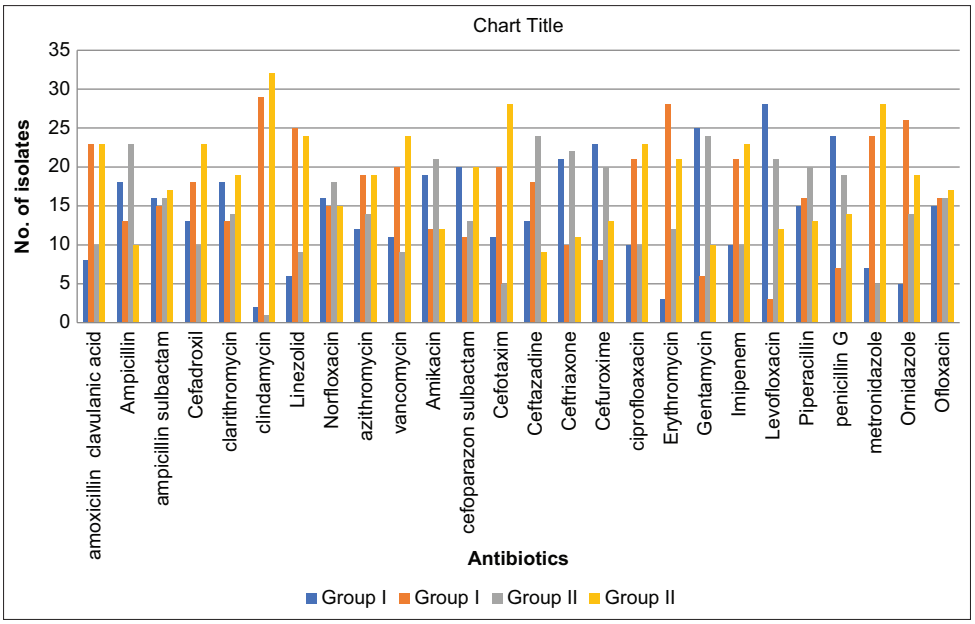
Antibiotic	Group I (%)		Group II (%)		*P*-value
	Resistant	Sensitive	Resistant	Sensitive	
Amoxicillin-clavulanic acid	8 (24.2)	23 (69.7)	10 (27.8)	23 (63.9)	0.864 (NS)
Ampicillin	18 (54.5)	13 (39.4)	23 (63.9)	10 (27.8)	0.585(NS)
ampicillin sulbactam	16 (48.5)	15 (45.5)	16 (44.4)	17 (47.2)	0.907 (NS)
Cefadroxil	13 (39.4)	18 (54.4)	10 (27.8)	23 (63.9)	0.585 (NS)
Clarithromycin	18 (54.5)	13 (39.4)	14 (38.9)	19 (52.8)	0.428 (NS)
Clindamycin	2 (6.1)	29 (87.9)	1 (2.8)	32 (88.9)	0.759 (NS)
Linezolid	6 (18.2)	25 (75.8)	9 (25)	24 (66.7)	0.708 (NS)
Norfloxacin	16 (48.5)	15 (45.5)	18 (50)	15 (41.7)	0.910 (NS)
Azithromycin	12 (36.4)	19 (57.6)	14 (38.9)	19 (52.8)	0.894 (NS)
Vancomycin	11 (33.3)	20 (60.6)	9 (25)	24 (66.7)	0.728 (NS)
Amikacin	19 (57.6)	12 (36.4)	21 (58.3)	12 (33.3)	0.919 (NS)
Cefoperazone sulbactam	20 (60.6)	11 (33.3)	13 (36.1)	20 (55.6)	0.124 (NS)
Cefotaxime	11 (33.3)	20 (60.6)	5 (13.9)	28 (77.8)	0.160 (NS)
Ceftazidime	13 (39.4)	18 (54.5)	24 (66.7)	9 (25)	0.042 (S)
Ceftriaxone	21 (63.6)	10 (30.3)	22 (61.1)	11 (30.6)	0.932 (NS)
Cefuroxime	23 (69.7)	8 (24.2)	20 (55.6)	13 (36.1)	0.479 (NS)
Ciprofloxacin	10 (30.3)	21 (63.6)	10 (27.8)	23 (63.9)	0.923 (NS)
Erythromycin	3 (9.1)	28 (84.8)	12 (33.3)	21 (58.3)	0.039 (S)
Gentamycin	25 (78.1)	6 (18.8)	24 (66.7)	10 (27.8)	0.517 (NS)
Imipenem	10 (30.3)	21 (63.6)	10 (27.8)	23 (63.9)	0.923 (NS)
Levofloxacin	28 (84.8)	3 (9.1)	21 (58.3)	12 (33.3)	0.039 (S)
Piperacillin	15 (45.5)	16 (48.5)	20 (55.6)	13 (36.1)	0.578 (NS)
penicillin G	24 (72.7)	7 (21.2)	19 (52.8)	14 (38.9)	0.224 (NS)
Metronidazole	7 (21.2)	24 (72.7)	5 (13.9)	28 (77.8)	0.700 (NS)
Ornidazole	5 (15.2)	26 (78.8)	14 (38.9)	19 (52.8)	0.066 (NS)
Ofloxacin	15 (45.5)	16 (48.5)	16 (44.4)	17 (47.2)	0.936 (NS)

S: Significant, NS: Non significant

and streptococci. With recent advances in the field of diagnostic microbiology and techniques, it is now known that odontogenic infections are poly microbial in origin.[14] Studies[5] comparing the microorganisms in diabetic and non-diabetic patients suffering from infection have also shown poly microbial origin with no significant differences between the groups.

Staphylococci produce coagulase, an enzyme which can cause fibrin deposition, and so are frequently associated with abscess formation. Streptococci produces enzyme such as streptokinase, hyaluronidase and streptodornase, enzymes that break down fibrin and ground substance of connective tissue, and therefor are often associated with so frequently present with cellulitis.[9]

Multiple authors[9,13,15,17,18] have observed and reported a distinct predilection for occurrence of maxillofacial infections among males, the lone exceptions being Mahalle *et al.* (2014)[19] who reported a female predilection and Hunt *et al.* (1989)[20] who reported an equal gender distribution. In the present study, over all there was no distinct gender predilection, an observation akin to that of Hunt *et al.*[20] However, the interesting observation was that of



Graph 8: Antibiotics

a complete reversal of sex ratio between the diabetic and non-diabetic cohorts. This observation is entirely different from that reported in the literature generally.

Sanchez *et al.* (2011)[23] showed that infections are found in almost all ages, his study showing a range of 4–80 years. Patients in our study however had the age ranging from 15 to 75 years. Haug *et al.* (1991)[24] in his study found that most common age range for all odontogenic infection was 25–30 year. Our observations are like those of Haug *et al.* with maximal patients (13 out of 56) belonging to the age group of 15–25 years. In contrast with the general population the diabetic patients presenting with maxillofacial infections are generally much older, findings that have been mentioned by Huang *et al.* (2005),[25] The mean age in the diabetic population affected with maxillofacial infection has been reported to vary between 45 and 60 years. The mean age of diabetic cohorts in present study was 51.8 years and that of non-diabetic cohorts was 31.16 years. These observations concur with those reported in the literature.

Multiple space involvement at the time of presentation was significantly higher in the diabetic group in our study. This agrees with observations forwarded by Huang *et al.* (2005),[25] Rao *et al.* (2010),[5] and Juncar *et al.* (2014).[16] The most frequently involved spaces in the present study were submandibular and buccal spaces in both the cohorts. Other cohort studies[5,29] have also mentioned similar findings. Although Huang *et al.* (2005)[25] reported parapharyngeal space to be the most involved space in diabetics, these studies essentially evaluated deep neck space involvement.

Fever occurs as an acute inflammatory response to bacterial endotoxins and cell wall fragments. About 53.5% patients in the present study were found to be febrile at the time of initial presentation. This observation is in agreement with that of Bridgeman *et al.* (1995),[26] who reported fever in 50% of the patients with maxillofacial infections but differs from the findings described by Mathew *et al.* (2012) [27] and Lee *et al.* (2007)[18] who recorded fever in only 35% and 14.6% patients, respectively.

Rao *et al.* (2000)[5] while comparing the deep neck infections in diabetic and non-diabetic patients, reported pyrexia in 60% of diabetic patients compared to 61.3% of non-diabetic patients. Rao *et al.* (2010),[6] on the other hand, found pyrexia in a significantly higher number of diabetic patients with maxillofacial infections as compared to non-diabetics which are observations like those of the present study. It has been suggested[6] that these differences may be due to a higher penchant for bacteremia in the diabetic patients.

Bacterial infection initiates neutrophil release from the bone marrow and thus induces a neutrophil leukocytosis. Rao *et al.* (2010)[5] in their comparative studies in diabetic and non-diabetic patients found no statistically significant difference in leukocytosis. Chang *et al.* (2013)[28] reported higher WBC count in diabetic patients compared to non-diabetic patients. In our study too, significantly higher proportion of patients (80.7%) in the diabetic group had leukocytosis as compared to non-diabetic patients (26.7%). None of the patients however had leukocytosis exceeding 20,000 cells/mm^3, with the majority showing

mild leukocytosis. It may be supposed that higher tendency for leukocytosis in diabetic patients could be due to the problem of impaired chemotaxis which probably reduces WBC availability at the target site. Increased WBC released into the peripheral circulation may therefore be a compensatory response to improve leukocyte emigration.

Direct smear studies of gram staining were done to identify the gross phenotypic characteristics of organisms in pus sample with the intention that it can help in determining the initial antibiotic to be given before the culture sensitivity reports. None of the studies reviewed have reported direct smear evaluations and comparison. Direct smear examination showed a predominance of Gram-positive cocci in both the groups without any significant statistical difference. This also validates our choice of Clindamycin as the empiric antibiotic.

Lewis *et al.* (1986),[21] Storoe and Haug (2001),[14] Huang *et al.* (2004)[15] and Robertson and Smith (2009)[22] covering diverse populations and performed at different time periods show that maxillofacial infections are polymicrobial in nature with aerobic, anaerobic, and mixed micro flora. Some studies[9,32] show that these infections are predominantly caused by anaerobic organisms. Rega and Ziccardi (2006)[1] stated that maxillofacial infection was caused predominantly by aerobes and facultative anaerobes. The results of our study are in concurrence with those of Rega and Ziccardi (2006)[1] and Rao *et al.* (2010).[5] Many studies[14,21] have shown successful isolation of obligate anaerobes. We were unable to isolate obligate anaerobes in any of the samples, but this had no impact on the outcome of treatment. It is possible that the empiric uses of Clindamycin helped to target obligate anaerobes as well since this antibiotic has proven record of effectiveness against obligate anaerobes. Isolation of anaerobic bacteria remains a technique sensitive and challenging issue.

There was a low occurrence of no growth in our study, there were only 7.2% of the sample which showed no growth which agrees with Sklavounos *et al.* (1986)[29] and Konow *et al.* (1992)[30] who reported only 9.5% and 1.6% negative growths, respectively.

In the present study, most common organism isolated in both the groups was *S. aureus* (23/56 patients) which is similar to several other reports.[6,10,19] In contrast, Kuriyama *et al.* (2005)[22] found Streptococci viridans to be the predominant aerobe involved in such infections. Isolation of *S. aureus* has clinical significance as resistant strains are known to occur which do not respond to routine microbial therapy. Cohort studies comparing maxillofacial infection in diabetics and non-diabetics such as those by Rao *et al.* (2010),[5] Huang *et al.* (2005),[25] reported *Klebsiella* as the predominant organism in diabetic patients with maxillofacial infection. Second to *S. aureus*, *Klebsiella* was the next most dominant organism in the diabetic cohorts.

A total of 25 antibiotics were tested in the present study. Over all excellent responses were evident for clindamycin, linezolid, and metronidazole in both the groups. Chang *et al.* (2005)[31] also reported the high sensitivity for clindamycin, while Boyanova *et al.* (2006)[32] reported clindamycin and metronidazole to be highly efficient against gram negative rods.

There was no statistically significant difference in antibiotic susceptibility and resistance between the two cohorts except for ceftazidime, erythromycin, and levofloxacin. Other published studies in literature have not assessed the cohort differences in the antibiotic susceptibility of the causative organisms. The susceptibility characteristics have been assessed and described only with relevance to organisms isolated. Antimicrobial sensitivity is significantly influenced by the previous exposure to antibiotics and varies from individual to individual.

Lee *et al.* (2007),[18] Chang (2013)[28] reported higher no. of complications in diabetic patients, although we did not encounter complication in any of the two groups. This could be due to the fact that majority of the diabetics did not have uncontrolled diabetes at the time of presentation.

CONCLUSION

There are many authors who have published their studies assessing microbiology, clinical presentation and antibiotic susceptibility of the patient suffering with maxillofacial infections. we have performed a prospective study. After the evaluation of the results of the study we were able to state that; diabetic males are at higher risk of getting infections. Diabetic patients are at a higher risk of bacteraemia, the spread of infection is higher in diabetic patients. The response to empirical antibiotic therapy (clindamycin) in both the groups provide satisfactory results. There were no significant differences in organism isolated and antibiotic susceptibility between the groups. *Kleibsiella* (facultative anaerobe) isolated in higher numbers in diabetic population. Diabetic patients have a longer duration of illness, which can be due to the time taken to control the blood glucose levels.

Management of maxillofacial infections remains the same for both diabetic and non-diabetic population although diabetic patients have to be trated with little more caution and precaution as they are at the higher risk of developing complication.

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Original Article

Study of Heart Rate Variability in Tobacco Smokers and Smokeless Tobacco Users

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Abstract

Introduction: Tobacco use is a public health concern worldwide. It is the leading preventable agent of death in the world. It is used both in smoked or smokeless form. It is a well-known fact that tobacco smoking predisposes to atherosclerosis leading to various diseases viz. high blood pressure, myocardial infarction, and stroke. Nicotine in tobacco is found to alter the cardiovascular autonomic functions. Deleterious effects of tobacco in the smokeless form are yet to be explored. Impact of nicotine on cardiovascular autonomic functions can be best diagnosed using the Heart rate variability (HRV) assessment.

Material and Methods: The study was conducted in the Department of Physiology, Pandit Bhagwat Dayal Sharma, Post Graduate Institute of Medical Sciences, Rohtak. A total of 90 healthy adult males were included in the study. They were grouped as 30 tobacco chewers (Group I), tobacco smokers (Group II), and tobacco nonusers (Group III). Subjects with a history of hypertension, cardiopulmonary or endocrine disorder were excluded from the study. HRV was recorded and frequency domain parameters were analyzed.

Results: There is a decrease in mean values of frequency domain parameters viz. Very-low-frequency (VLF) and heart failure (HF) (nu) in both the test groups with more decrease in Group II. The decrease is highly statistically significant ($P < 0.001$) for VLF and significant ($P < 0.05$) for HF (nu) in Group II. The mean value of low-frequency LF (nu) is decreased in both test groups but decrease is more in Group I though statistically insignificant. The mean value of LF/HF ratio is increased in both test groups with more increase in Group II. This increase in LF/HF ratio is highly significant ($P < 0.001$) in Group II.

Conclusion: HRV analysis in tobacco smokers and chewers has revealed the disturbances in cardiac autonomic regulation by increasing sympathetic activity predisposing the subjects to various cardiovascular diseases. However, disturbance was more in smokers than chewers. Hence, intervention to quit tobacco even in the smokeless form is required.

Keywords: Tobacco, Smoking, Smokeless tobacco, Heart rate variability, Autonomic

INTRODUCTION

Worldwide humans have been using tobacco for about a thousand years. Smoking of tobacco dates to 5000 BC. Earlier what started as something associated with spiritual awakening eventually transformed from sacred to iniquitous, sophisticated to vulgar, an elixir to a deadly and slow poison.[1,2] It is a practice where tobacco is burnt and smoke is tasted or inhaled. This can be achieved by means of beedis, cigarettes, cigars, hookahs, etc.[3,4]

Smoke contains nicotine (a highly addictive psychoactive drug), carbon monoxide (CO), hydrogen cyanide (HCN), phenol, and several carcinogenic products such as benzopyrene, Nnitrosamine (NNK). that bind to DNA and cause many genetic mutations leading to various cancers such as bronchogenic carcinoma, cancers of the mouth, larynx, pancreas, and liver.[5,6]

The use of tobacco without burning for similar purpose is known as smokeless tobacco (SLT). It can be taken in various forms such as chewing, sniffing (naswar), khaini, zarda, plug, twist, and snus. Tobacco chewing is the most common form of SLT practiced in India.[7] SLT garnered

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immense popularity after awareness regarding hazards of smoking began to spread.

It is presumed as a safe and non-toxic alternative for smoking.[8]

Cigarette smoking is a major risk factor for the development of atherosclerosis, coronary heart disease, acute myocardial infarction (MI), and sudden cardiac death.[5] The risk of a non-fatal heart attack increases by 5.6% for every cigarette smoked.[9] However, tobacco chewing increases the risk of MI more than two folds.[10] Hypertension is significantly prevalent in both tobacco smokers and chewers. The use of tobacco either by smoking or chewing changes the lipid profile significantly.[11]

Smokeless tobacco also contains substantial amounts of nicotine, which is a cardioactive substance.[12] Impact of the nicotine on cardiovascular autonomic functions can be best diagnosed using the Heart rate variability (HRV). Various studies have either shown the effects of tobacco smoking on HRV or the effect of SLT on HRV.[11,13,14] We in our study, have compared HRV in tobacco smokers and SLT users.

MATERIALS AND METHODS

The present study was conducted in the Department of Physiology, Pt. B.D. Sharma Post Graduate Institute of Medical Sciences (PGIMS), Rohtak after getting approval from the institutional ethical committee. A total of 90 male subjects of age group 25–50 years were included in the study. The subjects were divided into three groups.

- Group I – 30 male volunteers who were chronic tobacco chewers (non-smokers) for a minimum of 10 pouch years in continuation with a duration of 7 years or more.
- Group II – 30 male volunteers who were chronic smokers (non-chewers) for minimum 10 pack years in continuation with a duration of 7 years or more.
- Group III – 30 male volunteers who had never used tobacco in any form (control group).

Exclusion Criteria

- History or symptoms of any chronic cardiopulmonary, endocrine or metabolic disorder.
- History or symptoms of any oral lesion.
- History of any drug intake.

Pack Years

Cigarette smoking was quantified in pack years. A standard package contains 20 cigarettes. This was translated into pack years as:

Pack years = number of packs per day x years smoked.

Example: 10 cigarettes per day = 1/2 pack for 10 years = 5 pack years ($1/2 \times 10 = 5$).[8]

Pouch Years

Tobacco chewing was quantified in pouch years. This was calculated as:

Pouch years = No of pouches per day x years of chewing

Example: 1 pouch per day for 10 years = 10 pouch years ($1 \times 10 = 10$).[8]

Preliminary Preparation

Consent was obtained from every subject to undergo the whole procedure. All the tests were conducted from 10 am to 1 pm to avoid diurnal variation. Overnight abstinence from tobacco use in any form was recommended. Subjects were asked to avoid tea, coffee, carbonated drinks, or heavy meals at least two hours before the test procedure. The whole procedure was explained in detail to each subject in his own language to allay any apprehension or fear. The basic parameters such as age, weight, and height of subjects were recorded. Heart rate, respiratory rate, systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial blood pressure (MAP) were taken and noted down.

After preliminary history taking and examination, the subjects were asked to lie down on the couch and made to relax in front of the Polyrite D system. The three disposable adhesive electrodes were attached to the left arm, right leg, and left leg, respectively. The basal recording of electrocardiograph (ECG) (Lead II) was taken for 5 min. Utmost care to minimize the movements by instructing the subjects not to move and not to speak while the recording is in progress. From the ECG, the analysis of HRV was done automatically in the machine and the printed report of HRV provided the data of required variables. The HRV is based on the duration of the time interval between two R waves, graphically represented in the form of a RR interval tachogram. The functional value of the tachogram is the duration of a RR interval (in millisecond) at a certain point of time. For analysis of HRV, there are two domains mainly "Time domain" and "Frequency domain" as described earlier. Spectral analysis of ECG was done by the Fast Fourier Transformation method. Following HRV parameters were selected for study.

- Mean heart rate (beats/min)
- Mean RR interval (seconds)
- Very-low-frequency (VLF) (ms^2)
- LF (nu)
- Heart failure (HF) (nu)
- low frequency (LF/HF) ratio

Statistics

All the data obtained by the above two procedures were analyzed by a commercially available software package SPSS software. Statistical significance between the three groups was determined by ANOVA test and post hoc test. $P < 0.05$ was considered statistically significant and $P < 0.001$ was considered highly statistically significant.

RESULTS

The anthropometric parameters including age, height, weight, and BMI were comparable in the three groups with $P > 0.05$ Furthermore, there was no statical significance between heart rate, RR interval, SBP, DBP, and MAP in the three groups.

As evident from Table 1, the mean heart rate is increased in both Group I and Group II but the increase is more in Group II. The mean RR interval is decreased both Group I and Group II, but the reduction is more in Group I. However, changes in mean HR and mean RR are statistically insignificant. There is decrease in mean values of frequency domain parameters viz. VLF and HF (nu) in both the test groups with more decrease in Group II. The decrease is highly significant ($P < 0.001$) for VLF and significant ($P < 0.05$) for HF (nu) in Group II. The mean value of LF (nu) is decreased in both test groups but decrease is more in Group I though statistically insignificant. The mean value of LF/HF ratio is increased in both test groups with more increase in Group II, [Figure 1]. This increase in LF/HF ratio is highly significant ($P < 0.001$) in Group II.

Table 2 shows comparison in HRV parameters in Group I, Group II and Group III after post hoc analysis.

- Group I versus Group IIII- shows that there is a statistically highly significant ($P < 0.001$) difference for VLF, HF, and LF/HF ratio. There is a significant ($P < 0.05$) difference in HF- in normalized units.
- Group II versus Group III- shows that there is a statistically highly significant ($P < 0.001$) difference for VLF, HF, and LF/HF ratio. There is a significant ($P < 0.05$) difference in HF- in normalized units.
- Group I versus Group II- shows no statistically significant ($P < 0.05$) difference in the HRV parameters.

DISCUSSION

Cigarette smokers are more likely to develop both large-vessel atherosclerosis and small-vessel disease. There is a multiplicative interaction between cigarette smoking and other cardiac risk factors such that the increment in risk produced by smoking among individuals with hypertension or elevated serum lipids is substantially greater than the increment in risk produced by smoking for individuals without these risk factors. In addition to its role in promoting atherosclerosis, cigarette smoking also increases the likelihood of MI and sudden cardiac death by promoting platelet aggregation and vascular occlusion. Cessation of smoking reduces the risk of a second coronary event within 6–12 months.[8]

HRV is beat to beat variation of heart rate. It is a non-invasive method used to evaluate the autonomic regulation of heart rate. Alterations in HRV may have substantial clinical implications. Recent studies have shown decreased HRV to be associated with accelerated development of atherosclerotic coronary artery disease and increased cardiac mortality.[15] Smoking induces autonomic imbalance typically characterized by sympathetic hyperactivity. It acutely reduces baseline levels of vagal-cardiac nerve activity and completely resets vagally mediated arterial baroreceptor-cardiac reflex responses.[15]

In our study, we found in Group II, an increased heart rate even though it was statistically insignificant, indicating decreased vagal tone of heart. There was reduction in LF though statistically insignificant, suggesting impaired sympathetic activity. Furthermore, there was significant reduction in HF (nu) and highly significant increase in the LF/HF ratio suggesting that during smoking, associated with the decrease in the parasympathetic activity, there was increase in sympathetic activity.[13] Since HRV assesses the state of sympathovagal balance, it can be used to determine susceptibility to developing autonomic dysfunctions in

Table 1: Comparison of HRV in Group I, Group II, and Group III

Parameters	Group I (Chewers) (n=30) (Mean±SD#)	Group II (Smokers) (n=30) (Mean±SD)	Group III (Control) (n=30) (Mean±SD)	*P* value
HR (beats/min)	80.21±9.56	84.48±25.95	73.94±15.0	0.094
RR interval (s)	0.744±0.15	0.747±0.144	0.76±0.09	0.636
VLF (ms2)	501.58±416.83	443.79±253.85	1977.13±1104.22	<0.001**
LF (nu)	53.72±10.95	58.10±41.77	59.91±12.87	0.696
HF (nu)	22.94±6.39	17.76±11.39	47.07±63.16	0.009*
LF/HF	2.52±0.91	3.37±0.61	2.02±0.92	<0.001**

*P<0.05: Significant, **P<0.001: Highly significant, # SD: Standard deviation

Table 2: Post hoc test in HRV in Group I, Group II, and Group III

Groups	*P* value					
	Mean HR	Mean RR	VLF (ms^2)	LF (nu)	HF (nu)	LF/HF
Group I versus Group III	0.100	0.689	<0.001**	0.676	<0.001**	<0.001**
Group II versus Group III	0.061	0.344	<0.001**	0.2680	<0.001**	<0.001**
Group I versus Group II	0.673	0.584	0.749	0.489	0.372	0.246

*P<0.05=Significant, **P<0.001=Highly significant

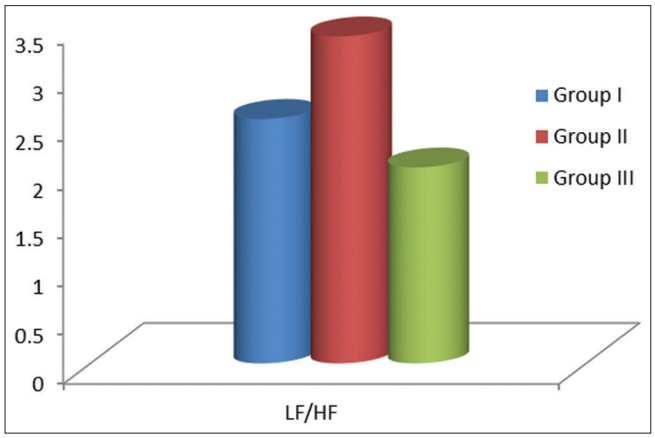

Figure 1: LF/HF in Group I, Group II, and Group III

conditions such as prehypertension and hypertension.[16] These results point towards autonomic imbalance with an increase in sympathetic tone in smokers.

In chewers, we observed, decrease in the mean RR interval and increase in the mean HR and though insignificant. Nicotine causes vasoconstriction possibly through alteration of a cyclic-GMP-dependent vasoactive mechanism. Significant rise in the diastolic blood pressure is of great concern as any increase in the diastolic BP is an indicator of hypertension.[14] Significant decline in VLF and LF (nu) suggests an increased sympathetic activity in chewers. And a highly significant decline in HF (nu) reflected decreased parasympathetic activity in. The significant increase in LF/HF ratio in Group I shows disturbances in the sympathovagal balance, with decreased vagal tone and increased sympathetic activity. Increased LF/HF ratio reflects decreased HRV.[16]

These effects are attributed mainly to the action of nicotine that binds to nicotinic cholinergic receptors present in the autonomic ganglia, neuromuscular junctions, and central nervous system, which on stimulation, increases the release of several neurotransmitters.[14] The nicotine and others substances found in cigarettes also stimulate the release of adrenalin into the sympathetic nervous system. In addition, the stimulation of the nicotinic receptors in the autonomic nervous system has been associated with the sympathetic excitatory effects of smoking.[17] There are three possible mechanisms to explain this sympathetic activation. (i) Direct effect on the central nervous system; (ii) stimulatory effect on the ganglionic sympathetic transmission that leads to a subsequent increase in the postganglionic efferent sympathetic activity; and (iii) effect on the sympathetic peripheral nervous terminations.[14,18,19]

CONCLUSION

Tobacco in any form affects the cardiovascular system adversely by altering the sympathovagal balance. Although deleterious effects of smoking were more than tobacco chewing, tobacco chewing should not be considered as a safe alternative. Awareness regarding cardiac effects of SLT is necessary. The use of tobacco in any form must be discouraged. Furthermore, HRV can emerge as a screening test for assessing cardiac autonomic disturbances in preclinical stages.

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Original Article

Assessment of Sarcopenia as an Independent Predictor of Post-operative Chest Complications in Patient Undergoing Elective Open Upper Abdominal Surgeries: A Prospective Observational Hospital Based Study

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Abstract

Introduction: Sarcopenia is a condition that becomes more prevalent with advancing age, as well as with many diseases and is increasingly recognized as an independent risk factor for adverse health outcomes. So Sarcopenia as a potential prognostic biomarker deserves attention. The present study demonstrated that sarcopenia itself, defined as reduced skeletal muscle mass plus low muscle strength and/or low physical performance, is an independent risk factor for pulmonary complications after elective open upper abdominal surgery.

Materials and Methods: This is a prospective study including patients who underwent elective open upper abdominal surgeries at our hospital. Sarcopenia was diagnosed by a combination of third lumbar vertebra Psoas muscle index (L3 PMI) using preoperative computed tomography scan of the abdomen and 6-m usual gait speed. The presence of postoperative pulmonary complications (PPC) was screened daily for 7 days using the Melbourne Group Scale (Version 2). Other complications were also identified and documented as per Clavien-Dindo classification.

Results: A total of 165 patients undergoing open upper abdominal surgeries were included in the study, and 20 patients were diagnosed as having sarcopenia. PPC occurred in 45 patients, including 11 with sarcopenia and 34 without sarcopenia. The sarcopenic group was significantly older and had significantly lower PMI, calf muscle circumference, and gait speed than non-sarcopenic group, but other physical parameters such as height, weight, and body mass index were not significantly different. The distribution of postoperative infectious and non-infectious diseases for 165 patients was as follows: diarrhea, 3 cases (1.82%); paralytic ileus, 11 cases (6.67%); urinary retention, 6 cases (3.64%); wound abscess, 17 cases (10.3%), with slightly more prevalence in sarcopenia group. The results of my study indicate that sarcopenia is a unique, independent preoperative predictor of pulmonary complications after elective open upper abdominal surgeries.

Conclusion: The present study demonstrated that sarcopenia itself, defined as reduced skeletal muscle mass plus low muscle strength and/or low physical performance, is an independent risk factor for pulmonary complications after elective open upper abdominal surgery.

Key words: Post-operative chest complication, Post-operative complications, Sarcopenia, Upper abdominal surgeries

INTRODUCTION

Sarcopenia- broadly defined as significant loss of muscle mass and function- is recognized increasingly as an important independent risk factor for numerous adverse outcomes.[1] The association of malnutrition with adverse clinical outcomes is well established in the literature and recognized as early as 1936. The European Union on Sarcopenia in Older People (EWGSOP) recommends using the presence of both low muscle mass and low muscle function (strength or function) for the diagnosis of sarcopenia.[2]

Loss of mass and functional capacity of skeletal muscle is a major cause of morbidity in older individuals as well as in patients affected by any acute and chronic

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conditions including infectious diseases, endocrine, and metabolic disorders, organ dysfunction, immunological diseases, vascular diseases, hematological disorders, and malignancies.[3]

Sarcopenia has also been shown to have a negative impact on patients undergoing surgery. The clinical implications of sarcopenia have been consistently associated with increased duration of hospital stay, higher costs of hospital care, higher risks of nosocomial infections, other post-operative complications and decreased survival outcomes. Sarcopenia leads to reduced mobilization, suboptimal deep breathing, and inability to perform simple activities of day-to-day life[3,4] partly explaining the increased post-operative chest complications observed in patients of sarcopenia undergoing open abdominal surgeries.

MATERIALS AND METHODS

Ethical clearance was obtained at the start of the study from the Institutional Review Board. This is an observational study. The sample size calculated to be 165, *n* (sample size) = $z_a^2 p(1-p)/e^2$; where p is proportion, e is precision. Here, a = 5% hence z_a =1.96, p (incidence) = 12%, e = 5%, n is coming out to be 163. We conducted on 165 patients over a period of 2 years from September 2018 to August 2020, in the Department of General Surgery at The Calcutta Medical Research Institute, Kolkata. A written informed consent was obtained from all the patients before enrollment. Patients were prospectively observed and followed up until discharge after surgery.

Inclusion Criteria

1. Patients between age group 18–70 years who underwent planned open upper abdominal surgeries defined as an incision above or extending above the umbilicus
2. Patients having previously done computed tomography (CT) scan of the abdomen as a part of their necessary investigations from within 30 days prior to surgery
3. Patients who agreed for follow-up for a postoperative period of 1 week or till discharge.

Exclusion Criteria

1. Patients who did not have a previously done CT scan of the abdomen from 30 days prior to the surgery
2. Patients having previous chest dysfunction such as COPD, or who were ventilated postoperatively
3. Patients with a physical deformity who were unable to be tested for muscle strength or physical performance
4. Patients who were immuno-compromised such as AIDS, undergoing chemotherapy, and who underwent palliative surgery.

We have performed a single institution, prospective review of 165 patients admitted for elective open upper abdominal surgeries in which CT scan of the abdomen was done.

For enrolled patients, the following preoperative factors: sex, age, height, weight, body mass index (BMI) were evaluated. Sarcopenia was evaluated using computed tomography and gait speed. Postoperative pulmonary complications (PPC) and other surgical complications were evaluated using Melbourne Group Scale-2 and Extended Clavien-Dindo Classification respectively.

Image Analysis of Skeletal Muscle Mass

A cross-sectional CT image at the third lumbar vertebra (L3) in the inferior direction was analysed, for example as shown in Figure 1.[5,6] The distinction between different tissues was based on Hounsfield units, using INFINITT PACS software. The muscles in the L3 region inferiorly contain paraspinal muscles-Psoas, erector spinae, quadratus lumborum. The cross-sectional area (cm^2) of the right and left psoas muscle at L3 level on CT scans was measured by manual tracing.[7] To minimize measurement bias, one investigator who was blinded to the patient outcomes was trained to identify and quantify muscle areas. The Psoas Muscle Index (PMI) was calculated as follows: PMI = total psoas muscle area/height^2 (cm^2/m^2). Sarcopenia was defined as the PMI under 3.70 cm^2/m^2 in males and 2.50 cm^2/m^2 in females, based on the morbidity criteria.

Measurement of Muscle Strength and Physical Performance

For measurement of the 6-m usual gait speed, patients were asked to walk over a 6 meter course at their usual speed. Patients begin walking from the starting line, following the examiner's command of "Go" and stop just past the finishing line. Timing was started with the first footfall and stopped when the patient's foot first completely crossed the finishing line.[8] The maximum value of three consecutive

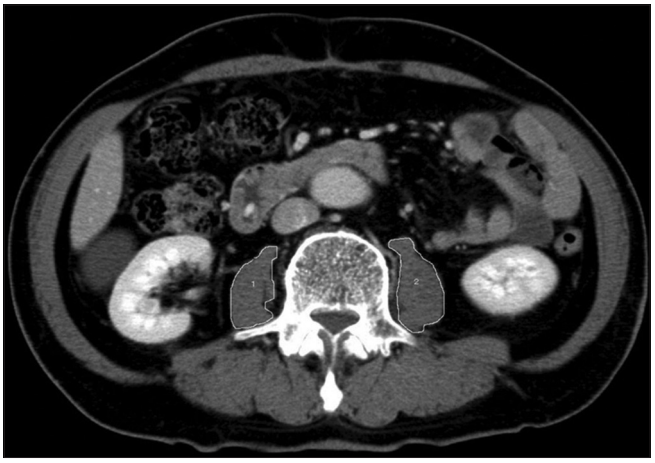

Figure 1: Cross sectional area (cm^2) of the psoas muscle at the level of the third lumbar vertebra (L3) measured by manual tracing on computed tomography

tests was recorded. The cut-off value for low physical performance was 6-m usual gait speed <0.8 m/s.

Calf muscle circumference will also be recorded at the nearest 0.1 cm at the mid level of the leg where calf girth is maximum using tape measure. Calf Circumference under 31 cm is the best clinical indicator of sarcopenia.

For BMI- Calculated as the weight divided by the height squared (kg/m^2). Patients were classified as obese (BMI ≥30 kg/m^2) or non-obese. The cut-off points for BMI to screen sarcopenia for males is 24.6 and for females is 26.2.

Presence of PPC

All participants received usual medical and nursing care as well additional monitoring from a specialized postoperative surveillance team of the hospital consisting of surgical residents and specialized intensive care unit (ICU) nursing staff during the first 7 days postoperatively (if directly admitted to the ward) or following ICU admission. No preoperative physiotherapy was provided and participants received usual care physiotherapy beginning on the 1st postoperative day. This commonly included early mobilization and education regarding the performance of deep breathing exercises and supporting coughing hourly. The presence of PPC was screened daily for the 1st week using the Melbourne Group Scale Version-2. Information collected included: oxygen saturation, temperature, auscultatory changes, and sputum colour. Sputum culture, white cell count, and chest radiograph results were reviewed when ordered by the treating doctor and were classified as normal or abnormal according to the pathology and radiology reports.

Presence of other Postoperative Surgical Complications

During the postoperative evaluation for PPC, participants were also looked for any other postoperative complications as per the definitions of Extended Clavien-Dindo Classification. Patients with Grade 2 or higher adverse events occurring during hospitalization were considered to have complications.

RESULTS

A total of 165 patients undergoing open upper abdominal surgeries were included in the study, and 20 patients were diagnosed as having sarcopenia. PPC occurred in 45 patients, including 11 with sarcopenia and 34 without sarcopenia. The sarcopenic group was significantly older and had significantly lower PMI, calf muscle circumference, and gait speed than non-sarcopenic group, but other physical parameters such as height, weight, and BMI were not significantly different. The various parameters with respect of sarcopenia are discussed in details in Table 1.

The distribution of postoperative infectious and non-infectious diseases for 165 patients was as follows: diarrhea, 3 cases (1.82%); paralytic ileus, 11 cases (6.67%); urinary retention, 6 cases (3.64%); wound abscess, 17 cases (10.3%), with slightly more prevalence in sarcopenia group. The results of my study indicate that sarcopenia is a unique, independent preoperative predictor of pulmonary complications after elective open upper abdominal surgeries.

DISCUSSION

Sarcopenia, as first reported by Rosenberg in 1989, was defined as the reduction of an elderly person's skeletal muscle. In 2010, the EWGSOP redefined sarcopenia as the progressive decline of skeletal muscle area, strength and function. It was initially introduced as long-term prognostic factor in patients with advanced cancer but subsequent

Table 1: Relation of Age, Weight, Height, BMI, Calf muscle circumference, PMI, Giat speed, sPO2, Temperature with respect to sarcopenia

Parameters	Sarcopenia						*P*-value	Significance
	No			Yes				
	Mean	Median	Std. Deviation	Mean	Median	Std. Deviation		
Age	53.47	53.00	5.78	59.50	60.00	4.63	<0.001	Significant
Weight	70.50	69.00	6.49	66.25	66.00	7.97	0.001	Significant
Height	1.68	1.69	0.04	1.67	1.69	0.07	0.437	Not Significant
BMI	24.84	24.40	2.21	23.79	23.45	2.31	0.022	Significant
Calf Muscle Circumference	31.82	31.80	0.58	30.67	30.35	0.82	<0.001	Significant
PMI	3.71	3.90	0.53	3.11	3.30	0.57	<0.001	Significant
Gait Speed	1.47	1.40	0.27	0.76	0.70	0.29	<0.001	Significant
SPO2	96.01	97.00	3.54	92.30	92.00	3.73	<0.001	Significant
Temperature	38.26	38.00	1.16	39.12	39.25	1.15	0.003	Significant

BMI: Body mass index, PMI: Psoas Muscle Index

studies found that sarcopenia can be used as a preoperative assessment tool to predict postoperative complications. Despite increasing knowledge and improved technology, a worldwide operational definition of sarcopenia applicable across racial/ethnic groups and populations lack consensus. It is unclear whether a decline in functional capacity results from the loss of muscle mass and/or the qualitative impairment of the muscle tissue. Thus, men and women present trajectories in the decline in skeletal muscle with aging. Men have a gradual decline, while women tend to have a sudden drop in muscle mass and function following menopause.

The current prevalence of sarcopenia in populations varies depending on the definition used, the limitations of past epidemiological and clinical data from small samples, and mixed information from the different measurement techniques employed. It is important to note that these studies used different measures of relative muscle mass, reference groups, and cutpoints, so it is difficult to compare prevalence among various studies.

Thus, a comprehensive approach to sarcopenia requires a multi-modal approach. Bioelectrical Impedance Analysis, dual-energy X-ray absorption,and magnetic resonance imaging have previously been used to measure the Skeletal Muscle Index. However, these three technologies have shortcomings and were therefore unsuitable for the present study.

We studied 165 patients, 20 (12.1%) patients were categorized as having sarcopenia. In the present study, the sarcopenic group was significantly older and had significantly lower PMI, calf muscle circumference, and gait speed than non-sarcopenic group, but other physical parameters such as height, weight, and BMI were not significantly different.

The elderly patients could have more aging-related complications following surgery. However, age was not an independent predictor of postoperative infections in multivariate analysis. The prevalence of PPC in this study was 27.27% (45/165) with 55% (11/20) in sarcopenia group and 23.45% (34/145) in non-sarcopenia group. The patients with sarcopenia had a significantly higher incidence of PPC. In my study population, the presence of respiratory comorbidity, smoking history, anesthesia duration, surgical category, duration of Nasogastric tube placement, and functional dependence was not identified as key risk factors which are in turn consistantly identified risk factors in studies and meta-analyses for PPC development. Skeletal muscle depletion with increasing adipose tissue leads to the synthesizing and secretion of several proinflammatory adipocytokines.

However, sufficient evidence to identify the effect of sarcopenia on outcome is lacking. The distribution of postoperative infectious and non-infectious diseases for 165 patients was as follows: diarrhea, 3 cases (1.82%); paralytic ileus, 11 cases (6.67%); urinary retention, 6 cases (3.64%); wound abscess, 17 cases (10.3%), with slightly more prevalence in sarcopenia group. Hence, It could be hypothesized that sarcopenia reflects the patients' frailty including impaired immune function which leads to the incidence of postoperative complications.

The results of my study suggest that sarcopenia may be a new and independent predictor of pulmonary complications after elective open upper abdominal surgeries. Improved understanding and treatment of sarcopenia would have a dramatic impact on improving the health and quality of life for the elderly, reducing the associated comorbidity and disability, and stabilizing rising health care costs. Identifying patients with preoperative sarcopenia help provide clinicians with useful clinical information to aid treatment decisions. However, continued research is needed to support a consensus operational clinical definition of sarcopenia applicable in clinical management and clinical and epidemiological research across populations. Furthermore, evidence indicates that exercise and nutritional support may improve complications and the prognosis in patients with sarcopenia. Therefore, appropriate perioperative management methods can be adopted, protein supplementation, and other methods that improve the condition of skeletal muscles and prevent postoperative complications. Currently, resistance strength training is the only treatment that affects the muscle aspects of sarcopenia. There are no pharmacological approaches that provide definite evidence in the ability to prevent the decline in physical function and sarcopenia. Current and future pharmacological and clinical trials and epidemiological studies could radically change our therapeutic approach to understanding and treating mobility and disability in elderly.

CONCLUSION

Sarcopenia is a condition that becomes more prevalent with advancing age, as well as with many diseases and exercise deficit disorder. Although there is continuing debate about the optimal application of clinical algorithms, diagnostic thresholds, and imaging techniques.

sarcopenia is increasingly recognized as an independent risk factor for adverse health outcomes. Muscle is routinely included on radiologic examinations, and imaging analysis of sarcopenia as a potential prognostic biomarker deserves further attention. The present study demonstrated that

sarcopenia itself, defined as reduced skeletal muscle mass plus low muscle strength and/or low physical performance, is an independent risk factor for pulmonary complications after elective open upper abdominal surgery. Including a functional aspect to the definition of sarcopenia may result in better prediction of postoperative complications.

However, further studies are needed to determine the value of sarcopenia for assessing long-term outcomes following open upper abdominal surgeries. This was a kind of study to externally validate the Melbourne score for risk prediction in an independent medically defined high-risk population. This observational study has identified several important points to consider in future trials. It is important to also consider that the pre-and peri-operative risk factors only accounted for approximately one-third of the variance in PPC. It is intuitive for the therapist to consider other factors such as adequate analgesia and time to mobilize that may also impact on the risk of PPC development. To my knowledge, no risk prediction model has been developed taking this into consideration, so lot of research still has to be done as a whole.

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Original Article

Cardiac Autonomic Function Tests in Tobacco Chewers

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Abstract

Introduction: Tobacco use is a public health concern worldwide as well as in India. It can be used in both smoked and smokeless forms. Smokeless tobacco is used either in chewed, sniffed, or sucked form. It affects the cardiovascular system and causes diseases such as high blood pressure, myocardial infarction, and stroke. Nicotine in tobacco is found to alter the cardiovascular autonomic functions. Impact of the nicotine on cardiovascular autonomic functions can be best diagnosed using the heart rate variability (HRV) assessment.

Materials and Methods: A total of 60 male subjects in the age group of 25–50 years – 30 tobacco chewers and 30 tobacco non-users of minimum 10 pouch years, were included in the study. Subjects with history of hypertension, cardiopulmonary, or endocrine disorder were excluded from the study. Overnight abstinence from tobacco use in any form was recommended. Basal electrocardiograph was recorded in lead II for 5 min using Digitalized Polyrite D. Frequency domain parameters – very low frequency (VLF), LF, high frequency (HF), and LF/HF ratio were recorded. Data obtained were analyzed statistically by unpaired *t*-test and statistical significance was set at $P < 0.05$.

Results: All the anthropometric parameters including age, height, weight, and body mass index were comparable among the two groups. There was no significant change in heart rate and RR interval in both groups. A highly significant ($P < 0.001$) decrease in VLF and HF was seen in chewers. A significant ($P < 0.05$) decrease in LF was seen in chewers. LF denotes both sympathetic and parasympathetic activity and HF reflects parasympathetic (vagal) influence. A significant ($P < 0.05$) increase in LF/HF ratio was seen in chewers. Increase in LF/HF ratio signifies increase in sympathetic activity.

Conclusion: HRV analysis in tobacco chewers has revealed the disturbances in cardiac autonomic regulation by increasing sympathetic activity predisposing the subjects to various cardiovascular diseases. Hence, active intervention to quit tobacco even in the smokeless form is required.

Key words: Autonomic, Chewers, Heart rate variability, Smokeless tobacco, Smoking

INTRODUCTION

Tobacco is one of the biggest public health threats the world is facing. Its use is the leading preventable agent of death in the world. According to the WHO, 5.4 million deaths are reported annually due to tobacco and the number is expected to rise to 8 million in the next 25 years. Nearly 80% of tobacco smoking population resides in developing countries.[1] Prevalence of smokeless tobacco (SLT) use is 26% which is far greater than smoking (14%) among adults as reported by Global Adult Tobacco Survey report of India.[2]

Tobacco is being used for about 1000 years by humans. Its consumption is mainly done in two forms: Smoked tobacco and SLT. Smoking is done in the form of bidis, cigarettes, hookahs, pipes, and cigars. Nicotine is the principal constituent of tobacco responsible for its addictive character, but other smoke constituents also contribute to the strength of the addiction. The use of tobacco without burning is referred to as SLT.

In India, SLT is consumed in several forms, for example, snuff/naswar (finely ground tobacco leaves), chewing

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tobacco (loose and sweetened tobacco leaves), zarda/kiwan (paste), paan (betel/quid), and khaini/mawa (tobacco with lime). Tobacco chewing is the most common form of SLT practiced in India. It is presumed to be harmless and a less "social evil" than smoking. Furthermore, due to various anti-smoking campaigns and law policies, it is considered as a safe alternative to smoking.[3]

Nicotine present in all tobacco products is well absorbed from mucosal surfaces, respiratory tract, and skin. In addition to nicotine, SLT contains nitrosamines, sodium, glucose, glycyrrhizinic acid, and grit.[4] It is one of the most important risk factors for the development of oral mucosal lesions including various oral pre-cancerous lesions such as lichen planus, lichenoid lesions, leukoplakia, and erythroplakia. Several cancers such as that of mouth, throat, cheek, gums, and lips are also attributed to tobacco chewing.[5] It also leads to teeth discoloration, dental cavities, and gum diseases due to the presence of glucose and flavoring agents present in SLT preparations.[4]

Cigarette smoking is major risk factor for the development of atherosclerosis, coronary heart disease, acute myocardial infarction (MI), and sudden cardiac death.[6] The risk of a non-fatal heart attack increases by 5.6% for every cigarette smoked.[7] However, tobacco chewing increases the risk of MI more than 2 folds.[8] Hypertension is significantly prevalent in both tobacco smokers and chewers. Use of tobacco either by smoking or chewing changes the lipid profile significantly.[9]

SLT also contains substantial amounts of nicotine, which is a cardioactive substance.[10] Impact of the nicotine on cardiovascular autonomic functions can be best diagnosed using the heart rate variability (HRV). Although local effects of SLT are widely known, systemic effects need exploration. Keeping this in mind, the present study has been undertaken to study the effect of SLT on HRV.

MATERIALS AND METHODS

The present study was conducted in the Department of Physiology, Pt. B.D. Sharma PGIMS, Rohtak, after getting approval from the Institutional Ethical Committee. A total of 60 male subjects of age group 25–50 years were included in the study. The subjects were divided into following two groups:

- Chewers – 30 male volunteers who were chronic tobacco chewers (non-smokers) for minimum 10 pouch years in continuation with the duration of 7 years or more
- Control – 30 male volunteers who had never used tobacco in any form (control group).

Chewers were further subdivided on the basis of number of pouch years of tobacco chewing as Group A and Group B. Group A consisted of chewers of <15 pouch years while Group B consisted of chewers of more than 15 pouch years.

Exclusion Criteria

- History or symptoms of any chronic cardiopulmonary, endocrine or metabolic, psychiatric disorder
- History or symptoms of any oral lesion
- History of any drug intake

Pouch Years

Tobacco chewing was quantified in pouch years. This was calculated as:

Pouch years = No. of pouches per day × years of chewing

Example: 1 pouch per day for 10 years = 10 pouch years ($1 \times 10 = 10$).[4]

Preliminary preparation: Informed consent was taken from every subject to undergo the whole procedure. All the tests were conducted from 10 am to 1 pm to avoid diurnal variation. Overnight abstinence from tobacco use in any form was recommended. Subjects were asked to avoid tea, coffee, carbonated drinks, or heavy meals at least 2 h before the test procedure. The whole procedure was explained in detail to each subject in his own language to allay any apprehension or fear. The basic parameters such as age, weight, and height of subjects were recorded. Heart rate, respiratory rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial blood pressure (MAP) were taken and noted down.

For recording HRV, Digitalized Powerlab26T Polyrite D was used. Sampling rate was 256 Hz. High and low filters were set at 99 and 0.1 Hz, respectively. The screen sweep speed was kept at 30 mm/s. For R wave detector, channel 3, that is, electrocardiograph (ECG) channel 3 was used. The whole channel was selected for HRV analysis. Position of event is taken as maximum after threshold. Retrigger delay is taken as 0. Ectopics were excluded from the analysis. A number of ectopics and artifacts are shown by the machine. Maximum frequency is 0.5 Hz. Window used is welch type. Frequency band used is 0.04 <low frequency (LF) <high frequency (HF) <0.4 Hz. HRV report comprises various things: HRV spectrum, HRV tachogram, HRV delta NN histogram, etc.

After preliminary history taking and examination, the subjects were asked to lie down on the couch and made to relax in front of the Polyrite D system. The three disposable adhesive electrodes were attached to the left arm, right leg,

and left leg, respectively. The basal recording of ECG (Lead II) was taken for 5 min. Utmost care was taken to minimize the movements from subjects by instructing them not to move or speak while the recording is in progress. From the ECG, the analysis of HRV was done automatically in the machine and the printed report of HRV provided the data of required variables. The HRV is based on the duration of time interval between two R waves, graphically represented in the form of a RR interval tachogram. The functional value of tachogram is the duration of a RR interval (in millisecond) at a certain point of time. For analysis of HRV, there are two domains mainly "Time domain" and "Frequency domain" as described earlier. Spectral analysis of ECG was done by fast Fourier transformation method. Following HRV parameters were selected for study.

- Mean heart rate (beats/min)
- Mean RR interval (seconds)
- Very low frequency (VLF) (ms^2)
- LF (nu)
- High frequency (HF) (nu)
- LF/HF ratio.

Statistics

All the data obtained by above two procedures were analyzed by a commercially available software package SPSS software. Statistical significance between chewers and controls was determined using Student's unpaired t-test. $P < 0.05$ was considered statistically significant and $P < 0.001$ was considered highly statistically significant.

RESULTS

There was no significant difference in the anthropometric parameters including age, height, weight, and body mass index of chewers. Furthermore, there was no statistical significance between heart rate, RR interval, SBP, DBP, and MAP in the two groups.

There was no significant change in heart rate and RR interval in both groups. A highly significant ($P < 0.001$) decrease in VLF and HF was seen in chewers. LF was seen to be decreased significantly ($P < 0.05$) in chewers. LF denotes both sympathetic and parasympathetic activities and HF reflects parasympathetic (vagal) influence. A significant ($P < 0.05$) increase in LF/HF ratio was seen in chewers. Increase in LF/HF ratio signifies increase in sympathetic activity. Significant decline in VLF and LF is suggestive of an increased sympathetic activity in chewers.

Group A consists of chewers with <15 pouch years of chewing and Group B consists of chewers with more than 15 pouch years of chewing tobacco [Table 2]. There was highly significant increase in the mean heart rate in Group B. The mean RR interval was decreased in Group B but the decrease was statistically insignificant. In Group B, the mean values of VLF and LF were increased. However, the change was highly significant ($P < 0.001$) for LF only. There was highly significant ($P < 0.001$) increase in LF/HF ratio in Group B. These suggest deterioration of cardiac functions with increase in pouch years of tobacco chewing.

DISCUSSION

Tobacco in any form trebles the risk of cardiac disease. About 30% of all deaths from heart disease are due to smoking. Cardiovascular effects of smoking occur within minutes with rise in HR up to 30% in the first 10 min.[11,12] Tobacco contains nicotine which increases heart rate and blood pressure.[9] SLT use results in considerable systemic exposure to nicotine.[13] The predominant cardiovascular effects of nicotine result from activation of the sympathetic nervous system. The state of sympathovagal balance is used for the prediction of many cardiovascular dysfunctions.[14] Studies in both SLT users and smokers have shown cardiac sympathovagal imbalance.[7,15-19] Nicotine increases the cardiac output by increasing both the heart rate and the myocardial contractility.[20] Furthermore, it may contribute to atherosclerosis by affecting lipid metabolism, coagulation, hemodynamic status, or causing endothelial injury. These effects lead to diseases such as MI, stroke, and high blood pressure.[15,21-23]

We found highly significant decline in VLF and LF in chewers [Table 1]. The LF power spectrum is evaluated in the range from 0.04 to 0.15 Hz. LF is thought to represent both sympathetic and parasympathetic activities. This indicates higher sympathetic activity in chewers.[15] Similar findings were reported by Glad *et al.* in their study of short-term HRV in dipping tobacco users. Pakkala *et al.*, while studying HRV among khaini users, reported a statistically significant decrease in VLF and LF after 3 months.[16] However, Itagi *et al.*, in their study on acute effects of

Table 1: Comparison of heart rate variability parameters in controls and chewers

Parameters	Control (Mean±SD#)	Chewers (Mean±SD)	*P* value
HR (beats/minute)	73.94±15.0	80.21±9.56	0.059
RR interval (seconds)	760.09±93.38	744.19±150.66	0.628
VLF (ms^2)	1977.13±1104.22	501.58±416.83	0.0001
LF (nu)	59.91±12.87	53.72±10.95	0.048
HF (nu)	47.07±63.16	22.94±6.39	0.0001
LF/HF	2.02±0.92	2.52±0.91	0.035

*P<0.05=Significant, **P<0.001=Highly significant, #SD=Standard deviation, VLF: Very low frequency, LF: Low frequency, HF: High frequency,

Table 2: Comparison of HRV in Group A (<15 pouch years) and B (>15 pouch years) of chewers

Parameters	Group A (<15 pouch years) (*n*=15) (Mean±SD#)	Group B (>15 pouch years) (*n*=15) (Mean±SD)	*P* value (Group A vs. Group B)
HR (beats/minute)	72.81±7.83	87.61±3.86	<0.001**
RR interval (seconds)	0.788±0.12	0.700±0.16	0.116
VLF (ms^2)	439.72±531.56	563.44±281.54	0.432
LF (nu)	45.01±6.13	62.43±6.44	<0.001**
HF (nu)	24.51±5.95	21.55±6.93	0.227
LF/HF	1.92±0.45	3.13±0.84	<0.001**

*P<0.05=Significant, **P<0.001=Highly significant, #SD: Standard deviation. LF: Low frequency, HF: High frequency, VLF: Very low frequency

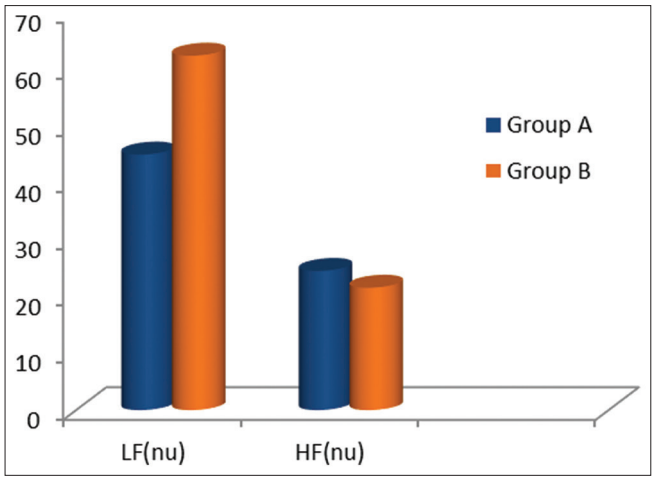

Figure 1: Low frequency and high frequency in Groups A (<15 pouch years) and B (>15 pouch years)

gutkha consumption on HRV, reported significant increase in LF after 5 min and 15 min of gutkha chewing.[17]

The HF power spectrum is evaluated in the range from 0.15 to 0.4 Hz.[18] There is highly significant decline in HF in our study in chewers reflecting a decrease in the parasympathetic activity [Figure 1].[24] Pakala *et al.*, on studying HRV in khaini users, reported that the mean value of the HF power was of lower magnitude after 3 and 6 months, but the decrease was not statistically significant.[16] However, contrary to our findings, few studies reported an increase in HF power.[17,25]

The LF/HF ratio is used to indicate balance between sympathetic and parasympathetic tones. A decrease in this score might indicate either increase in parasympathetic or decrease in sympathetic tone. It is considered together with absolute values of both LF and HF to determine what factor contributes in autonomic imbalance.[18] We observed a significant increase in LF/HF in chewers, indicating an increase in the sympathetic activity.[14] These values were in agreement with Pakkala *et al.*[16]

In our study, we observed, decrease in the mean RR interval and increase in the mean HR and BP in chewers or chewers, though insignificant. Nicotine causes vasoconstriction possibly through alteration of a cyclic GMP-dependent vasoactive mechanism.[25] Significant rise in the DBP is of great concern as any increase in the diastolic BP is an indicator of hypertension. This can lead to all possible cardiovascular diseases in near future.

CONCLUSION

HRV is an index of vagal tone and reflects the balance between parasympathetic and sympathetic maneuvers. HRV analysis in tobacco chewers has revealed the disturbances in cardiac autonomic regulation due to increased sympathetic activity predisposing the subjects to various cardiovascular diseases. HRV can be used as a non-invasive tool for screening in preclinical derangement of cardiac functions.

Thus, tobacco chewing is detrimental for cardiac functions. Hence, active intervention to quit tobacco even in the smokeless form is required.

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Original Article

A Randomized Controlled Trial to Assess the Efficacy of Topical Besifloxacin 0.6% versus Moxifloxacin 0.5% in Bacterial Conjunctivitis

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Abstract

Background: Bacterial conjunctivitis is an inflammation of the conjunctiva is defined as conjunctival hyperaemia associated with a mucopurulent or purulent discharge. Besifloxacin is a topical fluoroquinolone and developed specifically for ophthalmic use. The broad-spectrum activity of besifloxacin includes potent activity against the drug-resistant strain of various bacteria.

Aim: To compare the efficacy and tolerability of two drugs, Topical Besifloxacin 0.6% and Topical Moxifloxacin 0.5%, in patients diagnosed with bacterial conjunctivitis in a tertiary care hospital.

Methodology: 163 patients were recruited and randomized into either group A to receive Topical Besifloxacin 0.6% ophthalmic suspension three times for 5 days or group B to receive Topical Moxifloxacin 0.5% solution three times for 5 days. Clinical examination, screening with Cumulative sum scale score(CSS) and laboratory investigations were done at baseline,4th day, and 7th day. Efficacy was measured by improvement of symptoms assessed by CSS scoring. Tolerability was ensured by assessing the patient outcome on the 10th day using a four-step scale.

Results: The mean CSS score reduction from 9.85 at baseline to 0.88 in Group A (Besifloxacin) and from 10.49 at baseline to 1.08 in Group B (Moxifloxacin) on the 4th day of treatment and the 7th day of treatment, the scores were reduced to 0.00. The reduction in CSS score was statistically significant within groups (p-value <0.001). The mean CSS score reduction between Group A and Group B did not show a statistically significant difference (P-value = 0.40). The score for tolerability on the 10th day showed no significant difference between the group statistically. (p-value = 0.193)

Conclusion: This study confirms that both Besifloxacin and Moxifloxacin are equally effective in treating bacterial conjunctivitis. Tolerability profile is better for Besifloxacin suspension than Moxifloxacin solution in the treatment for bacterial conjunctivitis.

Key words: Conjunctivitis, Besifloxacin, Moxifloxacin, Cumulative sum score

INTRODUCTION

Conjunctivitis is an inflammation or infection of the transparent membrane(conjunctiva) that lines the eyelid and covers the white part of the eyeball. It is a common condition of the eye that occurs worldwide and affects all ages and social strata[(1)]. It can be caused by several different bacterial or viral pathogens but may also be caused by allergies, irritants or medications. Most types of conjunctivitis are self-limiting, but some may progress and cause serious ocular and extra-ocular complications. [(2)]

Most causes of conjunctivitis are benign, but depending on the immune status of the patient and the aetiology, conjunctivitis can progress to increasingly severe and sight-threatening infections. The incidence of bacterial conjunctivitis was estimated to be 135 in 10,000 in study Smith and Waycaster. [(3)] The prevalence of conjunctivitis varies according to the underlying cause, which may be influenced by the patient's age, as well as the season of the year. However, bacterial conjunctivitis is one of the most common ocular surface infections.

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Acute bacterial conjunctivitis is common and caused by direct eye contact with infected secretions. The most common isolates are H.influenza, S.pneumonia, S.aureus. and Moraxella catarrhalis. The most common pathogens for bacterial conjunctivitis in adults are Staphylococcal species, Streptococcus pneumoniae and Haemophilus influenza. In children, the disease is often caused by H influenzae, S pneumoniae, and Moraxella catarrhalis. [4] The course of the disease usually lasts for 7 to 10 days.

Common symptoms in acute bacterial conjunctivitis are redness, grittiness, stickiness, lacrimation and photophobia. Other possible symptoms are burning sensation and dryness of the eyes. Signs of acute bacterial conjunctivitis are hyperaemia or redness of the conjunctiva, conjunctival discharge, foreign body sensation. Marginal corneal ulcer, superficial keratitis, blepharitis or dacryocystitis are the complications of conjunctivitis. [5] For making appropriate treatment and management of conjunctivitis, focused ocular examination and history is necessary. The type of eye discharge and ocular symptoms are used for finding the cause of conjunctivitis. A purulent or mucopurulent discharge is mostly due to bacterial conjunctivitis, but a watery discharge is mostly due to viral conjunctivitis. [6] Itching is associated with allergic conjunctivitis. [7]

Topical antibiotic therapy is the mainstay of treatment. Ideally, the antibiotic should be specific for the causative organism. For example, chloramphenicol, aminoglycosides (gentamicin, neomycin, tobramycin), quinolones (ciprofloxacin, ofloxacin, levofloxacin, lomefloxacin, gatifloxacin, moxifloxacin,besifloxacin), macrolides (erythromycin, azithromycin), polymyxin B, fusidic acid and bacitracin are the available antibiotics.

Topical antibacterial drops are the standard treatment for bacterial conjunctivitis since they achieve higher antibiotic concentrations at the infection site to prevent contagious spread, disease course and recurrence are also reduced. It also decreases vision-threatening complications. However, inappropriate use of antibiotics leads to increased drug resistance, necessitating the continued development of new antibiotics.

In many clinical trials, besifloxacin demonstrated efficacy and safety in treating patients with bacterial conjunctivitis and was safe and well-tolerated with no observed contraindications. [8] Though multiple classes of drugs are available for pharmacological management of conjunctivitis, Fluoroquinolones are the mainstay of treatment for acute bacterial conjunctivitis.

The only fluoroquinolone specifically designed for ocular use is Besifloxacin. Therefore, it is not used for systemic infections like other older antibiotics. In bacterial conjunctivitis, a common source for treatment failure is bacterial resistance. Therefore, restriction to topical use only renders besifloxacin unique in its class and theoretically reduces the risk of developing resistance due to decreased systemic exposure.

Besifloxacin has improved pharmacodynamic properties compared with other commonly used fluoroquinolones and has shown to be safe and efficacious in clinical studies. For S. aureus, S. epidermidis and S. pneumonia, besifloxacin demonstrates a lower minimum bactericidal concentration than moxifloxacin, gatifloxacin, ciprofloxacin, azithromycin and tobramycin. For the pathogens mentioned above, besifloxacin is the most potent antibiotic. It has broad-spectrum activity against anaerobic bacteria, gram-positive and gram-negative bacteria. The purpose of this study is to compare two of the drugs from this class of fluoroquinolones, namely Besifloxacin 0.6% ophthalmic suspension versus Moxifloxacin 0.5% ophthalmic solution in terms of efficacy and tolerability among acute bacterial conjunctivitis patients attending the ophthalmology outpatient department in Chengalpattu Medical College and Hospital.

Aim

To assess the efficacy of Besifloxacin 0.6% ophthalmic suspension in Patients with Bacterial conjunctivitis.

Objective

To compare the clinical and antibacterial efficacy of Besifloxacin and Moxifloxacin in patients with bacterial conjunctivitis.

MATERIALS AND METHODS

A randomized, open-label, comparative active-controlled study was conducted in the Department of ophthalmology and microbiology at Chengalpattu medical college from January 2018 to December 2018. 150 male and female patients attending ophthalmology OPD who are clinically diagnosed with bacterial conjunctivitis were included.

Inclusion Criteria

1. Age: Above 18 years, both male and female
2. Patients who are clinically diagnosed with bacterial conjunctivitis.
3. Patients with visual acuity >6/60in both eyes.
4. Patients willing to give written informed consent.

Exclusion Criteria

1. Patients with other forms of conjunctivitis like viral or allergic conjunctivitis.
2. Patients already using any topical eye drops.

3. Patients with any history of ocular surgery within 6 weeks of study entry.
4. Patients with iritis, active ulcerative keratitis, recurrent corneal erosion syndrome.

The study was conducted after Institutional Ethical Committee approval. Patients who fulfilled the selection criteria were recruited for the study. The study was conducted according to good clinical practice guidelines. Written informed consent was obtained from all patients in regional language in the prescribed format and explained the study purpose and procedures before their enrollment in the study. In illiterate patients, the study procedure and their right to withdraw or contact the principal investigator were explained in case of any side effects, and a left thumb impression was obtained.

Randomization was done by the lots method. Among the 182 patients recruited and screened, 163 were enrolled in the study. Patients were assigned either to group A to receive study drug TopicalBesifloxacin 0.6% three times a day or to group B to receive Topical Moxifloxacin 0.5% three times a day for five days.

Demographic details and complete history were recorded during enrolment. In addition, clinical examination, screening with cumulative sum score and lab investigations were done at baseline.

Group A received TopicalBesifloxacin 0.6% ophthalmic suspension three times a day for five days. Group B received Topical Moxifloxacin 0.5% ophthalmic solution three times a day for five days.

Efficacy is measured by the response in terms of improvement of symptoms assessed by scoring with Cumulative sum score at baseline, at 4th day, and 7th day. **Tolerability** is assessed at the end of the 10th day using the 4-step scale, treatment outcome, and local tolerance of study medication.

The difference in cumulative sum scoring between two groups A and B was assessed by the student t-test. The culture was taken at 0 (baseline), 4th day and 7th day. The difference in cumulative sum score within the groups before and after treatment was analyzed using student paired t-test. The variations in the culture report between group A and group B were analyzed by chi-square test. In addition, the percentage of incidence of adverse effects among the study groups were analyzed.

RESULTS

In this study, 163 patients diagnosed with acute bacterial conjunctivitis were screened, randomized and included to participate in the study. Thus, 150 patients, i.e.,91.46 % of group A and 92.59% of group B, completed the study. In group A, 7 members lost to follow up. In Group B, 6 members lost to follow up. The highest number of patients were observed in the range of 41- 50 years [Figure 1].

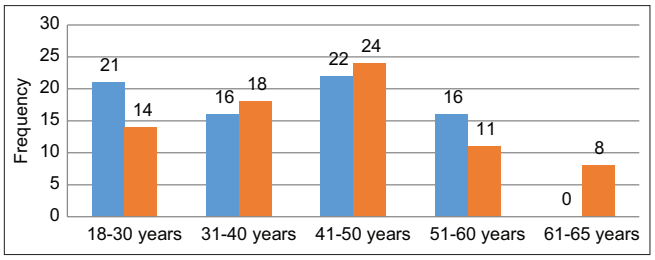

Figure 1: Age Distribution

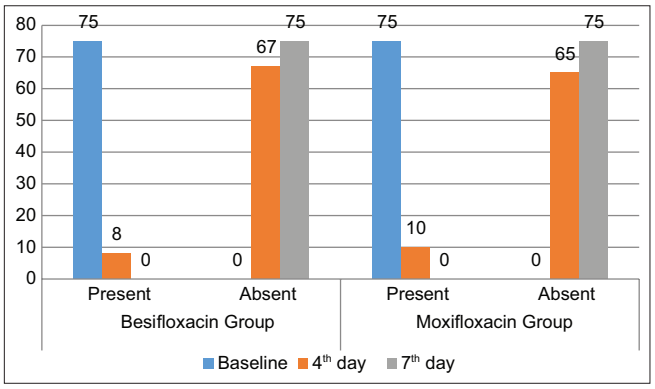

Figure 2: Comparison of bacterial culture between the Groups

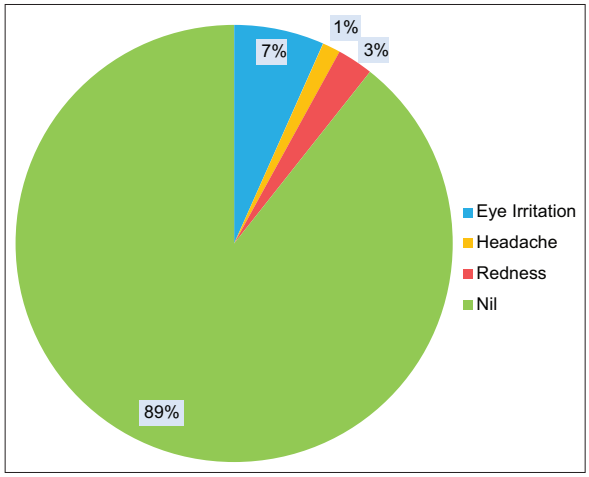

Figure 3: Adverse events in Group A

Common bacterial pathogens found in culture was Staph aureus, Streptococcus pneumonia, Staph. epidermidis, Klebsiella, E.coli, and mixed isolates found were Moraxella catarrhalis, proteus [Table 1].

By the 4th day, no bacterial colonies were observed in 89.3% of Group A and 86.7% of Group B. There was

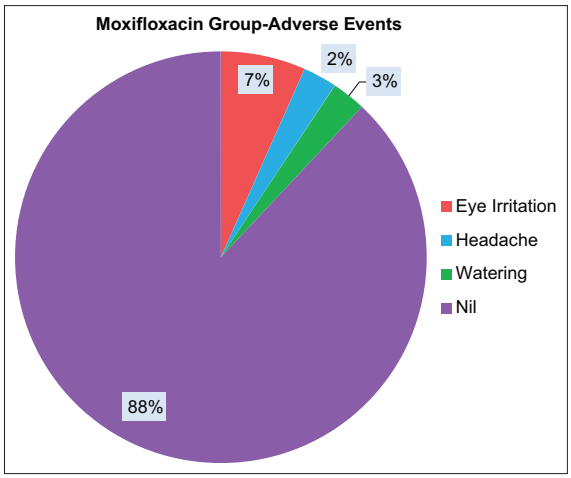

Figure 4: Adverse events in Group B

Table 1: Common Bacterial pathogens

Bacterial Pathogens	Besifloxacin Group		Moxifloxacin Group	
	Frequency	Percentage	Frequency	Percentage
Staph aureus	51	68	48	64
Streptococcus Pneumonia	9	12	12	16
Staph epidermidis	3	4	6	8
Klebsiella	3	4	5	7
E. Coli	6	8	1	1
Mixed Isolates	3	4	3	4
Total	75	100.0	75	100.0

Common bacterial pathogens found in culture was Staph aureus, Streptococcus pneumonia, Staph. epidermidis, Klebsiella, E. coli, and mixed isolates found were Moraxella catarrhalis, proteus

no significant difference between the treatment groups in terms of reduction in the bacterial growth in culture during the study [Figure 2].

There is no statistically significant difference in CSS from baseline to 4th day and 7th day [Table 2].

There are no serious adverse effects reported. Among adverse events reported, eye irritation was the most common ADR, followed by redness, Headache in Besifloxacin group [Figure 3].

Moxifloxacin group - common adverse effects reported were Eye irritation, followed by headache and watering [Figure 4].

There was a significant difference in 4-step scale tolerability scores on 10th day between groups. Besifloxacin is better tolerated than Moxifloxacin eye drops (p=0.319) [Table 3].

There was no significant difference in tolerability scores on 10th day between groups. Besifloxacin is better tolerated than Moxifloxacin eye drops (p=0.193) [Table 4].

Table 2: Comparison on cumulative sum score between groups

Cumulative sum score	Besifloxacin		Moxifloxacin		P value
Ocular Discharge					
Baseline	2.39	0.695	2.47	0.664	0.47
4th Day	0.24	0.43	0.31	0.464	0.36
7th day	0	0	0	0	-
Conjunctival Hyperaemia					
Baseline	2.4	0.678	2.4	0.658	1
4th Day	0.33	0.644	0.49	0.795	0.78
7th day	0	0	0	0	-
Ocular Itching					
Baseline	0.13	0.342	0.15	0.356	0.81
4th Day	0.08	0.273	0.04	0.197	0.3
7th day	0	0	0	0	-
Ocular Pain					
Baseline	1.71	1.063	1.97	1.013	0.11
4th Day	0.08	0.273	0.07	0.251	0.75
7th day	0	0	0	0	-
Ocular Watering					
Baseline	1.6	0.805	1.65	0.762	0.67
4th Day	0.08	0.395	0.13	0.502	0.47
7th day	0	0	0	0	-
CSS					
Baseline	9.85	3.84	10.49	3.51	0.28
4th Day	0.88	1.7	1.12	1.81	0.4
7th day	0	0	0	0	-

Statistically no significant difference in mean score reduction from baseline to 4th day and 7th day

Table 3: Tolerability score on the Tenth day

4-STEP SCALE 10TH DAY	Besifloxacin Group		Moxifloxacin Group	
	Frequency N=75	Percentage	Frequency N=75	Percentage
0 (Poor)	0	0	0	0
1 (Fair)	3	4.0	3	4.0
2 (Good)	60	80.0	66	88.0
3 (Excellent)	12	16.0	6	8.0

Table 4: Score for tolerability on 10th day

Tolerability score assesses on the 10th day	Mean	Std. Deviation	P-value
Besifloxacin Group	2.12	0.401	0.193
Moxifloxacin Group	2.04	0.346	

DISCUSSION

Our study findings show the highest prevalence of bacterial conjunctivitis was observed in 41-50 years with 29.3% and 32.0% in groups A and B, respectively. The mean age for group A is 40.29±12.41 years, and group B is 42.49 ±13.64 years. There was no significant statistical difference in mean ages between the two groups (P-value = 0.303). This was similar to a previous study by Agius-Fernandez *et al.*[9] The least prevalence was seen in 61-65 years.

Culture confirmed bacterial conjunctivitis study population were evaluated for bacteriological improvement during treatment with the study medications. At baseline, the bacterial species involved in Besifloxacin (Group A) and Moxifloxacin (Group B) treatment groups. Staphylococcus aureus (Group A 72%, Group B 64%) was the most prevalent organism, followed by Streptococcus pneumonia (Group A 12%, Group B 16%), Staphylococcus epidermidis (Group A 4%, Group B 8%) and Klebsiella (Group A 4%, Group B 7%). The predominance of staphylococcus aureus seen in our study is similar to the okesolo study, where it was 74.9%.[10] It was also similar in other studies, which demonstrated the same trend. [11] It was also similar to cavuota *et al.*[12]

Both the study medications resulted in a significant reduction in the mean score of the bacterial colony count during the trial period. By the 4th day, no bacterial colonies were observed in 89.3% of Group A and 86.7% of Group B. There was no significant difference between the treatment groups in terms of reduction in the bacterial growth in culture during the study.

The clinical efficacy was measured as the Cumulative Sum Score CSS[9]of 5 key signs and symptoms of acute bacterial conjunctivitis; these comprise ocular discharge, conjunctival hyperaemia, ocular itching, ocular pain and watering, which were recorded on a 4-step scale of 0 to 3: 0 = absent, 1 = mild, 2 = moderate and 3 = severe. Thus, the maximal CSS possible in any patient was 20, and the minimum score possible was 0. Therefore, the CSS was designated as the primary clinical efficacy variable. In addition, the success of treatment was assessed from the patients' statement and local tolerance of the study medications using a four-step scale.

In this study, the mean ocular discharge scores in group A and group B during baseline visits were 2.39 and 2.47. The scores in both groups are comparable during the baseline visit. There was a significant difference in reduction of ocular discharge within the groups on the 4th day and 7th day ($p<0.001$). But there was no significant difference in p-value($P =0.36$)between the groups statistically.

The mean conjunctival hyperemia score during baseline is 2.40 in group A. However, the conjunctival hyperemia score reduced from 2.40 to 0.33 on the 4th day and from 0.33 to 0.00 on the 7th day in group A. There was a significant difference in the reduction of conjunctival hyperemia within group A on the 4th day and 7th day ($p<0.001$).

In group B the conjunctival hyperemia score was reduced from 2.40 to 0.49 on the 4th day and 0.49 to 0.00 on the 7th day [p value<0.001]. Thus, both Besifloxacin (Group A) and Moxifloxacin (Group B) effectively reduced conjunctival hyperaemia on the 4th day and 7th day. This was similar to the study done by Garg *et al.*[13], But there was no statistically significant difference in reducing conjunctival hyperemia (p-value =0.78) between the two groups.

In this study, the mean ocular itching scores in group A and group B during baseline visits were 2.6 and 2.45, respectively. Thus, the itching scores in both groups are comparable during the baseline visit. Furthermore, there was a significant difference in reducing itching within groups A and B on the 4th and 7th days ($p<0.001$). But there was no significant difference (pvalue=0.30) between the groups statistically. Thus both treatments were effective in treating itching.

The mean ocular pain score in group A on baseline visit was 1.71, and group B was1.97. In group, A 1.71 was reduced to 0.08 on the 4th day, and group B 1.97 was reduced to 0.07 on the 4th day ($p<0.001$). There was a significant difference in the reduction of score in group A and Group B from baseline to 4th day. But the difference in reduction of ocular pain scores between group A and group B was not statistically significant (p-value = 0.75)

The mean ocular watering score in group A on the baseline was 1.60 and in group B is1.65. In group A, the score was reduced from 1.60 to 0.08 on the 4th day, and in group B, the score of 1.65 was reduced to 0.13 on the 4th day. Thus, in group A and Group B, treatments effectively reduced ocular watering scores from baseline score [P value <0.001]. But the difference in reduction of ocular watering scores between group A and group B was not statistically significant [P value= 0.47].

The mean CSS score in group A on baseline visit was 9.85, and group B was 10.49. In groups A and B, treatments effectively reduced the mean score from the baseline score [P value <0.001]. On the 4th day, the mean CSS score was reduced to 0.88 in Group A and on the 7th day, the mean CSS was reduced to 0.00 in Group A. On the 4th day mean CSS score of 10.49 was reduced to 1.08 in Group B

And on the 7th day mean CSS was reduced to 0.00. Both the study medications resulted in a significant ($p < 0.001$) reduction in the mean CSS of the signs and symptoms during the trial period in bacteriologically confirmed bacterial conjunctivitis within groups A and B. There was no statistically significant difference ($p=0.40$) between the Besifloxacin and Moxifloxacin treatment groups regarding reduction in the mean CSS. Our study findings correlate with the previous multicentre study, which demonstrated that besifloxacin was not

inferior to moxifloxacin in the treatment of bacterial conjunctivitis [12]

The adverse events occurred in 17 out of 150 participants, 8 in group A and 9 in Group B. The adverse events noted were eye irritation, headache and redness in GroupA. The adverse events noted in Group B were eye irritation, headache and watering. There were no serious adverse events observed during the study. During follow up visits on the 4th and 7th-day visual acuity changes, Anterior chamber examination, fundoscopic changes were examined. No changes in these safety parameters were noted in both groups. The Adverse events were similar to the study done by Comstock *et al*.[8]

The score for tolerability in group A was good, excellent and fair in 80%,16% and 4%, respectively. In Group B, the score was good, excellent and fair in 88%, 8% and 4%, respectively. Eventhough there was no statistically significant difference in tolerability among the two groups (p value=0.193), 16% of the patients in the Besifloxacin group came under the excellent category. In contrast, only 8% of the patients came under the excellent category under the Moxifloxacin group.

CONCLUSION

This study confirms that both Besifloxacin and Moxifloxacin are equally effective in the treatment of bacterial conjunctivitis. However, the tolerability profile is better for Besifloxacin suspension than Moxifloxacin solution. Hence Topical Besifloxacin suspension is an alternative to Topical Moxifloxacin solution in the treatment for bacterial conjunctivitis.

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Original Article

Accuracy of Acute Appendicitis Prediction Using Alvarado Score and Tzanaki's Score

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Abstract

Background: Appendicitis is the most often encountered abdominal emergency on a global scale. The lifetime risk of acute appendicitis is 8.6 percent for males and 6.7 percent for women. Clinical examination is useful in diagnosing acute appendicitis in approximately 70%–87% of cases.

Objective: To study the diagnostic accuracy of Alvarado and Tzanakis score in predicting the accuracy of acute clinical appendicitis.

Methods: The study involves a prospective analysis of 50 patients with acute appendicitis. Completing relevant history, exam, and lab tests were used to capture the proforma capture both Alvarado and Tzanakis rating for patients. In addition, both scoring systems' sensitivity, specificity, positive and negative predictive values were evaluated.

Results: Among the 50 patients analyzed, Tzanakis' specificity was 100%, but HPE expected Alvarado's was 81.82 percent. The accuracies of both scores likewise differed greatly. The Tazanakis score predicted 100% accuracy, while the Alvarado score predicted 50% accuracy. In a prior study, Tazanakis scored outperformed Alvarado in predicting acute appendicitis.

Conclusion: For diagnosing acute appendicitis, Tzanakis's scoring system is a relatively appropriate scoring system to use compared with that of Alvarado.

Key words: Acute appendicitis, Alvarado score, Tzanakis score

INTRODUCTION

The Appendix (Vermiform Appendix) is a vestigial organ in humans, as it has no purposeful function. However, its propensity to inflame makes it useful in surgery. An infection that results in "Acute clinical Appendicitis". Acute appendicitis is an inflammation of the appendix due to common pathology, blockage of the lumen[1]. It causes significant stomach pain that might be localized to generalized peritonitis varies in severity. Globally, acute appendicitis accounts for over 1% of all surgical procedures. Acute appendicitis affects between 6% and 7% of people in their lifetime. Appendicitis is most common in children due to submucosal lymphoid tissue hyperplasia; however, it is uncommon in infants[2]. It can occur in the elderly. Males have an average lifetime incidence of 8.6%, while females have an average lifetime incidence of 7.2 percent. Men are 3 times more likely than women to develop this disorder before the age of 30, and the ratio tends to equalize thereafter[3].

Because of the low-fibre, high-fat diet that is assumed to be responsible in most cases, appendicitis is more common in developed countries than in underdeveloped or developing countries. In the previous two decades, the diagnosis of acute appendicitis has been exclusively clinical. However, the sensitivity in detecting acute appendicitis has grown dramatically since the advent of imaging investigations such as Ultrasonography (US) and Computed Tomography (CT)[4].

The diagnosis of acute appendicitis is still a clinical one. The most common symptom is abdominal pain. The patient describes the discomfort as starting in the

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periumbilical or epigastric region and then spreading to the right iliac fossa in the classic presentation. Fever, anorexia, nausea, and vomiting are all symptoms of this condition[5]. The clinical presentation of acute appendicitis varies greatly due to the degree of inflammatory process involvement, the location of the appendix, and the patient's age. Because of the uneven clinical presentation, one out of every five cases of acute appendicitis is misdiagnosed, with negative appendicectomy rates ranging from 15 to 40%. Furthermore, "typical" symptomatology occurs in just 50-60% of patients, making diagnosis challenging[6].

The diagnosis was made on clinical grounds in the earlier era, and patients were brought to emergency surgery to limit the morbidity and death associated with severe appendicitis. However, the rate of negative laparotomy and negative appendectomy has risen dramatically due to routine emergency laparotomy for acute appendicitis on clinical grounds[7]. According to numerous researches, the rate of negative appendectomy varies between 15% and 30%. In a Swedish study, the percentage was approximately 15%, but it was only around 13% in a North American study. The imaging research was implemented to limit the number of negative appendectomies, but even so, the rate is not well managed[8].

Difficulties with the diagnosis are particularly prevalent in extremely young, elderly, and females of reproductive age. These patients are more prone to present with an atypical appearance and a variety of other illnesses may mimic acute appendicitis[9]. Numerous physicians advise early surgical surgery in acute appendicitis to avert perforation, accepting a negative appendectomy rate of approximately 15-20%. The removal of the normal appendix imposes a financial cost on both patients and health care resources. Misdiagnosis and surgical delay can result in complications such as perforation and, ultimately, peritonitis.

There are different scoring systems for acute appendicitis. However, the best scoring method for acute appendicitis to date is the Alvarado scoring system, which integrates clinical symptoms, signs, and laboratory test values and provides a clear approach to care. The purpose of this study is to validate the diagnostic accuracy of several established scoring systems and to compare the four most vital and relevant, easily quantifiable scoring systems, namely the Alvarado, Tzanaki, RIPASA, and AIR scores[5]. There are different scoring systems for acute appendicitis. However, the best scoring method for acute appendicitis to date is the Alvarado scoring system, which integrates clinical symptoms, signs, and laboratory test values and provides a clear approach to care[10].

Aim

To study the diagnostic accuracy of Alvarado and Tzanaki in predicting the accuracy of acute clinical appendicitis.

MATERIALS AND METHODS

This prospective study was conducted in the department of general surgery at the Government medical college Pudukottai. All patients admitted with the diagnosis of acute appendicitis was included.

Inclusion Criteria

All patients diagnosed with acute appendicitis undergoing open or laparoscopic appendicectomy

Exclusion Criteria

Patients not fit or not willing for surgery, Appendicular mass

Even when both the scores were below the cut-off value, patients were subjected to appendicectomy based on clinical judgement.

Relevant history, examination and laboratory investigations are done. Patients were scored according to both Alvarado Scoring System and Tzanakis Scoring, and both were documented in the proforma. Sensitivity, specificity, positive predictive value, negative predictive value were assessed and compared for both scoring systems.

The decision to operate on the patient (versus conservative line of management) was based solely on the clinical suspicion of an experienced Surgeon who was not part of/involved in the study. Scoring was performed at every review until a decision was made from either appendicectomy or continued conservative management line. The diagnosis of acute appendicitis was confirmed by operative findings and histopathological assessment of the appendicectomy specimen. The ultimate criterion for the final diagnosis of acute appendicitis was the histological demonstration of polymorphonuclear leukocytes throughout the thickness of the appendix wall. Data were analyzed using the Pearson chi square test to calculate sensitivity, Specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), and Diagnostic Accuracy.

RESULTS

50 patients admitted to the general surgery service with a diagnosis of acute appendicitis was included. The majority of patients were in the age group between 21 to 30 years. [Figure 1] 34 patients were male and 16 patients were female. [Figure 2] 42% of patients were presented within 12 hours [Figure 3].

The position of the appendix was retrocaecal in 62% of patients. [Figure 4] 56% of patients have a Tzanakis score of more than 8. 36% of patients have Alvarado score of more than 7 [Figures 5 and 6].

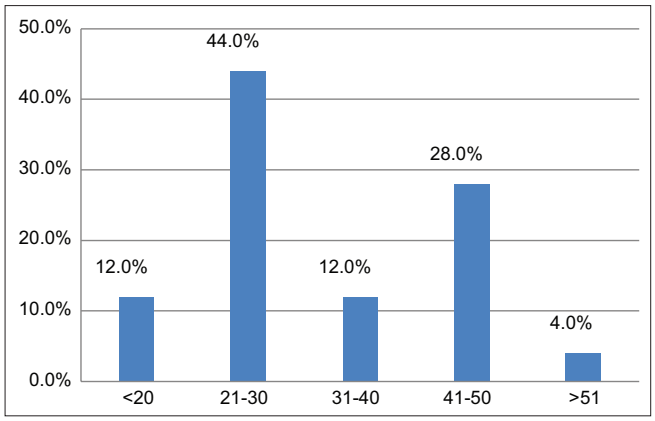

Figure 1: Age distribution

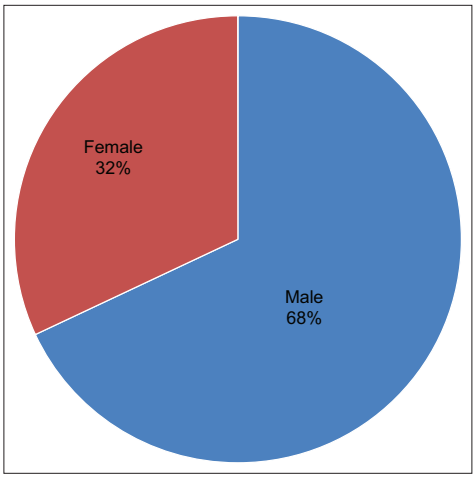

Figure 2: Gender distribution

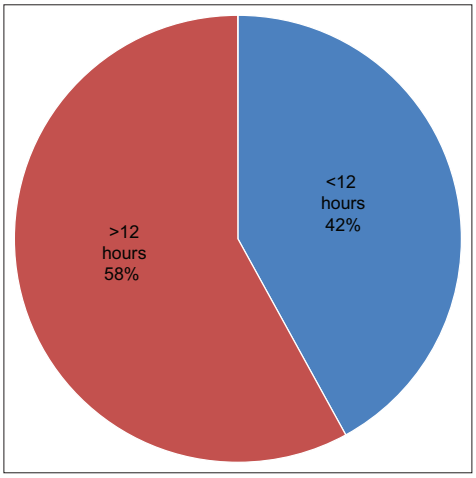

Figure 3: Time of presentation distribution

The histopathological examination has shown that 78% of patients had evidence of appendicitis [Figure 7].

The Tzanakis score had 65.52% sensitivity to correctly identify appendicitis with a confidence interval of 51.88% to 77.51%. Specificity of Tzanakis score is 100%, normal

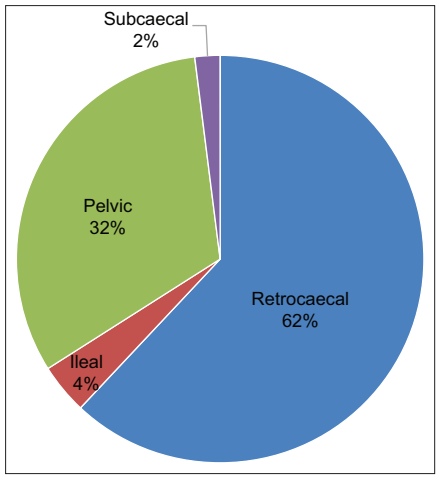

Figure 4: Position of appendix distribution

Table 1: Cross-tabulation of Tzanakis score with HPE

TZANAKIS Score	HPE		Total	P-value
	Positive	Negative		
>8	38	0	28	<0.0001
<8	20	12	22	
Total	39	11	50	

Table 2: Cross-tabulation of Alvarado score with HPE

ALVARADO Score	HPE		Total	P-value
	Positive	Negative		
>7	16	2	18	<0.0001
<7	23	9	32	
Total	39	11	50	

appendices are correctly identified with score <8 with a confidence interval of 73.54% to 100.00%. Tzanakis score had a 100% positive predictive value and having 37.50% negative predictive value. The accuracy of the Tzanakis score is 71.43%. [Table 1].

The Alvarado score indicated a sensitivity of 36.21 percent for correctly diagnosing appendicitis, with a confidence interval of 23.99 percent to 49.88 percent. Alvarado score has a specificity of 66.67 percent, while score 7 properly identifies normal appendices with a confidence interval of 34.89 percent to 90.08 percent. Alvarado score had a positive predictive value of 84% and a negative predictive value of 17.78%. Alvarado's accuracy is 41.43 percent. [Table 2].

DISCUSSION

Acute appendicitis is a common abdominal surgical disease. Since 1900, the disease's morbidity and fatality rates have

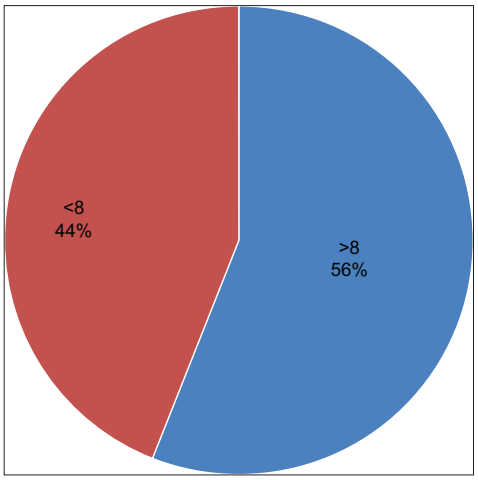

Figure 5: Tzanakis score distribution

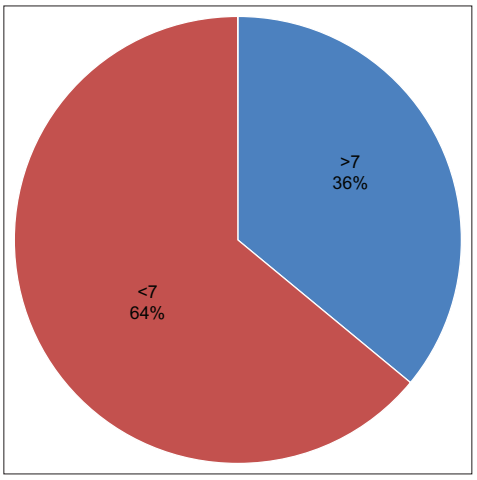

Figure 6: Alvarado score distribution

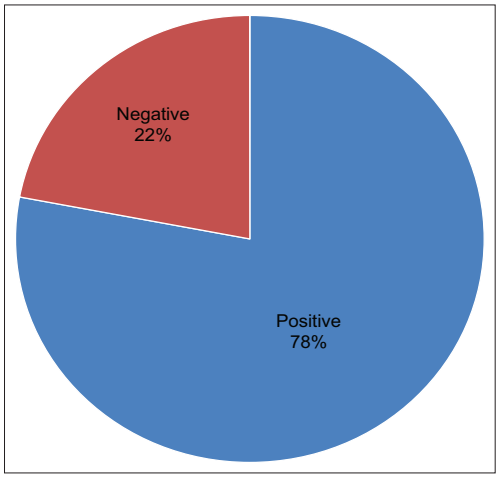

Figure 7: HPE distribution

fallen dramatically. Negative appendectomies have low mortality but a 10% morbidity rate. Many strategies have been investigated to reduce the removal of a normal appendix without increasing the perforation rate[11]. Radiological procedures, including ultrasonography and computed tomography, as well as laparoscopy, have all been studied. Many diagnostic ratings have been proposed, however, most are complex and difficult to apply in practise. The purpose of this study was to contrast Tzanaki and Alvarado in 50 appendicitis patients to develop a grading system for acute appendicitis and to determine the efficacy of these scoring systems for diagnosing acute appendicitis.

Incidence of acute appendicitis was higher in the patients below 40, with the highest prevalence occurring in those of age group 21 to 30. In addition, the predominance of occurrence in males was observed (68%). In a similar study conducted by Babu *et al.*[12], it was reported that the occurrence of acute appendicitis condition was predominant in males and documents the comparative surge in the frequency of the condition in the age group 21-30 years. A previous analysis performed by Anupriya *et al.*10 also reported a parallel statement on the existence of the condition more significantly higher in males and similar age groups. However, Sarla[13], in a likely study, has stated that age is not a limiting factor for the occurrence of acute appendicitis yet reported a higher rate of the condition among males and within a similar age group (20-30 years).

The position of the appendix is extremely variable – more than any other organ – and if it is too long, the appendix may extend to any part of the abdomen. The appendix is the only organ in the body that has no fixed anatomy[14]. The effect of the position of the appendix in relationship to acute inflammation was also determined. Appendix position in patients was found to be retrocaecal, ileal, pelvic and subcaecal. Among the four positions identified, the retrocaecal location of the appendix was found to be higher, followed by the pelvic position. Ileal as well as subcaecal appendix positions were found to be existent in very meagre numbers. In a previous study conducted by Fashina *et al.*[14], the retrocaecal appendix was dominant among 250 patients admitted for acute appendicitis. They also recorded that the length and position of appendices were not significantly different between those who had acutely inflamed and normal appendices ($P = 0.923$). This could also contribute to the majority of the appendix position being confined to the retrocaecal, even in general. Out of 377 cadavers autopsied, Souza *et al.*[15] recorded a vital number of appendix positions to the retrocaecal. Thus the length and position of the appendix might be excluded while fixing criteria for analyzing patients with acute appendicitis. Yet, further detailed analysis of the higher number of patients from various demographic locations shall be performed to substantiate this.

Tzanaki's scoring method is one of these systems; it incorporates clinical evaluation, elevated leukocyte count, and ultrasonography. There are just four variables worth

15 points, and a score of 8 or greater indicates acute appendicitis necessitating surgical treatment[16]. In our current evaluation, 56% of patients displayed Tzanaki's score of >8, while the remaining 22 patients were recorded with scores <8. In a previous study conducted by Anupriya *et al.*[10], more than half of patients recorded an optimum Tzanaki score. The overwhelming accuracy of Tzanaki's scoring method in predicting the positive diagnosis of acute appendicitis was recorded in many previous studies[5],[8],[10],[12]. In a study conducted by Sujeetha[8] also the patients admitted for acute appendicitis, most of them displayed scores above 10. Iqbal *et al.*[17] analyzed 214 appendicitis patients with Tzanaki's score and revealed the presence of scores >8 in more patients.

The Alvarado scoring system effectively detected acute appendicitis early in patients with a pre-operative clinical diagnosis of appendicitis, as established by numerous trials, and reduced the incidence of negative appendectomies without increasing morbidity or death[18]. The modified Alvarado Score is an easy, simple and cheap diagnostic tool for supporting the diagnosis of acute appendicitis. In our current observation, the scoring system using Alvarado's method revealed the presence of scores <7 in 64% of patients. However, patients with scores >7 were designated to be highly probable to be diagnosed with acute appendicitis. In previous analyses conducted in predicting acute appendicitis by the Alvarado scoring system, the predominant number of patients were recorded with scores >7, substantiating the existence of acute appendicitis with a histopathological cross examination[19].

A cross-sectional histopathological evaluation (HPE) of patients with acute appendicitis was compared with both the scoring systems. A total of 39 patients were positively diagnosed with acute appendicitis, while 11 of them were not. Hence the overall positive predictivity of acute appendicitis through HPE was recorded as 78%. In a similar study performed by Anupriya *et al.*[10], the predictivity accuracy of both scoring systems was also compared with HPEs. Our study found that out of the 50 patients, Tzanaki's scoring method, all the patients with scores>8 were confirmed with the presence of acute appendicitis. Also, 20 patients with <8 scores were also ascertained with the acute condition, thus revealing 71.79% sensitivity, 50% NPV rates, and 100% specificity and PPV. The overall analysis designates an accuracy score of Tzanaki's scoring system to fall to 78%. There was also no false diagnosis found in Tzanaki's scoring system.

In a parallel study conducted by Anupriya *et al.*[10] also, No patients were falsely diagnosed with appendicitis by the Tzanakis scoring system. Similar to our study, patients with a Tzanakis score of <8 and 12 among 32 patients analyzed were confirmed with appendicitis. However, in an investigation conducted by Iqbal, among 214 patients, HPE proven appendicitis condition was found in 89.7%, with 10.3% of them diagnosed with a normal appendix. Sensitivity, specificity, and the overall diagnostic score of Tzanaski were 99%, 91%, and 95%, respectively.

According to Alvarado score, 18 patients were diagnosed to have appendicitis through HPE. Out of these 18, 16 patients had evidence of appendicitis histopathologically, 2 patients were falsely diagnosed with appendicitis by the Alvarado scoring system. Out of the 32 patients diagnosed by Alvarado as not having appendicitis, 23 patients had evidence of appendicitis HPE. Thus revealing 41.03% sensitivity, 28.13% NPV rates, and 81.82 and 88.89% of specificity and PPV, respectively. The overall analysis designates an accuracy score of the Alvarado scoring system to fall to 50%. In Anupriya'*et al.*'s [10] study, 25 patients were diagnosed with appendicitis based on the Alvarado score. Out of these 25, 21 individuals had histological evidence of appendicitis, while four patients were misdiagnosed with appendicitis using the Alvarado grading system. Thus, of the 45 individuals Alvarado diagnosed as not having appendicitis, 27 had histological evidence of appendicitis.

Hsiao *et al.*[20] performed a retrospective analysis and discovered that the sensitivity and specificity for an Alvarado score of 7 were 60% and 61%, respectively. In their retrospective analysis, Rezak *et al.*[21] found a greater sensitivity and specificity of 92 percent and 82 percent, respectively. This study indicated that if patients with scores >7 were handled immediately by appendectomy without CT examination, CT scanning would have been reduced by 27%. Owen *et al.*[22] assessed 215 patients prospectively and discovered that Alvarado scoring had 93% and 81% sensitivity and specificity, respectively. In addition, 16 patients with an Alvarado score of less than 7 were compared to 45 patients with a Tzanakis score of greater than 8, indicating the presence of appendicitis on the histological investigation. Thus, 37 (82.2 percent) of 45 patients with an Alvarado score of less than 7 had histopathological evidence of appendicitis.

Comparing positive histological outcomes for patients with an Alvarado score of less than 7 patients with a Tzanakis score of less than 8 would reveal the better scoring system that could be adopted to predict acute appendicitis. In our present analysis, the specificity of Tzanakis score was 100%, but Alvarado was predicted as 81.82% based on HPE. There was also a huge difference in the accuracies of both scores. With the employment of the Tazanakis score, the accuracy was 100%, while the Alvarado score predicted only 50% accuracy. In a previous study also that compared both Tazanakis as well as Alvarado scores in

predicting acute appendicitis, Tazanakis score proved to be more accurate.

CONCLUSION

In conclusion, the Tzanakis score is a significantly superior diagnostic scoring system for acute appendicitis than the Alvarado score at the moment. Acute appendicitis is a frequently encountered surgical emergency. A combination of sound clinical judgement and an investigation rating system can assist lower the rate of negative appendectomy. In our study group, Tzanakis had significantly higher sensitivity, negative predictive value, and diagnostic accuracy. Thus, in remote locations or during an emergency, a swift decision on referral to an operating surgeon or observation might be made.

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