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Contents

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Case Report

Benign Fibrous Histiocytoma - Aneurysmal Variant as a Differential Diagnosis for Soft-Tissue Sarcoma, in a Physically Challenged and Mentally Retarded Child: Case Report

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Abstract

Santa Cruz and Kyriakos described a special variant of cutaneous fibrous histiocytoma (FH) which was characterized by large, blood-filled cystic spaces, and diffuse hemosiderin deposits. They proposed the term aneurysmal (angiomatoid) FH of the skin. We report and discuss a case of benign FH - aneurysmal variant, in a female patient aged 17 years who is physically challenged and mentally retarded visited our hospital.

Key words: Aneurysmal variant, Angiomatoid, Benign fibrous histiocytoma, Soft-tissue tumor

INTRODUCTION

Fibrous histiocytoma (FH) is a benign and often superficial subcutaneous proliferation of oval cells resembling histiocytes and spindle shaped cells resembling fibroblasts and myofibroblasts. The clinicopathological variants of FH include cellular FH, aneurysmal FH, atypical FH, epitheliloid FH, and atropic FH.

Aneurysmal FH (AFH) is a rare and distinct variant of benign FH (BFH) with a reported incidence of 1.7% of all BFH. BFH is also known as dermatofibroma which usually grows rapidly and may attain a very large size.[1-3] It shows extensive hemorrhage, with prominent cavernous such as pseudovascular spaces that are not lined by endothelial cells. It affects mostly children and young adults with median age of 14 years. The tumor is rare, accounting for approximately 0.3% of all soft-tissue neoplasms.[4] It arises in sites of normal lymphoid tissue such as antecubital fossa, axilla, inguinal, and supraclavicular regions. AFH has higher risk of local recurrence compared with dermatofibroma.

Clinically, AFH presents as a solitary polypoid, blue to brown cystic lesion most commonly on the extremities of young to middle aged adults. The nodule may be associated with rapid growth due to sudden hemorrhage with in the lesion leasing to suspicion of malignancy and may be associated with pain.[3-5]

The diagnosis of AFH is made based on histopathology and immunohistology. Immunohistological staining can be performed to differentiate AFH from other similar appearing lesions. This can be done with the S-100 stain for sarcoma, neurofibroma, and melanoma. Melan-A, which is less sensitive than S-100, but is more specific can also be used for melanoma.[6,7]

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CASE SUMMARY AND DISCUSSION

A 17-year-old female patient who is bedridden, mentally retarded, and physically challenged visited our hospital with complaint of swelling over left forearm which was ulceroproliferative with bleeding and foul smell discharge.

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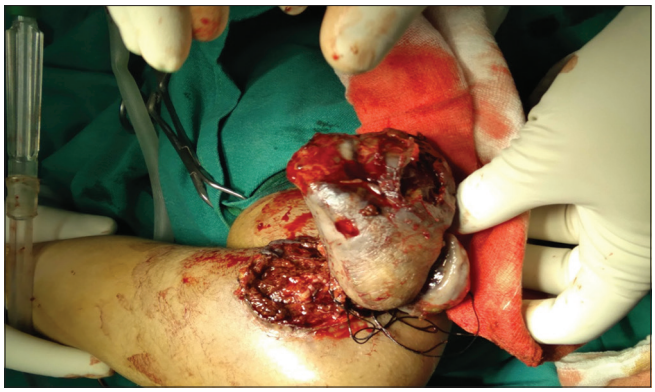

Figure 1: Swelling over left forearm which is ulceroproliferative with bleeding

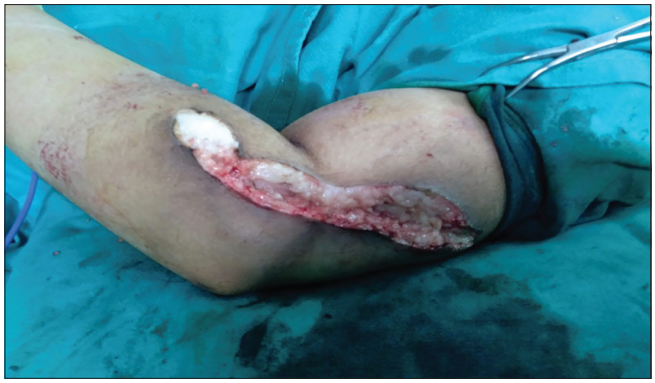

Figure 2: Before the closure of the wound

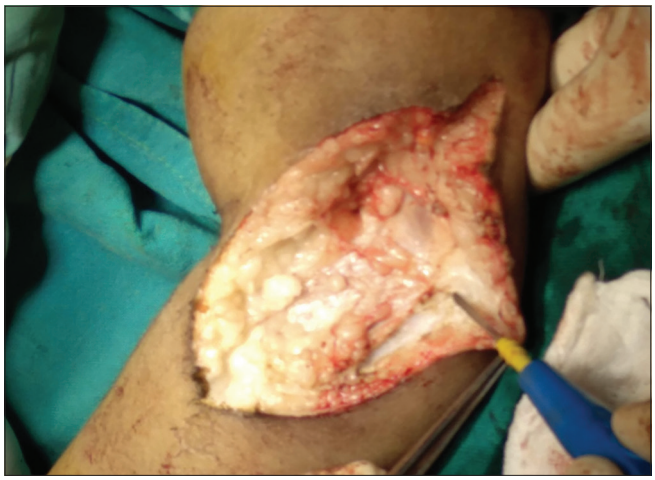

Figure 3: Wide local excision of the mass

Figure 1 show in the hematology reports revealed anisocytosis-anemia. Biochemistry reports reveal decrease in sodium, albumin, and globulin proteins. Ultrasound reveals mild splenomegaly. Patient is further evaluated for soft-tissue sarcoma of the left elbow. Incision biopsy of forearm lesion suggested Spindle Cell Neoplasm. Immunohistochemistry findings showed B cell lymphoma (Bcl)2 positive, cluster of differentiation (CD)99 positive, CD34 highlight blood vessels, negative in tumor tissue, S100 negative, smooth muscle antibody-negative, and Ki67-10-15%. In view of

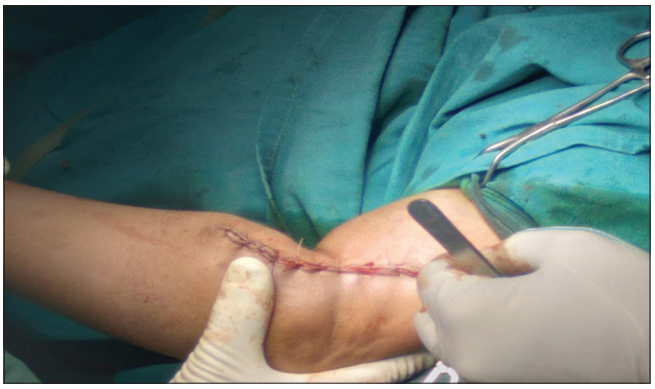

Figure 4: After the closure of wound

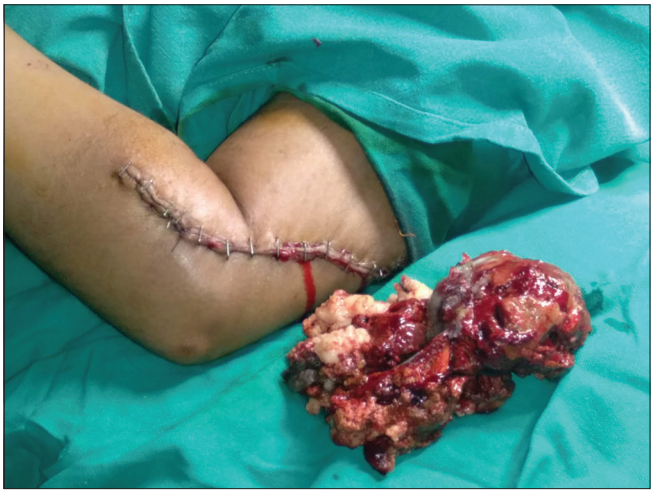

Figure 5: Post-operative image after the closure of wound with specimen aside

Bc12, CD99 positivity, and CD34 negativity, possibility of Synovial sarcoma to be considered. FDG PET-CT was done for disease staging, which was normal.

Wide local excision was done under high risk and informed consent was taken from patient attenders as the patient was physically and mentally challenged and bed ridden. Regional block anesthesia was given as the patient was not fit for general anesthesia. Operative and post operative images are shown in Figures 2-5.

Histopathology Findings

On gross examination mass contains skin covered soft tissue altogether measuring 6.5 × 5.3 × 2.4 cms. External examination shows ulceration. Cut surface shows grey white areas with extensive hemorrhagic areas. Microscopic examination shows skin with epidermis lined by squamous epithelium which shows elongated hyper pigmented rete ridges with focal ulceration. The dermis shows a lesion comprised of plump spindled to rounded cells dispersed among collagen bundles. The nuclei of these cells are rounded to elongated and vesicular. At some places, storiform pattern is seen. At the periphery, collagen is typically trapped, forming

collagen balls. Large blood filled spaces are seen. The lesion is extending into subcutaneous tissue with focal necrosis. Skin margin and posterior margin are involved by tumor. All these features suggest BFH and aneurysmal variant.

CONCLUSION

BFH should be a differential diagnosis while evaluating soft-tissue swellings where a major surgical amputation could be avoided in selected cases with poor performance status and at areas of critical importance such as joints. In our patient, incision biopsy was suggestive of spindle cell neoplasm but final diagnosis after wide local excision showed BFH – aneurysmal variant. In our patient with poor performance status, we have avoided major surgery where patient was unfit for general anesthesia.

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Case Report

Telecare of an Anxious Breathless Athlete in COVID-19 Pandemic: A Case Report Study

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Abstract

The COVID-19 pandemic has adversely impacted human history. It has familiarized us with new norms of living standards such as social distancing, quarantine, lockdown, and work from home. The COVID-19 Pandemic has a massive impact on healthcare which changes the trend toward telephonic Consultation for COVID-related as well as non-COVID related problems. However, there are still certain situations where Telecare should not be considered reliable. Therefore, we suggest that sufficient patient-physician communication is important before diagnosing any condition, particularly labeling any symptom as Anxiety.

Key words: Anxiety, COVID-19, Telecare

BACKGROUND

The COVID-19 pandemic has adversely impacted human history. It has familiarized us with new norms of living standards such as social distancing, quarantine, lockdown, and work from home. This pandemic has demonstrated the critical importance of telecommunication in different aspects of life from businesses, the economy, and societies to health medicine to keep the communities connected. There is no doubt that Telehealth has proved itself in providing health care services during this global emergency while also providing safety to patients and health care professionals. Although there are numerous benefits of Telehealth particularly in non-emergency conditions and few situations where direct physical review is not required such as psychological services, there are still certain definite limitations that exist. There are concerns about quality and safety through teleconsultation as compared to physical review.

Here, we are discussing a case of a young athlete who has been indirectly affected by the COVID pandemic due to a lack of face-to-face communication and labeled as Anxiety. Anxiety, among all human emotions, is one of the characteristics and most powerful emotions. It is a feeling of unease characterized by intense feelings of inner distress and anguish resulting in behavioral and physiological impact.[1] It can range from mild to severe and can include feelings of worry and fear. The most severe form of anxiety is panic. This can create a cycle of living "in fear of fear." The relationship between anxiety and cardiovascular health is complex as all the panic attack features can be seen in an acute cardiac event. The prevalence of anxiety disorder among patients with heart disorders are higher ranges from 15% to 40% than that of the general population.[2,3] In Athletes, studies show dilated cardiomyopathy is the main cause of heart failure (HF), while acute myocarditis is the most frequent cause of acquired dilated cardiomyopathy in young athletes.[4] The latter may run an asymptomatic course and present with normal resting electrocardiography in up to 32% of those affected.[5]

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CASE REPORT

A 42-years old young athlete presented in the Emergency department in the United Kingdom with 3 months history of recurrent episodes of shortness of breath, described as exertional dyspnoea, palpitations, sweating, trembling, and fatigability. He presented to his general practitioner (GP) with the above symptoms. His initial clinical review was completely unremarkable; therefore, and he was managed

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on the line of panic attacks. The patient's symptoms got worse over 2 months where he was unable to perform any exertional work. Except for the first GP surgery visit, his subsequent consultations were totally telephonic. He was a marathon runner, used to run kilometres routinely, now became debilitated, unable to perform the activity of daily living. He started using 3 pillows, and was unable to walk without being short of breath, he almost started crawling. Over the next 3 weeks, he noticed leg swellings and blood-stained cough, re-contacted GP Surgery, was advised to visit the hospital, and eventually landed in the emergency room. His past medical, drug, and family history was not significant. He was a non-smoker, non-alcoholic fit healthy person. There was no history of preceding viral illness or travel. His physical examination revealed sitting posture, cold clammy extremities, speaking in broken sentences respiratory rate 32, blood pressure 114/64, pulse rate 97, oxygen saturation 97% on 35% VM, Temp 36.6, thready radial pulse with raised jugular venous pressure up to ear lobule and bilateral pitting oedema. Chest examination revealed fine basal crackles, soft heart sounds with gallop rhythm, ascites, and palpable liver.

His investigations revealed Troponins 128.5, brain natriuretic peptide 22024, C-reactive protein 173.2, D Dimers 2578, deranged liver functioning test, glomerular filtration rate >90, and electrocardiogram showed left atrium enlargement, prolonged QTc and T wave inversions in lateral leads. Chest X-ray showed increased cardiothoracic ratio + congested lung fields.

A clinical diagnosis of acute decompensated HF was made. An echocardiogram showed ejection fraction 14%, severely dilated left ventricle (LV) with moderate biatrial and right ventricle dilatation, and LV Thrombus. Computed tomography (CT) Chest showed acute pulmonary emboli with pulmonary infarct and right kidney infarct. Blood tests for the autoimmune screen, thyroid profile, and blood cultures along with COVID polymerase chain reaction were negative.

He was treated for acute decompensated HF with furosemide, intravenous dobutamine, dalteparin and transferred to the cardiology unit where he was managed as a case of dilated cardiomyopathy of unknown cause. He responded well to the treatment and after stabilization, he was transferred to a specialized centre QE, Birmingham for Heart Transplant.

DISCUSSION

This is a case report of an anxious young athlete, in whom the diagnosis of breathlessness posed difficultly due to various factors, which included atypical presentation considered to be anxiety, slow progression, and subsequent telephonic conversations by the GP, rather than face-to-face consultation, due to COVID-19 pandemic. This led to difficulty in understanding the nature of his symptoms without a physical examination and may have contributed to a delay in the diagnosis. Clinical manifestation of chronic HF in an athlete as well as in non-athletes can be nonspecific, underestimated, and/or misdiagnosed, with possibly dire consequences. Thus, athletes suffering from HF may be asymptomatic or present with atypical symptoms. Dyspnea is a common complaint in seemingly otherwise healthy athletes. Asthma and exercise-induced bronchoconstriction are prevalent conditions in elite athletes. However, there are numerous factors, ranging from poor aerobic fitness to serious, potentially fatal respiratory and non-respiratory pathologies that can cause dyspnoea in athletes. For effective treatment of dyspnea, clinicians need to obtain an appropriate case history, ask relevant exercise-specific questions, and perform a proper examination to fully characterize the nature of the complaint, so that a targeted diagnostic plan can be developed.

In the case described above, although differentiation of evolving HF from panic disorder was difficult due to symptoms similarities. However, developments of such symptoms in young athletes should not be ignored or labeled as anxiety unless all other physical causes are excluded. According to the DSM-5, the diagnosis of panic disorder is applied in cases of repeated and unexpected panic attacks, where the condition is defined as not being caused by the physiological effect of a substance or other medical condition (e.g., hyperthyroidism or a cardiopulmonary disorder).[6] Panic attacks are psychiatric symptoms in which sudden severe fear or discomfort increases and peaks within a few minutes, and four of 13 symptoms (palpitations, sweating, trembling, sensations of shortness of breath, feelings of choking, chest pain, nausea, dizziness, chills, paresthesia, derealization, fear of losing control, or fear of dying) occur during that time.[6]

In this case, the patient exhibited palpitations, dyspnea, chest pain, lethargy, and fear of death. This gentleman contacted his GP in the early phase of illness, the examination was normal, and no other structural abnormalities were noted at the initial visit. Therefore, he was assumed to have these symptoms due to panic disorder. During the clinical course, his symptoms got worse. He repeatedly contacted his GP who arranged telephonic consultations due to the COVID-19 pandemic; no in-person visit was arranged. Hence, GP initiated psychotherapy and started him on psychotropic medication, but the patient observed no therapeutic effect and finally ended up in emergency in acute decompensated HF.

In the general population, the prevalence rate of panic disorder is reportedly 3.7%.[7] In contrast, some studies reported that up to 30% of patients with HF also exhibit clinically relevant anxiety symptoms.[2] In one of the first systemic studies conducted at a Sports Cardiology Clinic

in Denmark to investigate the prevalence of cardiac symptoms and diagnoses among 201 athletes, Cardiac disease was diagnosed in 44% of the patients, and atrial fibrillation was the most prevalent diagnosis (7.5%). Some patients receiving a delayed diagnosis of arrhythmia are initially misdiagnosed as having panic disorder.[8]

In other studies, an interesting relationship has been found between panic attacks and mitral valve prolapse. This benign condition is found to be more frequent in patients with panic disorder as compared to the general population.[1] A series of 73 patients were compared with a control group of acute coronary syndrome (ACS) patients. The authors found that Takotsubo Cardiomyopathy (TCM) patients had higher levels of chronic anxiety, in comparison with ACS patients. After a multivariable adjustment, it was found that chronic anxiety in TCM is associated with an emotional trigger.[9]

In one case report of a 57-year-old woman who appeared to have panic disorder, later diagnosed as transient complete atrioventricular block, associated with cardiac sarcoidosis. Her panic attacks were ameliorated after implantation of a permanent pacemaker and initiation of steroid treatment for cardiac sarcoidosis.[3]

CONCLUSION

The current case report highlights the importance of exclusion of all other physical causes before labelling any patient with anxiety. Anxiety should be last in our differential diagnosis unless proved otherwise. It is suggested that proper cardiac evaluation by examination, Holter monitoring, or echocardiography should be considered in athletes who develop new-onset breathlessness. This case report also emphasizes the significance of thorough clinical evaluation which is crucial to exclude illnesses with similar presentations like panic disorder.

The COVID-19 Pandemic has a massive impact on healthcare which changes the trend toward telephonic consultation for COVID-related as well as non-COVID related problems. It is believed under current circumstances that Telemedicine has shared a major burden in healthcare; however, it has deprived utmost important face-to-face clinical evaluation. This led to delay in diagnosis, early treatment, resulting in dire consequences, like our case. A qualitative interview study in Flemish GPs revealed that GPs found telephonic consultation difficult due to lack of non-verbal communication, less information, and subjective patient findings, think they will miss other diagnoses more frequently.[10]

In this regard, Greenhalgh and Greenhalgh *et al.*[11,12] gave guidance regarding the use of video consultations in primary care which has some important practical implications appropriate for both "COVID-related" or "non-COVID-related" consultations and provides tips on which patients may not be suitable for video consultations.

In the end, we suggest that sufficient patient-physician communication is important before labelling any symptom as a panic attack. The role of Telehealth should be prioritized on an individual basis rather than applying to every patient as there is a case-to-case variation in clinical presentation.

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Case Report

Fabrication of a Hollow Bulb Obturator using Altered Cast Technique: A Case Report

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Abstract

Surgical management of head and neck cancers affects the quality of life of the patients during and after treatment. Following a partial or total resection of the palate, the patient may experience difficulty in swallowing, speaking and difficulty in jaw movements. This leads to isolation from the society, and it hampers the well-being of the patient. This article presents a case report of a patient who had undergone partial maxillectomy requiring a definitive obturator.

Key words: Altered cast, Cast retained obturator, Hollow bulb obturator

INTRODUCTION

Rehabilitating patients with maxillofacial defects is one of the most difficult therapies of the stomatognathic system. The main purpose of rehabilitating these defects is to eliminate the disease and to improve the quality of life for these individuals. Following surgical resection, the conventional sequence of treatment includes the placement of a surgical obturator during the intervention.[1] After 5–10 days, the surgical obturator is removed, and a removable interim obturator is fabricated to facilitate healing of the wound. About 3–6 months later, a definitive obturator is fabricated and inserted at a stage when tissue changes are no longer expected.[2] This article presents the rehabilitation of a patient with Aramany Class II maxillary defect [3-5], where definitive prosthetic rehabilitation is carried out with a cast open bulb obturator.

CASE DESCRIPTION AND RESULTS

A 26-year-old female patient with a defect in the posterior left side of the palate reported to the Department of Prosthodontics in Government Dental College, Thiruvananthapuram. Intraoral examination revealed a maxillary defect on the left side of the palate. The defect extended from the premolar region anteriorly to the posterior aspect of the hard palate posteriorly. Medially, it extended from the mid-palatine region to the buccal mucosa laterally. The patient had partially dentate upper arch with only 7 maxillary teeth remaining (17, 13, 12, 11, 21, 22, and 23). The patient had partially dentate lower arch with 10 teeth remaining (37, 34, 33, 32, 31, 41, 42, 43, 44 and 45).

A maxillary cast open bulb obturator prosthesis and mandibular partial removable dental prosthesis were planned for this patient [Figure 1]. Diagnostic impressions of the upper and lower arches were made using irreversible hydrocolloid impression material (Vignette Chromatic Alginate, Dentsply Sirona). The defect was covered with wet gauze to prevent the flow of impression material into the defect.The impression of the defect was made using admix impression technique. The impression of the maxillary arch including the defect was made using thin mix of irreversible hydrocolloid impression material. This primary impression recorded the relevant intraoral structures on the nonresected side and part of the resection defect. The impressions were then poured in dental stone (Gem stone, Shruthi products, India) to obtain primary casts. The cast was surveyed and the cast partial denture design of the prosthesis was decided. The obturator

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prosthesis was to be retained by circumferential clasp and I bar clasps. Before making the secondary impression for the fabrication of metal framework, rest seats were prepared on the upper canines and molar. Secondary impression was made using putty impression material (Avue Gum Putty, Korea) and light body impression material (Avue Gum Light Body, Korea). The master cast was poured in Type IV stone (Ultra Real Dental stone, Shruthi products). The metal framework was fabricated and inserted into the patient's mouth to evaluate the fit.

Three metal clasps engaged the maxillary canines and maxillary right second molar to stabilize the framework for the secondary (altered cast) impression. The defect side was again molded using admix impression technique and secondary (altered cast) impression was made using light body impression material (Avue Gum Light Body, Korea). The stone cast was then modified to an altered cast; segment of the cast corresponding to the defect was reduced until the secondary (altered cast) impression of the defect could be placed on it without any interference. After positioning it, impression of the defect area was poured in Type IV stone to produce a definitive cast for the fabrication of the bulb. The wax pattern for the bulb was made using modeling

wax (3 mm thickness). The wax was extended till the superior extent of the lateral walls. To make the bulb hollow, dental plaster was poured into the wax pattern until 2 mm short of the metal framework border. Then, a layer of wax was placed just below the framework to enhance mechanical retention. The framework was positioned on the cast and waxed up. Putty impression material was placed on the framework to block the undercuts. Then, the cast was invested and bulb was fabricated using heat polymerized acrylic resin. The open bulb along with the framework was evaluated intraorally and checked for the extensions. Occlusal vertical and horizontal dimensions were determined and the casts were articulated. Artificial teeth were arranged and evaluated intraorally. Occlusion and esthetics were also verified. The partial removable dental prosthesis was processed with heat polymerized denture base acrylic resin. The maxillary hollow bulb obturator was trimmed and polished. It was evaluated intraorally and necessary adjustments made. The patient was instructed to follow hygiene procedures regularly. Follow-up appointments were recommended every 3–6 months to evaluate the fit of the prosthesis.

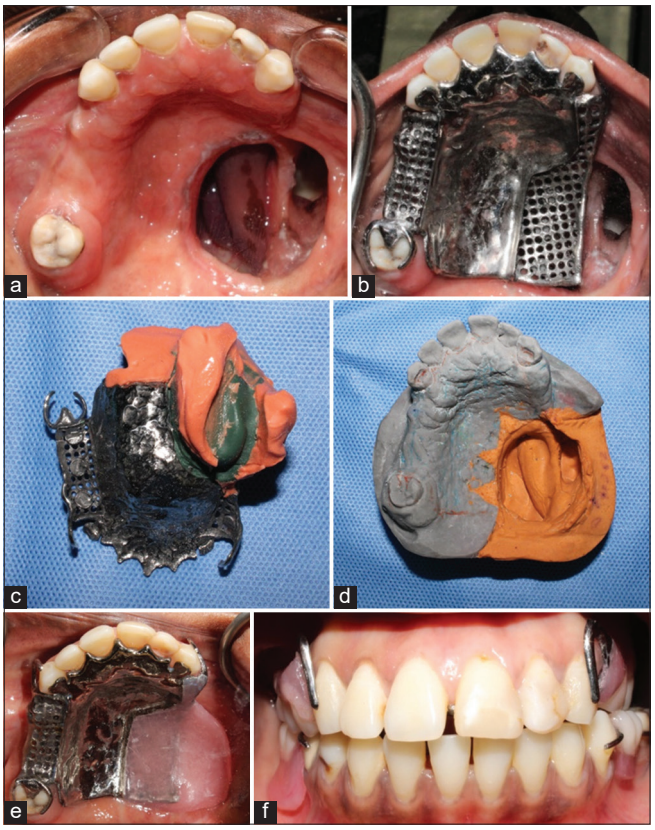

Figure 1: (a) Pre-operative intraoral photo. (b) Metal framework try in. (c) Secondary (altered cast) impression. (d) Altered cast. (e) Metal framework with hollow bulb inserted into defect. (f) Completed prosthesis in occlusion

DISCUSSION

Various factors that affect the management of maxillary defects are the presence of teeth, amount of remaining support area and characteristics of the defect. When these factors are detrimental on the treatment outcome, success of the prosthetic management of the defect becomes a major challenge. Adequate retention of the prosthesis is essential for good prognosis. The prosthesis should also maintain a harmonious relationship with the tissues adjacent to the resected site. The weight of the prosthesis is a major factor to consider in relation to the retention and comfort of the patient. Hence, it is always advisable to fabricate light weight prosthesis by making the obturator bulb hollow. The obturator bulb can be made hollow using a closed bulb or open bulb. The advantages of open hollow obturator are reduced weight, hygiene maintenance, easier fabrication and improved speech.

In case of maxillary defects, two-step (Altered Cast) impression technique provides an accurate registration to relate the functional tissues of the defect to the adjacent soft tissues and teeth. The impression made using metal framework helps in minimizing inaccuracies during jaw relation and final fit of the prosthesis. It ensures adequate closure of the maxillary defect with the obturator thereby improving the oral function, speech and esthetics.

CONCLUSION

The present case report shows the prosthetic rehabilitation of a partial maxillectomy patient with Aramany Class II defect using a hollow bulb cast obturator. It involved the fabrication of a cast partial denture framework onto which the hollow bulb was attached. This helped in restoring function by improving masticatory efficiency and speech by providing resonance to the voice and also improved esthetics of the patient. The hollow bulb obturator was more comfortable to the patient because of its reduced weight.

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Review Article

Oral Cues associated with Coronavirus Disease 2019 Infection – A Systematic Review

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Abstract

Introduction: A global pandemic has been broken out in December 2019 by human-to-human transmission of novel corona virus disease (COVID -19). Since then, it has affected more than million people worldwide and causing numerous death. Most of the cases are mild (80%), while 20% of the infected patients may develop severe disease, and 5% may become critically ill and develop pneumonia or acute respiratory distress syndrome. The general clinical manifestations include fever, chills, cough, fatigue, muscle or body aches, soreness of throat, shortness of breath, headache, nausea, vomiting or diarrhoea. In recent times, few studies have documented several oral manifestations associated with COVID-19. Hence we aim to summarize the oral cues associated with COVID-19.

Methodology: The review was reported as per the PRISMA checklist, and the literature search was conducted in 4 databases and in grey literature as well as a manual search across the reference lists of included studies. Studies published in only English language and those which mentioned oral signs and symptoms in patients with COVID-19 were included.

Conclusion: Taste disorder was the foremost common oral symptoms in patients with COVID-19. Identifying these lesions could help clinicians to treat their patients more efficiently. But several oral manifestations of this disease are underreported due to the lack of oral examination of patients with COVID-19 owing to the lockdown and the carelessness of patients regarding these manifestations that might be less serious compared to the typical COVID-19 manifestations. So, a thorough oral examination should be routinely performed for all suspected COVID-19 cases.

Key words: Coronavirus, COVID-19, Oral manifestations, Review

INTRODUCTION

A global pandemic has been broken out in December 2019 by human-to-human transmission of novel coronavirus disease (COVID-19). Since then, it has affected more than million people worldwide with death of many. Compared to other recent pandemics, COVID-19 shows in general, less severe clinical manifestations but is spreading with great ease. On January 8, 2020, the Chinese Center for Disease Control and Prevention announced officially the identification of a new strain of coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as the causative pathogen of the global COVID-19 pandemic.[1] SARS-CoV-2 is a single-chain RNA virus that is the cause of novel COVID known as COVID-19. Most human cases of COVID-19 are mild (80%), while 20% of infected patients may develop severe disease, and 5% may become critically ill and develop pneumonia or acute respiratory distress syndrome, which requires mechanical ventilation and intensive care unit hospitalization.[2] Coronavirus invades human cells through the receptor angiotensin-converting enzyme 2 (ACE2) through single cell RNA sequencing data analyses.[3] The study of Xu *et al.* found that the receptor-binding domain of the 2019-novel coronavirus (nCoV) S-protein supports strong interaction with human ACE2 molecules.[4] Thus ACE 2 expressing cells become the target for viral entry and infection. Type II alveolar cells of lung, absorptive enterocytes from ileum and colon, esophagus upper and stratified epithelial cells, myocardial cells, cholangiocytes, bladder urothelial cells, and kidney proximal tubule cells shows high ACE2 expression.[5] The general clinical manifestations shown by the patient

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infected with SARS-CoV-2 are fever, chills, cough, fatigue, muscle or body aches, soreness of throat, shortness of breath, headache, nausea, vomiting, or diarrhea.[6]

This meta-analysis presents the information available about the oral manifestations in COVID-19 with lesions presented at the mucosal level, salivary glands and alterations in the olfactory system and taste.

METHODOLOGY

Literature Search and Eligibility Criteria

We searched PubMed library, Scopus databases, Web of Science databases, and Google Scholar for published literature using the keywords "coronavirus," "SARS-CoV-2," "SARS-CoV-2," "COVID-19," "nCoV," "nCoV" and "2019-nCoV" from December 2019 to November 2020.

Reference lists of included studies were also screened for retrieving additional articles. Articles published in English language were taken during literature search. Eligible articles reported the epidemiological and clinical features of COVID-19 and the prevalence of oral manifestations in infected patients. The following studies were excluded: Duplicate publications, reviews, editorials, and studies pertaining to other coronavirus related illnesses, such as Middle East respiratory syndrome. A total of 37 articles that met the inclusion criteria were obtained [Table 1].

Data Extraction

The following information was extracted and tabulated [Table 2] with author, age, sex, oral manifestations, site, duration, systemic manifestations, any special investigations performed, and treatment of oral lesions.

RESULTS

Oral manifestations were swelling, cracked lip, extensive mucosal damage, ulcer, erosion, bulla, vesicle, pustule, fissured or geographic tongue, prominent papilla or depapillated tongue, macule, papule, plaque, pigmentation, halitosis, whitish areas, hemorrhagic crust, necrosis, petechiae, purpura, erythema, spontaneous bleeding, dysgeusia or hypogeusia, herpetiform stomatitis, edematous gingiva, angular cheilitis or burning sensation, and dry mouth. The most common sites involved in descending order were lips (46%), tongue (38%), hard palate (37%), buccal mucosa (14%), gingiva (13%), labial mucosa (6%), oropharynx (6%), tonsil (6%), and soft palate (4%). Provisional diagnoses of the lesions were angular cheilitis, aphthous stomatitis, herpetiform lesions, candidiasis, vasculitis, Erythema Multiforme (EM) like, mucositis, drug eruption, necrotizing periodontal disease (NPD), angina bullosa-like, atypical Sweet syndrome, Kawasaki-like Vascular inflammation Ischemic reperfusion injury, Zosteriform, Thrombocytopenia and enanthema due to COVID-19, and Melkerson Rosenthal syndrome. The results of literature are summarized in Table 2.[7-41]

Oral lesions in 68% of the cases were symptomatic including burning sensation, pain, or pruritus. Oral lesions were slightly higher in males (69% males and 57% females). The age of incidence ranged between 3 and 78 years. Oral lesions were more prevalent as age increases. Systemic manifestations included fever, cough, chills, vomiting, diarrhea, conjunctivitis, meningeal sign, lymphadenopathy, tachypnea, respiratory and gastrointestinal (GI) symptoms, anosmia, malaise, dyspnea, headache, sorethroat, pneumonia, asthenia, fatigue, respiratory distress, nasal congestion, dysgeusia, arthralgia, facial edema, loss of apetite, and weakness. Latency time period between appearance of systemic symptoms and oral lesions was 4 days up to 12 weeks after onset of systemic symptoms. The longest latency period was noticed in Kawasaki-like lesions. Oral lesions healed within 2–4 weeks after appearance. Medications prescribed for oral lesions depend on the etiology. Treatment done was chlorhexidine and metronidazole mouthwash, Nystatin, non-steroidal anti-inflammatory drugs (NSAIDs), Vitamins C and D,

Table 1: Literature search methodology

Identification	Screening	Eligibility	Included
• Pubmed-364 • Scopus-560 • Web of science-270 • Embace-480 • Records identified through first database searching (*n*=1700) • Records after duplicates removed (*n*=1300)	• Grey literature • Google scholar (*n*=50) • Full text article assessed in phase 2 (*n*=80)	• Reviews, letters, conference abstracts, personal opinion, book chapters (*n*=4) • Non-confirmed COVID-19 (*n*=2) • Case reports for taste disorders (*n*=7) • Population selection criteria based on another main disease (*n*=3) • Studies containing data included in other studies or other • studies in which it is not possible to state if they contain duplicate data (*n*=2) • Taste disorder as criteria for population inclusion (*n*=19)	• Studies included in systematic review (*n*=37)

Table 2: Detailed characteristics of included studies

Sl. No.	Author	Age/Sex	Oral Lesions	Site	Duration	Systemic Manifestations	Covid-19 Diagnostic Tests	Treatment Done
1	Verdoni *et al*.[7]	7/5 9-16	Mild swelling	Lip Oral cavity (80%)		Fever Diarrhea Conjunctivitis Meningeal sign lymphadenopathy	PCR-20% IgG-80% IgM 30%	------
2	Jones *et al*.[8]	6M	Cracked lip Prominent papilla in tongue	Lip tongue	------	Fever Conjunctivitis Tachypnea	PCR	
3	Pouletty *et al*.[9]	10(M=8, F=8)	Cracked lip	lip	-------	Fever Respiratory and GI symptom Anosmia	PCR-+69 %	IVIG CS ANTI IL1, IL6 HCH
4	Singh *et al*.[10]	44/F	Extensive mucosal damage	Lip Tongue	----	Malaise Dyspnea		
5	Chiotoset al.[11]	5/F	Fissured lip					
6	Chiotos *et al*.[11]	9/F	Fissured lip	lip		Fever Diarrhea		
7	Chiotos *et al*.[11]	12/M	Fissured lip	lip		Fever Diarrhea conjunctivitis		
8	Chiu *et al*.[12]	10/M	Cracked lip Erythema	Lip oropharynx		Fever Cough diarrhea	PCR	
9	Mazzotta *et al*.[13]	58/M	Unilateral multiple small ulcers	Palate	7	----		Mouthwash
10	Carreras-Presas *et al*[14]	56/M	Dysgeusia Herpetiform stomatitis	Hard palate	10	Fever Asthenia LAP	2	
11	Carreras-Presas *et al*[14]	60/M	Macule Petechiae	Palate	---	----	19	AZT HCH L/R
12	Jimenez-Cauhe *et al*.[15]	60/M	Macule Petechiae	Palate	---	----		L/R HCH AZT T CS L/R HCH AZT Toclizomab CS
13	Jimenez-Cauhe *et al*.[15]	40/M	Purpura	Palate	---	---		
14	Jimenez-Cauhe[15]	60/M	Macule Petechiae	Palate	---	---	PCR	L/R HCH AZT
15	Jimenez-Cauhe[15]	40/M	Purpura EM like	Palate		Enanthema due to covid 19		L/R HCH
14	Patel and Woolley[16]	35/F	Bleeding Halitosis Generalized edematous gingiva Necrosis	Gingiva		Fever LAP submandibular		Metronidazole mouthwash
15	Chaux-Bodard *et al*.[17]	45/F	Patch	Tongue	10	Asthenia	PCR	Vasculitis
16	Dominguez-Santas *et al*.[18]	19/M	Minor aphthous	Lip	---	Fever Headache Anosmia Malaise Dyspnea	PCR	----

(Contd...)

Table 2: *(Continued)*

Sl. No.	Author	Age/Sex	Oral Lesions	Site	Duration	Systemic Manifestations	Covid-19 Diagnostic Tests	Treatment Done
17	Dominguez-Santas *et al*.[18]	37/M	Minor aphthous	Tongue	----	-----	PCR	---
18	Dominguez-Santas *et al*.[18]	33/M	Minor aphthous	Mucogingival junction	-----	Pneumonia Fever Malaise	PCR	---
19	Dominguez-Santas *et al*.[18]	43/F	Minor aphthous	Buccal	----	Bilateral pneumonia Fever Malaise	PCR	
20	Putra *et al*.[19]	29/M	Papule Aphthous stomatitis		---	Fever Myalgia Sore throat Dry cough	PCR	Paracetamol AZT HCH Oseltamivir Vitamin C Vitamin D
21	Carreras-Presas *et al*.[14]	65/F	Rash Desquamative gingivitis	Tongue Gingiva		Fever Diarrhea	-----	Antibiotics CS HCH HA L/R
22	Kämmerer *et al*.[20]	46/M	Multiple ulceration covered by yellow gray membrane	Oral cavity Gingiva	---	Fever Fatigue Dry cough Respiratory distress LAP submandibular	PCR	AZT Meropenam Acyclovir
23	Tapia *et al*.[21]	42/M	Burning	Hard palate	7	Fever Malaise Dysgeusia Headache	PCR	Acetaminophen Mouthwash CS
24	Tapia *et al*.[21]	55/F	Tongue enlargement Purple blister	Tongue	5	Fever Headache Nasal congestion	PCR	Acetaminophen
25	Tapia *et al*.[21]	51/F	Vascular like purple macule Non bleeding Purple plaque	Palate	--	Fever Malaise Dysgeusia Arthralgia	PCR	Acetaminophen
26	Tapia *et al*.[22]	41/F	Erythematous blister	Hard palate	----	Fever Malaise Dysgeusia Hyposmia	PCR	Acetaminophen Fexofenadine
27	Rodríguez *et al*.[22]	78/F	Dry mouth Atrophy of surface of tongue White and red patches Fissured tongue	Tongue Hard palate Soft palate Lip	----	---	PCR	Artificial saliva Nystatin Neomycin CS
28	Rodríguez *et al*.[22]	43/M	Angular chelitis with burning sensation	Lip	10	Dysguisea Anosmia Diarrhea Pneumonia	PCR	Mouthwash CS
29	Chérif *et al*.[23]	35/F	Chapped lips Ulcer Hypogeusia	Tongue Lip	10	Fever Myalgia Dyspnea Dry cough Vomiting Diarrhea	PCR	AZT Mouthwash
30	Ansari *et al*.[24]	75/M	Painful Irregular ulcer in erythematous background	Hard palate	7	Hypoxia	PCR	AZT Mouthwash

(Contd...)

Table 2: *(Continued)*

Sl. No.	Author	Age/Sex	Oral Lesions	Site	Duration	Systemic Manifestations	Covid-19 Diagnostic Tests	Treatment Done
31	Ansari *et al*.[24]	56/F	Painful Irregular ulcer in erythematous background	Hard palate	7	Fever Dyspnea	PCR	Remisidivir AZT
32	Biadsee *et al*.[25]	36.25/F	Plaque bleeding swelling Xerostomia Dysgeusia	Tongue Palate Gingiva	--	Fever Cough Myalgia Sore throat Anosmia GI symptoms	PCR	
33	Olisova *et al*.[26]	12/F	Swollen irritated Pronounced lingual papilla	Tongue	3	Fever Fatigue Headache	PCR	Paracetamol
34	Tomo *et al*.[27]	37/F	Erythematous Depapillation of tongue	Tongue	14	Fever Asthenia Dysgeusia Anosmia	PCR	CS Dipyrone Mouthwash
35	Ciccarese *et al*[28]	19/F	Erosion Ulcer Hemorrhagic crust Petechial	Lip Palate Gingival Oropharynx	5	Fever Fatigue Hyposmia Sore throat	PCR	IVIG CS
36	Sakaida *et al*[29]	52/F	Erosion	Lip Buccal	---	Fever Dyspnea Drycough	PCR	
37	Brandiao *et al*.[30]	72/M	Painful Aphthous like necrosis Hemorrhagic ulcer	Lip	7	Fever Dyspnea	PCR	Increased levels of CRP Lymphocytopenia Positive PCR for HSV
38	Brandiao *et al*.[30]	81/M	Aphthous like necrosis Hemorrhagic ulcer	Lip Tongue	11	Dry cough Dyspnea Fever Chills Dysgeusia	PCR	AZT Cefriaxone Acyclovir PBMT
39	Malih *et al*.[31]	38/M	Erythema Aphthous like	Tonsil	---	Fever Asthenia Cervical LAP	PCR	Acetaminophen
40	Labé[32]	3/M	Cheilitis Glossitis Stomatitis	Lip Tongue Oral cavity	---	Loss of appetite	PCR	---
41	Aghazadeh *et al*.[33]	9/F	Vesicles Erosion	Lip Tongue Buccal	7	Fever Weakness Loss of appetite Abdominal pain	PCR	AcetaminophenI
42	Indu[34]	NS/M	Burning ulcer	Lip tongue	10	Fever	PCR	---
43	Taskin *et al*.[35]	61/F	Minor aphthous ulcer	Hard palate Buccal	---	Fever Fatigue Myalgia Arthralgia	PCR	AZT HCH Oseetamivir Toclizomab Favipiravir
44	Taşlıdere *et al*.[36]	51/F	Swollen lip Fissured tongue	Lip Tongue	---	Malaise Unilareral facial paralysis Facial edema	---	HCH AZT CS
45	Brandiao *et al*.[30]	29/M	Painful Aphthous like aguesia	Lip Tongue	6	Fever Cough Headache Myalgia Chills Anosmia	PCR	Mouthwash

(Contd...)

Table 2: *(Continued)*

Sl. No.	Author	Age/Sex	Oral Lesions	Site	Duration	Systemic Manifestations	Covid-19 Diagnostic Tests	Treatment Done
46	Brandiao *et al*.[30]	35/M	Aphthous like	Tonsil	8	Fever Malaise Sore throat Cough Hyposmia Ageusia Odynophagia	PCR	---
47	Brandiao *et al*.[30]	32/F	Aphthous like	Tongue	5	Dysgeusia Fever Cough Headache Anosmia	PCR	Dipyrone
48	Soares *et al*.[37]	42/M	Ulcer Blister Vesicle	Buccal mucosa Tongue Lip Hard palate	21	Fever Cough Dyspnea	PCR	CS Dipyrone
49	Dos Santos *et al*.[38]	67/M	White plaque multiple yellowish ulcer Geographic tongue Erythema Hypogeusia	Tongue Palate Tonsil	14	Fever Diarrhea Dyspnea	PCR	Mouthwash Fluconazole Nystatin AZT Cefriaxone HCH Meropenem T/S
50	Corchuelo and Ulloa[39]	40/F	Petechiae Whitish area Brown pigmentation	Tongue Lip gingiva	20	LAP of neck	IgG	Ibuprofen Vitamin D AZT Mouthwash Nystatin
51	Jimenez-Cauhe *et al*.[40]	66/F	Petechiae Macule	Palate	14-21	EM like	---	AZT Cefriaxone Cs HCH L/R
52	Kahraman and Çaskurlu[41]	51/M	Large erythematous petechiae Pustules	Hard palate Oropharynx Soft palate Ageusia	A few days	Fever Fatigue Dry cough Sore throat Anosmia	IgM	clarithromycin

PCR: Polymerase chain reaction, Ig: Immunoglobulin, EM: Erythema Multiforme, CRP: C-reactive protein, HSV: Herpes simplex virus, GI: Gastrointestinal

oral Fluconazole, topical or systemic corticosteroids, systemic antibiotics, systemic Acyclovir, artificial saliva, and photobiomodulation therapy.[7-41]

DISCUSSION

An increasing number of studies have reported the involvement of the oral lesions in patients with COVID-19. The occurrence of oral lesions is due to

1. Presence of ACE2 receptors in the oral cavity which leads to direct inoculation of the virus
2. Decreased host immunity
3. The effect of high dose steroids administered to the patient for managing general symptoms of COVID-19 infection.

ACE2 Expression in the Oral Cavity

The ACE2 receptor, which the SARS-CoV-2 binds to infect the host cells, is highly expressed in the epithelial cells of the tongue.[5] The interaction of SARS-CoV-2 with gustatory components and ACE2 receptors supports a direct effect in COVID-19 – related taste disorders.[42] A study was conducted to investigate the potential routes of 2019-nCov infection on the mucosa of oral cavity by Xu *et al*. and was found that ACE2 could be expressed in the oral cavity.[4] Among the different oral sites, ACE2 expression was higher in tongue than buccal and gingival tissues. These findings indicated that the mucosa of oral cavity may be a potentially high risk route of 2019-nCov infection.[43] The expression of ACE2 in minor salivary glands was found higher than that in lungs.[44] Thus, salivary glands could be potential target for

COVID-19 and the salivary gland could be a major source of the virus in saliva. In addition, before lung lesions appear SARS-CoV RNA can be detected in saliva. This suggests that COVID-19 transmitted by asymptomatic infection may originate from infected saliva.[45]

We aimed to investigate the pooled prevalence of oral manifestations in patients with COVID-19. This study presented several cases of SARS-Cov-2 infection, with oral manifestations developing during the infectious period of the disease. The loss of taste and smell also appeared concomitant with oral manifestations. The oral lesions were more severe and widespread in older patients with more severe COVID-19 infection. The common oral manifestations were as follows:

Taste Disorders

Taste disorders were the foremost common oral symptoms in patients with COVID-19. Chemosensory disorders are defined as diseases related to the sense of smell and/or taste. Taste disorders are classified as quantitative or qualitative disorders, of which hypogeusia may be a decreased sense of taste, ageusia is that the absence of a way of taste, and dysgeusia could be a qualitative distortion of gustatory sensation. It was the higher prevalence in Europe and North America than in Asia and a significant association with COVID-19– positive diagnosis, mild/moderate COVID-19 severity, and female patients.[46] In this meta-analysis, patients with COVID-19 presented a prevalence of 20% for overall taste disorders, 14% for dysgeusia, 4% for hypogeusia, and 2% for ageusia. These results confirm that taste disorders may be a significant and specific symptom of mild/moderate COVID-19 cases.

Aphthous-like Lesions

Aphthous-like lesions appeared as multiple shallow ulcers with erythematous halos and yellow-white pseudomembranous on the both keratinized and nonkeratinized mucosa. Oral lesions appeared concomitant with systemic symptoms. Latency time period was between 2 and 10 days. Lesions healed within 5–15 days. Regression of oral lesions was seen with improvement of systemic disease. One patient had positive history of recurrent aphthous stomatitis. The lesions were of two types, one resembling aphthous-like ulcers in young patients with mild cases of COVID-19 and another with more widespread patterns resembling herpes simplex virus (HSV)-1 necrotic ulcers and hemorrhagic crust in the more severe and immunosuppressed older individuals. An overall prevalence was 20% of aphthous like lesions with 10% of patients had painful lesions. There was necrosis observed in 10% of cases and there was no necrosis in 40% of cases.[30,22] The interaction between SARS-CoV-2 and ACE2 might disrupt the function of oral keratinocytes and the epithelial lining of salivary glands ducts, resulting in painful oral ulcers.[30] Furthermore, the increased level of tumor necrosis factor (TNF)-α in COVID-19 patients can lead to chemotaxis of neutrophils to oral mucosa and development of aphthous like lesions. Stress and immunosuppression secondary to COVID-19 infection could be other possible reasons for appearance of such lesions in COVID-19 patients.[47]

Necrotizing periodontal disease (NPDs)

A 35-year-old female presented with fever, submandibular lymphadenopathy, halitosis, and oral lesions. Oral manifestation included necrosis of inter-papillary areas. Gingiva was painful, diffuse erythematous, and edematous. Provisional diagnosis was NPD due to bacterial coinfections (especially *Prevotella intermedia*) along with COVID 19. The lesions were healed after 1 week. The major etiological bacterial species for several acute periodontal lesions is considered as *P. intermedia* along with Fusobacterium and Treponema species. This constitutes a major proportion of the microbiota present in NPDs lesions. SARS-CoV-2 infection may predispose individuals to NPDs through bacterial co-infection caused by P. intermedia.[16]

Enanthema

Enanthema occurs in various types of viral diseases including dengue fever disease, Ebola virus disease, herpangina, human herpes virus infections, measles, and roseola infantum. Approximately 88% of enanthema are caused by infectious diseases, especially of viral etiology.[2] Petechiae, macules, papules, or vesicles may present with enanthema in the mouth. Erythematous-vesicular and petechial patterns were also present in association with viral infections. It is more frequent in adults.[40] This is consistent with the present study, in which 7 patients (13%) had petechiae as a main component of the enanthema. It occurred 2 days after the onset of COVID-19 symptoms, making association with the drug intake unlikely. The presence of enanthema is a strong clue that suggests a viral etiology rather than a drug reaction, especially when a petechial pattern is observed.[15,19] Different types of enanthema such as aphthous-like ulcers, Koplik's spots, Nagayama's spot, petechiae, papulovesicular, or maculopapular lesions, white or red patches, gingival and lip swelling have been reported with various viral infections. Both keratinized (hard palate, gingiva, and dorsum of tongue) and nonkeratinized (labial and buccal) mucosae can be involved.[2]

Ulcer and Erosion

Ulcerative or erosive lesions were one of the most commonly reported oral manifestations of COVID-19. These lesions appeared as painful lesions with irregular borders. These are mainly seen on the tongue, hard palate, and labial mucosa. Latency time period of lesions was 4–7 days. But in one case, lesions appeared 3 days before the onset of systemic

symptoms. Two studies performed laboratory investigations such as polymerase chain reaction (PCR) for HSV-1 and HSV-2 and showed negative herpes antibodies.[24] Lesions healed after 5–21 days. Different factors including drug eruption (to NSAID in one case), vasculitis, or thrombotic vasculopathy secondary to COVID-19 were suggested as etiology for development of ulcerative and erosive lesions.[48]

Vesiculobullous Lesions

Eight studies reported oral vesiculobullous lesions in patients with COVID-19. The clinical presentations varied greatly, ranging from blisters, to erythematous lesions, to petechial, and erythema multiform-like lesions.[48] Oral lesions were present on the tongue and buccal mucosa as vesicular eruptions and erosions. Prodromal symptoms were also present. Lesions regressed after 1 week.

EM-like lesions presented as cutaneous target lesions in the extremities. There were blisters, desquamative gingivitis, erythematous macules, erosions, and painful cheilitis with hemorrhagic crust in patients with EM like lesions. These lesions are observed in 4% of cases Lesions appeared within 7–24 days after the onset of systemic symptoms. These are healed after 2–4 week.[15]

Melkerson-Rosenthal Syndrome

A 51-year-old female patient presented with complaint of unilateral lip swelling, fissured tongue and right facial paralysis. She had past history of Melkersson-Rosenthal syndrome since 4 years that spontaneously cured with no relapse. Laboratory data demonstrated an increased level of C-reactive protein (CRP). Ground-glass opacities in both lungs was observed in computed tomography scan. The patient cured completely after treatment of COVID-19 disease.[36]

Melkersson–Rosenthal syndrome is characterized by orofacial edema, facial paralysis and fissured tongue. Orofacial edema is the most common component of the triad and the upper lip is usually involved. Peripheral facial paralysis is often unilateral. It is thought to develop due to granulomatous infiltration and edema of the nerve tissue.[49] In this case, orofacial edema was unilateral and located in the lower lip. Peripheral facial paralysis was present on the right side, and the classic triad of the syndrome was completed by the fissured tongue.[36]

Kawasaki-like Disease

Kawasaki-like disease in COVID-19 patients (Kawa-COVID) presented oral lesions including cheilitis, glossitis and erythematous and swollen tongue (red strawberry tongue). The latency period between appearance of systemic symptoms (respiratory or GI) and onset of oral or cutaneous symptoms was long. This could be due to a delayed hyperactivation response of the immune system and secondary release of acute inflammatory cytokines rather than direct effects of virus on the skin and oral mucosa.[7-9]

Post-inflammatory Pigmentation

A 40-year-old female reported with pigmentation in the attached and interpapillary gingiva. Increased levels of inflammatory cytokines (including interleukin-1 [IL-1] and TNF-α) and arachidonic acid metabolites (prostaglandins) secondary to production of stem cell factor and basic-fibroblast growth factor from keratinocytes of basal layer led to post-inflammatory pigmentations.[39]

Herpetiform Lesions

Herpetiform lesions presented as multiple painful, unilateral, round yellowish-gray ulcers with an erythematous rim on the both keratinized and nonkeratinized mucosae. These lesions preceded, coincided with, or followed systemic symptoms. Laboratory test showed increased level of CRP, IL-6, eosinopenia, positive PCR and serology for HSV. Stress and immunosuppression associated with COVID-19 were also suggested as etiology for secondary herpetic gingivostomatitis.[14,20,38]

Zosteriform Lesions

Zosteriform lesions appear as ulcers with symptoms such as painful, burning, and itching occurred mainly on lip and tongue. The lesion healed after 10 days.[34]

Atypical Sweet Syndrome

A 61-year-old female presented with chief complaint of fever, fatigue, arthralgia, myalgia, several erythematous nodules on the scalp, trunk and extremities, and minor aphthous ulcers on the hard palate and buccal mucosa. Reverse transcription PCR for COVID-19 was positive. Diffuse neutrophilic infiltration in the upper dermis and granulomatous infiltration in the lower dermis and subcutaneous area were present in skin biopsy. This was compatible with erythema nodosum-like Sweet syndrome.[35]

Red and White Lesions

Red and white lesions were observed on dorsum of tongue, gingiva, and palate of patients with confirmed or suspected COVID-19. Long-term antibiotic therapy, deterioration of general health, and decline in oral hygiene can be the cause of white or red patches or plaques. Stress and immunosuppression also can be the etiology.[38,39]

Limitations

The limitations of the present study are as follows:

i. No clarity is given about the severity of COVID disease
ii. Majority published data are only case reports and many were published as letter to the editor which led to incomplete reported outcomes.

CONCLUSION

Oral manifestations are common in patients with COVID-19 that may help clinicians identify suspected cases. However, many oral manifestations of this disease are underreported due to the lack of oral examination of patients with COVID-19 due to the lockdown and the carelessness of patients regarding these manifestations that might be less serious compared to the typical COVID-19 manifestations.[48] Hence, a thorough oral examination should be routinely performed for all suspected COVID-19 cases. Dental follow-up must be provided after the patient is dismissed from the hospital. Dentists should also be familiar with all potential orofacial manifestations of COVID-19. Further studies are recommended to document all COVID-19-associated orofacial manifestations using large cohorts of patients. Future studies will help to verify this hypothesis by correlating the symptomatic condition to the viral loads from the swabs or saliva.

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Original Article

Clinico-demographic Profile of Malignant Gliomas at a Tertiary Cancer Centre

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Abstract

Background: Gliomas have traditionally been classified as astrocytic, oligodendroglial, oligoastrocytic (mixed), or ependymal tumors based on light microscopic features as defined in the World Health Organization (WHO) classification of the central nervous system tumors of 2007. The WHO additionally assigns each tumor a histologic grade, ranging from WHO Grade I to WHO Grade IV, reflecting the range from low to high grade of malignancy. Historically gliomas have been shown to be associated with certain risk factors. There are analyses correlating these factors with race/ethnic group, gender, age, life style, and dietary habits in adult gliomas and various subtypes of gliomas.

Aims and Objectives: The aim of the study was to analyze the clinicodemographic profile of gliomas at a tertiary care center.

Materials and Methods: Clinical profile of thirty patients was analyzed in the years 2018–2020 with respect to various demographic parameters.

Results: Male gender and advancing age seem to be risk factors associated with glioma incidence.

Conclusion: We have concluded that advancing age and female gender are two important determinants which are effecting the clinic-demographic outcome. For other parameters we need large cohort of patients.

Key words: Malignant Gliomas, Clinico-Demographic Profile, Outcome

INTRODUCTION

Gliomas are neuroepithelial tumors originating from the supporting glial cells of the central nervous system (CNS). They range in behavior from benign low-grade gliomas (LGGs), amenable to resection or observation, to aggressive histologies such as diffuse intrinsic pontine gliomas and supratentorial glioblastomas (GBMs) with nearly uniform poor prognoses despite aggressive therapy. They account for 29–35% of the CNS tumors in adolescents and young adults (AYA), with approximately two-thirds being LGG and the remaining being high-grade glioma (HGG).[1] Neoplasms of the CNS are the most frequently encountered solid tumors of childhood, but are less common in AYA.

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NCCN categorizes gliomas on the basis of the World Health Organizations (WHOs) morphologic classification as Grade I - Pilocytic astrocytoma, pleomorphic xanthoastrocytoma (PXA), ganglioglioma, and suependymal giant cell astrocytoma, Grade IIb- diffuse astrocytoma, and oligodendroglioma, Grade III - Anaplastic astrocytoma and oligodendroglioma, and Grade IV - GBM.

Incidence of gliomas varies across all age groups. Their types and grades are predominant in specific age groups with certain grades predominant in particular age groups. Pilocytic astrocytoma occurs mostly in children and young adults under age 20.[2] Likewise PXA is a rare brain tumor, most commonly affecting children and young adults.[3] Diffuse astrocytomas and oligodendrogliomas represent the third most common type of glioma, comprising 4–15% of all gliomas and can be classified by degree of malignancy into Grade II and Grade III, according to the WHO classification. These are seen mostly in young and middle aged adults.[4] GBM multiforme, which is the most common malignant tumor of the CNS considering all ages, accounts for nearly 50% of all primary malignant CNS

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tumors. The average age at diagnoses has been reported to be sixth or seventh decade of life.[5]

In a Danish national population based analysis the male: Female ratio did not differ significantly between various grades of gliomas[6] whereas in another analysis on gliomas patients across all age groups, the population comprised 58.3% male patients and 41.7% female patients. The ratio of males to females was 1.4:1.[5]

Genetic factors that contribute to glioma etiology are poorly understood[7] however segregation analyses and other genetic models suggest that inherited factors may contribute to 5–12% of all brain/CNS cancers.[8] Cancers other than glioma in family members also may be related to glioma risk and usually are not taken into account in heritability estimates. Risk of glioma has been somewhat elevated among adults who report a relative with a cancer of the brain/nervous system.[8]

Although cigarette smoking and alcohol drinking increase the risk of several cancers and certain components of cigarette smoke and alcohol can penetrate the blood-brain barrier, it remains unclear whether these exposures influence the risk of glioma.[9] A Japanese analysis found a significant inverse association between coffee consumption and brain tumor risk in subjects who consumed ≥3 cups/day. No association was seen between green tea and brain tumor risk suggesting that coffee consumption might reduce the risk of brain tumor, including that of glioma, in the Japanese population.[10]

This study suggests that there is no association between meat or iron intake and adult glioma.[11] A number of occupations and industries have been inconsistently associated with the risk of brain cancer. Among men, the industries and/or occupations that had a significantly increased risk for employment of more than 10 years included roofing, siding, and sheet metalworking; newspaper work; rubber and plastics products, particularly tires and inner tubes. Among women, significant excess risk was observed for occupations in agricultural services and farming, apparel and textile products, electrical and electronic equipment manufacturing, various retail sales, record-keeping, and restaurant service. Workers in industries with a potential for gasoline or motor exhaust exposures experienced a non-significant excess risk of brain glioma.[12]

Radiation-induced gliomas though relatively rare, are a well-characterized entity in the neuro-oncologic literature. Retrospective analyses in pediatric populations after therapeutic intracranial radiation have shown a clear increased risk in glioma incidence, that is both patient age- and radiation dose/volume-dependent. Data in adults are more limited but show heightened risk in certain groups exposed to radiation. In both populations, there is no evidence linking increased risk associated with routine exposure to diagnostic radiation.[13]

MATERIALS AND METHODS

This was a retrospective, analytical study conducted in the Departments of Radiotherapy GMC Srinagar, Jammu and Department of Neurosurgery Government Super Speciality Hospital, Jammu from January 2018 to December 2020. Data of each patient were collected from registration counter Radiotherapy department, SMHS Hospital and Medical Records Department Susper-Speciality Hospital Jammu. All patients who were enrolled for the analysis had histopathological documentation of a malignant brain tumor through either a decompressive surgery or a biopsy from the representative site. Data were then analyzed for clinico-demographic information such as age, gender, residence, dietary habits, tobacco consumption, alcohol intake, presenting symptoms, and signs. These parameters were then correlated with each other. Histological grading was done as per the WHO grading system. Grading was done on morphological basis only. Genetic analysis was not done as many patients had declined the proposal due to financial implications associated with the test.

RESULTS

This study included 30 patients who had histologically proven malignant glioma.

Patients were evaluated for headache, vomiting, and seizures which were the most common modes of presentation, seen in more than 80% of the patients. Computed tomography brain was the first investigation carried out, coupled later with contrast enhanced magnetic resonance imaging (MRI) brain for the suspected cases. Fronto-parietal was the most common location of the tumor seen in nearly 50% patients. Of 30 patients analyzed 24 were subjected to decompressive surgery or subtotal resection, whereas in five only biopsy could be taken and one patient was treated on the basis of radiological features, in view of high operative risk due to eloquent site of the lesion. Post-operative period was uneventful in 24 of the thirty patients (80%). In six patients, there were minor post-operative complications which were addressed conservatively. Majority (>70%) of the patients (22 of 30) had HGGs (the WHO Grade III or IV) and warranted some kind of adjuvant treatment (Radiation therapy/Chemotherapy) for which patient was referred to radiation oncology department. Patients were followed up at 6 months whence 18 patients reported improvement in clinical condition while as six patients still

had intermittent presenting symptoms. Four patients had deteriorated at 6 months and two patients were reported to have died [Table 1].

Male to female ratio was 2:1 [Table 2]. The age distribution varied from 18 to 76 years with the youngest patient being a female one. The age and gender distribution is shown in Table 2. Majority of the patients were more than 40 years of age (60%). Age group <40 years constituted 40% of patients of which 10% were males. Moreover, majority of the females were in the age group of >60 years. Family history was not significant; only three patients had family history of brain tumor. Only eight patients had history of tobacco consumption and all patients were of same ethnic background. Majority of patients were of rural background (80%). None of the patients had any history of radiation exposure in the past or in the near past. Only five patients were strict vegetarian and the rest were Mixetarian. Over 30% of the patients had some sort of medical comorbidity.

DISCUSSION

Gliomas account for 24% of brain tumors in adults and as a group are the second most common brain tumors in adults.[14] GBM is the second most frequently reported primary intra-cranial tumor and the most common malignant tumor of the CNS when considering all ages. GBM accounts for 15.4% of all primary brain tumors and 45.6% of primary malignant brain tumors. This disease is less common in children, comprising ~2.9% of all brain and CNS tumors reported among 0–19 year olds, and 3.2% of all brain and CNS tumors reported among 15–19 year olds.[14] Our analysis showed similar results with respect to the age of patients. Most of the gliomas were of high grade and that too were seen in patients more than 40 years of age.

Various international studies have analyzed variations in the incidence of adult primary brain cancers with respect to various demographic parameters. While as white populations in the west have been shown to have highest incidence rates, the southeast Asian populace have been shown to have lowest incidence rates.[15] All our patients were of a single ethnic and racial background.

Our study did not show any familial aggregation of brain tumors or history of any brain tumors. Although, its deliberate that cancers other than glioma in family members also may be related to glioma risk our analysis did not take into account any heritability risk estimates (genetic analysis).

Table 1: Clinical parameters of all the thirty patients

S No	Clinical parameters	%
1.	Presentation	
	Headache=30	100
	Vomiting=26	86
	Seizures=24	80
2.	Tumor location by MRI	
	Fronto-parietal=14	46.6
	Temporal=08	26.6
	Frontal=06	20
	Parietal=02	06
	Occipital=0	0
3.	Surgical intervention	
	Decompression=24	80
	Biopsy=05	16
	No intervention=01	3
4.	Tumor grade	
	WHO Gr I=04	13.3
	WHO GrII=04	13.3
	WHO GrIII=06	20
	WHO GrIV=16	53.3
5.	Post op complication (s)	
	Yes=06	20
	No=24	80
6.	Adjuvant treatment	
	Radiotherapy=24	80
	Chemotherapy(oral)=24	80
	Chemo.+ RT=24	80
	None=06	20
7.	Outcome at 6 months	
	Improved=18	60
	Same=06	20
	Deteriorated=04	13.3
	Death=02	6

Table 2: Demographic parameters

S. No.	Demographic parameters	%
1	Gender	
	Males=20	66.6
	Females=10	33.3
2	Age	
	>40=18	60
	<40=12	40
3	Family history	
	Yes=03	10
	No=27	90
4	Tobacco	
	Yes=08	26.6
	No=22	73.3
5	Residence	
	Rural=24	80
	Urban=06	20
6	Radiation exposure	
	Yes=0	0
	No=30	100
7	Diet	
	Veg=05	16.6
	Non Veg=25	83.3
8	Occupation	
	House wife=08	26
	Farmer=06	20
	Private job=04	13
	School teacher=04	13
	Mechanic=04	13
	Mason=02	6
	Government servant=02	6

Risk of glioma has been seen to be elevated among adults who report a relative with a cancer of the brain/nervous system.[8] In an analysis carried out by SEER to assess the age standardized and relative risk variation by race/ethnic groups in HGGs, it was found that rates varied about three-to-four-fold, with the highest rates among non-Hispanic Caucasians, followed by Hispanic Caucasians, Africans, Asian/Pacific Islanders, and American Indians/Alaskan Natives. As with GBM, rates for non-GBM were highest among non-Hispanic Whites, followed by Hispanic Whites, with rates among Blacks, Asian/Pacific Islanders, and American Indians/Alaskan Natives each about 40% of the rates among non-Hispanic Whites.[15] All of our patients belonged to same ethnic background.

Males have been seen to have higher incidence rate than females for any race/ethnic group. Although this difference is limited to incidence and outcome, little is known about sex differences in GBM at the disease phenotype and genetical/molecular level.[16] Our study too revealed a male preponderance in the ratio of 2:1. However, another analysis by Birthe Krogh Rasmussen did not show any significant gender difference.[6]

Association of diet with gliomas is not well established. Data from three large prospective trials have not shown any significant association of pattern of diet with incidence of brain tumors.[17] Our analysis was primarily based on vegetarian or non-veg habits. Non-veg patients outnumbered as majority of the population is assumed to be non-vegetarian. Occupation and glioma risk have been reported in the literature. In a study conducted by Department of Epidemiology and Biostatistics, School of Rural Public Health, Texas, increased incidence of gliomas was seen in populations associated with specific works such as painters, petroleum and gas workers, aircraft and motor vehicle operators, and textile workers. White collar jobs too have been seen to have association with various gliomas.[18]

Our study cohort was less in number so any significant association could not be inferred. Of the thirty patients occupation, glioma distribution was more or less equal and none had a high risk occupation except four mechanics involved in vehicle repair as shown in Table 2.

Retrospective data in pediatric populations have shown a clearly increased risk in glioma after therapeutic intracranial radiation incidence that is both patient age- and radiation dose/volume-dependent. Data in adults are more limited but show heightened risk in certain groups exposed to radiation.[13]

Moreover, there is no evidence linking increased risk associated with routine exposure to diagnostic radiation. None of the patients in our study had history of any radiation exposure, either accidental or therapeutic. The association between cigarette smoking or tobacco consumption and the risk of developing malignant glioma remains unclear. Various analyses have shown mixed results as far as tobacco as incriminating agent in glioma is concerned. The role of cigarette smoking and the risk of glioma studied in three large prospective studies of men and women with detailed and updated smoking information, with over 350 glioma cases, and 26 years of follow-up suggested no additional risk of association by any of the exposures evaluated.[19] However, in yet another analysis from the Korean National Health Insurance System cohort, 9,811,768 people over 20 years old without any cancer history in 2009 were followed until the end of 2017. They documented 6100 malignancy glioma cases during follow-up period of over 7 years. Current smokers were found to have a higher risk of developing malignant glioma (hazard ratio [HR] = 1.22, confidence interval [CI]: 1.13–1.32) compared with never-smokers, after adjusting for confounders. This association was stronger for those who smoked ≥20 cigarettes daily (HR = 1.50, CI: 1.36–1.64). Furthermore, having 30 or more pack-years of smoking over the course of one's lifetime was associated with an increased risk of developing MG in a dose-dependent manner. Paradoxically our study shows over 70% of patients being never smokers. This in part might be due to less powered study due to less number of patients.

In west the incidence of glioma has been seen to be high in societies with high socioeconomic status (SES) as compared with low SES. These differences are more pronounced among white non-Hispanic individuals and white Hispanic individuals residing in urban areas.[20]

Moreover, better survival was observed in high SES counties, even when adjusting for extent of surgical resection, and when restricted to those who received radiation and chemotherapy for GBM. Differences in incidence and survival were associated with SES and race, rather than rural versus urban status. Our study had more patients from rural population. To the best of our knowledge, no randomized analysis has been done in India comparing incidence of gliomas in rural versus urban population. They are indirect extrapolation of high socioeconomic status assumed to be prevalent in urban population.

CONCLUSION

Male gender and advancing age seem to be the only determinants affecting incidence of gliomas in our study.

Our analysis was limited by the small cohort of patients, indirectly affecting statistical inference for any demographic or clinical parameter.

AUTHORS DECLARATION

Genetic analysis of gliomas was not done due to financial constraints.

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Original Article

Morbidity and Mortality Profile of Neonates Admitted in Special Newborn Care Unit in Tertiary Care Centre in Rural Area of Telangana State, India

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Abstract

Background: India contributes to one-fifth of global live births and >25% of neonatal deaths. In spite of advances in perinatal and neonatal care, neonatal mortality is still high in developing countries, such as India. Special neonatal care units (SNCUs) have been set up to provide quality newborn care services to meet this challenge. This study aims to determine the causes of morbidity and mortality in admitted neonates.

Materials and Methods: This is a retrospective observational study carried out at SNCU, Government Medical College Siddipet, providing advanced level II Neonatal care at rural part of Telangana State. Data of all the admitted babies during 2015–2021 were recorded from by case sheets from records section and SNCU online software database. Excel sheet and Epi info were used for analyzing and tabulating the data.

Results: In the mentioned study period, a total of 7141 neonates were admitted. Major causes of admission were Sepsis 1439 (20.15%), Prematurity 1356 (19%), Transient Tachypnea of Newborn 1104 (15.46%), Jaundice 1100 (15.40%), and Birth asphyxia 688 (9.8%). Extreme low birth weight (23.61%) was the major cause of mortality. Discharge percent among the patients was 85.73%, 2.61% had left hospital against medical advice, 1% died and 10.33% were referred. The overall survival rate of SNCU is 98.49%.

Conclusions: Establishing SNCU's in high delivery points has great impact in reduction of Neonatal mortality and morbidity in India. With the availability of this unit the indicators of mortality and morbidity was reduced significantly as the common causes are identified and treated appropriately.

Key words: Morbidity, Mortality, Neonate, Rural India, Special neonatal care unit

INTRODUCTION

The first 28 days of life – the neonatal period – is the most vulnerable time for a child's survival. The growth and development of any nation is reflected in its health indicators especially the neonatal and child health indicators. Globally, 2.5 million children died in the 1st month of life in 2018, approximately 7000 newborn deaths every day with about one third dying on the day of birth and close to three quarters dying within the 1st week of life.[1]

In India, 26 million babies are born every year and 1.2 million die in the newborn period, which accounts for a quarter of global neonatal death. India thus faces the biggest newborn health challenge in the world.[1]

Neonates face the highest risk of dying in their 1st month of life. The average global neonatal mortality rate (NMR) is 17 deaths/1000 live births in 2019, down by 52% from 37 deaths/1000 live births in 1990. Neonatal mortality has reduced at much lesser rate than post-neonatal deaths, thereby increasing the contribution of neonatal deaths from 41% of under-5 deaths in 1990 to 56% in 2012.[2] Even

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now, 0.76 million newborns die each year mainly due to preventable causes.

Many health programs were launched by Government of India (GOI) and Facility-Based Newborn Care (FBNC) program is one of the key initiatives under the National Rural Health Mission (NRHM) and Reproductive Child Health II to improve the status of newborn health in the country.[3] Under this program, Newborn Care Corners (NBCCs), Newborn Stabilization Units (NBSUs), and Special Newborn Care Units (SNCUs) are being established at different levels of health care facilities. In this regard, the GOI has recently developed a FBNC Operational Guideline to facilitate the states in planning, establishment, operationalization, and monitoring of newborn care.

SNCUs have been established at district hospitals and sub district hospitals with annual delivery load more than 3000 to provide care for sick newborns, that is, all type of neonatal care except major surgeries. It is a separate unit in close proximity to the labor room with 12 or more beds, and managed by adequately trained doctors, staff nurses and support staff to provide 24 × 7 services. GOI started 253 SNCUs throughout the country in April 2011 and increased to 391 by March 2013. Till March 2015, 525 SNCUs (3), 1904 NBSUs and 14,163 NBCCs were functional in the country.[4]

NBSUs

NBSUs are established at community health centers (CHCs)/first referral units. These are 4 bedded units with (Neonatal Resuscitation Program [NRP] trained doctors and nurses for stabilization of sick newborns).

NBCCs

These are 1 bedded facility attached to the labor room and operation theatre for provision of essential newborn care.

With the launch of various initiatives under National Health Mission, India has made a concerted push to increase access to quality maternal and newborn health services and reduce the large number of preventable, neonatal and infant deaths. Schemes such as Janani Suraksha Yojana and Janani Shishu Suraksha Karyakram brought significant gains in increasing institutional deliveries and helped in improving coverage as well reducing out of pocket expenditures. As a result, institutional delivery rates improved from a mere 38% in 2005 to 79% in the year 2015–2016.

India Newborn Action Plan (INAP) is India's committed response to the Global Every Newborn Action Plan, launched in June 2014 at the 67th World Health Assembly, to advance the Global Strategy for Women s and Children's Health. INAP lays out a vision and a plan for India to end preventable newborn deaths, accelerate progress, and scale up high-impact yet cost-effective interventions toward attainment of the goals of "Single Digit NMR by 2030" and "single digit stillbirth rate by 2030."[5]

Despite ongoing challenges, major progress has been made in improving neonatal survival. In India, the NMR is 21.66/1000 live births in 2019 from 25.87/1000 live births in 2015 at the beginning of the plan.

As per the National Family Health survey (NFHS) 5 by GOI, Telangana State, has at present Neonatal Mortality of 16.8 mean (Urban 13.8 and Rural 18.8) when compared the NMR of Telangana State in NFHS survey 4 was 20 (2015–2016). In India, highest NMR is seen in Bihar state which has reduced from 36.7 to 34.5 where as in Kerala state lowest NMR which has reduced from 4.4 to 3.4. The NMR of all states of India is decreasing with implementation of such programs.[6]

The government has also set a target of fewer than ten neonatal deaths per 1000 live births by 2030 under the INAP. The majority of newborn deaths (80%) are due to complications related to preterm birth, intrapartum events such as birth asphyxia, or infections such as sepsis or pneumonia. Thus, targeting the time around birth with proven high impact interventions and quality care for small and sick newborns may prevent up to 80% of newborn deaths.

KCR Kit Scheme

The KCR Kit scheme was announced by the Telangana state government in 2017 for pregnant women and new born baby. Under this scheme, along with financial assistance to below poverty pregnant women, a kit is provided containing some essential items for pregnant women and new born baby to manage the pregnancy complications and encourage institutional delivery and newborn care. The scheme is designed to get pregnant women nutritious food and to take care of the new born after delivery. KCR Kit scheme is aimed at well-being of mother and child and reducing the NMR. After the KCR Kit scheme initiation, there is 22% increase in public sector institutional deliveries there by better obstetric and Neonatal care would be given.[7]

Advancement in perinatal and neonatal care has significantly helped in reducing NMR in developed countries, but the mortality and morbidity are still high in developing countries. This study was undertaken to study the disease pattern and outcome of neonates admitted to the SNCU of a secondary care teaching hospital located in Siddipet district, a rural area in Telangana state, India, to provide a facility based view of morbidity and mortality profile of

rural area for further evaluation, assessment and planning of future programs.

MATERIALS AND METHODS

This is an observational retrospective study carried out in the SNCU, Department of Pediatrics, Government Medical College Siddipet located in rural area of Telangana State, India, after approval by the institute review board, for 6 years from July 2015 to July 2021.

This SNCU caters to the population of Siddipet District with babies delivered in-house and referrals from CHCs, primary health centers (PHCs) and private hospitals of the district. Approximately, 6200 deliveries are conducted per year in the hospital. Each delivery is attended by Pediatrician and NRP trained staff nurse. A retrospective case record review and analysis of all the newborn babies admitted to the SNCU during the study period was done and neonates satisfying inclusion and exclusion criteria were included in the study.

Inclusion Criteria

All live newborn weighing 500 g or more and gestational age 24 weeks or more, admitted in the neonatal care unit during the study period.

Exclusion Criteria

Neonates who left hospital against medical advice (LAMA) and neonates who were referred due to surgical intervention and other high-risk cases were excluded from the study. These neonates were categorized as inborn if delivered in the Medical college Hospital and rest as out born. The data were recorded in predesigned Pro forma.

Statistics

Data collected were compiled and entered in MS Excel 2010 spreadsheet and analyzed using appropriate statistical tools in Open Epi statistical software version 3.01.

RESULTS

A total of 7141 neonates [Table 1] were admitted during the study period. Out of this 5910 (82.76%) babies were inborn and rest 1231 (17.23%) were out born. Total male babies were 4074 (57.05%), and female babies were 3067 (42.94%) giving a male: female ratio of 1.3:1 (1.3:1 inborn vs. 1.27:1 out born). Term and preterm babies were 5776 (80.88%) and 1359 (19.04%), respectively. Out of all admitted neonates 4138 (57.94%) general category, 1186 (16.60%) Other Backward Classes (OBC), 1615 (22.61) Scheduled Castes (SC), 202 (2.82%) shows that all category of neonates are being treated at public sector.

In the admitted babies 4938(69.14%) delivered by lower segment Cesarian section (LSCS), 2203 (30.85) Normal vaginal delivery.

The majority of inborn babies [Table 2] admitted were in the First 72 h of life 5308 (89.83%), while 10% of babies were admitted from day 4th to 7th. Significantly higher number of inborn babies were admitted compared to out born babies in first 3 days of life (75.75% vs. 14.07%). Average stay duration of babies in SNCU is 5.9 days with 72 (1%) neonates stayed in SNCU for more than 30 days.

Table 1: Patient demographic data

Demography	Inborn (%)	Outborn (%)	Total	Percentage
Place of delivery	5910 (82.76)	1231 (17.24)	7141	100
Gender				
Male	3385 (47.40)	689 (9.65)	4074	57.05
Female	2525 (35.36)	542 (7.59)	3067	42.95
Total	5910 (82.76)	1231 (17.24)	7141	100.00
Gestation				
Term	4934 (69.09)	842 (11.79)	5776	80.89
Preterm	970 (13.58)	389 (5.44)	1359	19.03
Post term	6 (0.084)	0	6	0.08
Total	5910 (82.76)	1231 (17.24)	7141	100.00
Category				
General	3436 (48.12)	702 (9.83)	4138	57.95
OBC	951 (13.32)	235 (3.29)	1186	16.61
SC	1359 (19.03)	256 (3.58)	1615	22.62
ST	164 (2.29)	38 (0.53)	202	2.83
Total	5910 (82.76)	1231 (17.24)	7141	100.00
Delivery type				
NVD	1796 (25.15)	407 (5.70)	2203	30.85
LSCS	4114 (57.61)	824 (11.54)	4938	69.15
Total	5910	1231	7141	100.00

OBC: Other backward classes, SC: Scheduled castes, ST: Scheduled tribes, NVD: Normal vaginal delivery, LSCS: Lower segment cesarian section

Table 2: Stay duration and intervention at birth data

Stay duration (Days)	Inborn (%)	Outborn (%)	Total	Percentage
0	235 (3.29)	102 (1.43)	337	4.72
1	291 (4.08)	104 (1.46)	395	5.53
2	397 (5.56)	126 (1.76)	523	7.32
3	467 (6.54)	114 (1.60)	581	8.14
4	884 (12.38)	167 (2.34)	1051	14.72
5	1173 (16.43)	178 (2.49)	1351	18.92
6	794 (11.12)	121 (1.69)	915	12.81
7	510 (7.14)	71 (0.99)	581	8.14
8–30 days	1107 (15.50)	228 (3.19)	1335	18.69
31+days	53 (0.73)	19 (0.28)	72	1.01
Total	5910	1231	7141	100.00
Resuscitation at birth				
No resuscitation	4533 (63.48)	933 (13.07)	5466	76.54
Only O_2	1135 (15.89)	260 (3.64)	1395	19.54
Tactile stimulation	131 (1.83)	23 (0.32)	154	2.16
Bag and mask	84 (1.18)	11 (0.15)	95	1.33
Chest compression	16 (0.22)	3 (0.04)	19	0.27
Intubation	8 (0.11)	0	8	0.11
Adrenaline	3 (0.04)	1 (0.01)	4	0.06
Total	5910	1231	7141	100.00

Among the babies admitted neonates, 5466 (76.54%), did not require any kind of intervention at birth. While resuscitation measures required for remaining includes tactile stimulation 154 (2.15%), Bag and Mask ventilation 95 (1.33%), chest compression 19 (0.26%), intubation 8 (0.11%) adrenaline 4 (0.05%), and 1395 (19.53%) required only oxygen supplementation at the time of delivery.

Major cases of morbidity [Table 3] of admissions were sepsis 1439 (20.15%), prematurity 1359 (19%), transient tachypnea of newborn (TTNB) 1104 (15.46%), jaundice 1100 (15.40)%, meconium aspiration syndrome (MAS) 887 (12.42%), birth asphyxia 703 (9.8%); others were respiratory distress syndrome (RDS) 244 (3.4%), low birth weight (LBW) 766 (10.7%), Extreme prematurity 128 (1.7%), seizures 77 (1%), congenital malformations 74 (1%), hypoglycaemia 110 (1.5%), shock 97 (1.35%), and hypothermia 52 (0.7%).

If respiratory distress is taken as morbidity of admission in broad term it includes TTNB, MAS, RDS, and Birth Asphyxia which will then be a major morbidity cause comprising 41.08% of all admissions. Extreme LBW (ELBW) 17(23.61%) was the major cause of mortality [Table 4], followed by RDS 14 (19.44%), MAS 10 (13.8%), prematurity 10 (13.88%), birth asphyxia 6 (8.3%), and sepsis 5 (6.9%).

In our study [Table 5], 6122 (85.73%) neonates were discharged successfully, 187 (2.61%) had LAMA, 72 (1%) died, and 738 (10.33%) were referred to neonatology department, institute of child health institutions for specialized treatment. Our SNCU survival rate is 98.49% (excluding the referrals and LAMA cases [6122/7141–(187 + 738)*100]).

Table 3: Morbidity data

Diagnosis	Inborn	Outborn	Total	Percentage
Sepsis	1177 (16.48)	262 (3.67)	1439	20.15
TTNB	942 (13.19)	162 (2.27)	1104	15.46
Jaundice	960 (13.44)	140 (1.96)	1100	15.40
MAS	789 (11.05)	98 (1.37)	887	12.42
LBW	512 (7.17)	254 (3.56)	766	10.73
Birth asphyxia	578 (8.09)	110 (1.54)	688	9.63
Others	261 (3.65)	25 (0.35)	286	4.01
RDS	210 (2.94)	34 (0.48)	244	3.42
Extreme prematurity	85 (1.19)	43 (0.60)	128	1.79
Hypoglycemia	97 (1.36)	13 (0.18)	110	1.54
Shock	79 (1.11)	18 (0.25)	97	1.36
Nseizures	5 (.80)	20 (0.28)	77	1.08
Cong malformations	63 (0.88)	11 (0.15)	74	1.04
Hypothermia	34 (0.48)	18 (0.25)	52	0.73
Pneumonia	22 (0.31)	13 (0.18)	35	0.49
ELBW	15 (0.21)	4 (0.06)	19	0.27
HIE	12 (0.17)	3 (0.04)	15	0.21
HDN	9 (0.13)	2 (0.03)	11	0.15
Hyperthermia	5 (0.07)	0	5	0.07
ARF	2 (0.03)	1 (0.01)	3	0.04
Pneumothorax	1 (0.01)	0	1	0.01
Total	5910	1231	7141	100.00

TTNB: Transient Tachypnea of Newborn, MAS: Meconium aspiration syndrome, RDS: Respiratory distress syndrome, LBW: Low birth weight, ELBW: Extreme low birth weight, HIE: Hypoxic ischemic encephalopathy, ARF: Acute renal failure

Table 4: Mortality data

Cause of mortality	Inborn	Outborn	Total	Percentage
ELBW	14 (19.44)	3 (4.17)	17	23.61
RDS	10 (13.89)	4 (5.56)	14	19.44
MAS	9 (12.50)	1 (1.39)	10	13.89
Prematurity	9 (12.50)	1 (1.39)	10	13.89
Others	7 (9.72)	0	7	9.72
HIE	5 (6.94)	1 (1.39)	6	8.33
Sepsis	3 (4.17)	2 (2.78)	5	6.94
Major cong anomaly	1 (1.39)	2 (2.78	3	4.17
Total	58 (80.56)	14 (19.44)	72	100.00

MAS: Meconium aspiration syndrome, RDS: Respiratory distress syndrome, LBW: Low birth weight, ELBW: Extreme low birth weight, HIE: Hypoxic ischemic encephalopathy

Table 5: Survival data

Outcome	Inborn	Outborn	Total	Percentage
Discharged	5172 (83.20)	950 (15.28)	6122	98.49
Expired	57 (0.92)	14 (0.23)	71	1.14
On bed	20 (0.32)	3 (0.05)	23	0.37
Total	5249 (84.44)	967 (15.56)	6216	100.00

DISCUSSION

Data pertaining to disease pattern and mortality are useful for health care providers and policy makers to modify and plan treatment or interventions and evaluate the effectiveness of health care initiatives respectively. In our study, total of 7141 neonates were admitted of which 5910 (82.76%) neonates were inborn and rest were out born babies 1231 (17.23%), Significantly higher number of inborn babies (82.76%) were admitted compared to out born (17.24%) babies%). As ours is the only referral center in the district for high-risk pregnancies the admissions are more of inborn babies which is similar in studies of Kumar *et al*.[8] (60.80% vs. 39.20%), Randad *et al*.[9] (76.46% vs. 23.54%), Mundlod and Thakkarwad[10] (62.5% vs. 37.4%), and Prasanna *et al*.[11] (58.3% vs. 41.7%) but outborn are more in the study of Sharma and Gaur[12] (45.13% vs. 54.86%).

There is a male preponderance in admissions with 57.05% were male babies and 42.95% babies were female. Similar findings were reported from various studies conducted in different rural parts of India like Modi *et al*.[13] (67.51% vs. 32.49%), Kumar *et al*.[8] (59.54 vs. 40.46), Mundlod and Thakkarwad[10] (58.78% vs. 41.22%), Prasanna *et al*.[11] (53.4% vs. 46.6%), and Sharma and Gaur[12] (63.07% vs. 36.92%).

Average stay duration of babies in SNCU is 5.9 days, 72 (1%) babies have stayed more than 1 month in the SNCU for the Newborn care and Kangaroo Mother Care (KMC). With early intervention and appropriate use of noninvasive ventilation continuous positive airway pressure and mechanical ventilation and reduction of exposure to NICU environment with early shifting of baby to KMC which reduced further morbidity and the duration of stay of babies were significantly reduced along with effective implementation of breastfeeding. All high-risk babies were screened for retinopathy of prematurity and hearing test as per standard guidelines at our institute.

Out of all admitted neonates 4138 (57.94%) general category, 1186 (16.60%) OBC, 1615(22.61) SC, 202 (2.82%) Scheduled Tribes (ST) shows that this SNCU is rendering services to all categories of neonates at public sector which shows that they have faith in public sector hospitals, and it is mainly serving the low income generation.

According to the United Nation Children's Fund, "The state of world's children's report 28% of neonates were born with LBW in India However, in our study, overall 35.8% of neonates were LBW and 19.03% of neonates are born prematurely. In other studies, the LBW admissions were Mundlod and Thakkarwad[10] 59%, Sharma and Gaur[12] 51.47%, Anupama *et al*.[14] 46.53%, which are higher than our study. This may probably be due to poor maternal health condition, low socioeconomic status, less visits to health care facility, and the delivery points attached are referral centers of high-risk deliveries of that area.

Neonatal Jaundice (NNJ) is also one of the important neonatal morbidities which requiring phototherapy as in our study 15.4% similar studies are Som *et al*.[15] 25.99%, Kumar *et al*.[8] 24.72%, Anupama *et al*.[14] 19.04% which required more babies for phototherapy for NNJ, where as in other studies Sharma and Gaur[12] 10.65%. Prasanna *et al*.[11] 9.9% have lower incidence of NNJ than our study.

In our study, clinical sepsis is 20.15%, is comparable with studies of Kumar *et al*.[8] at Uttarakhand 20.48%, Anupama *et al*.[14] Assam 21.61%, Sharma and Gaur[12] 13.77%, Prasanna *et al*.[11] 13.3%, Som *et al*.[15] 9.79% and Mundlod and Thakkarwad[10] 7.7%. At SNCU Siddipet rationale antibiotic policy is followed and adopted guidelines of AIIMS antibiotic policy for our unit. Strict hand hygiene is being maintained before touching each baby, hand sanitizes are used at every next baby touch. AIIMS WHO CC PTC and STPs are being followed for management of preterm and sick newborn at out institute.[16] Birth asphyxia is important cause of morbidity and mortality. At this hospital morbidity of birth asphyxia is 9.8% but its high in studies of Mundlod and Thakkarwad[10] (36.1%), Som *et al*.[15] 29.09%, Sharma and Gaur[12] 24.61%, Prasanna *et al*.[11] 19.1%, Kumar *et al*.[8] 18.5%, Anupama *et al*.[14] 11.65%' At SNCU Siddipet every delivery is being attended by pediatrician and staff who are trained in NRP. With high reach of maternal and child health services through PHCs, Accredited Social Health Activists, and Anganwadi Centres most of the high risk and at risk pregnancies are being identified and followed meticulously at community level and are sent to high risk delivery centers such as our institute for delivery, due to which the outcome has improved very much and cases of stillborn and birth asphyxia has reduced.

In our study, ELBW 17(23.61%) was the major cause of mortality, followed by RDS 14 (19.44%), MAS 10 (13.8%), Prematurity 10 (13.88%), Birth asphyxia 6 (8.3%) and sepsis 5 (6.9%) which is comparable with Prasanna *et al*.[11] (SNCU Nellore) but RDS is high 40.2%, mortality is similar as RDS (11.3%), hypoxic ischemic encephalopathy (HIE) (9.3%), Sepsis (12.6%). When mortality pattern is compared with studies of other SNCUs in India such as Mundlod and Thakkarwad[10] (SNCU Adilabad) HIE (36.1%), RDS (27.7%) prematurity (21.9%), and sepsis (21.9%) were major causes of mortality. It is comparable to Sharma and Gaur[12] SNCU Gwalior RDS (37.6%), HIE (26.75%), major congenital malformation 10.35%.

In our study 6122 (85.73%) neonates were discharged successfully, 187 (2.61%) had LAMA, 71 (1%) died and 738 (10.33%) were referred to Institute of Child Health for further treatment. The mortality rate of SNCU is comparable with study of Randad *et al*.[9] SNCU Mumbai where mortality rate is 1.5%, discharge rate of 95.66%, LAMA 1.3%, referrals 1.5%. Whereas the mortality rate is high in studies of Sharma and Gaur[12] (25.45%), Mundlod and Thakkarwad[10] (13.7%), Anupama *et al*.[14] (12.37%) Prasanna *et al*.[11] (10.1%), and Kumar *et al*.[8] (8.15%) as these are studies in various parts of developing country India. Our SNCU survival rate is 98.49% (excluding the referrals and LAMA cases).

The data of NFHS 4 and NFHS 5 show that major causes of morbidity and mortality has been reduced which can be attributed due to allotting SNCUs, NBSUs and NBCCs at rural and tribal parts of Telangana State playing a major role in reduction of morbidity and mortality due to prematurity, RDS, MAS, HIE, and neonatal sepsis.[17]

CONCLUSIONS

ELBW, Prematurity, RDS, MAS and Perinatal asphyxia and its complications are the leading causes of mortality

in our SNCU. LBW and prematurity were preventable causes of mortality, which are been well addressed through improvement of obstetric care and scaling up of neonatal care skill through NSSK, integrated management of neonatal and childhood illnesses (IMNCI), FIMNCI, and FBNC programs.

Establishing FBNC centers in various parts of Telangana state and entire country and government schemes such as NRHM and KCR KIT have great impact in reducing the morbidity and mortality of Neonates by increasing institutional deliveries.

ETHICAL APPROVAL

The study was approved by the Institutional Review Board.

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Original Article

Assessment and Comparison of Human Pulp Tissue Dissolution Capacities of Endodontic Irrigating Solutions: An *In Vitro* Study

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Abstract

Background: Over the past few decades practice of endodontics has been transformed by newer technology and materials and increased the success rate of endodontic treatment. Disinfecting and cleaning by chemomechanical procedures are the prerequisites for successful root canal treatment. Organic tissue dissolution is considered as one of the most vital and desirable property of endodontic irrigant, any soft tissue remnant, harboring bacteria, left in the canal after endodontic therapy may be the cause of failure treatment.

Aim: The present study aimed at assessing and comparing the human pulp dissolution (thereby eliminating the bacteria) capacity of some potential endodontic irrigants, viz., sodium hypochlorite (NaOCl) (2.5–5.25%), chlorine dioxide (5%), and peracetic acid (5%).

Materials and Methods: Sixty human pulp specimens from extracted premolars were taken and weighed. They were immersed in test solution for 30 min, dried on filter paper and weighed again. The weight loss in percentage was calculated and statistically analyzed.

Results: Both 5.25–2.5% NaOCl showed mean value of 100%. Whereas, mean reduction for 5% ClO 2 was 55.30 ± 1.87%, whereas the same for 5% peracetic acid was 65.70 ± 1.69%.

Conclusion: NaOCl showed the best tissue dissolution capacity, followed by 5% peracetic acid.

Key words: Chlorine dioxide, Dental pulp, Endodontic irrigant, Peracetic acid, Sodium hypochlorite

INTRODUCTION

The field of endodontics has modernized with the developments of several techniques and materials over the past decades.[1] Disinfecting and cleaning by chemomechanical procedures are the fundamentals for successful root canal treatment. With advanced instrumentation technology, though root canal shaping can be efficiently achieved, effective cleaning of the entire root canal system, still, remains a challenge.[2,3] The attainment of endodontic therapy depends mainly on the efficiency of the chemomechanical preparation done during the process.[4] Any tissue residue left in the canal may prove to be a source for the surviving bacteria which ultimately result in endodontic failure.[5] The antimicrobial substances used as endodontic irrigant should possess tissue dissolution property,[6] enhance bacterial eradication,[7,8] and at the same time have low systemic toxicity.[9] Therefore, endodontic irrigation plays a most important role in completely debriding the canal.

Sodium hypochlorite (NaOCl) solution is one of the irrigant of choice because of its antimicrobial activity and pulp dissolution capacity.[10] The prewarming of NaOCl is an easy, and the most commonly used method to increase the reaction rate and enhance the dissolution of

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organic residues. About, a temperature range of 50–60°C is suggested for warming the NaOCl.[11] NaOCl also have cytotoxic property. Hence, the need for finding an alternative to NaOCl has been raised in various studies.

Chlorine dioxide is chemically similar to chlorine or hypochlorite but is less toxic and it is one of the familiar household bleach. It is reported to be tuberculocidal, bactericidal, virucidal, and fungicidal.[12] It is mostly commonly used for sewage water disinfection, industrial process water treatment, industrial air treatment. However, there is lack of literature regarding human pulp tissue dissolution capacity of ClO_2.[12] Peracetic acid is one of the most commonly used disinfectants in hospitals and industries areas.[13] Preliminary studies have shown that it can remove the smear layer,[14] which has been attributed to its acetic acid content.

It has antibacterial, sporicidal, antifungal and antiviral properties.[15] However, some issues related to its caustic effect at higher concentration have been raised.[15] In most of the previous studies, tissue solubility of numerous irrigants has been measured using bovine mucosa and bovine pulp tissue. Very few studies have been done on solubilizing effects of various irrigants on human pulp tissue.

Therefore, the aim of this *in-vitro* study is to compare the human pulp tissue dissolution by different concentrations of, NaOCl, chlorine dioxide and peracetic acid.

MATERIALS AND METHODS

This is *in-vitro* study conducted to compare the human pulp tissue dissolution by different concentrations of, NaOCl, chlorine dioxide and peracetic acid. The study protocol was approved by the Scientific Advisory committee and Institutional Ethics Committee. Sixty freshly extracted premolars were obtained from the outpatient department of the Department of Oral and Maxillofacial Surgery and from private clinics. Teeth extracted for orthodontic reasons were considered. Any tooth with restoration, caries, endodontic treatment, or wasting disease was excluded from the study. After extraction, the tooth was cleaned with a brush and stored in saline. The teeth were divided into four groups with 15 teeth in each group ($n = 15$), Group I: NaOCl 5.25%, Group II: NaOCl 2.5%, Group III: ClO2 5%, and Group IV: Peracetic acid 5%.

For retrieving the pulp tissue, the teeth were divided into two halves. Two longitudinal grooves were made on the proximal surface of the tooth with the help straight bur. They were split with the help of chisel and mallet. Pulp specimens were washed with help of distilled water to remove any remnants of blood remnants and refrigerated for 1 h for assist in sectioning.

Pulp tissue samples were standardized to weight range of 0.023–0.028 g by cutting them with the help of No. 15 BP blade. The samples were weighed on an analytical balance (MX-7301A Anamed, India). After weighing, the samples were submerged in test solution (10 ml) in a small plastic vial and kept for 30 min. They were placed on a vibrator (Unident, India) at 3000 rpm for 1 min to achieve proper immersion and simulate conditions present in the pulp canal during biomechanical preparation. After 30 min, the solution was filtered using a filter paper (Whatman) and left overnight for drying. The weight of the residual pulp tissue was measured. Readings were noted, and percentage weight reduction was calculated.

Statistical analysis was performed using SPSS version 15.0. Analysis of variance, followed by Tukey's *post-hoc* test significant difference test was used to compare differences between groups. The confidence level of the study was kept at 95%. Hence, a $P < 0.05$ indicated a statistically significant intergroup difference.

RESULTS

Both 5.25% and 2.5% NaOCl showed mean value of 100% [Table 1]. Whereas, mean reduction for 5% ClO_2 was 55.30 ± 1.87%, whereas the same for 5% peracetic acid was 65.70 ± 1.69%. Statistically, there was a significant difference among groups ($P < 0.001$). On comparing the data, no difference was observed between 5.25% and 2.5% NaOCl. However, both 5% ClO_2 and 5% peracetic acid solution displayed significantly lower mean value than 5.25% and 2.5% NaOCl groups ($P < 0.001$). On comparing 5% ClO_2 with 5% peracetic acid solution, mean reduction was found to be significantly lower in 5% ClO_2 than 5% peracetic acid group ($P < 0.001$) [Table 2].

DISCUSSION

Chemomechanical preparation is essential procedure for the success of root canal instrumentation. Pulp tissue

Table 1: Mean percentage reduction in different groups

Test Solution	n	Mean± SD
5.25% NaOCl	15	100.00 ±0.00
2.5% NaOCl	15	100.00 ±0.00
5% Chlorine dioxide	15	55.30±1.87
5% Peracetic acid	15	65.70±1.69
Total	60	80.25±28.45

(NaOCl- Sodium Hypocloride, SD- Standard deviation)

Table 2: Between group comparison (Tukey's post hoc test)

Comparison between groups	Mean difference	p
5.25% NaOCl versus 2.5% NaOCl	0.000	1.000
5.25% NaOCl versus 5% Chlorine dioxide	65.800	<0.001
5.25% NaOCl versus 5% Peracetic acid	55.540	<0.001
2.5% NaOCl versus 5% Chlorine dioxide	45.600	<0.001
2.5% NaOCl versus 5% Peracetic acid	55.540	<0.001
5% Chlorine dioxide versus 5% Peracetic acid	-15.100	<0.001

(NaOCl- Sodium Hypocloride)

dissolution capability is one of the desired properties of an endodontic irrigant. The principal properties expected from an ideal irrigation solution are antimicrobial activity, water solubility, low toxicity to periradicular tissues with tissue solvent ability.[16] Over the years, several chemicals and their combinations have been studied for potential use as endodontic irrigant. From various literatures, it can be seen that NaOCl, though toxic, named "gold standard" as it is an excellent antimicrobial agent and solvent of organic tissue.

Therefore, NaOCl was used as a positive control group.[17] Various different types of tissues have been used in earlier studies such as bovine pulp,[18,19] umbilical cord,[20] pig palatal mucosa,[21] and rat dermal connective tissue.[22] However, these tissues do not simulate the conditions present clinically within the human root canal. Hence, human pulp tissue was better to considered for this study. Tissue dissolution capacity depends on various factors, such as amount of irrigant, amount and area of the tissue being tested, and the frequency of agitation.[23]

In our study, the study showed that 5% NaOCl was the most effective pulp tissue solvent among all irrigants. This is because of the ionization of NaOCl to liberate hypochlorous acid (HOCl) and hydroxyl ions in an aqueous environment.[24] When hydroxyl ion levels decrease as a result of the saponification and amino acid neutralization reactions, the pH also decreases, thereby favoring the formation of HOCl molecules.[12] The chloramination reaction is then initiated which results in degradation and hydrolysis of amino acids.[12]

In our study, it was found that 100% in Groups I and II, 55.3% in Group III and 65.7% in Group IV. Group I (5.25% NaOCl) served as control because complete dissolution was anticipated in this group as various studies done in the past have demonstrated this effect.[18,23,25] This effect of NaOCl has been attributed to its proteolytic activity. Group II (2.5% NaOCl) showed similar results. Various studies have demonstrated similar results for 2.5% NaOCl, but for a longer time tested (2 h).[26,27] We found similar results in 30 min, which may be explained on the basis of tissue specimen used (human pulp tissue than the bovine pulp tissue and palatal mucosa).

In our study, 2.5% NaOCl and 5% NaOCl showed no significant difference in pulp dissolution at 30 min. Whereas study done by Taneja *et al.*[12] found that 5% NaOCl was less effective than 5% NaOCl at 30 min. Hand *et al.*[22] have also suggested that 5.25% NaOCl was a more effective solvent than 2.5% NaOCl.

In our study, significant difference was found between Groups II and III, Group II and Group IV, signifying NaOCl to be a better tissue solvent. Group IV showed significantly better tissue dissolution than Group III, suggesting peracetic acid also to be a better tissue solvent than ClO_2. ClO_2 has been shown to be toxic at higher pH, besides having antimicrobial effect.[28] The percentage of peracetic acid tested in this study was within the safe limits as suggested by Kühlfluck and Klammt.[29] Moreover, smear layer removal capacity of peracetic acid adds to its advocation as a possible root canal irrigant.

CONCLUSION

It can be concluded that both 2.5–5.25% NaOCl are a more effective pulp tissue solvent that chlorine dioxide and peracetic acid.

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Original Article

Study of Management of Post-Burn Flexion Contracture of Finger by Glabrous and Non-Glabrous Split Skin Graft

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Abstract

Background: Young males are the most common victims of hand burn and mostly sustain injury at work place. Healing by secondary intention, inappropriate positioning, and lack of physiotherapy lead to contractures causing functional disability. Conventionally, non glabrous skin grafts of variable thickness (intermediate or thick split thickness or full thickness) are mostly used for coverage of palmar skin defects.

Materials and Method: A detailed history of each patient was taken and patients were randomly divided in two groups by simple randomization method. Group A was offered treatment with split thickness graft from glabellar region and other Group B was offered treatment with split thickness graft from non-glabellar skin. Frequencies and percentages of both recipient and donor sites complications such as infection, hypertrophic scarring on Vancouver scar assessment scale, recurrence, and difficulty in walking were noted. Patient satisfaction for color and texture match to neighboring skin at recipient site was assessed 3 months after the operation using five points Likert scale.

Results: At follow-up of the group A, the donor areas were completely healed in all the cases 100%. The grafted area showed excellent color and texture match with the adjacent palmer skin. The graft was mobile, stable and without any pigmentation. There was also no hypertrophic scarring, hyper pigmentation or pain at the donor site as compared to ordinary skin graft. Walking and weight bearing was smooth and the instep curvature appeared normal. And in Group B, 100% patients had hyperpigmentation, 20% had marginal scarring, and scar hypertrophy at hand. While, 40% had scar hypertrophy at 80% had hyperpigmentation over donor site. Recurrence was noted in 32% patients in Group B as compared to 8% in Group A.

Conclusion: Glabellar skin of the instep is the best replacement for the palmar skin of the digits and hand because of the similarities in their characteristics. Results are excellent in terms of color and texture match, no hyperpigmentation, less marginal scarring, scar hypertrophy, and less recurrence of contracture in patients with area grafted with glabellar skin to conclude for management of post burn flexion contracture of finger. Ideal skin substitute is glabellar skin grafts from the instep region of foot.

Key words: Burn, Glabella, Skin

INTRODUCTION

Burns constitute the second highest incidence of trauma related deaths globally, second only to vehicular trauma both in developed and developing countries.[1] Burn injury is a common form of trauma affecting hands. Young males are the most common victims of hand burn and mostly sustain injury at workplace.[2] Inadequate management (healing by secondary intention, inappropriate positioning, lack of physiotherapy, and inadequate scar therapy) of these burn injuries leads to hypertrophic scarring and contractures causing functional disability. Individuals with burn injuries are at risk for developing contractures due to multitude of factors. Patients with burns often are immobilized, both globally, as a result of critical illness in the severely burned, and focally, as a result of the burn itself because of pain, splinting, and positioning. Post-burn contractures (PBC) need releases to improve hand function. Coverage of defects after releases of these contractures on palmar aspect of hand requires skin with structural and functional characteristics

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similar to palmar skin. Palmar skin is thick, inelastic and hairless. It is designed to combat the daily strong and tough work of an individual.[3] Conventionally, non glabrous skin grafts of variable thickness (intermediate or thick split thickness or full thickness) harvested from medial arms, thighs, buttocks, or groin are mostly used for coverage of palmar skin defects. These non-glabrous skin grafts lack similarities with palmar skin and use of these skin grafts is associated with hyper-pigmentation, scarring, recurrent contractures, hair growth, and unacceptable cosmetic appearance.[4] Glabrous Plantar skin is the only area of body sharing characteristics of palmar skin. Plantar skin can be harvested as split thickness, dermal only, or full thickness skin graft.[5,6] There are few studies available describing effectiveness of use of intermediate thickness plantar (ITP) skin graft for coverage of defects after release of PBC of hand. This prospective study is designed to determine the outcome of split thickness glabellar skin graft for the coverage of defects on Palmar aspect of hand after release of PBC in terms of graft take, complications, recurrence, and patient satisfaction for color and texture match.

MATERIALS AND METHODS

This prospective comparative study was carried out on patients of Department of Burns and Plastic Surgery, Civil Hospital and B. J. Medical College, Ahmedabad, Gujarat, India, from December 2018 to December 2020. A total of 50 patients with PBC of hand satisfying inclusion criteria were included in the study. Patients were randomly divided in two groups by simple randomization method of dividing patients into alternate study group after assigning serial no. Group A consisted patients with odd number were offered treatment with split thickness graft from glabellar region and Group B consisted patients with even number were offered treatment with split thickness graft from non-glabellar skin.

Study Design

This was a prospective comparative study.

Study Location

This is tertiary hospital-based study done in the Department of Burns and Plastic Surgery, Civil Hospital and B. J. Medical College, Ahmedabad, Gujarat, India.

Study Duration

This study was from December 2018 to December 2020.

Sample Size

The sample size was 50 patients.

Inclusion Criteria

All the patients presenting to outpatient department with PBC fingers or indoor patients developing contractures during their stay for treatment of acute burns in the aforementioned time frame were included in the study. For the purposes of analysis, a limitation in the range of motion (ROM) in at least one plane of motion at a specified joint was considered to be a contracture at that joint.

1. Patients with PBC of fingers were included in the study.
2. Patients with good passive ROM at joints were included in the study.
3. Patients who had agreed to take part in study were included in the study.

Exclusion Criteria

The following criteria were excluded in the study:

1. Patients refusing for treatment.
2. Patients with contractures due to any other etiology other than burns.
3. Joint stiffness.
4. Acute infective condition.
5. Patients having wounds with exposed vessels, tendon, or bone.
6. Patient with wound size more than 20 cm^2 were excluded from the study.
7. Patients with history of diabetes mellitus, hypertension were excluded from the study.

Procedure Methodology

Collection of data

A detailed history of each patient was taken covering the duration of deformity, cause of contracture, effect of deformity on daily activities, any previous surgery for the deformity, and any associated medical problem. Active ROM was measured before and after surgery. Preoperatively and postoperatively photographs were taken for records purposes X-rays for the involved digits including anteroposterior and lateral views, full blood count and screening for hepatitis B/anti-hepatitis C virus was performed.

Procedure

The classification of Sheridan *et al.* and McCauley for the hand was modified for the current study involving all sites with contractures. Patients with contractures in Grades III and IV of this modified classification were considered for surgical release of their contractures.

All patients were operated under general anesthesia with tourniquet using tumescent solution. One dose of intravenous antibiotic was injected, at the starting of surgery to every patient. Incision was marked and infiltration was performed with tumescent fluid of 2% lidocaine with 1:200,000 adrenaline. Surgery was started 7 min after infiltration of tumescent solution. Contracture was released and all abnormal tissue was excised down to healthy tissue Figure. Depending on treatment group

assigned, coverage with either split thickness graft from non-glabellar (preferably thigh) or glabellar (Instep area of foot) area was taken.

In case of Group A with glabellar split thickness graft, resultant defect was measured and marked out on instep of foot in 1:1 fashion. ITP skin graft was harvested with Watson knife (Downs Surgical Sheffield England) and was stabilized to recipient site. Recipient site was dressed with Vaseline gauze dressing. This was reinforced with tie over wet cotton dressing followed by dry gauze and crepe bandage. Donor site was also dressed with Vaseline gauze dressing covered with dry gauze and crepe bandage.

Similarly intermediate split thickness graft was harvested from thigh in Group B with non-glabellar donor site group and similar procedure was performed for donor site region. Operated hand was splinted in postoperative period with POP caste. Patients were allowed to bear weight after surgery as tolerated. First change of dressing and recipient site inspection was done at 7th post-operative day. Patients were discharged at 7th postoperative day.

Donor site was inspected at 14th postoperative day. Graft take (defined as graft which is well adherent to its bed without the aid of sutures) was measured on 14th postoperative day in terms of percentage using formula (Graft take %= size of graft take/total size of graft applied × 100). Massage with coconut oil twice to thrice daily was advised 3–4 weeks after surgery and continued for 3 months at both recipient and donor sites. Patients were advised to wear pressure garments on hand as well as donor foot for 1 year. Patients were followed till 3 months postoperatively.

Frequencies and percentages of both recipient and donor sites complications such as infection (defined as discharge of pus), hypertrophic scarring (defined as red and raised scar measured on Vancouver scar assessment scale), recurrence (defined as development of new flexion contracture at operated site), and difficulty in walking (defined as pain on walking and abnormal gait) were noted. Patient satisfaction for color and texture match to neighboring skin at recipient site was assessed by adult patients themselves 3 months after the operation using five points Likert scale, where score 1 was considered as not at all satisfied, and score 5 was considered as highly satisfied. In case of children this assessment was done by their parents.

Statistical analysis was done using Statistical Package for the Social Sciences software. Continuous variables (age, pain, graft take, and patient satisfaction for color and texture match) were presented as mean ± standard deviation. Categorical variables (gender, complications, and recurrence) were presented as frequencies and percentage.

RESULTS

A total of 50 patients with post burn flexion contracture (PBC) of fingers were studied over period from December 2018 to December 2020. The duration of deformity varied from 6 months to 20 years (mean = 4.11 years). About 48% (24 patients) of them were males and 52% (26 patients) were female accounting to ratio of almost 1:1. 44% (22 patients) belonged to the most active age group of 10–25 years, followed by adults within age group 26–50 years which were 36% (18 patients). Patients above 50 years were the least involved people 2% (1 patient) and patients below 10 years constituted 18% (9 patients) of the study model.

All patients in study had contractures post burn. Out of which 80% (40 patients) had PBC finger post flame burns, 10% (5 patients) were post scald burns, and remaining 10% (5 patients) were post electric burns.

The contractures mainly affected the proximal interphalangeal joints (PIP). Pre-operative median active ROM at PIP joint was 60°–90° (extension/flexion). In majority of the patients (70%) Left hand was involved.

About 34% (17 patients) presented with one finger involvement mainly affecting the interphalangeal joints. There were 26% (13 patients) with two fingers, 22% (11 patients) with more than 2 fingers, and 18% (9 patients) had PBC finger associated with scar syndactyly or finger webbing.

Among all the patients who were included in study, 45 patients 90% were operated for 1st time and five patients 10% were operated for recurrence of PBC 2nd time, all of which were operated for PBC with non-glabellar STG from thigh.

In those with glabellar skin as donor, separation and peeling of corneal layer and the appearance of pink Palmar skin underneath was considered as the criterion for graft take and healing which usually occurred on 14th day in 92% cases (23 patients). Partial loss of glabellar skin graft happened in 8% cases (2 patients) either due to infection or inadvertent removal of skin along with corneal layer. These hands were allowed to heal by secondary intention. In all the patients of plantar donor areas healed completely. In four patients defects after release of PBC were big that skin graft was harvested from both feet at the same time.

Among other half of patients in whom PBC finger defect was covered with non-glabellar split skin grafts from thigh with graft take in 88% (22 patients), Grafts were lost in 12% cases (3 patients) due to infection. Among these patients

areas of only one patient was covered secondarily by grafting after the infection subsided and wounds become clean. Remaining 2 patient's area recovered by secondary intention.

In non-glabellar donor area thigh, and glabellar donor area plantar instep area, donor site did not show delayed healing in any cases and there was no need for grafting on donor area in any case.

PBC Release with Glabellar STG

At follow-up all those with glabellar skin grafts showed excellent color and texture match with the adjacent palmar skin with 5 points on Likert's scale. The graft was soft, supple, mobile, and stable, without any pigmentation. About 12% (3 patients) had slight marginal scarring and scar hypertrophy in the operated area of fingers, which was taken care with intralesional steroid injections and pressure garments.

Grafted areas showed smooth contour merging with rest of the palm.

Contracture recurred in 8% (2 patients), both were below 10 years of age prime cause of recurrence was mainly due to infrequent use of splintage and poor compliance with post-operative physiotherapy protocol.

None of these patients developed scar hypertrophy, marginal scarring hyper-pigmentation, arch deformity or persistent pain at the plantar donor sites. About 4% (1 patient) developed marginal scarring with hyper-pigmentation at donor plantar site. Walking and weight bearing was smooth with most of the patients starting weight bearing from 4 to 7 post-operative day in case of glabellar skin as donor site.

PBC Release with Non Glabellar STG

Non-glabellar skin grafts from thigh were used in remaining 25 patients. All had color and texture mismatch with the rest of the hand with 2 out of 5 points on Likerts scale. All 25 patients had hyperpigmentation, that is, 100% patients exhibited hyperpigmentation. Some of the grafted areas were smooth, soft, stable, and mobile while others were with dry and thickened skin. About 20% (five patients) had marginal scarring and scar hypertrophy of hand.

Out of 25 patients incidence of recurrence was in 32% (eight patients) of which five patients belonged to age group below 10 years of age.

Hyperpigmentation is seen on non-glabellar area of thigh in 80% (20 patients) and scar hypertrophy at donor area reported in 40%, that is, in ten patients.

About 20% of patients with glabellar skin grafts had a hospital stay of up to 3 weeks as compared to About 30% in those with grafts from non-glabellar skin 80% of the patients with graft from glabellar skin went home in 2 weeks. Recovery of sensation and sweating was not done as patient failed to come for long-term follow-up [Figures 1-4] and [Tables 1 and 2].

DISCUSSION

Glabrous skin is unique because of its specialized function and appearance. Found on the plantar surface of the feet and the palmar surface of the hands, glabrous skin differs from hair-bearing skin. Functionally, glabrous skin needs to withstand greater forces, pressures, and shear. It has greater capacity to perceive sensations, to protect, and to heal. The anatomy of glabrous skin has evolved to perform these functions. This also affects the appearance of glabrous skin. It is hairless without sebaceous glands and contains few melanocytes. Southwood in 1955 demonstrated that the skin and its epidermis and dermis vary in thickness, depending on the location on the body, age, and sex, and between hair-bearing and glabrous skin. He showed that the epidermis is thicker in glabrous skin, measuring 529–1377 m in the sole and 420–673 m in the finger. Southwood[7] reporting on the thickness of human skin at different sites states that the epidermis on the sole is thicker than that on the hair bearing skin but the dermal thickness is similar. The epidermis of the instep is thinner than the epidermis of the neighboring weight bearing areas but is not significantly thicker than the epidermis of the palm and fingers.

Release of flexion contracture of digits and palm is one of the most commonly performed procedures in the plastic surgery unit. Plantar skin is the most suitable replacement for the skin defects onto the palmar aspect of hand. For the sake of convenience traditionally the thigh or buttock skin is used as split skin graft donor sites. The skin from these areas is too dissimilar for the volar aspect of hand. Webster[8] was the first to introduce full thickness skin grafts to the volar aspect of the hand from the instep area of the foot in his attempt to obtain appropriate tissue. A second split skin graft was needed to cover the donor defects in those cases. Le Worthy[9] advocated the use of split skin graft from the insteps to resurface the palm of the hand. LeWorthy in 1963 introduced the first split-thickness glabrous skin graft. He treated 12 patients with 13 wounds with this method. In his series, however, he experienced significant loss of grafts, and three patients needed their donor sites skin grafted from hair-bearing areas. Since these reports, there have been many variations of these two techniques.

Nakamura *et al.*[10] presented a series of 64 patients and favored very thick split thickness skin graft from instep to palm. They reported satisfactory healing in 2 ± 3 weeks, good color match, stability and lack of hyperpigmentation in their results. Zoltie *et al.*[11] described full thickness plantar grafts to hand in syndactily repair.

Roboti and Edstrom[12] used split thickness skin grafts from instep area of foot in their cases and found it as an excellent technique for avoiding hyperpigmentation, marginal scarring, and hyperkeratosis resulting from the use of skin graft from the traditional donor sites. Recovery of sensation and sweating was optimum with a superb color and texture match.

Recently, Tanabe *et al.*[13] reported a modification of the use of plantar skin grafts in eighteen cases of Granulating and fresh wounds of the volar aspect of hands. Two skin grafts were harvested from the same site, first the split thickness skin graft and then the dermal graft exposing subcutaneous fat. Split skin graft was returned to the original site and dermal graft applied over the defect. Good cosmetic and functional results were obtained at both donor and recipient sites.

Hyperpigmentation, scarring, and recurrence of contracture are the common problems encountered with the traditional skin grafts to palm. Skin grafts from plantar area of foot prove better probably because they have sparse pigment cells and tend to contract less because of the less elastic and more compact connective tissue in the dermis.

In Bunyan[14] series, who used medium thickness split skin graft, the donor area did not heal in three patients and had to be covered with the skin graft. Wendt[15] harvested full thickness skin graft from lateral great toe skin but this was associated with the additional split thickness skin graft placed on the donor site. Tenabe *et al.*[13] used planter dermal graft to resurface the palm but the harvest was limited to the planter instep. In our technique split thickness skin graft could be harvested from almost the entire sole or from both sole at the same time. The reason for restricting the harvest in the present series to the planter instep was to avoid risk of complication at the donor area that would restrict early ambulation

Tanabe *et al.*[13] used dermal grafts from plantar skin to cover palmar defects in eighteen of their cases.

They mention that it is not always easy to harvest sufficiently thick graft to prevent recurrence of contracture, and another skin graft may be needed to cover the donor area if a thick split or full thickness graft is harvested in which the donor site could end up with scar hypertrophy and deformity.

Recurrence rate of contracture is very important indicator of success in the management of digital contracture. The low recurrence rate in the present study was attributed to the fact that glabellar skin graft has minimal or no primary contraction (contraction of graft soon after its removal from the donor area). Furthermore, the secondary contraction which developed late is less as compared to skin graft from the conventional donor areas. This fact is also provided by Jang *et al.* and Southwood.[7]

Table 1: Comparison between surgical management and their outcomes between PBC finger grafted with glabellar and non-glabellar skin

	Glabellar STG (Instep of foot)	Non glabellar STG (Thigh)
	No of patients	
Total cases	25 (100%)	25 (100%)
>95% graft take	23 (92%)	22 (88%)
Partial of complete graft loss	2 (8%)	3 (12%)
Second surgery required	None	1 (4%)
Donor area grafted	None	None

Table 2: Comparison of colour match, texture, scarring, scar hypertrophy, and recurrence of contracture between PBC finger grafted with glabellar and non-glabellar skin

	Glabellar skin	Non-glabellar skin	
	Changes at grafted site (Operated PBC finger)		
Colour and texture match	Likert scale 4–5 point	Likert scale 2–3 point	
	Complications at grafted PBC finger		
Hyperpigmentation at hand	Nil (0%)	All (100%)	
Marginal scarring and scar hypertrophy at hand	3 (12%)	5 (20%)	(*P* value 0.6) Not Significant
	Complications at donor site		
Hyperpigmentation at donor site	Nil (0%)	20 (80%)	(*P* value 0.0005) Significant
Scar hypertrophy at donor site	1 (4%)	10 (40%)	(*P* value 0.002) Significant
	Recurrence at follow-up		
Recurrence of contracture	2 (8%)	8 (32%)	(*P* value 0.06) Not significant

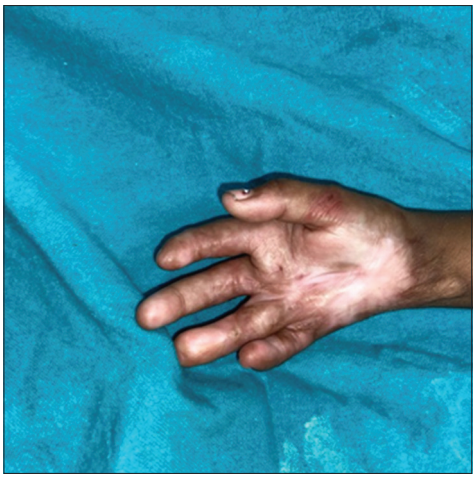

Figure 1: Follow-up of post burn contractures finger with glabellar skin with good color and texture match

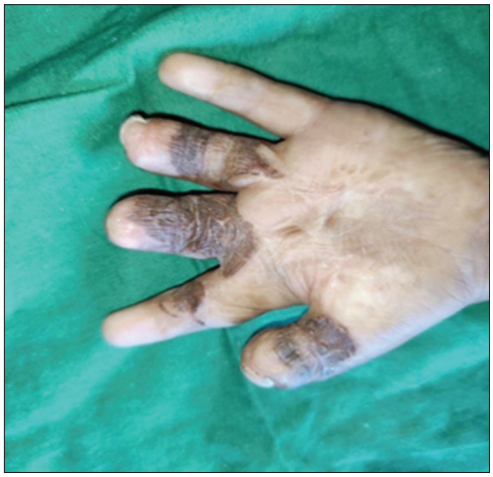

Figure 2: Follow-up of post burn contractures finger with non-glabellar skin with poor color and texture match

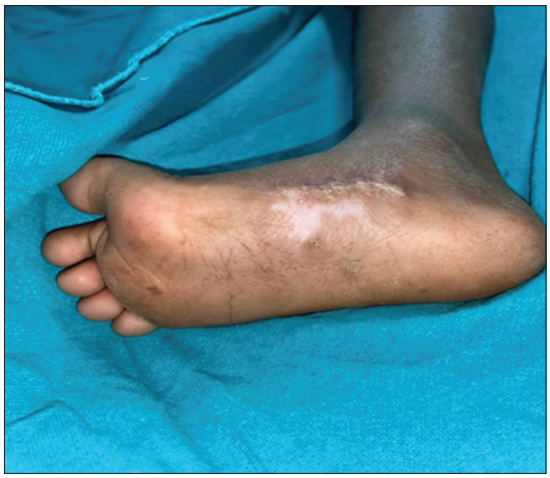

Figure 3: Follow-up of glabellar donor site at 3 months follow-up with healed donor area

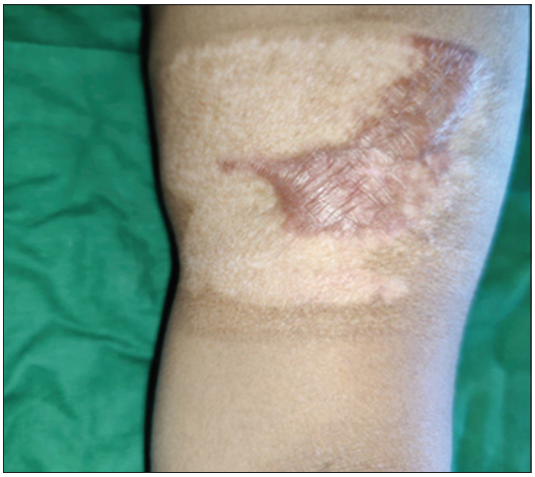

Figure 4: Follow-up of non-glabellar donor site at 3 months follow-up, with hyperpigmentation and scar hypertrophy

It is clear that replacing glabrous skin defects with like tissue is superior with regard to restoring function and aesthetics. Glabrous skin grafts demonstrate durability without hyperkeratosis and hyperpigmentation, and have even demonstrated improved recovery of sensation when compared with hair-bearing grafts.[16,17] However, when taking full-thickness glabrous grafts, the donor site is always limited. With split-thickness glabrous grafts, donor-site morbidity is significant, with prolonged healing, hypertrophic scarring, hyperpigmentation, and pain. Because of these problems, we have evolved to using glabrous dermal grafts to resurface palmar and plantar defects for the past many years similar to the technique reported by Tanabe and associates in 1998.[13]

CONCLUSION

Glabellar skin of the instep is the best replacement for the palmar skin of the digits and hand because of the similarities in their characteristics. Results are excellent in terms of color and texture match, no hyperpigmentation, less marginal scarring, and scar hypertrophy. There is less recurrence of contracture in patients with area grafted with glabellar skin. Split thickness graft from non glabellar area doesn't provide good color, texture match, with hyperpigmentation, scarring, and scar hypertrophy. Donor site of non glabellar skin showed signs of hyperpigmentation and scar hypertrophy. Proper splinting and physiotherapy are key factors in the prevention of recurrence of contracture in the glabellar skin grafted areas. The excellent color, texture match, and the functional advantages in terms of active ROM and sensitivity offered by the split thickness in the long run. Glabellar skin graft is of no match to split thickness conventional skin grafts taken from non-glabellar skin. Cosmetic results of planter skin graft are far superior to any other skin substitute. Donor site morbidity is very low and hardly any donor site scar is visible. So in conclusion for management of

post-burn flexion contracture of finger ideal skin substitute is glabellar skin grafts from the instep region of foot.

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Original Article

Efficacy and Outcome of Bubble Continuous Positive Airway Pressure in Newborn with Respiratory Distress at Special Newborn Care Unit in Rural Area of Telangana State, India

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Abstract

Background: Management of respiratory distress (RD) in newborn in a developing country with limited resources in rural parts in India is still a challenge. A low cost bubble continuous positive airway pressure (CPAP) device has been shown a great promise to fulfill this difficulty. Even though CPAP therapy has been shown to be successful, studies documenting its efficacy and outcome from rural India are very rare.

Materials and Methods: These were a retrospective observational study carried out at special newborn care unit of Siddipet, Telangana, from January 2019 to December 2020. Neonates with RD at birth or after birth that required bubble CPAP were included in the study. The efficacy of CPAP on immediate outcome of these infants was analyzed.

Results: A total of 154 newborns (124 inborn and 30 outborn) were included in the final analysis who received bubble CPAP. Mean gestational age was 35–36 weeks, mean birth weight of 2156 g. Morbidities required bubble CPAP most common were RD syndrome 81 (52.6%) followed by transient tachypnea of newborn 51 (33.1%), meconium aspiration syndrome 13 (8.4%), perinatal asphyxia 7 (4.5%), and congenital pneumonia 2 (1.3%). Of the study population, 119 (77.3%) neonates have successfully been discharged with CPAP only, 14 (19%) babies required further invasive ventilation, and 6 (3.9%) babies required surfactant administration along with CPAP.

Conclusion: Proper and early initiation of low cost non-invasive CPAP for newborn with significant RD has good results in outcome and decreased the need for invasive mechanical ventilation and surfactant administration which helped in early kangaroo mother care and discharge with fewer morbidities.

Key words: Bubble continuous positive airway pressure, Efficacy, Respiratory distress, Special newborn care unit

INTRODUCTION

Approximately one in 10 newborn requires assistance to begin breathing in an extrauterine environment at birth. The most common conditions that compromise respiratory function include prematurity, birth asphyxia, and pneumonia, which are responsible for more than 50% of 3.6 million deaths every year globally.[1]

Respiratory distress (RD) is said to be present when tachypnea (respiratory rate >60/min) is accompanied with chest retractions and/or grunt. RD can be due to respiratory and non-respiratory causes. Common respiratory causes include RD syndrome (RDS), meconium aspiration syndrome (MAS), pneumonia, transient tachypnea of newborn (TTNB), persistent pulmonary hypertension, pneumothorax, tracheoesophageal fistula (TEF), and congenital diaphragmatic hernia (CDH). Congestive heart failure, congenital heart disease, hypothermia, hypoglycemia, metabolic acidosis, and perinatal asphyxia constitute common non-respiratory causes.[2]

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Continuous positive airway pressure (CPAP) is a non-invasive respiratory support option which provides continuous distending pressure in a spontaneously breathing neonate, increases functional residual capacity of lung resulting in better gas exchange. It is also meant to avoid harmful effects of positive pressure ventilation.[3]

In India, nearly 26 million infants are born every year and assuming an incidence of RD in newborn to about 10%, 2.6 million infants are at need for the treatment of RD of various causes. Despite advances in neonatal care such as mechanical ventilation, surfactant therapy, and CPAP technologies, the accessibility and cost constraints are making neonatal care still a challenging area in most of the developing countries like India. Even though early CPAP therapy has been shown to be successful on some clinical trials in the management of RD, studies documenting its efficacy and outcome in rural areas are very few.

With this background, the present study was done to document the outcome and efficacy of CPAP in newborn with RD in a special newborn care unit (SNCU), rural part of Telangana State in India.

Objectives

The objectives of the study were as follows:

1. To assess the outcome of bubble CPAP in premature and term neonates with RD in a rural SNCU
2. To assess the efficacy of CPAP by comparing the outcome and complications in similar studies conducted in India both rural and urban.

MATERIALS AND METHODS

Study Design

Retrospective observational study analysis.

Study Setting

SNCU of Government Medical College, Siddipet, a tertiary care teaching hospital in rural part of Telangana State, India.

Study Period

The study period was from January 2019 to December 2020.

Inclusion Criteria

The following criteria were included in the study:

- Term neonates with RD with Downes score 4–7
- Preterm neonates with RD with Silverman Anderson score 4–6
- To prevent respiratory failure (apnea of prematurity)
- To treat airway obstruction.

Exclusion Criteria

The following criteria were excluded from the study:

- Neonates with a history of significant birth asphyxia (Stages 2 and 3)
- Term neonate with RD with Downes score <4 and >8
- Preterm neonate with RD with Silverman Anderson score <4 and >7
- Babies with congenital anomalies and surgical conditions such as cleft palate, bilateral choanal atresia, CDH, and TEF.

Sample Size

A total of 154 eligible newborn babies both preterm and term were included in this study of 2 years.

Study Procedure

Whenever neonatal baby presented to SNCU with RD as per protocol to maintain temperature, airway, breathing, and circulation, babies after keeping under the radiant warmer babies are given supplemental oxygen with nasal prongs 1–2 l/min to all babies with mild RD keeping target oxygen saturation of 90–95% as per NRP. As per the criteria of Silverman Anderson score for premature babies and Downes score for term neonates, babies with RD were started on bCPAP with rule of 5, as 50% FIO_2, 5 L of flow, and 5 positive end-expiratory pressure (PEEP) with target SPO_2 saturations for the neonates between 90% and 95% in the right upper arm. CPAP machine settings of flow, FIO_2, and PEEP were changed as per clinical improvement of the neonates. Whenever baby RD comes down, we gradually tapered the FIO_2 by 5% (from 50% to 45%) later from 45% to 40% in stepwise, followed by flow from 5 L to 4 L. Then FIO_2 40–35%, next 35–30% followed by flow changed from 4 L to 3 L. We kept the PEEP constant in maximum cases. Once the baby is stable on FIO_2 30%. Flow 3 L and PEEP 5, when the baby is hemodynamically stable, the baby is gradually weaned off to hood oxygen or nasal prongs with oxygen 1–2 L/min. Vice versa whenever required to increase the settings. We have used Neotech Company bubble CPAP machine with appropriate size nasal prongs of small, medium, and large as per the weight, gestational age of the baby. Orogastric tube was inserted in all newborns on CPAP for abdominal decompression and early initiation of OG feeds once baby is hemodynamically stable, neonates were monitored clinically and regular arterial blood gases (ABGs) were done when ever required. Chest X-rays (CXRs) were done in all neonates on bubble CPAP. Respiration rate, heart rate, SPO_2, and blood pressure were monitored regularly.

Babies were observed for outcomes until discharge. Premature babies with hyaline membrane disease (HMD) whenever there is high requirement of oxygen of more than 50% FIO_2, surfactant is given by INSURE technique and those babies

requiring further respiratory support and not maintaining saturations on CPAP and surfactant, were mechanically ventilated and termed as CPAP failure. If there were signs of shock such as tachycardia, prolonged capillary refill time, dull activity volume expansion by fluid boluses, and inotropic support were given. If there were symptoms and signs of sepsis, antibiotics were started as per unit protocol. All premature neonates admitted in SNCU were screened for retinopathy of prematurity and neurosonogram as per protocol.

CPAP failure is defined as: [4]

1. Increased work of breathing (intercostal retractions and accessory muscle contribution for respiration) with respiratory rate >60/min
2. Increased apnea and bradycardia and/or desaturations >2 in 1 h for a previous 6 h period
3. Increased oxygen requirement: SpO_2 <90% on FiO_2 >60% for >30 min with requirement of CPAP >8 cm of H_2O.
4. Blood gases showing
   a. PH <7.2
   b. PCO_2 >65 mm of Hg
   c. PO_2 <50 mm of Hg on FiO_2 >60%
5. Major apnea/bradycardia requiring resuscitation.

Outcomes

Initiation of CPAP, duration, neonates discharged successfully from CPAP, CPAP failure, requiring surfactant, mechanical ventilation, nasal damage, incidence of pneumothorax, intraventricular hemorrhage, periventricular leukomalacia, retinopathy of prematurity, chronic lung disease, and duration of hospital stay were analyzed.

RESULTS

During the study period, a total of 1963 babies were admitted in our unit of which 1264 (64.39%) were given supplemental oxygenation in view of minimal RD which got resolved with oxygen only. Among the admitted neonates with significant RD, 154 neonates were started with bCPAP in the final study as per the inclusion criteria. Beyond those 71 neonates required mechanical ventilation that had severe RD.

The maternal characteristics [Table 1] of neonates who received CPAP support for RD when analyzed showed a predominance primigravida mothers who constituted 50.60% (78) of study group, second gravida mothers are 26.60% (41) followed by G3 16.90% (26), and higher order pregnancies consist of 5.8% (9). Maternal age of <25 years comprises >75% of study population. Of the 77 preterm deliveries, full course of antenatal steroids (two doses of Betnesol 12 mg with 24 h gap or dexamethasone injection 6 mg, 4 doses with 12 h interval) was given in 42 (54.54%), incomplete steroids (at least one dose of antenatal steroids) given in 28 (36.36%), and not given antenatal steroids in 7 (9.10%). Five twin deliveries were present in the study and remaining all are singleton pregnancies. Urinary tract infection (maternal fever) is the most common complication seen in 15.6% (24) of mothers followed by diabetes mellitus in 7.1% (11), hypertension in 4.5% (7), and patient-reported outcome measures in 3.2% (5) of cases.

Term deliveries [Table 2] comprise 50.1% (77) while 34.4% are with gestational age of 33–36 weeks, 12.3% are 29–32 weeks, and 3.2% with gestational age <28 weeks. The mean gestational age of the study group was 35.48 weeks. Of the 154 deliveries, 124 were C-section and 30 were vaginal deliveries. When weight of the baby is taken for the criteria, 36.4% of neonates were more than 2500 g appropriate for gestational age, 42.9% are between 1500 g and 2500 g low birth weight (LBW), 16.2% are between 1000 g and 1499 g very LBW, and 4.5% are <1000 g extremely LBW with mean birth weight of 2156 g.

In gender variation, study shows that 101 (65.6%) neonates were male and 53 (34.4%) are female with M: F ratio of 1.9:1. There is increase admission rate in male newborn babies. Appearance, pulse, grimace, activity, and respiration (APGAR) score at 5 min in the study group shows 100 (64.9%) babies having an APGAR of 8–10, 50 (32.5%) with 5–7 score and 4 (2.6%) babies had APGAR score of 4.

Orogastric tube [Table 3] was inserted in all newborns on CPAP for abdominal decompression and early initiation of OG feeds which was done in 18% of study neonates once they were hemodynamically stable. In the study group, 21 (13.6%) of newborn babies with RD were started with bCPAP soon after birth and 133 (86.4%) newborn babies required bubble CPAP after 6 h of life. Twenty-six (16.9%) newborn babies required initial FiO_2 of <40% at the beginning of CPAP therapy and 128 (83.1%) required more than 40% FiO_2 which was gradually decreased as per clinical improvement. If FiO_2 requirement of more than 50% with significant RD in premature babies with CXR features suggestive of HMD, surfactant was given by INSURE technique.

RDS is the most common primary diagnosis with 81 (52.6%) babies requiring CPAP followed by TTNB 51 (33.2%), MAS 13 (8.4%), mild perinatal asphyxia 7 (4.5%), and congenital pneumonia 2 (1.3%). Clinical sepsis was a comorbid factor in 82 (53.2%) neonates of study group. Complications of CPAP therapy were nasal septum injury which was seen only 2 (1.29%) babies which subsided later without any complication with

local antibiotic ointment application. None of the babies developed nasal bridge injury, abdominal distension, and pneumothorax in our study.

In the study group, 130 (84.40%) neonates with significant RD were successfully discharged with CPAP alone and 24 neonates [Table 4] being required mechanical ventilation of which six premature babies required surfactant administration and three babies who were ventilated from CPAP got expired due to other complications. Three babies were referred to higher center in view of complex cardiac disease. The overall success rate of our study group is 98% and success rate with exclusive CPAP is 86.1%.

DISCUSSION

This is a retrospective observational study conducted in a level 2 neonatal unit of rural part of Telangana state, India, with a high-risk delivery unit that conducts at an average of 4500 deliveries per year with about 1000 newborn admitted annually in our unit. During the study period, a total of 1963 newborn babies were admitted of which 1264 (64.39%) with mild RD got resolved with oxygen supplementation only. Among the babies with significant RD, 154 babies required bubble CPAP as per the inclusion criteria. With such a background, this study was done to find the efficacy and immediate outcome of bCPAP when started timely and escalated/de-escalated appropriately based on babies clinical condition. Diagnosis was done mainly clinically and was aided by CXR, ABGs, and Downes score and Silverman Anderson scores.

In the present study, the success of bCPAP was 84.4% which is much higher than earlier studies by Byram *et al.*[5] (64%), Shamil *et al.*[6] (66%), and Sethi *et al.*[7] (60%). This may be due to the structured approach followed in our unit in assessing the newborn and early and timely initiation of bCPAP.

BCPAP was started to babies with RD irrespective of gestation age and weaned off as per clinical improvement. All term babies were weaned within the first 48 h of life than those of early and preterm babies. Babies with gestation age <32 weeks required CPAP for longer duration and CPAP failure was seen exclusively in this group. Three babies were referred due to complex cardiac disease and three babies in the study group expired secondary to extreme prematurity associated comorbidities. Of the six babies administered with surfactant, four were discharged successfully and two expired. Overall CPAP failure rate in our unit was 15.58% which is comparatively less when compared with studies by Koti *et al.*[8] (25%), Sethi *et al.*[7] (40%), and consistent with study by Roberts *et al.*[9] (13%).

Table 1: Maternal characteristics

Maternal age	Number	Percentage
<20 years	67	43.5
20–25 years	50	32.5
26–30 years	23	14.9
31+years	14	9.1
Gravida status		
Primi	78	50.6
G2	41	26.7
G3	26	16.9
G4 and above	9	5.8
Mode of delivery		
NVD	40	26.0
C-section	114	74.0
No. of babies delivered		
Singleton	149	96.8
Twins	5	3.2
Triplets	0	
Place of delivery		
Inborn	124	80.5
Outborn	30	19.5
Antenatal steroid		
Yes (complete two doses)	42 (among 77 preterm)	54,5
Incomplete (at least one dose received)	28 (among 77 preterm)	36.4
No	7 (among 77 preterm)	9.1
Complications		
DM	11	7.1
Hypertension	7	4.5
PROM	5	3.2
UTI	24	15.6

NVD: Normal vaginal delivery, DM: Diabetes mellitus, PROM: Patient-reported outcome measures, UTI: Urinary tract infection

Table 2: Neonatal characteristics

Gestation age	Number	Percentage
<28 weeks	5	3.2
29–32 weeks	19	12.3
33–36 weeks	53	34.4
37–40 weeks	77	50.1
Gender		
Male	101	65.6
Female	53	34.4
Birth weight		
<1000 g	7	4.5
1000–1499 g	25	16.2
1500–2499 g	66	42.9
>2500 g	56	36.4
Resuscitation at birth		
Routine	146	94.8
Bag and mask ventilation	8	5.2
5 min APGAR score		
0–4	4	2.6
5–7	50	32.5
8–10	100	64.9
RD signs		
Tachycardia	102	66.2
Grunting	134	87
Retractions	27	18.1
Cyanosis	17	11.2
Apnea	6	4

RD: Respiratory distress, APGAR: Appearance, pulse, grimace, activity, and respiration

Table 3: Characteristics of bubble CPAP therapy in neonates

Starting age of CPAP therapy	Number	Percentage
At birth	21	13.6
>6 h	133	86.4
FiO_2 needed on CPAP therapy		
<40%	26	16.9
>40%	128	83.1
Orogastric tube insertion	154	100
Feeding while on bCPAP	46	18.2
CPAP therapy duration		
<24 h	34	22.1
24 h–48 h	113	73.4
>48 h	7	4.5
Primary diagnosis		
RDS	81	52.6
TTNB	51	33.2
MAS	13	8.4
Mild perinatal asphyxia	7	4.5
Congenital pneumonia	2	1.3
Comorbidities		
Sepsis (probable)	82	53.2
Complications		
Nasal septum injury	2	
Nasal bridge injury	Nil	
Abdominal distension	Nil	
Pneumothorax	Nil	

CPAP: Continuous positive airway pressure, bCPAP: Bubble continuous positive airway pressure, RDS: Respiratory distress syndrome, MAS: Meconium aspiration syndrome, TTNB: Transient tachypnea of newborn

Table 4: Outcome

Primary outcome	Number	Percentage
Discharge		
130	84.40	
CPAP failure requiring ventilation	24	15.58
Referred	3	1.94
Secondary outcome		
Deaths	3	1.94
Surfactant therapy	6	3.89

The analysis of maternal characteristics showed that mothers of <25 years form 75% of the study group with 50% of the babies are born to primi mothers. This can be attributed to our high-risk delivery unit which acts as a referral center for the district and depicted with 74% of deliveries being conducted by C-section. The present study showed that of the preterm deliveries, seven mothers did not receive any antenatal steroid of which 2 (28.6%) babies expired and 28 mothers received single dose of steroid 1 (3.6%) baby died. No mortality was seen in babies of mother who received two doses of antenatal steroids before delivery. This is similar to studies by Sanghvi and Rasania[10] Robert and Dalziel.[11]

CONCLUSION

This study concludes that early initiation of non-invasive CPAP in newborn with significant RD has definitely reduced the need of invasive mechanical ventilation, need of costly surfactant administration, and aids in early recovery and discharge with least morbidities in the neonate.

It is a safe and cost-effective method that can be employed in resource-limited settings and requires good monitoring and supportive care. Antenatal steroids have good impact in outcome of babies with RD on CPAP and CPAP failure is mainly seen in preterm babies whose mother did not receive no or full dose of antenatal steroids.

ETHICAL APPROVAL

This study was approved by Institutional Review Board.

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Original Article

Age Estimation using Orthopantomographs by Demirjian's Method

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Abstract

Objectives: The aim of this study was to pursue a survey on age estimation for dental patient using for orthopantomographs (OPGs). The 30 OPGs were selected by us with respect to criteria and evaluated. The results were compared to chronological ages (CAs). The accuracy of estimates synchronously made using OPGs.

Materials and Methods: This is a retrospective study, the OPGs of 30 individual children of age group 3–16 years of non CA were measured using the Demirjian's Method of age estimation on the bases of development of 7 mandibular molars on the left side using radiographs.

Results: The results indicate that the Demirjian method is most accurate method for Age estimation using OPGs and it is also most reliable method for age estimation. There is no significant difference between CA and dental age.

Conclusion: Age estimation with OPGs can be used to make a significant percentage of forecasts in areas such as forensic medicine and forensic dentistry, especially in young patients.

Key words: Age estimation, Orthopantomigraphs, Demirjian's Method

INTRODUCTION

Age estimation is a scientific process/method that estimates and individual's True chronological age (CA) by evaluating skeletal and dental development and maturation.[1] Age estimation is one of the essential factors in human identification.[2]

Age determination versus it's used in several situations in forensic odontology such as ~Identification of unknown individuals, In scenes of crime and accidents, it is probably used to estimate the CA of children of unknown birth records.[3] There are other methods available, but dental age (DA) plays an important role in the age estimation of the individual. *Other methods: skeletal maturation, physical examination using anthropometric measurement, combination of all.[3]

Tooth formation is broadly used to evaluate maturity and anticipate age, also this information aids in diagnosis and treatment planning.[4]

In archeology and forensic odontology, this method can aids the estimation of age at that of a deceased child and also give importance with regard to past population.[5] Nowadays, the radiographic method of age estimation on basis of tooth development has been found to be an accurate method, because the eruption of teeth into oral cavity is generally influenced by local factors e.g.: lack of space, systemic sectors, hands dental maturity is considered as a more accurate master of biologic maturity in children because tooth mineralization stages are much less affected by nutritional and endocrine status.[3] In this article, the study aimed to determine possibility of age estimation with the Orthopantomographs (OPGs).

The study was done retrospectively at the "Oral Medicine and Radiology, Department, Siddhpur Dental College and Hospital (SDCH), Gujarat, India."

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MATERIALS AND METHODS

In this study panoramic radiographs of 30 individual children of known CA, with ages ranging from 3 to 16 years in which 18 females and 12 males are included.

There are various methods of age estimation. *This study is based on "Radiographic methods:" it is a Simple, Non-invasive technique used in forensic odontology for living and unknown dead.

The Demirjian *et al.* Method has been the most commonly used method for DA estimation using radiographic technique as it is based on tooth developmental changes and easy to apply.

In this method, development of 7 mandibular teeth on the left side as it appears on the radiograph were divided into 10 stages for each stage; different maturity scores were given for the tooth[6,7].

Study Groups

The selected dental patients were divided into two main groups according to biological sex (Group A [Males] and Group B [Females]).

There are at least two participants per age group.

Data Collection

Dental patients and personal information related to the CA of each subject, such as the date of birth (DOB) and date of radiograph (DOR), were collected from the existing records.

The CAs of the participants were calculated by subtracting the DOB from the DOR and were recorded as years with two decimal places. All of the dental patients were scored independently and randomly by one of the authors, who was blinded to the CA and sex of each subject. The DA was calculated using Demirjian's method. All of the 7 teeth in the lower left jaw (with the exception of the third molar) were assessed. The DA was calculated according to the tables proposed by Demirjian *et al.* [Tables 1-4].[8] When a tooth on one side was missing or difficult to read, the contralateral tooth was assessed.

Reproducibility

About 20% of the dental patients were randomly selected and the tooth developmental stages were re-evaluated 2 weeks later (retest) to test the inter-examiner and intra-examiner reliability. Then, the intra- and inter-examiner agreement was calculated.

Statistical Testing

All data were collected, tabulated, and statistically analyzed. Quantitative data are presented as the range, mean, and standard deviation (SD), and qualitative data are presented as the number (*n*) and percentage (%). The statistical analyses were performed using an independent samples student *t*-test for analysis of quantitative data.

For all tests, probability (*P*) was categorized as follows:

- Non-significant if ≥0.05
- Significant if <0.05

Table 1

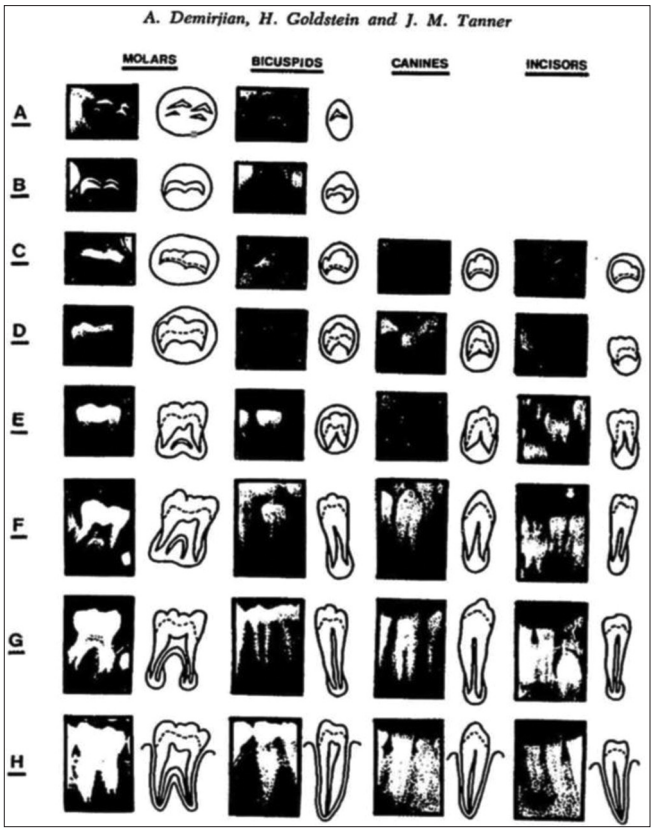

Table 2

Self-Weighted Scores for Dental Stages
7 Teeth (Mandibular Left Side)

Boys

Tooth	Stage 0	A	B	C	D	E	F	G	H
M_2	0.0	2.1	3.5	5.9	10.1	12.5	13.2	13.6	15.4
M_1				0.0	8.0	9.6	12.3	17.0	19.3
PM_2	0.0	1.7	3.1	5.4	9.7	12.0	12.8	13.2	14.4
PM_1			0.0	3.4	7.0	11.0	12.3	12.7	13.5
C				0.0	3.5	7.9	10.0	11.0	11.9
I_2				0.0	3.2	5.2	7.8	11.7	13.7
I_1					0.0	1.9	4.1	8.2	11.8

Girls

Tooth	Stage 0	A	B	C	D	E	F	G	H
M_2	0.0	2.7	3.9	6.9	11.1	13.5	14.2	14.5	15.6
M_1				0.0	4.5	6.2	9.0	14.0	16.2
PM_2	0.0	1.8	3.4	6.5	10.6	12.7	13.5	13.8	14.6
PM_1			0.0	3.7	7.5	11.8	13.1	13.4	14.1
C				0.0	3.8	7.3	10.3	11.6	12.4
I_2				0.0	3.2	5.6	8.0	12.2	14.2
I_1					0.0	2.4	5.1	9.3	12.9

NB: Stage 0 is no calcification

Table 3

Conversion of Maturity Score to Dental Age 7 Teeth (Mandibular Left Side)

Age	Score	Age	Score	Age	Score	Age	Score
			Girls				
3.0	13.7	7.0	51.0	11.0	94.5	15.0	99.2
.1	14.4	.1	52.9	.1	94.7	.1	99.3
.2	15.1	.2	55.5	.2	94.9	.2	99.4
.3	15.8	.3	57.8	.3	95.1	.3	99.4
.4	16.6	.4	61.0	.4	95.3	.4	99.5
.5	17.3	.5	65.0	.5	95.4	.5	99.6
.6	18.0	.6	68.0	.6	95.6	.6	99.6
.7	18.8	.7	71.8	.7	95.8	.7	99.7
.8	19.5	.8	75.0	.8	96.0	.8	99.8
.9	20.3	.9	77.0	.9	96.2	.9	99.9
4.0	21.0	8.0	78.8	12.0	96.3	16.0	100.0
.1	21.8	.1	80.2	.1	96.4		
.2	22.5	.2	81.2	.2	96.5		
.3	23.2	.3	82.2	.3	96.6		
.4	24.0	.4	83.1	.4	96.7		
.5	24.8	.5	84.0	.5	96.8		
.6	25.6	.6	84.8	.6	96.9		
.7	26.4	.7	85.3	.7	97.0		
.8	27.2	.8	86.1	.8	97.1		
.9	28.0	.9	86.7	.9	97.2		
5.0	28.9	9.0	87.2	13.0	97.3		
.1	29.7	.1	87.8	.1	97.4		
.2	30.5	.2	88.3	.2	97.5		
.3	31.3	.3	88.8	.3	97.6		
.4	32.1	.4	89.3	.4	97.7		
.5	33.0	.5	89.8	.5	97.8		
.6	34.0	.6	90.2	.6	98.0		
.7	35.0	.7	90.7	.7	98.1		
.8	36.0	.8	91.1	.8	98.2		
.9	37.0	.9	91.4	.9	98.3		
6.0	38.0	10.0	91.8	14.0	98.3		
.1	39.1	.1	92.1	.1	98.4		
.2	40.2	.2	92.3	.2	98.5		
.3	41.3	.3	92.6	.3	98.6		
.4	42.5	.4	92.9	.4	98.7		
.5	43.9	.5	93.2	.5	98.8		
.6	45.2	.6	93.5	.6	98.9		
.7	46.7	.7	93.7	.7	99.0		
.8	48.0	.8	94.0	.8	99.1		
.9	49.5	.9	94.2	.9	99.1		

Table 4

Conversion of Maturity Score to Dental Age (7 Teeth)

Age	Score	Age	Score	Age	Score	Age	Score
			Boys				
3.0	12.4	7.0	46.7	11.0	92.0	15.0	97.6
.1	12.9	.1	48.3	.1	92.2	.1	97.7
.2	13.5	.2	50.0	.2	92.5	.2	97.8
.3	14.0	.3	52.0	.3	92.7	.3	97.8
.4	14.5	.4	54.3	.4	92.9	.4	97.9
.5	15.0	.5	56.8	.5	93.1	.5	98.0
.6	15.6	.6	59.6	.6	93.3	.6	98.1
.7	16.2	.7	62.5	.7	93.5	.7	98.2
.8	17.0	.8	66.0	.8	93.7	.8	98.2
.9	17.6	.9	69.0	.9	93.9	.9	98.3
4.0	18.2	8.0	71.6	12.0	94.0	16.0	98.4
.1	18.9	.1	73.5	.1	94.2		
.2	19.7	.2	75.1	.2	94.4		
.3	20.4	.3	76.4	.3	94.5		
.4	21.0	.4	77.7	.4	94.6		
.5	21.7	.5	79.0	.5	94.8		
.6	22.4	.6	80.2	.6	95.0		
.7	23.1	.7	81.2	.7	95.1		
.8	23.8	.8	82.0	.8	95.2		
.9	24.6	.9	82.8	.9	95.4		
5.0	25.4	9.0	83.6	13.0	95.6		
.1	26.2	.1	84.3	.1	95.7		
.2	27.0	.2	85.0	.2	95.8		
.3	27.8	.3	85.6	.3	95.9		
.4	28.6	.4	86.2	.4	96.0		
.5	29.5	.5	86.7	.5	96.1		
.6	30.3	.6	87.2	.6	96.2		
.7	31.1	.7	87.7	.7	96.3		
.8	31.8	.8	88.2	.8	96.4		
.9	32.6	.9	88.6	.9	96.5		
6.0	33.6	10.0	89.0	14.0	96.6		
.1	34.7	.1	89.3	.1	96.7		
.2	35.8	.2	89.7	.2	96.8		
.3	36.9	.3	90.0	.3	96.9		
.4	38.0	.4	90.3	.4	97.0		
.5	39.2	.5	90.6	.5	97.1		
.6	40.6	.6	91.0	.6	97.2		
.7	42.0	.7	91.3	.7	97.3		
.8	43.6	.8	91.6	.8	97.4		
.9	45.1	.9	91.8	.9	97.5		

- Highly significant if <0.01
- Very highly significant if <0.001. Cohen's kappa test with a $P < 0.05$ indicating significance was used to test the inter- and intra-examiner reliability.

RESULTS

The study consisted of 18 females and 12 males. The student *t*-test is used for statistic evaluation for this study.[9] The mean CA of the sample was 10.13333 years, while the mean DA was 10.3866. The mean CA for male 10.64 ± 3.70 years and that for females was 9.75 ± 1.82 years. The mean DA for males was 10.92 ± 3.42 years and that for females was 10.03 ± 2.09 years [Table 5 and Figure 1]. Mean absolute error (MAE) in the age estimation was classified by dividing the sample into eight different age groups which ranged from 7 to 15 years. The highest MAE was in the age 12 years age group (0.46 ± 1.01),while lowest in the age group 7 years (–0.8 ± 2.1) [Table 6].

Table 5: Descriptive statistics of male and female

Variable	Males (mean)	SD (*n*=30)	Females (mean)	SD (*n*=30)	*P*-value
CA	10.64	3.70	9.75	1.82	0.05*
DA	10.92	3.42	10.03	2.09	0.02*
P-value	0.01*		0.003*		

*Indicates statistically significance at *P*=0.05, CA: Chronologic age, DA: Dental age, SD: Standard deviation

Table 6: MAE in different age groups

Age groups (year)	No of subjects	Mean	SD
7	6	–0.8	2.1
8	4	–0.2	1.09
9	4	0.3	1.14
10	2	0.4	
11	4	0.3	0.95
12	6	0.46	1.01
14	2	0.1	
15	2	–1	

MAE: Mean absolute error, SD: Standard deviation

DISCUSSION

The age estimation of age is an important aspect in medico-legal practice.[10] The estimation of age is based on the developmental stages of teeth taking into consideration associated calcification process. The original Demirjian's method excluded the Third molar due to the variability in its development, eruption, and anatomy. However, the pitfall of its exclusion was that age prediction by the original Demirjian's

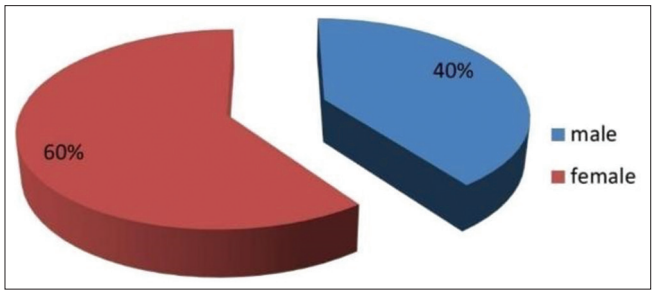

Figure 1: Graph showing gender distribution of the sample

method is not feasible after about 16 years of age, since by this age all the permanent teeth, except the third molar, would have completed their development. The tooth improvement is a continuous process, but determining the end point of tooth development is very difficult. Thus, the calculation of a mean age for each phase is difficult; further research is needed to determine the apex closure stage of teeth. Measurement using dental radiographs may be useful as a non-invasive technique for estimating the age of adults, both living and dead, in archeological studies and in forensic work, but the method should be tested on an independent sample.

DA estimation is commonly used worldwide and is thought to correlate with CA better than other maturity indicators of a child's development. Several methods have been introduced to estimate DA depending on either calcification (tooth development) or eruption patterns. Relying on eruption dates when attempting to assess DA is complicated by the fact that tooth emergence may be significantly affected by local exogenous factors, such as infection, obstruction, crowding, and premature extraction of the deciduous predecessor or adjacent permanent teeth. These mishaps can be avoided by interpreting radiographic data representing the tooth development stages.[11]

One of the most commonly used radiographic methods is the method reported by Demirjian *et al.*, which established a standard based on a large sample that included 1446 males and 1482 females of French-Canadian origin. Although observer agreement is usually reported when using Demirjian's method, there is an evident tendency toward overestimation of a subject's age, which may be a result of ethnic differences between populations 26 and a positive secular trend over the last 50 years. The debate regarding the applicability of Demirjian's method to all races and populations. Encouraged the authors to assess the applicability of Demirjian's method and to develop new prediction equations if needed.[11]

Prabhakar *et al.* tested the applicability of Demirjian's method among 151 Indian children living in Davangere. They found that the Davangere children were dentally more advanced and that Demirjian's method did not apply to their study group.[11]

Our study found that Demirjian's original standards accurately estimate the CA in our studied sample and that the exploratory data analysis generally almost similar to the CA on application of Demirjian's method. The authors strongly believe that each population requires its own adaptive dental maturity score. This concept of developing a specific prediction equation for each population is becoming more strongly supported.

CONCLUSION

Age estimation through the evaluation of OPG revealed the most reliable results for the first decade of life. Age estimation with OPGs can be used to make a significant percentage of forecasts in areas such as forensic medicine and forensic dentistry, especially in young patients. To achieve accurate and reliable age estimation, in addition to mill metric measurements of the teeth, skeletal measurements and examinations should be performed.

Demirjian's method was found most accurate method for age estimation and suitable for children living in Siddhpur, Gujarat.

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Original Article

Health Seeking Behavior of Mothers toward Acute Respiratory Tract Infection in Under-five Children in a Rural Area in Goa, India

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Abstract

Background: One of the major causes for mortality and morbidity among under-five children with acute respiratory tract infections (ARI) is a delay in seeking health care by the mothers. Even though early treatment in ARI has the potential to substantially reduce child mortality, health care seeking behavior (HCSB) is lacking among mothers of under-five children in developing countries Mother needs to identify the danger signs of ARI and to seek prompt treatment. The aim of this study was to assess mothers' health-seeking behavior for ARI in under-five children in a rural area in Goa, India.

Methods: A community-based cross-sectional study was carried out on a sample of 302 mothers in Sanquelim town in Goa from June to August 2020. A systematic random sampling method was used for sample selection. Data were entered using Epidata Version 3.1 and transferred to SPSS version 22 software for analysis. Odds ratio (OR) with $P < 0.05$ and 95% confidence interval (CI) was used to show the strength of association.

Results: A total of 302 mothers were enrolled in the study by systematic random sampling. It was observed that 237 (77.4%) mothers sought treatment from a qualified medical practitioner. Mothers with a male child had odds of seeking health care 4.40-fold (OR: 4.40, 95% CI: 2.510, 7.730) higher than the girl child. Mothers with parity of one had odds of health-seeking 0.359-fold (OR: 0.359, 95% CI: 0.197, 0.655) lower than mothers with parity of two and above. Mothers who were married had odds of seeking healthcare 41-fold (OR: 41.488, 95% CI: 13.95–123.334) than mothers who were single/divorced/widowed. Mothers with higher educational status were 2.08-fold (OR: 963, 95% CI: 0.336–2.757) likely to seek health care than those with no formal education. It was also observed in the current study that mothers with a sick child less than a year were 3-fold (OR = 1.78, 95% CI: 1.02, 4.13) more likely to seek healthcare than those whose child was >1 year. It was observed that 33 (11%) mothers sought health care for their sick child within a day of onset of illness, whereas 97 (32%) mothers availed of health care in <3 days of symptom onset and 172 (57%) mothers availed health care after 3 days of symptom onset. Hence, in the current study, it was observed that there was delayed HCSB of mothers toward ARI in under-five children in a rural area in Goa.

Conclusions: It was observed in the current study that there was a delay in seeking healthcare by the mothers for their sick child with ARI. Age and sex of the child, marital status of the mother, level of education, and parity were associated with the mother's HCSB for under-five children with ARI.

Key words: Health seeking behavior, Acute respiratory tract infection, Mothers

INTRODUCTION

Acute Respiratory tract infection (ARI) in under-five children is one of the major public health problems accounting for 15–30% of all under-five deaths in India.[1,2] It has been estimated that respiratory infections account for 6% of the total global burden of disease.[3] Furthermore, every year at least 300 million episodes of ARI occur in India, out of which about 30–60 million are moderate to severe ARI. Globally, every sixth child with ARI is Indian and every fourth child who dies due to ARI is from India.[4]

ARI accounts for 30–50% of visits to health facilities and 20–40% of hospital admissions.[5,6] Most of the infants die despite the implementation of evidence-based interventions such as Integrated Management of Childhood

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Illnesses that put a substantial premium on early diagnosis and management of infants with ARI.[7] This calls for investigations into factors that may be associated with increased infant morbidity and mortality including delayed health-seeking. Studies suggest that common causes of under-five morbidity and mortality in developing countries could substantially be reduced with timely healthcare-seeking behavior (HCSB) of their families.[8,9] The survival of an infant from the physical stressors associated with acute illness is dependent on the identification of cues for the illness, time lag, and the decision to seek expert help by the mother "the so-called health-seeking behavior."[10] A large number of children under 5 years of age die of ARI without ever reaching a health facility due to delays in seeking health care. The WHO has estimated that seeking health care on time could reduce child deaths due to acute respiratory infections by 20%.[7] Even though early treatment in ARI has the potential to substantially reduce child mortality in developing countries, HCSB is lacking among mothers of under-five children in India.[1] This calls for investigations into factors that may be associated with increased infant morbidity and mortality including delayed health-seeking.

To decrease mortality and morbidity due to ARI in under-five children at the community level, it is important to study the HCSB of mothers for acute respiratory infection. Hence, the current study seeks to assess the proportion of mothers seeking health care for ARI in under-five children, from a registered medical practitioner and to determine factors influencing mother's HCSB.

METHODS

A cross-sectional study was conducted in Sanquelim town to assess mother's HCSB for children under 5 years with ARI. The current study was conducted from June to August 2020.

Sanquelim is a town in Bicholim Taluka of the North Goa, India. The study participants were chosen from 9 different localities in Sanquelim town namely Navelim, Harvalim, Honda, Karapur, Surla, Cudnem, Virdi, Amona, Podocem. The study population comprised of mothers who were residents of Sanquelim for a minimum duration of 1 year before the commencement of the study and had at least one child under 5 years of age. Data were collected in a structured questionnaire on sociodemographic characteristics, HCSB among mothers with children under 5 years of age and various factors affecting healthcare-seeking.

Sociodemographic variables were age, marital status, religion, education, employment, sex of the child, socioeconomic status, and parity. Child-related factors were the sex and age of the child.

Inclusion Criteria

Mothers who had at least one under-5-year-old child and living in Sanquelim for at least 1-year duration before the commencement of the study. The mothers of under-five children who had ARI in the last 1-month recall period and were willing to give informed consent were included in the current study.

Exclusion Criteria

Mothers who are not willing to give informed consent for participating in the study and those who were not permanent residents of Sanquelim for the last 1 year were excluded from the study.

Sample Size Determination

With an estimated proportion of health care seeking taken as 50% among mothers of under-five and d = 6%, the sample size was calculated using the formula,

$$n = \frac{4pq}{d^2} \quad n = \frac{4 \times 0.5 \times 0.5}{0.0036}$$

$$n = \frac{4 \times 0.5 \times 0.5}{0.0036}$$

n = 277, rounded to n=302.

Operational Definition

Health seeking behavior was defined as a mother who took treatment for her child with ARI at a health facility - hospital, health center, private clinic from a registered medical practitioner.

The factors which were assessed in the present study were child-related (age, sex) maternal factors (age, marital status, socioeconomic status, education, and parity).

The study was commenced in June 2020 after getting approval from the Institutional Ethics Committee of Goa Medical College.

Data Collection

Face-to-face interviews were conducted using a structured questionnaire. A systematic random sampling technique was used for the selection of mothers from the household. Data were entered into EpiData version 3.1, and data analysis was performed using IBM SPSS Statistics version 22. The associations between independent variables and Health seeking behavior in terms of health care sought or not were tested for significance using the Chi-square test, and the odds ratio (OR) was estimated

RESULTS

Sociodemographic Characteristics of Respondents

A total of 302 mothers whose children aged under five (birth–59 months) were recruited in the study, making the response rate of 100%. The mean age of the mothers was 27 ± 6 SD years. Out of the total mothers 196 (64.9%) were Hindu by religion followed by 67 (22.2%) were Muslims and 39 (12.9%) were Christian. Of the total mothers, 269 (89.40%) of them had attended formal education and out of which the majority of the mothers had completed their primary schooling 114 (42.4%) and 89 (33.10%) mothers had attained secondary education and above. It was observed that 102 (33%) mothers were housewives while 96 (31.7%) of the mothers were farmers by occupation. Of the total number of mothers 256 (84.76%) were married while 46 (15.3%) were single/divorced/widowed [Table 1].

Table 1: Sociodemographic characteristics of the respondents (mothers) 2020 (*n*=302)

Mothers characteristics'	*n* (302)	Percentage
Age (years)		
15–20	36	
21–24	82	
25–30	103	
31–35	57	
>35	24	
Religion		
Hindu	196	64.9
Christian	39	12.9
Muslim	67	22.2
Education		
Illiterate	13	4.3
Primary schooling	129	42.4
Secondary schooling	108	36
Higher education	52	17.3
Occupation		
Housewife	102	33.77
Un skilled	21	6.95
Farmer	96	31.7
Skilled	46	15.2
Professional	37	12.2
Marital status		
Married	256	84.76
Single/Divorced	46	15.23
Socioeconomic status		
Class I	18	5.9%
Class II	49	16.22%
Class III	83	27.5%
Class IV	124	41.06%
Class V	28	9.3%
Age of the child in months		
<6 months	37	12.3%
6–11	67	22.2%
12–23	86	28.5%
24–59	112	37.1%
No of children		
≤2	183	60.5%
>2	119	39.5%
Sex of the child		
Male	169	56%
Female	133	44%

Perception of the Magnitude of the Child's Illness and Time Taken by the Mothers to Avail Health Care for Their Sick Child

The most frequent symptoms perceived by the mothers during their child's illness were fever 163 (53.9%), cough 128 (42.4%), excessive crying 89 (29.5%), fast breathing 36 (11.9%), and drowsiness 13(4.3%).

It was observed that 33 (11%) mothers sought health care for their sick child within a day of onset of illness, whereas 97 (32%) mothers availed themselves of health care in <3 days of symptom onset and 172 (57%) mothers availed health care after 3 days of symptom onset. Hence, in the current study, it was observed that there was delayed HCSB of mothers toward ARI in under-five children in a Sanquelim, Goa [Figure 1].

HCSB of Mothers for Their Sick Child

Figure 1 depicts the percentage of mothers who have availed of health care. In the present study, 77.4% of mothers sought health care for ARI in under-five children from a registered medical practitioner whereas 23.6% of mothers did not avail treatment. Of the mothers who did not avail health care from a registered medical practitioner sought non-medical health care for their sick child such as home remedies or visiting a traditional healer [Figure 2].

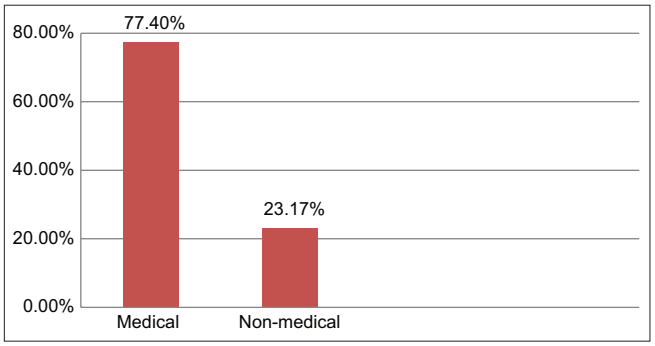

Figure 1: Health care availed by the mothers

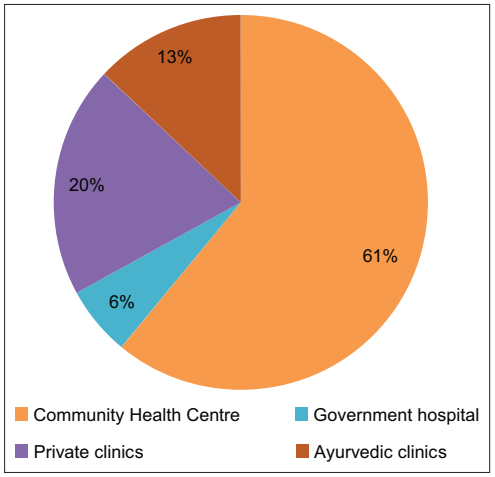

Figure 2: Various health care facilities visited by mothers

More than half of the mothers who sought health care took their child to a community health center (61%) while 20% of the mothers availed of treatment from private practitioners and very few mothers (6%) took the child to a government hospital [Figure 3].

Reasons for Not Seeking Health Care by the Mothers for their Sick Child

Figure 4 shows various reasons why the mother did not seek health care for their child with an ARI. In the current study, of the total mothers who did not seek health care, 34 (53%) of mothers treated their child with home remedies while 14 (21%) of the mothers could not avail treatment during child's illness due to non-availability of transport. Whereas, nearly one fourth (19%) of the total mothers could not avail health care for their sick child due to financial constraints. Of the total 5 (7%) mothers were unable to seek health care due to busy work schedules [Figure 4].

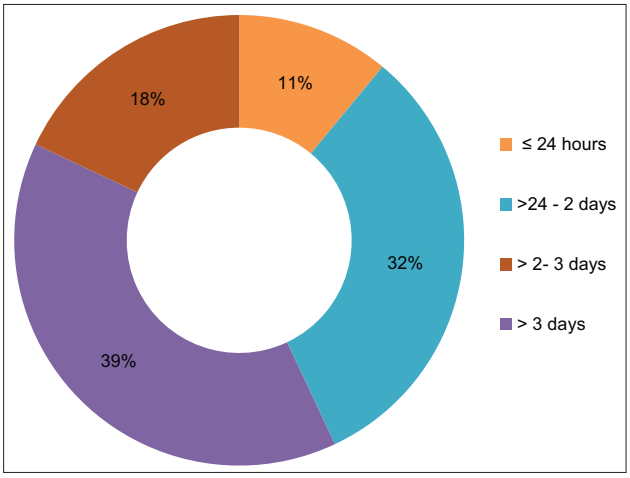

Figure 3: Time taken by the mother to seek health care for the sick child

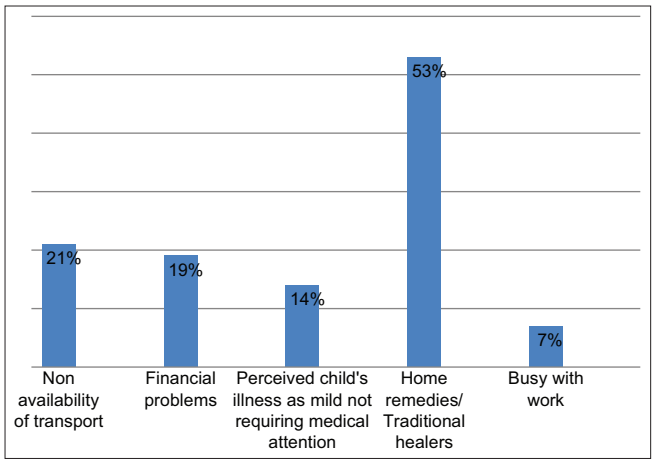

Figure 4: Reasons why mother did not seek health care for their child with acute respiratory tract infection

Factors Associated with Mothers' HCSB toward ARI in Under-five Children

Mothers with a male child had odds of seeking health care 4.40-fold (OR: 4.40, 95% confidence interval [CI]: 2.510, 7.730) higher than the girl child. Mothers with parity of one had odds of health-seeking 0.359-fold (OR: 0.359, 95% CI: 0.197, 0.655) lower than mothers with parity of two and above. Mothers who were married had odds of seeking healthcare 41-fold (OR: 41.488, 95% CI: 13.95–123.334) than mothers who were single/divorced/widowed. Mothers with higher educational status were 2.08- fold (OR: 963, 95% CI: 0.336–2.757) likely to seek health care than those with no formal education. It was also observed in the current study that mothers with a sick child less than a year were 3-fold (OR = 1.78, 95% CI: 1.02, 4.13) more likely to seek healthcare than those whose child was >1 year [Table 2].

DISCUSSION

This study primarily aimed to assess the health-seeking behavior of mothers toward ARI in under-five children in Sanquelim, Goa.

In the current study, it was observed that the proportion of mothers seeking healthcare care for ARI in under-five children, from a registered medical practitioner was 77.4% which was similar to the finding reported in a study conducted by Ghosh *et al.*[11] among mothers of children in the age group 0–59 months in a rural area in Darjeeling district, in West Bengal which reported the proportion of health-seeking behavior among mothers to be 72.3%.

However, a study conducted by Astale *et al.*[12] on Help-Seeking behavior for Children with Acute Respiratory Infection in Ethiopia reported only 27.2% of mothers took their child to a health care facility. A similar study conducted by Wardlaw *et al.*,[13] reported the prevalence of Health seeking behavior in developing countries to be 54% and South Asia was about 59%.

It was observed in our study that more than half of the mothers who sought health care took their child to the community health center (61%) while 20% of the mothers availed of treatment from private practitioners and very few mothers (6%) took the child to the government hospital. However, in a study conducted by Minz *et al.*[14] in an urban slum of Lucknow, the respondents primarily preferred a qualified private practitioner (65.4%), followed by an unqualified private practitioner (26.9%) and a tertiary care health center (7.8%). Another study by Annadurai *et al.*[15] in Tamil Nadu reported that around 81.15% of the caregivers preferred a private doctor during any childhood illness and as few as 18.85% preferred a government health center

Table 2: Factors associated with mothers' health care seeking behavior toward childhood ARI in under five children in Sanquelim, Goa 2020

Variables	Mothers seeking treatment from health care facility			
	Healthcare sought	No healthcare sought	Chi-square	OR (95% CI)
Marital status				
Married	223	43	0.00	41.488 (13.95–123.334)
Single/Divorced	4	32		
Educational status				0.046 (0.16–0.134)
Illiterate	3	10	0.00	0.322 (0.124–0.837)
Primary schooling	52	77		0.963 (0.336–2.757)
Secondary schooling	67	41		
Higher education	35	17		
Sex of the child			0.000	4.404 (2.510–7.730)
Male	137	32		
Female	95	38		
Parity				
<2	125	58	0.001	2.784 (1.52–5.075)
>2	102	17		

In the current study, mothers with a sick child less than a year were 3-fold (OR = 1.78, 95% CI: 1.02, 4.13) more likely to seek healthcare than those whose children were >1 year. The finding was consistent with the studies by Sreeramareddy *et al*.,[16] Dey *et al*.,[17] Sankarapandian *et al*.,[18] and Page *et al*.[19] who had shown that the younger the age group of children, more health care utilization than others. In our study, we observed that female children had lower odds of being taken to a health facility during the time of illness. A study done by Sreeramareddy *et al*.[16] had shown similar findings, wherein a female child had lower odds of being taken to healthcare providers (AOR 0.87, 95% CI: 0.78–0.97) which is consistent with the findings in our study which shows that female children had lower odds while a male child had higher odds of seeking health care. A study by Yerpude *et al*.[20] done among the rural population of Gujarat had a difference in the health-seeking behavior with male children given earlier access and better care toward the ailments in comparison to their female counterparts.

In the present study, mothers with higher educational status were 2.08-fold (OR: 963, 95% CI: 0.336–2.757) likely to seek health care than those with no formal education. Similar findings were observed in a study conducted by Manna *et al*.[21] wherein, there was a significant association between education and health-seeking behavior among mothers.

Our study reported that of the total mothers who did not seek health care, 34 (53%) of mothers treated their child with home remedies while 14 (21%) of the mothers could not avail treatment during child's illness due to non-availability of transport. Whereas, nearly one fourth (19%) of the total mothers could not avail health care for their sick child due to financial constraints. Of the total 5 (7%) mothers were unable to seek health care due to busy work schedules. A study conducted by Mishra *et al*.[22] revealed that the reasons for not seeking healthcare were mainly due to the use of home remedies suggested by family members and neighbor's (48.79%), loss of wages (17.07%), previous experience with the health services (17.07%), and lack of knowledge about the danger signs of acute childhood illness (17.07%).

ACKNOWLEDGMENTS

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DECLARATIONS

Ethical Approval

Approval taken from Institutional Ethics Committee of Goa Medical College, Bambolim.

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Original Article

Oral Manifestations of Coronavirus Disease-2019: A Questionnaire-Based Study

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Abstract

Introduction: Coronavirus disease 2019 (COVID-19) is an infectious disease caused by a recently discovered coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Aim: The questionnaire survey aims to raise awareness about the importance of the oral manifestations in COVID-19 patients.

Methodology: An online questionnaire survey was conducted, which included 150 patients who were confirmed reverse transcription polymerase chain reaction-positive cases of COVID-19. The questionnaire consisted of four sections. The 1st section included demographic data. The 2nd section included questions about the commonly reported COVID-19 symptoms that patients suffered. The 3rd section included questions that referred to oral manifestations the patients complained of while being infected with COVID-19. The 4th section included questions regarding general measures to be taken to prevent COVID-19.

Results: A total of 121 patients (50.4% of males and 49.6% of females) were included in this survey as they fulfilled all the criteria. It was reported that 21.5% experience taste disorder/alteration of taste, 15.7% experienced non-specific oral ulcerations, gum ulcerations, colored pin point lesions, infections, 6.6% experienced burning sensations in mouth, and 17.4% experienced change in the consistency of saliva.

Conclusion: As per the results in our study, patients who had tested positive for COVID-19 infection also had associated symptoms in the oral cavity, which emphasizes the role of oral examination of patients with COVID-19 infection.

Key words: Oral manifestations, Taste disorder, Saliva consistency, COVID-19

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by a recently discovered coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In December 2019, a case series was reported and confirmed in Wuhan, China.[1,2] On March 11, 2020, the World Health Organization declared it as a pandemic.[3] This disease can cause mild symptoms or cause progressive respiratory failure in adult patients, leading to death.[2] The most frequently reported signs and symptoms in a study involving 138 hospitalized patients in Wuhan, China, included fever (98.6%) and fatigue (69.6%). Other documented symptoms are dry cough, diarrhea, nausea, dizziness, vomiting, headache, myalgia, and dyspnea.[4,5]

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Coronavirus attacks human cells by angiotensin-converting enzyme 2 (ACE2) receptors since the current evidence indicated that ACE2 acts as the primary host cell receptor for SARS-CoV-2.[6] As such, the virus will bind to ACE2 using the spike-like protein on its surface, and ACE2 will serve as a cellular portal for viral entry into the cell to cause COVID-19 infection.[7] Hence, organs with high ACE2 expression (e.g., lung) can become target cells during SARS-CoV-2 infection that causes inflammatory reactions in related organs and tissues, such as salivary glands and tongue, which could explain

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the occurrence of both loss of taste and oral ulceration due to destruction of keratinocytes and oral fibroblasts.[2]

The oral signs and symptoms related to COVID-19 are taste disorders, unspecific oral ulcerations, desquamative gingivitis, petechiae, and coinfections such as candidiasis.[8]

The oral cavity is known to be an indicative mirror reflecting the underlying health condition. Therefore, careful examination of the mouth will assist in early diagnosis and treatment since some oral symptoms that can be associated with certain systemic disorders.[9] The aim of present work was to evaluate the oral manipulation which could be associated with mild-to-moderate cases of COVID-19 infection.

Aims and Objectives

The main objective of this study was to highlight the oral manifestations which could be reported in mild-to-moderate cases of COVID-19. Moreover, our goal was to spread awareness among physicians, general and dental practitioners, about these oral symptoms so that early diagnosis could be achieved, thus maintaining patient's ultimate health and welfare.

SUBJECTS AND METHODS

Study Design

An online questionnaire was designed for this investigation. A total of 150 patients from the Jammu (J and K), who recovered from COVID-19 were included, and voluntarily participated in answering the questionnaire. A web-based survey tool (Google Forms) was used to design the questionnaire. A sharable link on Google Drive was sent through a WhatsApp message.

Exclusion Criteria

The following criteria were excluded from the study:

- Failure to complete the whole questionnaire
- Patients with poor oral hygiene or suffering from any of the oral symptoms investigated before the pandemic
- Patients with chronic illnesses
- Smokers
- Alcoholics
- Patients with serious COVID-19 infection, who experienced severe respiratory failure (severe pneumonia, severe dyspnea, an increased respiratory rate of >30 breaths/min, and a decreased oxygen saturation of <93%) or patients who required hospitalization.

Inclusion Criteria

The following criteria were included in the study:

- Laboratory-confirmed COVID-19 infection (the polymerase chain reaction test)
- Non-smokers
- Non-alcoholics
- Medically free patients
- Patients with mild-to-moderate symptoms; patients with good oral hygiene and not suffering from any oral manifestations before the pandemic.

Questionnaire Tool

The questionnaire consisted of four sections and a total of 16 questions. The 1st section included demographic data. The 2nd section contained questions included questions about the commonly reported COVID-19 symptoms the patients suffered. The 3rd section included questions that referred to oral manifestations the patients complained of while being infected with COVID-19. The 4th section included questions regarding general measures to be taken to prevent COVID-19 transmissions.

Statistical Methods

The recorded data were compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0. Continuous variables were expressed as Mean±SD and categorical variables were summarized as frequencies and percentages. Graphically, the data were presented by pie and bar diagrams. Chi-square test or Fisher's exact test, whichever appropriate, was employed for comparing oral manifestations as per age and gender. $P < 0.05$ was considered statistically significant. All P-values were two tailed.

RESULTS

A total of 121 patients who fulfilled all the prerequisite criteria in this questionnaire study were divided into two age groups ≤25 years, 42.1% ($n = 51$) and >25 years, and 57.9% ($n = 70$). The mean age of patients was 28.7 ± 9.17 (range: 18–55) [Table 1 and Figure 1]. There were 61 male and 60 female (50.4% of males and 49.6% of females)

Table 1: Age distribution

Age (Years)	Number	Percentage
≤ 25 Years	51	42.1
> 25 Years	70	57.9
Total	121	100
Mean±SD (Range)=28.7±9.17 (18-55)		

[Table 2 and Figure 2], among them 45 (37.2%) were health care workers.

In this study, we mainly included patients with mild-to-moderate symptoms, without severe respiratory failure, who were not hospitalized. The percentage of the respondents who suffered from any of the following symptoms such as fever, shortness of breath, headache, muscle pain, sore throat, diarrhea, exhaustion, and smell disorder was 44.6% ($n = 54$) and fever with chills was 21.5% ($n = 26$) [Table 3 and Figure 3].

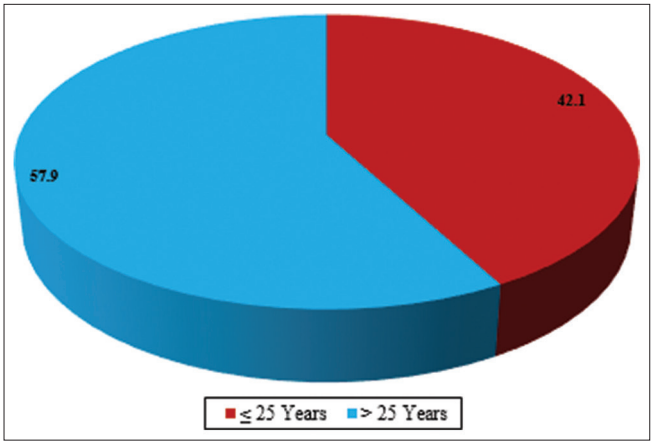

Figure 1: Age distribution

Table 2: Gender distribution

Gender	Number	Percentage
Male	61	50.4
Female	60	49.6
Total	121	100

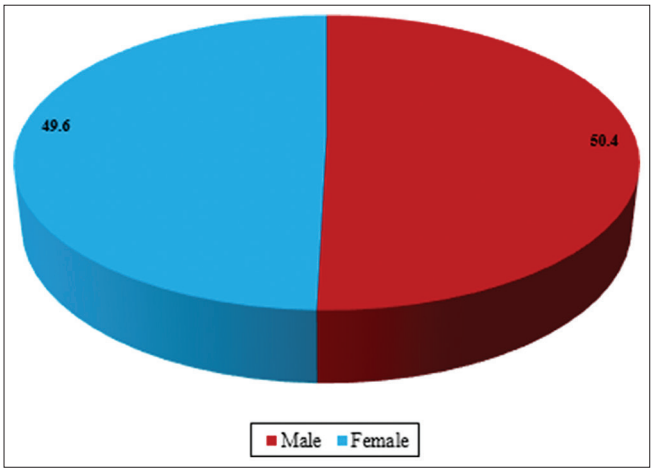

Figure 2: Gender distribution

Our results found that 48.7% ($n = 59$) of the patients had at least one of the oral manifestations, while about 51.3% ($n = 62$) did not have any symptoms related to the oral cavity.

Regarding taste disorder/alteration of taste, it was expressed as 21.5% ($n = 26$), oral ulcerations – 15.7% ($n = 19$), burning sensations in mouth – 6.6% ($n = 8$), and any change in the consistency of saliva – 17.4% ($n = 21$) [Table 4 and Figure 4].

The assessment of the incidence of oral manifestations in relation to the two investigated parameters (gender and age) was performed as follows:

- The assessment of the incidence of oral manifestations in relation to the patient's gender – the statistical analysis identified a significantly increased number of ulcerations in male patients as compared to females ($P = 0.014$); however, taste disorder/alteration of taste

Table 3: General systemic symptoms in study patients

Question	Response	Number	Percentage
Do you experience any of the following symptoms such as ,fever, shortness of breath, headache, muscle pain , sore throat, diarrhoea, exhaustion, smell disorder	Yes	54	44.6
	No	67	55.4
Fever with chills	Yes	26	21.5
	No	95	78.5

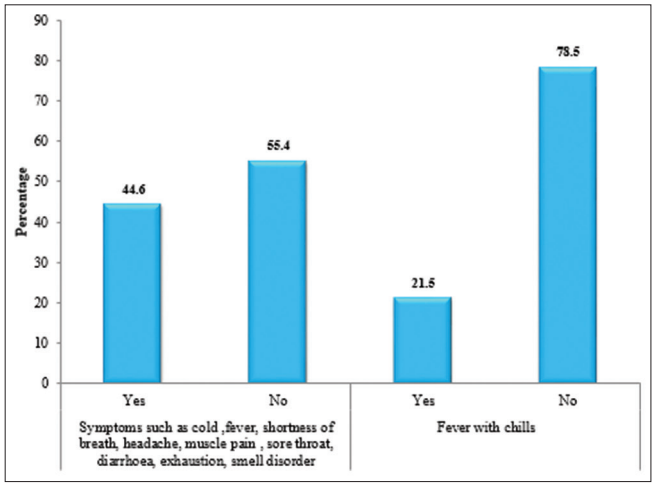

Figure 3: Analysis of COVID-19 symptoms in mild-to-moderate cases

Table 4: Oral manifestations in study patients

Oral manifestations	Number	Percentage
Taste disorder/ alteration of taste	26	21.5
Oral ulcerations	19	15.7
Burning sensations in mouth	8	6.6
Any change in the consistency of saliva	21	17.4
Oral manifestations (59, 48.7%)		

Table 5: Comparison of oral manifestations as per gender in study patients

Oral manifestations	Male		Female		P-value
	No.	%age	No.	%age	
Taste disorder/ alteration of taste	13	21.3	13	21.7	0.962
Oral ulcerations	15	24.6	4	6.7	0.014*
Burning sensations in mouth	2	3.3	6	10.0	0.137
Any change in the consistency of saliva	12	19.7	9	15.0	0.497

**Statistically Significant Difference (P-value<0.05)*

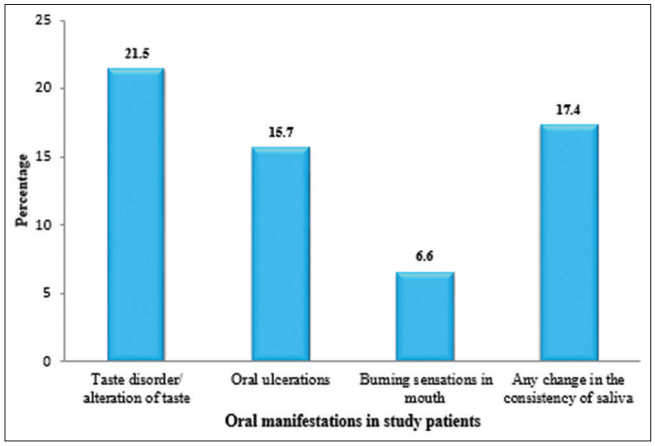

Figure 4: Analysis of the oral manifestations of COVID-19 in the respondents

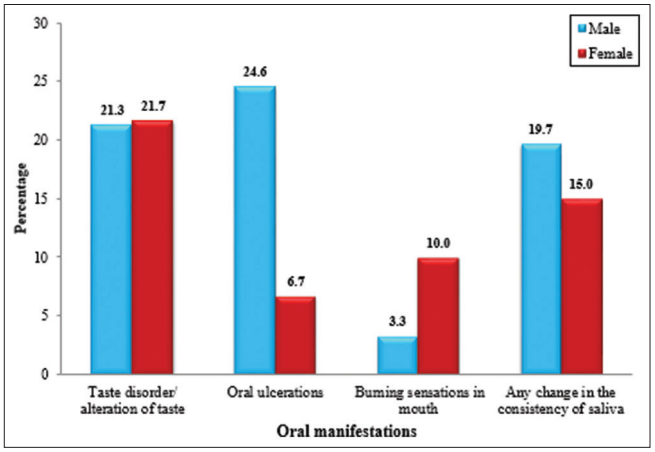

Figure 5: Incidence of oral manifestations according to the gender of the patients

($P = 0.962$), burning sensations in mouth ($P = 0.137$), and any change in the consistency of saliva ($P = 0.497$) were increased in females as compared to males [Table 5and Figure 5].

- The assessment of the incidence of oral manifestations in relation to the mean age of the respondents – the statistical analysis showed a non-significant difference in the mean age between the patients who complained of oral manifestations and those who did not ($P > 0.05$) [Table 6 and Figure 6].

DISCUSSION

COVID-19 patients have a wide variety of signs and symptoms, so the study of these manifestations will contribute to the early diagnosis and isolation of infected patients.[10] Furthermore, COVID-19 as an acute infection with multiple therapeutic measures could adversely affect oral health leading to opportunistic infections (e.g., recurrent herpes simplex virus [HSV-1] infection and oral ulcerations) due to the compromised immune system and xerostomia associated with the reduced salivary flow.[11] Clinical evidence shows that the oral mucosa is a primary site of entry for SARS-CoV-2, and is considered possibly at high risk of susceptibility to the 2019 novel coronavirus (2019-nCoV) infection. However, there is still uncertainty whether the above-mentioned oral manifestations result from direct viral infection or from systemic health deterioration and impaired immune system.[12]

In the present work, patients experienced the general signs and symptoms of COVID-19 infection, which are fever, cough, a sore throat, malaise, a headache, diarrhea, the loss of smell, the loss of taste, muscle pain, and dyspnea. This is in accordance with several clinical studies, which reported these symptoms as the most prevalent ones in mild and moderate cases of COVID-19 infection.[13]

In the current study, 21.5% of patients manifested taste disorder/alteration of taste. Taste disorders have been reported in a variety of clinical problems.[14] Amblygeustia, a diminished sensitivity of taste, was shown to be manifested by a relatively high proportion of patients

Table 6: Comparison of oral manifestations as per age in study patients					
Oral manifestations	≤ 25 Years		> 25 Years		P-value
	No.	%age	No.	%age	
Taste disorder/ alteration of taste	8	15.7	18	25.7	0.185
Oral ulcerations	6	11.8	13	18.6	0.087
Burning sensations in mouth	3	5.9	5	7.1	0.783
Any change in the consistency of saliva	11	21.6	10	14.3	0.296

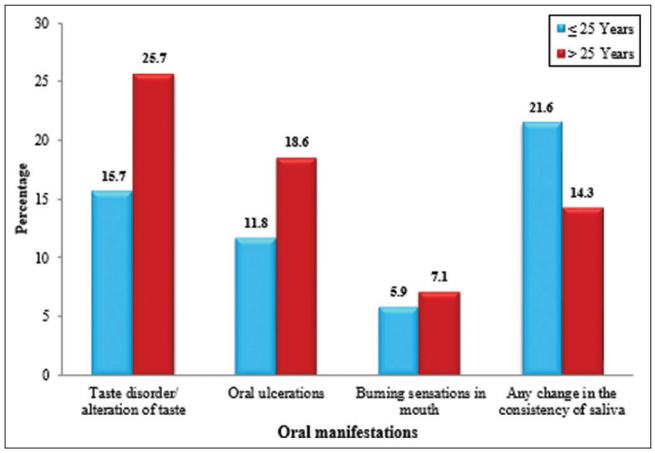

Figure 6: Incidence of oral manifestations according to the age of the patients

with COVID-19.[15] A possible reason for the loss of taste in COVID-19 might be due to the increasing number of ACE-2 receptors on the tongue keratinocytes, and the keratinocyte cell death and slough production can block taste buds which can adversely affect taste perception.[16,17] Taste loss (ageusia) occurs due to the viral infection to the olfactory cranial nerve or from rhinitis and nasal obstruction. The loss of smell (anosmia) is related to retronasal olfaction which is a sensory process, combining orthonasal smell and taste patterns and enabling people to perceive flavor. This mechanism is temporarily disrupted during upper respiratory infections due to mucosal inflammation and obstruction of the nasal passages, thereby physically blocking flavor and odor molecules from entering the olfactory cleft.[18] In this study, consistent with the current evidence, olfactory dysfunction was the primary factor identified either with or without gustatory dysfunction.[8] Song *et al.* found that a loss of taste was more frequent (21%) than a loss of smell (11%) in hospitalized patients, with the loss of taste but not smell being associated with severe COVID-19.[19] Most patients recovered their smell and taste dysfunctions within 2 weeks.[19,20]

In the current study, 17.4% of patients manifested change in the consistency of saliva. This could be because of hyposalivation associated with COVID-19. In COVID-19, the impaired salivary gland secretions are often associated with xerostomia and taste loss.[21] In SARS-CoV infections, xerostomia could be aggravated by impaired nasal breathing due to nasal congestion and rhinorrhea, where the oral breathing increases and it can impaired salivary gland function and xerostomia is secondary.[22] Similar to COVID-19-induced oral mucosal lesions, pandemic-induced psychosocial factors have a greater impact on normal salivary gland function and quantitative secretions.[22,23]

Furthermore, 15.7% of COVID-19 patients reported the appearance of ulcers in their oral cavities. This is in accordance with several cases, in which blisters and oral ulcers occurred during COVID-19 infection.[12] It has been demonstrated that psychological upsets, such as anxiety and stress, contribute to the development and progression of oral lesions like recurrent aphthous ulcers, and this applies to COVID-19 patients.[24] It has also been proven that psychological distress stimulates the immunoregulatory mechanism by elevating the leukocyte count at inflammatory sites.[25] In addition, ACE2 is detected in the oral cavity and appears in high amounts in epithelial cells. It is elevated in the tongue, gingival, and buccal mucosa. These findings demonstrate that the oral mucosa may be a target for COVID-19 infection.[26]

In the current study, burning sensations in mouth were manifested in 6.6%. It could be due to several reasons (e.g., candidal infection, dry mouth, oral ulceration, or drug induced). Evidence show that viral infection could weaken the immune system, thus creating secondary infections such as oral candidiasis. Candidiasis is the most prevalent opportunistic infection in HIV and is also reported in COVID-19.[27]

In addition, 48.7% (n = 59) of COVID-19 patients in the current study showed two or three of the above-mentioned oral manifestations concurrently. This could be due to the interaction of several mechanisms in the oral cavity, where ACE2 plays the major role due to its presence in various oral tissues.[26]

The assessment of the incidence of oral manifestations in relation to the two investigated parameters showed that regarding gender, ulcerations were significantly more common in males than females. This is in accordance with a previous study, which showed the preponderance of ulcers among males.[28] However, this is opposite to the findings of other investigation, which reported female prevalence.[29] In the present study, it was probably hard

to say what type of ulceration was present in the infected patients, since clinical examination was not applicable in those patients. However, we assumed that these ulcerations might be aphthous ulcers, as it has been reported that psychological stress plays an important role in the progression of recurrent aphthous ulcers, which is the case in nearly all COVID-19 patients, who experienced a very stressful situation.[24] Regarding the age of the patients, most of the manifestations were significantly more common in >25 years of age group.

CONCLUSION

Our study had few limitations. First, the main methodological limitation is the limited sample size. Second, this is an online questionnaire; thus, we have not been able to document the patient's full history and a clinical oral examination (e.g., length of infection, the severity of the case, oral hygiene, habits, and the taken medications), which might have a misleading impact on the results. Despite the limitations, this online questionnaire study's findings could help understand the oral manifestations associated with COVID-19. It was proven that mild-to-moderate cases of COVID-19 infection were associated with oral manifestations, with variable incidence. Further clinical studies with larger sample sizes and detailed patient's history are required to confirm our results and clarify the full impact of COVID-19 on the oral tissues.

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Original Article

Local Infiltration and Intraperitoneal Instillation of Ropivacaine versus Local Ropivacaine Infiltration alone for Post-Operative Pain Control in Elective Cesarean Section

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Abstract

Introduction: The post-operative period is as important as the pre-operative and intraoperative period for an anesthesiologist. The aim should be to get pain free and comfortable patients after every surgery whether it is done in regional or general anesthesia. Spinal anesthesia is used routinely for cesarean sections, but its effect lasts for few hours only, so to make patients pain free, different multimodal analgesia techniques with minimal side effects have been tried for post-parturient as they may also have a negative impact on the health of a newborn infant. As already studied, inj. ropivacaine is comparatively safer option than inj. bupivacaine. For post-operative analgesia in patients underwent cesarean surgery, we tested local infiltration of injected ropivacaine alone against both intraperitoneal instillation and local infiltration.

Aims and Objectives: Inj. ropivacaine 0.2% intraperitoneal instillation and local infiltration for the management of post-operative pain after elective cesarean section under spinal anesthesia were evaluated against inj. ropivacaine 0.2% inj. local infiltration alone in the present study.

Materials and Methods: An American Society of Anesthesiologists Grades I and II pregnant woman undergoing spinal anesthesia for an elective cesarean section was separated into two groups randomly (R1 and R2 group, each have 30 patients). A 20 mL injection of 0.2% ropivacaine was administered to Group R1 patients before the skin closure at an incision site and patients in Group R2 administered with intraperitoneal instillation of inj. ropivacaine 0.2% in 5 mL Inj. before peritoneum closure and local infiltration of 15 mL inj. ropivacaine at the site of incision, before skin closure. During the post-operative period, visual analog scale (VAS) was used to measure pain intensity, and the analgesia duration was evaluated by timing the beginning of the sensory block to the time at which additional analgesia was requested. Patients' hemodynamic and side effects data were also collected.

Results: Group R2 had a considerably extended analgesia duration than Group R1 ($P < 0.05$). 147.17 ± 4.67 and 170.33 ± 3.69 min were the mean (±SD) analgesia duration in R1 and R2 groups, respectively. At the time of the initial analgesic request, the following mean (±SD) VAS values were observed: Group R1 – 36.7 ± 5.14 and Group R2 – 32.6 ± 6.52.

Conclusion: Combining inj. ropivacaine 0.2% local infiltration with intraperitoneal instillation improves post-operative analgesia in cesarean section than using inj. ropivacaine 0.2% local infiltration alone under spinal anesthesia.

Key words: Cesarean section, Intraperitoneal instillation, Local infiltration, Ropivacaine, Spinal anesthesia

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INTRODUCTION

Nowadays, the use of a cesarean section for delivery has become very frequent.[1] About 15–20% of all deliveries are done with cesarean section over the world whereas the numbers (40%) are more in developing countries.[2] We can use multiple anesthesia techniques for cesarean sections such

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as spinal, epidural, spinoepidural, or general anesthesia. Like any surgery, cesarean section is also associated with intense pain postoperatively that can be treated with opioids or nonsteroidal anti-inflammatory drugs, or combination. We cannot use IV opioids in parturients as they need to nurture their newborn baby and are associated with side effects such as urinary retention, respiratory depression, vomiting, pruritus, as well as nausea.[1,3] The pain after surgery makes the post-anesthesia period more uncomfortable and it interferes with emotional bonding to develop with the newborn and to start breastfeeding, also increases hospital stay and cost of the stay.[3,4]

Opioids are necessary for the treatment of severe pain and epidural analgesia needs close supervision, but non-opioid systemic analgesics are ineffective in reducing pain.[1,5] Ropivacaine, a long-acting local anesthetic, is a pure left isomer with lower toxicity potential on the central nervous system and cardiovascular system than bupivacaine. Ropivacaine lowers opioid intake by blocking painful impulses from the injury site through reversible hyperpolarization of peripheral nerve fibers.[6]

MATERIALS AND METHODS

Informed approval and consent from the Institutional Ethics Committee were required for this prospective randomized clinical study on 60 pregnant women with American Society of Anesthesiologist Grades I and II undertaking elective cesarean sections, scheduled under spinal anesthesia which were involved and operated by the same surgical team. All patients were blinded about group allocated, exclusion criteria for the study were known sensitivity background to local anesthetics of amide-type, patient's refusal, skin site infection, patients on opioids, valvular heart disorders, elevated intracranial tension, endocrinal diseases, renal diseases, metabolic disorders, coagulation disorders, hepatic disorders, as well as cesarean section under epidural/general anesthesia. The envelope method was used to randomly divide the patients into two groups.

Group R1 (n = 30) – 20 mL of local infiltration inj. ropivacaine 0.2% at site of incision.

Group R2 (n = 30) – 15 mL inj. ropivacaine 0.2% is injected locally at the incision site, and 5 mL inj. ropivacaine 0.2% is injected intraperitoneally. As a preoperative preparation, an intradermal sensitivity test for ropivacaine was performed on all patients. Inj. glycopyrrolate 0.2 mg I.M was administered 30 min before induction of anesthesia, inj. ranitidine 50 mg and inj. metoclopramide 10 mg to all patients. Preloading with ringer lactate in a dose of 10 ml/kg BW with 18G cannula was done before induction of anesthesia. On the surgery day, the patient was brought into the OT, and the multipara monitor consisted of heart rate (HR), non-invasive blood pressure (BP), SpO_2 (pulse oximeter), as well as electrocardiography was attached. In the left lateral decubitus site, a Quincke spinal needle of 25-gauge was used to execute a midline subarachnoid block at L3/4 or L2/3 intervertebral space, as well as all aseptic precautions were followed. After the free flow of cerebrospinal fluid, inj. bupivacaine 0.5% 2 ml was injected intrathecally. After that, the patients were put in a supine posture and prepared for the procedure. After completion of surgery, 20 ml of 0.2% inj. ropivacaine hydrochloride was infiltrated in group R1 subcutaneously while in Group R2, intraperitoneal instillation, as well as local infiltration both, was done. A 26-gauge needle was used to measure the degree of sensory block and the results were reported as a lack of feeling to a pinprick. The Bromage scale was used to record motor blocks. The aim was to study the efficacy of ropivacaine when used in combination in relieving pain compared to ropivacaine used locally alone. "Visual analog scale" [VAS] evaluates the degree of pain which was already explained to all patients beforehand. The highest point on the scale, 100, indicates very severe pain, whereas the lowest point, 0, denotes no pain at all.

Rating of VAS Score

1. 0: No pain
2. 1–25: Mild pain
3. 26–50: Moderate pain
4. 51–75: Severe pain
5. 76–100: Very severe pain.

Criteria of Bromage Score Grade

1. Grade 0 – Feet and legs can move
2. Grade 1 – Knees just flexed, feet free to move
3. Grade 2 – Knees are unable to bend and feet are just slightly able to move
4. Grade 3 – Feet and legs are unable to move.

Before spinal anesthesia, baseline measurements were taken. HR, systolic and diastolic BP (DBP), electrocardiogram, SpO_2, as well as respiratory rate were monitored perioperatively. After intrathecal injection, data were collected at 0, 5, 10, 20, 30, 45, and 60 min and then every hour for the next 8 h. During the intraoperative and post-operative periods, patients were constantly monitored for problems such as vomiting, nausea, respiratory depression, hypotension, dyspnea, shivering, chest pain, bradycardia, dysrhythmia, and any other symptoms within the first 24 h

after surgery. No cases of any complications were recorded in this study.

The observations were analyzed to statistical analysis with Student's "*t*-test," and for qualitative parameters, "Chi-square test" has been employed. Statistical analysis was performed on the data collected from all three study groups and represented in tabular form using Statistical Package for the Social Sciences version 17 statistical software. For intergroup comparison, $P > 0.05$ and $P < 0.05$ were deemed as insignificant and significant, respectively. In this case, the level of significance was fixed at $P < 0.01$.

RESULTS

Table 1 represents parturient in both the groups is similar in the context of weight, mean age, sex, height, duration of anesthesia, as well as surgery type.

Pre-operative and intraoperative HR, systolic BP, DBP, mean BP, and SpO_2 were comparable in both groups.

At the time of the initial request for analgesic, the following mean (±SD) VAS values were observed: Group R1 – 36.7 ± 5.14 and Group R2 – 32.6 ± 6.52 [Table 2].

DISCUSSION

Cesarean section is associated with moderate pain after the wearing-off effect of spinal anesthesia. The multimodal approach is quite convincing to reduce post-operative pain in the parturient. More recently, anesthesiologists are focusing on preemptive analgesia which means that analgesics are sufficiently given before patient experiences pain so that pain intensity can be reduced postoperatively and the requirement of painkillers also can be minimized. Wound infiltration with long-acting or intermediate-acting local anesthetics is simple as well as safest technique, used by anesthesiologists all over the world.

Table 1: Demographic variables of two groups

Demographic data	Group R1	Group R2	*P*-value
Age (years)	26.5±5.871	25.1±4.4	0.300
Weight (kg)	58.2±5.1	57.3±5.57	0.516
Sex (female)	100%	100%	–
Height (cm)	150.73±3.16	150.97±2.73	0.745

Table 2: Mean (±SD) time for first rescue analgesia in two groups

Variable	Group R1 (*n*=30)	Group R2 (*n*=30)	*P*-value
	Mean±SD	Mean±SD	
Time for first rescue analgesia (min)	147.17±4.67	170.33±3.69	<0.0001

Ropivacaine 0.2% intraperitoneal instillation as well as local infiltration, as opposed to 0.2% ropivacaine local infiltration alone, extends the analgesia duration as well as gives satisfactory analgesia (reduced VAS rating). When performing surgical operations, local infiltration around the incision site and even deeper in the surgical cavity may limit the formation as well as spread of injury-induced release. The effect of certain local anesthetics may be attributable in part to their ability to suppress nociception transduction as well as sensitization phases. By suppressing certain inflammation stages (such as neutrophil priming) and block several of the neuronal routes activated due to inflammation (such as some G protein-coupled receptors and protein kinase C), local anesthetics can impede inflammatory and local sensitizing responses on the affected area.[7,8]

Nguyan *et al.*[1] also identified that ropivacaine infusion after cesarean surgery considerably extended the duration it took to achieve rescue analgesia in comparison to the control group. Ropivacaine is a local anesthetic of long-acting amide type with chemical properties comparable to that of bupivacaine but it is less toxic than it.[9]

Intraperitoneal inj. of ropivacaine before and after laparoscopy considerably reduced post-operative pain in comparison to a placebo, according to a study by Labaille *et al.*[10] Table 3 demonstrates that 147.17 ± 4.67 and 170.33 ± 3.69 min were the mean (±SD) analgesia duration in R1 and R2 groups, respectively. The analgesia duration in R2 group was considerably longer as compared to R1 group based on comparison and statistical analysis ($P < 0.0001$).

Gautam *et al.*[11] found that intraperitoneal instillation of inj. ropivacaine 0.2% intraperitoneal infiltration as well as local infiltration provided greater post-operative analgesia after cesarean section than only inj. ropivacaine 0.2% local infiltration under spinal anesthesia. Yong *et al.*[12] conducted a meta-analysis and systematic review comparing intraperitoneal ropivacaine instillation versus no instillation to alleviate the pain during laparoscopic cholecystectomy and discovered that pain at 4–8 h and 9–24 h was considerably lowered with intraperitoneal ropivacaine instillation.

In another study, Kaushal-Deep *et al.*[13] compared the effectiveness of 0.2% ropivacaine injected intra-incisional and intraperitoneally in patients receiving an uncomplicated laparoscopic cholecystectomy and found that this was a cost-effective method for discharging an estimated nine out of 10 patients on the same day.

Other investigations have represented comparable outcomes.[14-16] At the time of the initial request of analgesic,

Table 3: Comparison of Mean±SD VAS scores in two groups

Variable	Group R1 (*n*=30)	Group R2 (*n*=30)	*P*-value
	Mean±SD	Mean±SD	
VAS score	36.7±5.14	32.6±6.52	0.009

VAS: Visual analog scale

the following mean (±SD) VAS values were observed: Group R1 – 36.7 ± 5.14 and Group R2 – 32.6 ± 6.52 ($P = 0.009$). Ropivacaine infiltration following hemorrhoids surgery decreased VAS ratings considerably and reduced total morphine use, as shown by Vinson-Bonnet *et al.*[17] Callesen *et al.*[18] demonstrated that ropivacaine by combining field block and intraperitoneal instillation to alleviate pain following laparoscopic sterilization results in a considerably lower cumulative pain rating when contrasted with the placebo group during coughing as well as movement. The greatest disparity in pain levels was noticed 1 h after the procedure, however, there was no difference between groups after 4 h. Several additional researches have found comparable results.[19-22]

CONCLUSION

Ropivacaine 0.2% intraperitoneal instillation as well as local infiltration were shown to provide greater post-operative analgesia after cesarean section in comparison to ropivacaine 0.2% local infiltration alone while the patient was under spinal anesthesia, as per the outcomes of the clinical tests. Intraperitoneal instillation of 0.2% ropivacaine local inj. also increased the analgesia duration as well as gave better analgesia (reduced VAS value) than 0.2% local infiltration of ropivacaine alone.

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Original Article

Preemptive Glycopyrrolate and Hemodynamic Consequences in Spinal Anesthesia

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Abstract

Background: Hypotension is most common side effect of spinal anesthesia caused by decrease in systemic vascular resistance or cardiac output.

Materials and Methods: This randomized study was conducted in 104 patients of physical status American Society of Anesthesiologists I and II, who have to undergo total abdominal hysterectomy for various gynecological reasons. Patients were allocated into their respective groups by computer-generated random numbers in blocks of 52 to receive either 2 mL of 0.9% sodium chloride (Group A) or glycopyrrolate 4 mcg/kg made up to 2 mL with 0.9% sodium chloride (Group B). Parameter (heart rate, systolic blood pressure (BP), diastolic BP, mean BP, respiratory rate, and saturation of peripheral oxygen) were recorded at 1 min, 5 min, 10 min, 20 min, 30 min, 45 min, and 60 min after spinal anesthesia. Vasopressor requirement and any side effect were recorded.

Results: It was found that glycopyrrolate group was more hemodynamically stable than control group. There was significant reduction in spinal induce hypotension in Group B (study group) with $P < 0.0001$ after spinal anesthesia. Thus, there was reduced need of vasopressor in the glycopyrrolate group which was statistically significant. Study was also showed that glycopyrrolate prevent spinal induce bradycardia after 10 min of spinal anesthesia. It was also statistically significant with *P*-value at 10 min = 0.04 and at 20 min = 0.003.

Conclusion: Intravenous glycopyrrolate before spinal anesthesia prevents spinal induce hypotension and bradycardia and also reduces requirement of vasopressor for the treatment of hypotension.

Key words: Bupivacaine, Glycopyrrolate, Hypotension, Normal saline, Spinal anesthesia

INTRODUCTION

Hypotension following spinal anesthesia occurs in up to 83% of cases if no steps are taken to prevent it.[1] Performance of a spinal/epidural block produces vasodilatation within the blocked area and a reflex vasoconstriction in unblocked areas of the body to maintain blood pressure (BP).[2] Imbalance between vasodilatation and vasoconstriction is the most common mechanism underlying hypotension associated with spinal/epidural analgesia and occurs if the block is widespread or in the presence of hypovolemia, even with a limited block.[3] The mechanism for vasodilatation is blockade of the sympathetic nerve fibers at the preganglionic level. It has been generally believed that the sympathetic block extends one to two segments higher than the somatic level.[4] The heart rate (HR) during a high neuraxial block typically decreases as a result of blockade of a cardioaccelerator fibers arising from T1 to T4. The HR may decreases outflow from intrinsic chronotropic stretch receptors located in the right atrium and great veins.[5] Despite more than three decades of research, hypotension during spinal anesthesia remains a common clinical problem that is associated with morbidity for the patient. An effective method for preventing hypotension has been referred to as the "Holy Grail" of anesthesia and has yet to be described.[6]

A number of strategies for preventing hypotension have been investigated. These strategies have included the

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use of intravenous fluid preload, gravity (Trendelenburg or leg rising), compression devices on the legs, and prophylactic vasopressor.[7] Ephedrine and phenylephrine are common vasoconstrictor drugs and their effects on hypotension during anesthesia have been compared in many studies. Although no definite difference has been observed between two drugs regarding the prevention of hypotension following spinal anesthesia, some prefer ephedrine and others preferred phenylephrine depending upon the condition of the cardiac status of the patient, that is, whether the patient is able to tolerate tachycardia or not. Each vasopressor, either ephedrine or phenylephrine, has their own pros and cons.[8]

The physiopathological mechanism involved in the occurrence of hypotension is systemic vascular resistance and central venous pressure from sympathetic block with vasodilatation.[9,10] Bradycardia can occur from shift in cardiac autonomic balance toward the parasympathetic system, from activation of the left ventricular mechanoreceptors from a sudden decrease in the left ventricular volume (Bezold-Jarisch reflex).[11] Glycopyrronium bromide is a medication of the muscarinic anticholinergic group. It does not cross the blood–brain barrier and consequently has no to few central effects.[12] Its actions include among others a prolonged inhibition of gastro-intestinal tract motility and secretion. The antisialagogue effect was shown to be about 5 times as potent as that of atropine. Studies in conscious healthy volunteers have consistently shown an absence of significant effects on HR and rhythm following doses of glycopyrrolate which might be used in premedication in anesthetized patients, using larger intravenous doses, glycopyrrolate, and atropine both produced a rise in HR with glycopyrrolate being approximately twice as potent (w/w) as atropine. The effects of the drug on HR in conscious adult patients are not well documented, particularly with reference to dose-response relationships. However, the effects on HR are quite apparent in anesthetised patients.[13] Most recently study has been shown that glycopyrrolate has a significant and prolonged bronchodilating action, leading to an increase in dead space similar to that following the administration of atropine but persisting for a longer period of time.[14,15]

The purpose of this study is to investigate whether the combination of rapid crystalloid cohydration with 0.2 mg of glycopyrrolate would be more effective at preventing hypotension than crystalloid infusion alone and whether this technique would prove to be an effective method for eliminating intraoperative hypotension.

MATERIALS AND METHODS

A total of 104 patients were enrolled for the study of age group 18–65 years of physical status American Society of Anesthesiologists I and II, after the approval from Institutional Ethics Committee. The design of the study was prospective randomized, comparative study. Patients who have undergone total abdominal hysterectomy for various gynecological reasons and fulfilling the criteria for regional anesthesia were taken for study after written informed consent. A detailed history, thorough physical examination, routine investigation such as complete blood count, blood sugar, renal profile, serum electrolytes, and any special investigation if required was done for the study. Patients who had coagulopathy, sepsis at the site of intrathecal injection, major organ pathology such as heart disorder, hepatic, and renal disorder were excluded from the study. After all standard preparations, routine monitoring devices such as electrocardiogram leads, noninvasive BP cuff, and pulse oximetry probe, were attached to patient. An intravenous access with 18 gauge intravenous cannula was secured. Patients were allocated into their respective groups by computer-generated random numbers in blocks of 52 to receive either 2 mL of 0.9% sodium chloride (Group A) or glycopyrrolate 4 mcg/kg made up to 2 mL with 0.9% sodium chloride (Group B), prepared with the identical syringe, contents of which were unknown to the anesthetists involved in the case. Preload of 15 mL/kg Ringer's lactate solution was given over 10 min. The study drug or placebo was then given over 2 min. The subarachnoid space was then located using a 26-guage Quincke needle and 0.5% hyperbaric bupivacaine 3.0 mL injected intrathecally. Parameter (HR, systolic BP [SBP], diastolic BP [DBP], mean BP [MBP], respiratory rate [RR], and saturation of peripheral oxygen [SPO_2]) was recorded at 1 min, 5 min, 10 min, 20 min, 30 min, 45 min, and 60 min after spinal anesthesia. Atropine atropine was given if HR is <60, and mephentermine was given if BP falls below 30% from baseline values. Vasopressor requirement was reported if needed during procedure. Any side effect also to be recorded if occurs such as nausea, vomiting, and dryness of mouth. Sample size was estimated using formula for simple random sampling as given below-

$$n = \frac{Z^2 p(1-p)}{l^2}$$

where n = required sample size, z = 1.96 at 95% confidence intervals (CIs) and 80% power, 5% alpha (type I error), p is the probability of difference in HR changes between glycopyrrolate and saline groups which was considered 23% based on pertaining literature as reported by Yentis[1] 2000. l = precision (marginal error) which was considered as 11.5% (a 50% relative precision to given p) this accumulation 51.44, thus we planned to enroll 52 samples in each group for the proposed study.

RESULTS

Table 1 shows the demographic parameters of age in both the groups [Graph 1].

Table 2 depicts the comparison of preoperative vital parameters among both the groups [Graph 2].

Table 3 depicts the comparison of vasopressor requirement [Graph 3]. In Group A, 44 required vasopressor and in Group B, only eight patient required vasopressor. $P < 0.05$ which was statistically significant.

Table 4 shows the comparison of frequency of vasopressor requirement in both the groups [Graph 4]. All the patients in Group A and only eight patients in the Group B required vasopressor. Only once in glycopyrrolate group whereas 14 patients in NS group required once, 15 patients required twice, 14 patients required thrice, and one patient required the vasopressor for the 4th time. $P < 0.05$ was statistically significant. Thus, there was higher frequency of vasopressor requirement in Group A in comparison to glycopyrrolate group.

Table 5 depicts the comparison of HR. Trend of HR showed that the groups differ significantly at 10, 20, and at 30th min with a $P = 0.04$, 0.003, and 0.028, respectively [Graph 5].

Table 6 shows the comparison of SBP where *P*-value of SBP at 5 min, 10 min, 20 min, and 30 min among the groups was <0.0001 which was statistically significant [Graph 6].

Table 7 shows the comparison of DBP where *P*-value of DBP at 1 min, 5 min, 10 min, 20 min, and 30 min among the groups was <0.0001 which was statistically significant [Graph 7].

Table 1: Demographic data: Age (years)

Age group	Treatment group (%)		Total (%)
	NS	Glycopyrrolate	
28–30 years	2 (3.8)	2 (3.8)	4 (3.8)
31–40 years	13 (25)	18 (34.6)	31 (29.8)
41–50 years	13 (25)	13 (25)	26 (25)
51–60 years	19 (36.5)	13 (25)	32 (30.8)
61–70 years	5 (9.6)	6 (11.5)	11 (10.6)
Total	52 (100)	52 (100)	104 (100)

Chi-square=2.02; *P*=0.73

Table 2: Comparison of pre-operative vital parameters

Variables	Group				*t*-test	*P*-value
	NS		Glycopyrrolate			
	Mean	SD	Mean	SD		
Age	48.33	10.504	46.94	10.513	0.672	0.503
Preop Pulse	77.79	7.212	77.31	8.886	0.303	0.763
Preop Sys	110.56	8.123	111.52	9.076	0.569	0.57
PreopDia	74.04	5.495	74.85	5.906	0.722	0.472
Preop MBP	86.19	5.671	86.98	6.494	0.659	0.511
Preop RR	12.38	0.565	12.67	0.964	1.861	0.066
Preop Spo2	100	0	100	0	0	1

MBP: Mean blood pressure, RR: Respiratory rate, SPO_2: Peripheral oxygen saturation

Table 3: Comparison of vasopressor requirement

Requirement of vasopressor	Treatment group (%)		Total (%)
	NS	Glycopyrrolate	
No	8 (15.4)	44 (84.6)	52 (50)
Yes	44 (84.6)	8 (15.4)	52 (50)
Total	52 (100)	52 (100)	104 (100)

Chi-square=49.85; *P*<0.0001

Table 4: Comparison of frequency of vasopressor requirement in both groups

Frequency of requirement of vasopressor	Treatment group (%)		Total (%)
	NS	Glycopyrrolate	
0	8 (15.4)	44 (84.6)	52 (50)
1	14 (26.9)	8 (15.4)	22 (21.2)
2	15 (28.8)	0 (0)	15 (14.4)
3	14 (26.9)	0 (0)	14 (13.5)
4	1 (1.9)	0 (0)	1 (1)
Total	52 (100)	52 (100)	104 (100)

Chi-square=56.56; *P*<0.0001

Table 5: Comparison of HR

Variables	Group				*t*-test	*P*-value
	NS		Glycopyrrolate			
	Mean	SD	Mean	SD		
HR 1 min	72.92	6.151	73.54	7.815	0.446	0.656
HR 5 min	69.6	5.825	71.13	7.035	1.215	0.227
HR 10 min	66.81	5.402	69.17	6.183	2.078	0.04
HR 20 min	64.94	5.758	68.35	5.551	3.069	0.003
HR 30 min	65.62	5.918	67.9	4.429	2.232	0.028
HR 45 min	67.23	5.386	68.65	5.387	1.347	0.181
HR 60 min	69.13	5.194	69.85	5.062	0.707	0.481

HR: Heart rate

Table 6: Comparison of SBP

Variables	Group				*t*-test	*P*-value
	NS		Glycopyrrolate			
	Mean	SD	Mean	SD		
SBP 1 min	100.6	7.027	103.9	7.887	2.258	0.026
SBP 5 min	90.27	7.497	99.75	6.998	6.666	<0.0001
SBP 10 min	83.71	4.816	97.6	7.754	10.969	<0.0001
SBP 20 min	84.6	5.278	94.67	7.142	8.183	<0.0001
SBP 30 min	88	6.466	94.5	8.941	4.248	<0.0001
SBP 45 min	92.25	5.884	96.13	8.765	2.653	0.009
SBP 60 min	96.9	6.763	100.73	8.975	2.456	0.016

SBP: Systolic blood pressure

Tables 8 and 9 show comparison of RR and saturation, respectively, where p value >0.05 among both the groups was statistically not significant [Graphs 8 and 9].

DISCUSSION

Hypotension is the most common side effect of spinal anesthesia. Hypotension is caused by decrease in systemic vascular resistance or cardiac output. As a result of the sympathectomy caused by spinal anesthetics, as many as one-third of patients receiving a spinal anesthetic become hypotensive with a SBP <90 mm Hg and 10–15% of patients become bradycardia. There are several reasons why hypotension occurs in spinal anesthesia. First, it may be due to decreases in systemic vascular resistance.

Table 7: Comparison of DBP

Variables	Group				*t*-test	*P*-value
	NS		Glycopyrrolate			
	Mean	SD	Mean	SD		
DBP 1 min	66.71	3.907	70.42	5.403	4.014	<0.0001
DBP 5 min	58.31	6.821	67.83	5.956	7.58	<0.0001
DBP 10 min	52.29	5.482	64.77	6.345	10.733	<0.0001
DBP 20 min	52.38	5.221	62.29	6.539	8.535	<0.0001
DBP 30 min	55.08	6.312	60.94	7.8	4.215	<0.0001
DBP 45 min	58.96	6.417	62.29	8.069	2.327	0.022
DBP 60 min	62.46	5.758	65.08	7.211	2.044	0.044

DBP: Diastolic blood pressure

Table 8: Comparison of RR

Variables	Group				*t*-test	*P*-value
	NS		Glycopyrrolate			
	Mean	SD	Mean	SD		
RR 1 min	12.21	0.457	12.4	0.869	1.412	0.161
RR 5 min	13	0.686	13.19	0.864	1.257	0.212
RR 10 min	13.29	0.915	13.21	1.016	0.406	0.686
RR 20 min	12.71	0.893	12.88	0.9	0.984	0.327
RR 30 min	12.88	0.832	12.87	0.991	0.107	0.915
RR 45 min	13	0.863	12.92	1.082	0.401	0.689
RR 60 min	12.94	0.916	13.04	0.885	0.544	0.587

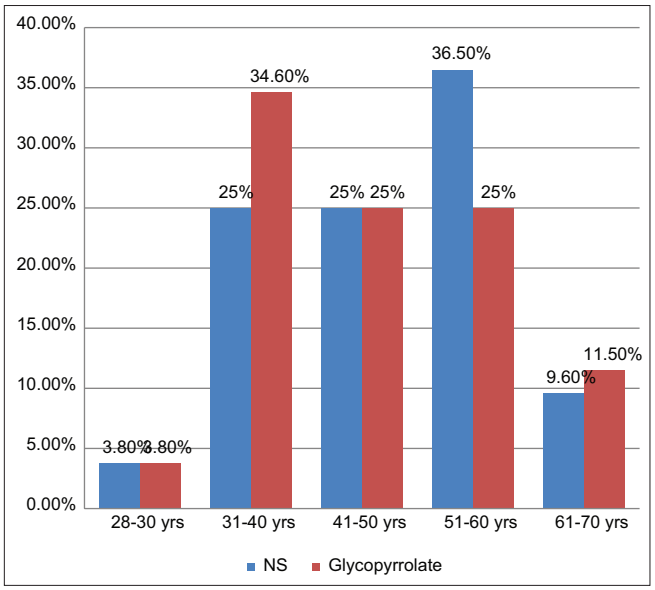
RR: Respiratory rate

Table 9: Comparison of saturation

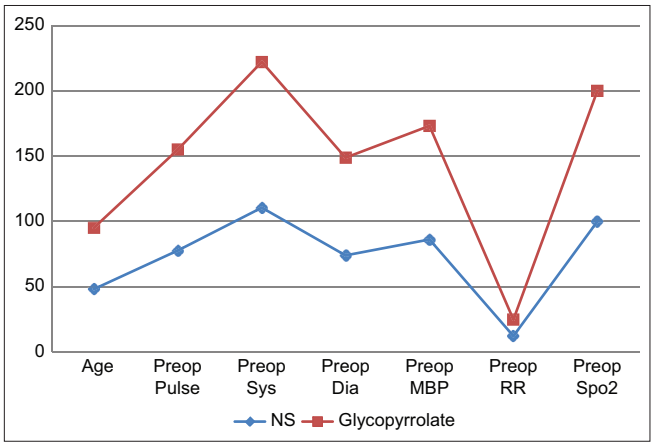
Variables	Group				*t*-test	*P*-value
	NS		Glycopyrrolate			
	Mean	SD	Mean	SD		
SPO2 1 min	99.98	0.139	99.9	0.298	1.689	0.094
SPO2 5 min	99.83	0.382	99.92	0.269	1.484	0.141
SPO2 10 min	99.85	0.364	99.88	0.323	0.57	0.57
SPO2 20 min	99.67	0.474	99.83	0.382	1.823	0.071
SPO2 30 min	99.75	0.437	99.83	0.382	0.955	0.342
SPO2 45 min	99.81	0.398	99.81	0.398	0	1
SPO2 60 min	99.65	0.653	99.85	0.364	1.854	0.067

SPO_2: Saturation of peripheral oxygen

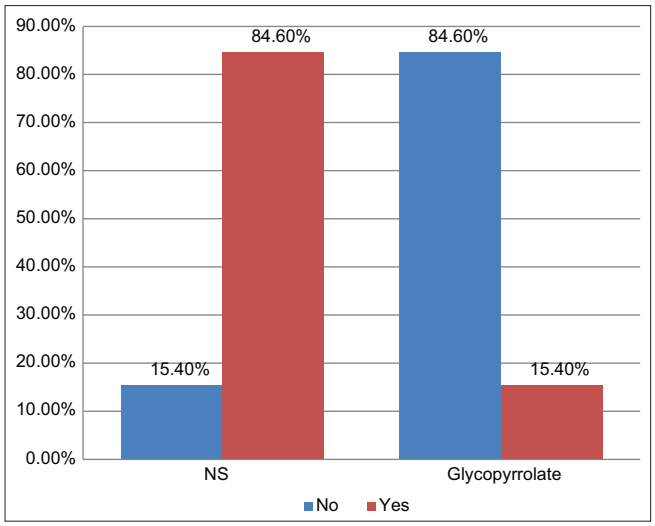
Second, it may be due to decreased venous return to the heart and subsequent decrease in cardiac output. Finally, if blockade of the cardioaccelerator fibers occurs, bradycardia results and there is even greater decrease in cardiac output. Blockade of cardioaccelerator fibers occurs when the dermatomal level of the sympathetic nervous system blockade is at or above the T1 level since the cardioaccelerator fibers originate from T1 to T4. When the hypotension is modest it is probably due to decreases in systemic vascular resistance. When hypotension is severe, it is believed to be due to decreases in cardiac output.[16] Hypotension may cause nausea, vomiting, unconsciousness, pulmonary aspiration, and hypoxia. Management of hypotension during spinal anesthesia includes oxygenation, fluid therapy, positional changes, pharmacotherapy, and other non-pharmacological method. In the study by Manem and Krishnamurthy[17] patients were randomly allocated into two groups of 30 each. Group G - received intramuscular



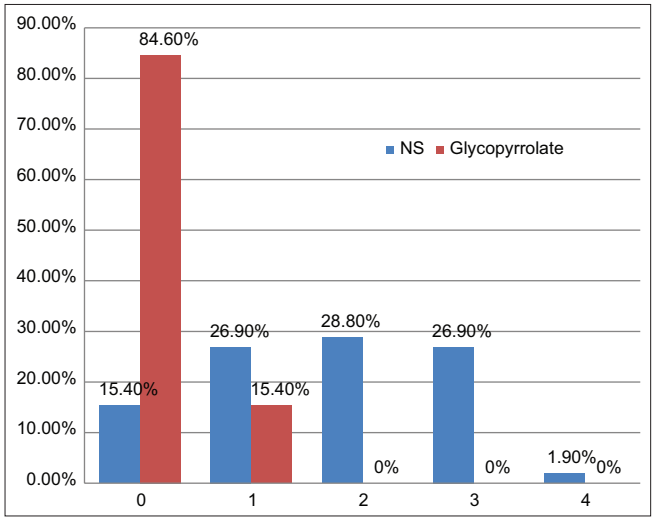
Graph 1: Demographic data: Age (years)



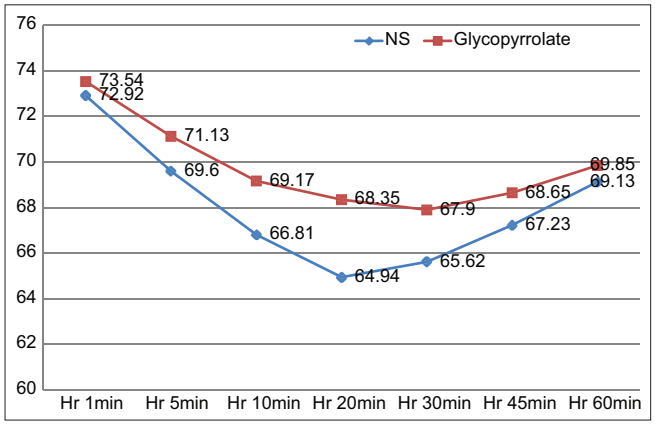
Graph 2: Comparison of preoperative vital parameters



Graph 3: Comparison of vasopressor requirement

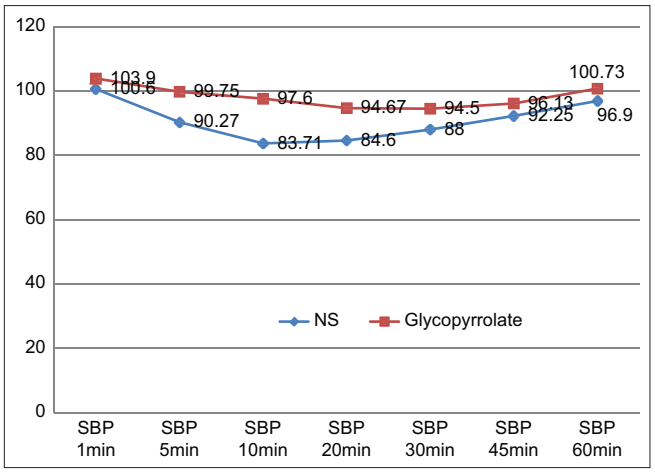


Graph 4: Comparison of frequency of vasopressor requirement in both groups

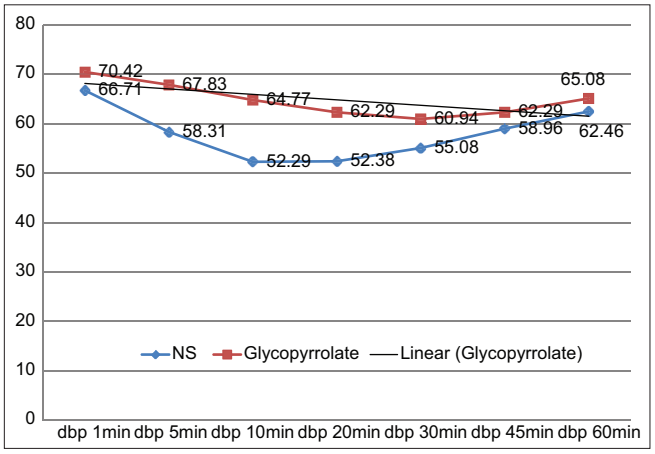


Graph 5: Comparison of heart rate

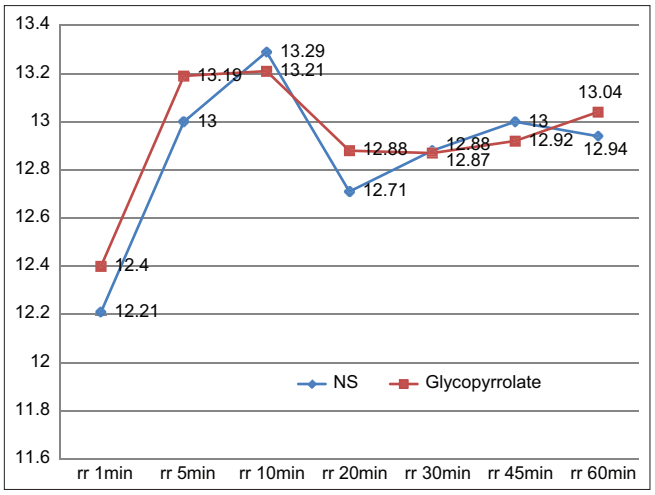
0.2 mg glycopyrrolate and Group S - received 1ml saline, 15 min before spinal anesthesia. 13 out of 30 patients had hypotension in G group. Whereas, 22 out of 30 patients



Graph 6: Comparison of systolic blood pressure

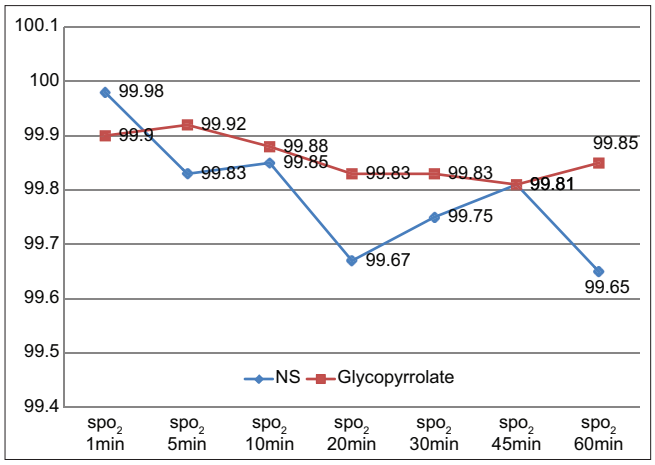


Graph 7: Comparison of diastolic blood pressure



Graph 8: Comparison of respiratory rate

developed hypotension in saline group with $P = 0.018$. Median dose of rescue vasopressor used in G group was 0 mg and in saline group was 6 mg. This difference in total dose of rescue vasopressor used between two groups was statistically significant with $P = 0.008$. In the study by



Graph 9: Comparison of saturation

Hwang *et al.*,[18] 66 patients were randomly divided into two groups. They received either glycopyrrolate 0.2 mg (Group G) or normal saline (Group S) intramuscularly, 15 min before spinal anesthesia. They found that, 23 out of 33 (70.0%) patients in Group S, experienced hypotension compared with 9 of 33 (27.3%) patients in group G (Difference = 42.7%; 95% CI 18.4–60.2; P = 0.0001). The median amount of vasopressor (ephedrine) required was 5 mg in Group S compared with 0mg in group G (difference = 5.0 mg; 95% CI: 2.7–7.3 P = 0.0001). In the study by Kee *et al.*,[19] 104 patients randomly received intravenous glycopyrrolate 4 ug/kg or saline placebo. The primary outcome, the cardiac output, 5 min after spinal injection was greater in the glycopyrrolate group. Both cardiac output and HR were greater over time in the glycopyrrolate group versus the control group (both the $P < 0.001$) but there was no difference in stroke volume over time ($P = 0.95$) and decrease in vasopressor dose when glycopyrrolate given before a phenylephrine infusion. In the study by Ure *et al.*,[20] a total of 50 patients were randomly divided in two groups of 25 each. In the glycopyrrolate group, ten patients developed nausea and vomiting compared with 17 of 25 in the placebo group. Patients in the group pretreated with glycopyrrolate reported a reduction in the frequency ($P = 0.02$) and severity ($P = 0.03$) of nausea. Incidence of hypotension was similar in each group but significantly higher total doses of vasopressor (ephedrine) were given to the placebo group (P = 0.02). In the study by Chamchad *et al.*,[21] patients were randomly allocated into two groups of 35 each. Group G received 0.4 mg glycopyrrolate and Group S received equal volume of saline and they found that none of the 35 patients who were given glycopyrrolate and 6 of the 35 (17%) patients who received saline experienced bradycardia ($P = 0.02476$, Fisher's exact test) In the study by Yentis[1] patients were allocated by computer generated random number in blocks of 40 to receive either glycopyrrolate 4 ug/kg made up 2 ml by 0.9% sodium chloride (group G) or 2 ml of 0.9% sodium chloride (Group S). Intraoperative HR increased by a greater amount in Group G than in Group S ($P = 0.002$). In the study by Patel *et al.*,[22] a total of 311 patients were included in the study; 153 received glycopyrrolate and 158 placebo. The maximal HR achieved in the glycopyrrolate group was significantly higher when compared to control (MD, 15.85 bpm [5.40–26.31]; $P < 0.0001$); however, the incidence of bradycardia was not statistically different. The vasopressor (phenylephrine) dose required was significantly reduced with glycopyrrolate group. This study was planned to evaluate for prevention of spinal induce hypotension and bradycardia by giving prophylaxis intravenous 4 ug/kg glycopyrrolate and reduce the need of vasopressor and observe hemodynamic changes. Study sample population was randomly divided into two groups (each group, $n = 52$) in which the observation were recorded and statistically evaluated. Patient in either group received an intravenous access with 18 gauge intravenous cannula. Preload of 15 ml/kg ringer's lactate solution was given over 10 min. Patients received either glycopyrrolate 4 mcg/kg (group G) made up to 2 ml with 0.9% sodium chloride or 2 ml 0.9% sodium chloride (group S). Subarachnoid space was then located using a 26-gauge Quinke spinal needle and 0.5% hyperbaric bupivacaine 3.0 ml injected intrathecally. Our study found that glycopyrrolate group was more hemodynamically stable than control group. There was significant reduction in spinal induce hypotension in group G with $P < 0.0001$ of SBP at 5 min (90.27 vs. 99.75), 10 min (83.71 vs. 97.6), 20 min (84.6 vs. 94.67), and at 30 min (88 vs. 94.5). Similar statistical difference was also observed in DBP at 1 min (66.71 vs. 70.42), 5 min (58.31 vs. 67.83), 10 min (52.29 vs. 64.77), 20 min (52.38 vs. 62.29), 30 min (55.08 vs. 60.94) and of mean arterial pressure at 5 min (68.98 vs. 78.52), 10 min (62.83 vs. 75.9), 20 min (63.13 vs. 73.13), and 30 min (65.98 vs. 72.23) after spinal anesthesia. Our study also showed that glycopyrrolate prevent spinal induce bradycardia after 10 min of spinal anesthesia. It was also statistically significant with P-value at 10 min = 0.04 and at 20 min = 0.003. Our study also showed statistically significant result in that there was reduced need of vasopressor in the glycopyrrolate group, 8 (15.4%) out of 52 patients, whereas 44 (84.6%) out of 52 patients in the Group NS required vasopressor (Chi-square = 49.85; $P < 0.0001$). 14 (26.9%) patients in Group NS required vasopressor only once whereas 8 (15.4%) patients in the glycopyrrolate group required the vasopressor once. 15 (28.8%) patients of Group NS required vasopressor twice whereas none of the patients needed vasopressor for the 2nd time in Group G. 14 patients (26.9%) of Group NS required vasopressor thrice and 1 (1.9%) patient required vasopressor for the 4th time in group NS. (Chi-square = 56.56; $P < 0.0001$). Group NS patients required more vasopressor than glycopyrrolate group (Group G) to maintain hemodynamic stability. Thus,

we can conclude that glycopyrrolate reduce the incidence of hypotension in comparison to control group.

CONCLUSION

Our study concluded that intravenous glycopyrrolate before spinal anesthesia prevents spinal induce hypotension and bradycardia and also reduce requirement of vasopressor for treatment of hypotension. Our study demonstrated that intravenous glycopyrrolate when used before spinal anesthesia, provided the most acceptable intraoperative hemodynamic stability.

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Original Article

Impact of COVID Pandemic on the Training of Postgraduate Residents: Comparison between Clinical versus Basic Specialty Residents

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Abstract

Introduction: COVID pandemic has come up as a challenge for the global health-care system, leaving no other option but to redistribute the staff and resources of the health sector toward the aid of the patients affected due to COVID. Out of all health care workers, postgraduates trainees are among the most vulnerable group. Postgraduate medical students especially are under stress to watch over potentially infectious patients, so several effective interventions can be implemented by institutions, supervisors and employers can help to mitigate this problem.

Materials and Methods: Fifty postgraduate students each from clinical and non-clinical specialty were distributed with study questionnaire and their response was compiled and statistically analyzed.

Results: It was observed that clinical specialty residents suffered more levels of anxiety, fear, and stress compared to non-clinical specialty residents and out of them more anxiety levels were observed in female postgraduate students.

Conclusions: COVID-19 had put a large impact on the mental health of postgraduates and suffered anxiety and depression from the pandemic. Appropriate measures must be taken both at management levels and at college levels to supply all the necessities required by the postgraduates so that they can work without any hindrance. Furthermore, their physical and mental well-being should be taken care of.

Key words: Anxiety, COVID-19, Depression, Mental health

INTRODUCTION

On December 31, 2019, the Chinese authorities notified the World Health Organization regarding a novel coronavirus that has spread in Wuhan city as a highly contagious disease that affects the respiratory system.[1]

This COVID pandemic has come up as a challenge for the global health-care system, leaving no other option but to redistribute the staff and resources of the health sector toward the aid of the patients affected due to COVID. Amidst this sudden change, there has been widespread effect on the medical education and the training of the postgraduate residents. Because of the pandemic and its social distancing measures, regular face-to-face trainings of the residents are not possible. In such an extraordinary scenario of pandemic, our health-care systems had to rapidly mold their organization to handle the emergency, aiming to efficiently optimize resources and curb further spread of the infection. Hence, most of the trainees/residents were diverted toward the management of COVID patients. There was appreciably reduced number of outpatient clinics, ward work, and multidisciplinary meetings because of redeployment of the residents to support the emergency response to COVID-19-centered approach.

On the contrary in some hospitals, there has also been reduction in the inpatient service due to the pandemic

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again leading to decrease clinical exposure to the residents. As hospitals have now created different COVID wards to combat this pandemic, residents have to spend maximum amount of their time in these COVID services leading to less clinical exposure of their respective branches.

If we talk about the psychological impacts, the work-related anxieties about provision of personal protective equipment, and risks to self and to colleagues are superimposed on concerns for family and friends and domestic disruption. These seismic changes have had consequences for wellbeing and mental health. In these unprecedented times, there has been frequent postponement or even cancellations of examinations, leading to slowing down of the preparations of the residents. All these factors contribute to increase psychological distress among medical students. There is insufficient data availability regarding prevalence of depression during the pandemic.

However, in India according to a recent survey, a very high (32.6%) prevalence of depression was found in health care workers (HCWs) during COVID pandemic.[2] Out of all HCWs, postgraduates trainees are among the most vulnerable group.[3] Postgraduate medical students especially are under stress to watch over potentially infectious patients, so several effective interventions can be implemented by institutions, supervisors and employers can help to mitigate this problem. Hence, we need to seek out the measure to establish balance between the needs of the residents and the service provision to prevent any kind of frustration among the residents.

MATERIALS AND METHODS

After taking permission from the Institutional Ethics Committee, Government Medical College, Amritsar, a cross-sectional survey will be conducted among postgraduate residents of Guru Nanak Dev Hospital attached to GMC, Amritsar, Punjab, to study the "impact of COVID-19 pandemic on postgraduate residents." A written informed consent was taken from each medical resident. The survey involved a questionnaire that was distributed in either a paper based or online version by means of email or social media, to the residents. The residents were divided into two set of batches, one batch of 50 residents comprising the clinical specialty (medicine, chest and tuberculosis, surgery, anesthesia, etc.) postgraduate residents, and another batch of 50 residents comprising the basic specialties (anatomy, physiology, biochemistry, etc.).

Questionnaire

The questionnaire included 13 questions regarding the COVID-19 infection and its impact on daily lifestyle of the residents. A friendly reminder was sent to potential respondents to ensure highest possible response rate. Unreturned questionnaire was recorded as missing. Participants were aware of study aim or outcomes to reduce the risk of any possible bias. The questionnaire was self-administered without intervention by the authors or any specific person, and it did not contain any identifying data of the participants to ensure confidentiality.

Study Tool

The questionnaire covered participants basic demographic data, such as their gender, age, marital status, as well as general questions about their financial status, faculty, level of medical education, history of health problems, psychological illness, and learning disabilities, if present. The survey requested information about participants medical education status during the pandemic, such as their work status, type of educational activities conducted, how COVID-19 affects their career plan, their personal attitude toward the pandemic, and questions on their personal opinions about authorities response to the pandemic and about their well-being. It also covered mental health assessment that measures the level of anxiety and depression in the form of depression, anxiety, and stress scale (DASS) questionnaire. It was in English language.

We used the DASS21 questionnaire for the assessment of psychological impact of COVID pandemic on the residents. The DASS-21 items are a set of three self-report scales designed to measure the emotional states of depression, anxiety, and stress. Each of the three DASS-21 scales contains seven items, divided into subscales with similar content. The depression scale assesses dysphoria, hopelessness, devaluation of life, self-deprecation, lack of interest/involvement, anhedonia, and inertia. The anxiety scale assesses autonomic arousal, skeletal muscle effects, situational anxiety, and subjective experience of anxious affect. The stress scale is sensitive to level of chronic nonspecific arousal. It assesses difficulty relaxing, nervous arousal, and being easily upset/agitated, irritable/over-reactive, and impatient. Scores for depression, anxiety, and stress are calculated by summing the scores for the relevant items. The DASS-21 is based on a dimensional rather than a categorical conception of psychological disorder. The assumption on which the DASS-21 development was based (and which was confirmed by the research data) is that the differences between the depression, anxiety, and the stress experienced by normal subjects and clinical populations are essentially differences of degree. The DASS-21, therefore, has no direct implications for the allocation of patients to discrete diagnostic categories postulated in classificatory systems such as the Diagnostic and Statistical Manual of Mental Disorders and International Classification of Diseases.[4]

Statistical Analysis

The data from the present study were systematically collected, compiled, and statistically analyzed to draw relevant conclusions. Counts and proportions (%) were used for descriptive values. The comparison on the trainings and psychological behavior was assessed using the Chi-square test. $P < 0.05$ at 95% confidence interval was considered statistically significant. Statistical Package for the Social Sciences (SPSS), version 21 (SPSS, Chicago, IL, USA) was used for all statistical data.

RESULTS

We collected 100 responses from clinical and non clinical postgraduate students from online questionnaires, sent to them via mails and social media from May 2021 to June 2021. Out of 100 residents, 70% of the clinical group and 26% ofnon clinical group residents had direct involvement in the management of COVID 19 patients ($P < 0.05$).

During this pandemic, teaching, trainings and clinical activities were some of the major concerns being faced by the postgraduates and out of all, 66% students from clinical and 32% from non clinical department residents acknowledged that they did not get enough time to study. Hence, due to lack of time for studying, majority of the clinical group residents i.e. 80% and 46% of non clinical residents felt psychological stress about their upcoming exams during this pandemic ($P < 0.05$).

Major cause of anxiety and stress during this pandemic was related to self infection while treating the covid patients. We have observed that, 52% of the residents from the clinical and 30% from non-clinicaldepartment were infected with COVID disease while treating and handling these patients and almost equal proportion of trainees from both groups i.e. 28 and30%felt that their family members contracted the disease from them.

Majority of the clinical undertraining postgraduates (82%) vs 24% in the non-clinical group suffered changes in their sleep pattern which further attributed to their stress and anxiety levels.

DASS 21 questionnaire was used to calculate anxiety, stress and depression among residents of both groups. From the responses, wehave observed that, overall, 43.8% residents had stress, 39% anxietyand depression was found in 17.2% which was further divided into mild, moderate, severe, and extremely severe. Many of the postgraduates experienced more stress than anxiety.

The higher anxiety and depression levels were observed in clinical residents as compared to non-clinical subject residents (22%). But no one in any of the two groups experienced an extreme depression levels.

In non-clinical group postgraduate residents there was more anxiety (63%) as compared to clinical group ofresidents (44%), where stress and depression levels were more common. In the clinical group, 48 % suffered fromstress and 56 % from depression, which was much higher when compared tonon-clinical group (i.e. 22% and 29% respectively) ($P < 0.05$), but none of the residents in any group suffer from extreme levels of depression and stress.

It has also been witnessedin our survey that, the gender, female (63%), suffered more anxiety and stress compared to male (20%) postgraduates in both clinical and nonclinical groups ($P < 0.05$) Also, postgraduatesfrom clinical groups were more anxious and stressful and suffered more problems in learning and their teaching was affected more compared to non-clinical undertraining postgraduates.

DISCUSSION

With covid pandemic, clinical trainings and health education is affected harshly. Clinical postings, elective opds, surgeries and other works were suspended and hence there was marked reduction in clinical teaching and learnings of the students which was one of the major contributing factor leading to stress and anxiety in the postgraduates.

For the PGs involved in COVID-19 duties, there is more mental stress because of the possibility of getting the viral infection. Various researchers observed significant levels of anxiety and stress in the students and faculty who were directly and indirectly involved in treating covid patients and also in those in whom additional covidduties were assigned during the pandemic.[5]

Medical students experience more symptoms of anxiety and stress compared to general population.[6,7] They had higher burnout rates relative to similarly aged people and students involved in other courses and activities.8Students involved in medical field, experience more mood changes, anxiety disorders, suicidal ideation and psychological distress because of their nature of work.[8] Our survey findings also suggested the same results about the experience of anxiety, stress and depression among the working postgraduate students.

Postgraduate students not only feel burnout because of excessive workload, compromised sleep patterns, exposure to terminal illness[9] but also, some students raise their bars high about their studies and come under more pressure and stress which further can exaggerate the mental health

problems in these students. The other contributing factor is, most of the postgraduates are far from their home place, so despite of their emotional distress, they were unlikely to seek help from the fellow colleagues because of their own busy schedules and rotatory duties.[10] Some students knowingly do not seek help for their mental conditionsbecause of fear of compromising academic and career progressions.[11]

Researchers also found that, females have higher prevalence for anxiety and depression in general may be because of their harmonal and emotional levels.[12] Among medical students, female postgraduates, are affected more both mentally and socially and suffered more mood or anxiety disorder and severe psychological distress.[7,8] As viral diseases are more transmissible, so fear of contracting this disease was much higher while working in the medical field.

Fear, anxiety and depression among the medical students was much higher when the disease was at its peak leading to psychological disturbances among the resident students. Approximately, 84.71% medical students declared about their fear of getting covid infection and 70.8% medical students observed that this pandemic has affected their financial status and which may compromise their course continuity.[13] In such cases, of postgraduate students, support system needs to be emanate from their own universities.[14] Hence, we can say that the COVID-19 pandemic had caused potential impact not even on emotional as well as mental health state of the postgraduate undertrainee students. Also, the level of anxiety and stress was more in those students who were directly involved in the management of the critically ill patients i.e. in the clinical group postgraduates.

The purpose of this study was to find out the possible causes for anxiety and stress among the postgraduates of different specialities involved in the management of covid patients, so that their physical and psychological well being can be taken care of with best possible alternatives related whether to studies or with their support system. So, at medical college level, administrators and leaders should take lead in providing adequate support system for those students who needs help for their mental and psychological wellness.

CONCLUSIONS

To conclude, though covid 19 had put a large impact on health care workers, but among all health care workers, medical postgraduate undertrainees were the highest affected. Further, among the postgraduate trainees, female doctors and residents from the clinical speciality suffered more levels of anxiety and depression compared to non clinical batch students because of their direct exposure with the covid patients. So there must be a solution and protection to mental health and social well being of all medical students. Also, they should be appropriately trained before giving them the exposure to a highly infectious disease as quality of patients care depends upon the physician's physical and mental wellness.

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Original Article

A Comparative Study of Intravenous Esmolol and Labetalol in Low Doses for Attenuation of Sympathomimetic Responses to Laryngoscopy and Endotracheal Intubation

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Abstract

Introduction: Direct laryngoscopy and endotracheal intubation are a noxious stimulus and induce sympathomimetic responses. Although properly tolerated in normal and healthy subjects, it is able to impose serious arrhythmias, left ventricular failure, or rupture of cerebral aneurysm in vulnerable patients. Esmolol and labetalol attenuate those responses however are related to some untoward outcomes such as bradycardia and hypotension. In low doses, chances of those expected untoward outcomes are relatively low.

Purpose: We designed this prospective observational clinical study to assess the efficacy of intravenous esmolol and labetalol in low doses for attenuation of sympathomimetic responses to endotracheal intubation.

Materials and Methods: Fifty consenting patients of American Society of Anesthesiologists physical repute I or II of age between 20 and 60 years, scheduled for surgeries requiring general anesthesia, were randomly allocated to two groups; group ES and group LB, given esmolol hydrochloride (HCL) 0.5 mg/kg and labetalol HCL 0.25 mg/kg body weight, respectively. Final result variables were heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP). These variables had been recorded immediately after intubation (AI) and then at 1, 3, 5, 7, and 10 min AI.

Results: There was no statistically considerable distinction regarding the demographic traits of both the groups. HR and SBP were significantly lower throughout the study period in labetalol group. Values of MAP were slightly higher in labetalol group but it was much higher in esmolol group throughout the study period. DBP was higher in both the groups.

Conclusion: Labetalol 0.25 mg/kg is an effective and safe drug to be used for attenuation of sympathomimetic responses to endotracheal intubation. Esmolol 0.5 mg/kg is also safe and effective to some extent.

Key words: Endotracheal intubation, Esmolol, Labetalol, Laryngoscopy, Sympathomimetic reflexes

INTRODUCTION

Cardiovascular stress response is frequently induced by laryngoscopy and endotracheal intubation results in tachycardia and hypertension due to increase in serum catecholamine.[1]

These hemodynamic changes are well tolerated in healthy individuals, but are life threatening in susceptible patients having multiple coexisting diseases.[2-4] In susceptible individuals, these hemodynamic stress responses can evoke life-threatening conditions such as myocardial ischemia, left ventricular failure, and cerebral hemorrhage.[5] Esmolol is a cardio selective b1-blocker having quicker onset and ultra-short duration of action. It causes depressor action on myocardium; hence, its place still remains to be defined

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especially in cardiac risk patients. Labetalol, a combined α and β blocker, has also been found to be effective for prevention of perioperative detrimental cardiovascular events,[6-9] but it can cause hypotension and bradycardia, when used in the higher doses.

Various efforts have been made to attenuate these untoward reflexes by the use of a variety of drugs. Selection of a pharmacological adjunct is tricky because efficacy has to be weighed against its safety. Hence, this clinical study was carried out to evaluate the effects of IV esmolol hydrochloride (HCl) and labetalol HCl in low doses for attenuation of hemodynamic response to laryngoscopy and intubation.

Aim and Objectives

The objectives of the study are as follows:

1. To assess and compare the efficacy of esmolol and labetalol for attenuation of sympathomimetic response to laryngoscopy and endotracheal intubation
2. To observe any adverse or beneficial effects.

MATERIALS AND METHODS

After approval of the institute ethical committee and informed consent, this study was conducted on 50 patients between the age of 20 and 60 years of either sex of American Society of Anesthesiologists (ASA) Grade I or II scheduled for different surgeries requiring general anesthesia was included in this study. Patients of ASA Grade III or more, pregnant and lactating women, morbid obesity, hypertension, and anticipated difficult intubation were excluded from the study.

Intervention Plan and Group Allocation

Patients were kept blinded by sealed envelope method and observer anesthesiologist was also uninformed of which drug was injected to which patient to avoid observer bias. The anesthesiologist who injected the study drugs took no further part in the study. Selected 50 patients were randomly allocated into two groups based on the study drug to be given:

1. Group ES: Inj. Esmolol 0.5 mg/kg body weight diluted to 10 ml with normal saline was given intravenously 5 min before intubation over 60 s
2. Group LB: Inj. Labetalol 0.25 mg/kg body weight diluted to 10 ml with normal saline was given intravenously 5 min before intubation over 60 s.

Pre-anesthetic Assessment

All the selected patients were carried out with complete history, general examination, airway assessment, and systemic examination along with routine investigations, electrocardiogram, and chest X-ray.

Premedication

All the patients were kept nil orally for at least 8 h before procedure. Tablet Lorazepam 1 mg and tablet ranitidine 150 mg were given night before surgery. Inj. Glycopyrrolate 0.2 mg intramuscularly had given to all the patients as premedication, 30 min before shifting the patient to operation theater.

Anesthesia Management

After taking the patient in the operation theater, intravenous cannulation was done and ringer lactate infusion was started. Basal parameters such as heart rate (HR), mean blood pressure (MBP), systolic blood pressure (SBP), and diastolic blood pressure (DBP) had been recorded. Study drug was given 5 min before intubation over 60 s.

Thereafter, preoxygenation with 100% oxygen was started and general anesthesia was induced with inj. fentanyl 2 μg/kg and inj. Thiopentone up to 5 mg/kg body weight. After securing mask ventilation, inj. vecuronium 0.1 mg/kg body weight administered intravenously for endotracheal intubation. Mask ventilation with 100% oxygen was continued for three or more min to time endotracheal intubation after 5 min of administration of study drugs, followed by endotracheal intubation. Anesthesia was maintained with 50% oxygen in air and isoflurane with intermittent doses of fentanyl and vecuronium, along with intermittent positive pressure ventilation. After intubation (AI) till conclusion of surgery and reversal of anesthesia, continuous monitoring of vital parameters was done. The incidence of bradycardia and hypotension was noted. After surgery, reversal done with combination of inj. Glycopyrrolate 0.01 mg/kg body weight and Neostigmine 0.05 mg/kg body weight. Any complications occurred perioperatively were noted.

Frequency of Data Recordings

Readings of hemodynamic parameters were taken before starting study drug and were taken as basal value (BV) and then during laryngoscopy (DL) and endotracheal intubation DL. Five more readings were recorded at 1 (AI 1), 3 (AI 3), 5 (AI 5), 7 (AI 7), and 10 (AI 10) min after endotracheal intubation.

Statistical Analysis

Statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS) version 19 (SPSS, IBM, Chicago, IL, USA). The study data were presented as mean ± standard deviation. Student's "*t*"-test was used for inter-group comparison. $P > 0.05$ and <0.05 were considered statistically insignificant and significant, respectively.

RESULTS

In the present study, both the study groups were comparable on demographic pattern such as age, weight, and sex [Table 1]. Basal hemodynamic variables such as mean HR, SBP, DBP, and mean arterial pressure (MAP) [Tables 2-5] were also comparable between the groups ($P > 0.05$ insignificant).

The increase in mean HR was observed in both the groups but lower in labetalol group [Table 2]. There was increase in SBP in group esmolol but not in labetalol group [Table 3]. DBP increased in both the groups almost similarly [Table 4]. Increase in MBP was higher in group ES than that in group LB [Table 5].

DISCUSSION

Our study showed a sudden increase in all the hemodynamic parameters up to variable extent DL and endotracheal intubation in different groups. Thereafter, all hemodynamic variables started to fall throughout the study. These hemodynamic changes were reduced to varying degrees by both the study drugs used but the most effectively attenuated by labetalol. Esmolol was not as effective as labetalol to attenuate the hemodynamic response. The hemodynamic changes resulted from laryngoscopy and intubation are due to sympathoadrenal discharges caused by epipharyngeal stimulation.[10] Reid and Brace had reported the circulatory responses to laryngeal and tracheal stimulation in anesthetized man as tachycardia and increase in arterial blood pressure.[11] Takeshima *et al.* found rise in MAP of 20 mmHg at the time of laryngoscopy and tracheal intubation and they concluded that laryngoscopy was a more potent stimulus to hypertension than intubation.[12]

In our study, we used 0.5 mg/kg of esmolol, given 5 min before intubation, which though attenuated the HR but showed significantly less effective attenuation as compared to labetalol group. The reason might be that both the drugs showed their maximum effect in 5 min and peak hemodynamic effects occurred within 6–10 min of administration[13] but esmolol had a shorter duration of action (elimination half-life of 9 min) as compared to labetalol (elimination half-life of 5–8 h). Even in study with bolus dose of esmolol 2 mg/kg was found to be successful for attenuation of rise in HR due to laryngoscopy and endotracheal intubation and the augmentation of blood pressure was not completely and effectively abolished.[14]

Table 1: Demographic pattern of the study population

Parameters	Group ES	Group LB	*P*-value
Age (years)	41.12±10.23	42.32±10.63	0.686
Weight (kg)	58.08±6.62	61.48±9.35	0.144
Sex (male/female)	15/10	14/11	–

Table 2: Comparison of mean HR among different groups

Recording time	Group ES (Mean±SD)	Group LB (Mean±SD)	*P*-value
BV	97.64±11.98	98.52±8.53	0.76
DL	109.16±9.84	103.4±8.73	0.03
AI 1	106.44±8.84	101.08±8.65	0.03
AI 3	104.28±5.01	96.68±8.43	0.00
AI 5	102.28±3.63	97.4±6.91	0.00
AI 7	100.76±6.93	96.48±7.10	0.03
AI 10	100.08±6.12	97.6±6.91	0.18

BV: Basal value, DL: During laryngoscopy, AI: After intubation, SD: Standard deviation, HR: Heart rate

Table 3: Comparison of mean SBP among different groups

Recording time	Group ES (Mean±SD)	Group LB (Mean±SD)	*P*-value
BV	121.32±6.56	122.76±7.76	0.48
DL	133.88±9.40	127.72±9.41	0.01
AI 1	130.36±11.63	123.12±6.10	0.00
AI 3	130.04±6.95	121.72±6.52	0.00
AI 5	128.56±5.51	120.28±7.71	0.00
AI 7	128.92±7.26	121.08±8.23	0.00
AI 10	127.44±7.42	120.08±9.78	0.00

BV: Basal value, DL: During laryngoscopy, AI: After intubation, SD: Standard deviation, SBP: Systolic blood pressure

Table 4: Comparison of mean DBP among different groups

Recording time	Group ES	Group LB	*P*-value
BV	77.76±6.90	78.88±2.94	0.46
DL	89.12±11.79	87.16±8.28	0.50
AI 1	88.40±8.45	85.16±5.94	0.12
AI 3	87.16±8.48	84.32±7.15	0.20
AI 5	87.08±4.99	85.04±8.83	0.32
AI 7	89.68±5.58	86.00±7.76	0.06
AI 10	86.47±7.8	83.6±10.22	0.26

BV: Basal value, DL: During laryngoscopy, AI: After intubation, SD: Standard deviation, DBP: Diastolic blood pressure

Table 5: Comparison of MAP among different groups

Recording time	Group ES	Group LB	*P*-value
BV	92.280±5.69	93.507±3.67	0.37
DL	104.040±9.74	100.68±7.95	0.18
AI 1	102.386±8.19	97.813±5.57	0.02
AI 3	101.453±6.35	96.786±6.37	0.01
AI 5	100.906±4.05	96.786±7.74	0.02
AI 7	102.760±5.64	97.693±6.96	0.00
AI 10	100.133±6.89	95.76±9.33	0.06

BV: Basal value, DL: During laryngoscopy, AI: After intubation, SD: Standard deviation, MAP: Mean arterial pressure

There was only slight and statistically insignificant increase in SBP in labetalol group at 1 min AI [Table 3]. Thereafter, up to 10th min of intubation, SBP was significantly lower than baseline values. Contrary to labetalol group, SBP was significantly higher in esmolol group at DL and intubation, and remained higher till 10th min of study period. We found that, labetolol was more effective than esmolol for attenuation of rise in SBP due to laryngoscopy and intubation. Esmolol is a β1 (cardio selective) adrenergic receptor blocking agent with no action on peripheral vasculature whereas labetalol is selective α1 and non-selective β1 and β2 adrenergic receptor blocking agent, it decreases blood pressure by lowering peripheral vascular resistance (α1 action) and also attenuates reflex tachycardia. It also has weak β2 agonistic activity therefore may cause vasodilatation. Cardiac output remains unchanged.[13]

In our study, the increase in DBP was not significantly decreased ($P < 0.05$) by esmolol, whereas labetalol showed statistically significant attenuation at least up to 3 min [Table 4]. It is stated in the pharmacology of labetalol that "Increase in SBP rise during exercise is reduced by labetalol but corresponding changes in DBP are essentially normal." Esmolol also has more effect on SBP than on DBP.[15,16] Labetalol was found to be more effective than esmolol for attenuation of MAP in response to endotracheal intubation. However, this effect was not observed at DL and immediately thereafter. However, grossly the change in MAP was most effectively attenuated by labetalol, followed by esmolol. Our results concurred with the study of Bensky *et al.*[17] They found that esmolol at dose of 0.2–0.4 mg/kg resulted in 21.7–11.1% increase in MAP just after endotracheal intubation. Whereas, the increase in MAP was 27% in control group.

Bradycardia was noted in one patient in group esmolol. Hypotension was seen in two patients of group labetalol. Bradycardia was treated with injection atropine 0.3 mg and for the treatment of hypotension injection Mephentermine 6 mg IV was given. These three cases were excluded from the study. Moreover, three other patients were recruited to complete the study. With both intra- and inter-group comparison, labetalol found to be better for the attenuation of HR, SBP, DBP, and MAP during and after laryngoscopy and endotracheal intubation. The hemodynamic parameters were relatively more stable in labetalol group intraoperatively as compared to esmolol.

CONCLUSION

Laryngoscopy and endotracheal intubation is consistently associated with increase in hemodynamic variables. Labetalol 0.25 mg/kg is a safe and effective drug which can be used for attenuation of sympathomimetic responses to laryngoscopy and endotracheal intubation. Esmolol 0.5 mg/kg is also safe and effective to some extent.

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Original Article

Comparison of Ultrasound-Guided Transversus Abdominis Plane Block versus Ultrasound-Guided Ilioinguinal/Iliohypogastric Nerve Blocks in Infraumbilical Surgeries

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Abstract

Background: Infraumbilical surgeries are associated with acute or chronic post-operative pain. Ultrasound (USG)-guided regional nerve block provides the best option as they provide better and precise analgesia. The aim of present study is to compare the efficacy of USG-guided ilioinguinal nerve (IIN) and iliohypogastric nerve (IHN) versus transversus abdominis plane (TAP) block for post-operative analgesia in patient undergoing infraumbilical surgeries.

Study and Design: A prospective, randomized, and double blinded study was conducted on 60 patients of American Society of Anesthesiologists Grades I and II undergoing lower abdominal surgery at Guru Nanak Dev Hospital attached to Government Medical College, Amritsar.

Materials and Methods: Patients were randomly divided into two groups of 30 each. Group T received TAP block with 20 ml 0.25% levobupivacaine and injection fentanyl 1 μg/kg. Group L (IIN/IHN) received IIN/IHN block with 20 ml 0.25% levobupivacaine and injection fentanyl 1 μg/kg.

Results: Mean duration of analgesia was prolonged in Group L as compared to Group T ($P < 0.05$). The visual analog scale score was lower in Group L as compared to Group T.

Conclusion: USG-guided ilionguinal block with 0.25% levobupivacaine and injection fentanyl 1 μg/kg was found to be better than USG-guided TAP block.

Key words: Levobupivacaine, Fentanyl, TAP Block, VAS Score, Post operative analgesia

INTRODUCTION

A substantial component of pain experienced in patients after infraumbilical surgeries is derived from the anterior abdominal wall incision.[1] Even a relatively small incision may be followed by risk of chronic pain in about 20% of patients.[2] Infraumbilical surgeries are associated with acute or chronic post-operative pain. The most of the pain subsides with healing of tissues and removal of noxious stimulus but sometime it may persists.[3] Post-operative pain is associated with many negative outcomes such as fear, anxiety, discomfort, inability to cough and deep breathing, late mobility, with risk of deep vein thrombosis, and pulmonary embolism, thus prolonged hospital stay.[4] Post-operative pain relief comes within the realm of anesthesiologists.

Numerous modalities are being used for post-operative pain relief including nonsteroidal anti-inflammatory

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drugs (NSAIDS), opioid, paravertebral blocks, regional blocks,[5] epidural analgesics, local infiltration, and opioid remained a gold standard for post-operative analgesia but they are not devoid of side effects such as nausea, vomiting, sedation, respiratory depression, tolerance, addiction, and delayed post-operative recovery.[6] Over the time, scenario of post-operative analgesia management changed from pharmacological interventions to regional techniques.

Recent advance in ultrasound (USG) technology and its utilization in regional anesthesia have enabled the practioner's to perform block under direct visualization with successful outcome. Transversus abdominis plane (TAP) block and ilioinguinal-iliohypogastric nerve blocks are regional anesthetic techniques in which local anesthetics are deposited to block the sensory nerves supplying the anterior abdominal wall.[7] Both TAP block and ilioinguinal nerve (IIN)/iliohypogastric nerve (IHN) block the same nerve. However, the only difference is that TAP is a compartment block while IIN/IHN is a truncal block. The present study is designed to compare the efficacy of USG-guided TAP block and USG-guided IIN and IHN block for post-operative analgesia in infraumbilical surgeries.

MATERIALS AND METHODS

After obtaining clearance from institutional ethical committee, we carried out randomized prospective study in 60 patients of American Society of Anesthesiologists (ASA) Grades I and II in the age group of 18–60 years posted for elective Inguinal hernia surgeries under spinal anesthesia. Patients were randomly divided into two groups of 30 each. Group T received TAP block with 20 ml 0.25% levobupivacaine and injection fentanyl 1 μg/kg. Group L (IIN/IHN) received IIN/IHN block with 20 ml 0.25% levobupivacaine and injection fentanyl 1 μg/kg. Patients were kept NPO 8 h preoperatively after thorough pre-anesthetic checkup and lab investigations.

On arrival of patient in operation theater, routine monitoring (electrocardiogram, pulse oximetry, and non-invasive blood pressure) was done and baseline vitals recorded. 18 G i/v canula was used to preload the patient with crystalloids. With patient in the lateral decubitus position, under all aseptic conditions, L3-L4 or L4-L5 space located and Quincke's needle number 25 or 26 G introduced into subarachnoid space through midline approach. After free flow of cerebrospinal fluid (CSF), 2.5–3 ml of 0.5% bupivacaine injected into CSF. Surgery started under adequate anesthesia. Oxygen started through simple oxygen mask.

After giving the subarachnoid block, the patient will be positioned supine, the skin over the anterior abdominal wall will be disinfected and draped. Blocks were placed under ultrasound guidancefor allotted groups.In T groups, drug was injected in between internal oblique andtransversus abdominis whereas drugs was given near to IIN and IHN nerves in group L after identifying the structures with linear transducer with frequency of 5-8 MHZ. Pulse, blood pressure and oxygen saturation were assessed for 24 hours from the time of administration of block at 0, 2, 4, 6, 8, 12, 24 hour interval. "0" reading was taken when there was two segment regression of pain on the opposite side of block. Pain was assessed by Visual Analog Scale and the duration of postoperative analgesia was recorded in both the groups.

Statistical Analysis

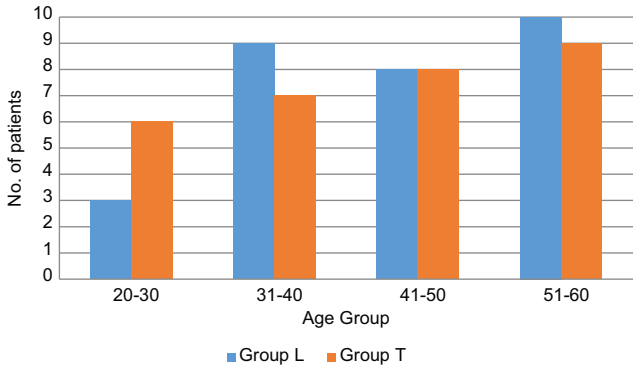
The data from the present study were systematically collected, compiled, and statistically analyzed to draw relevant conclusions. Sample size was calculated in consultation with statistician taking mainly the duration of post-operative analgesia and VAS score and based on the previous studies to get the power of study more than 85%. The continuous data were represented as standard deviation (mean ± SD). Number of patients and percentage of cases expressed discrete categorical data. Categorical variables were analyzed using independent Chi-square test. The *P*-value was calculated finally to evaluate the level of significance. $P > 0.05$ was considered non-significant, $P = 0.01–0.05$ was considered significant, and $P < 0.001$ was highly significant. The results were then analyzed and compared to the previous studies.

RESULTS

While comparing the distribution of age, sex, and ASA grade between the two groups was statistically non-significant, heart rate, blood pressure, and oxygen saturation were statistically non-significant in both the groups.

The mean duration of analgesia was prolonged in Group L as compared to Group T. It was 10 ± 1.96 h in Group L and 7.40 ± 1.97 h in Group T. The VAS score was significantly lower in group L as compared to group T ($P < 0.05$). The VAS score was assessed at 0 hours which was taken whentheir was two segment regression of pain on the opposite side of body. VAS score was assessed further at 1,2,3,4,6,8,10,12,16,20,24 hrs.

Rescue analgesia was given when the VAS score was more than 3, injection diclofenaci/m was given in rescue analgesia. In group T first dose of rescue analgesia was given between 5 to 9 hours when the patient started feeling



pain and the VAS score was more than 3. The second dose of rescue analgesia was given between15 to 19 hours .In group Lfirst dose of rescue analgesia was given between 8 to 12 hours when the patient started feeling pain and the VAS score was more than 3.the second dose of rescue analgesia was given between 18 to 22 hours.

DISCUSSION

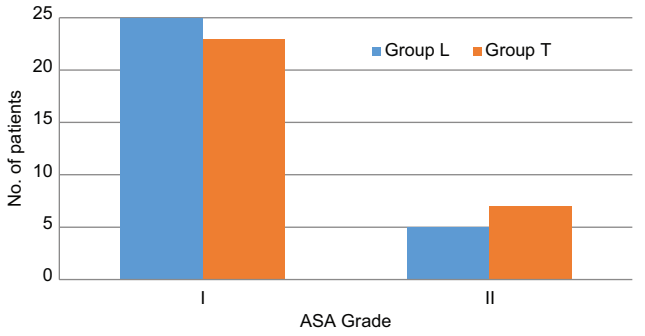
Pain and discomfort are important components which are experienced after abdominal wall incision; the anterolateral abdominal wall is innervated by thoracolumbar nerves T7 to L1 which emerges from the anterior rami of spinal nerves. The anterior abdominal wall incision is responsible for the most of the pain experienced after abdominal surgeries.[8] Adequate post-operative analgesia is vital to ensure early mobilization and discharge of patients, as stress response to pain may lead to tachycardia, hypertension, inability to cough, decreased lung compliance, and increased risk of deep vein thrombosis due to immobilization of patient.[4] Thus, anesthetic and analgesic techniques should aim to reduce post-operative morbidity to improve outcome. Nowadays, multimodal analgesia techniques are used and among them regional nerve block techniques offer great advantage.

In this study on comparison, duration of post-operative analgesia was prolonged in L group compared with T group and the result is supported by study conducted by Kamal *et al.* 2018.[9] In study conducted by Sundaram *et al.*[10] in 2019, the mean duration of rescue analgesia was higher in ilioinguinal/iliohypogastric block than transverse abdominis plane block. This can be explained as TAP is a compartment block whileIlioinguinal/iliohypogastric (IIIH) nerve block is a truncal block.

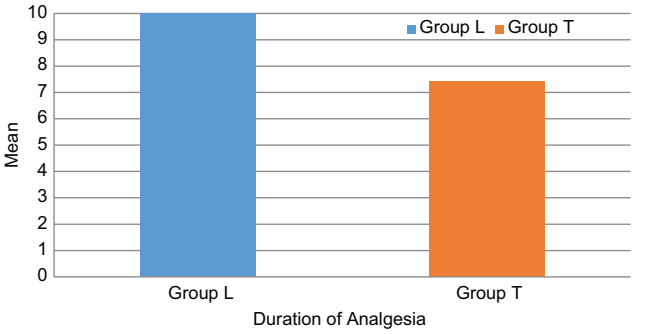
In our study, post-operative VAS score was recorded and was lower in group L at 1, 2, 3, 4, 6, and 8 h. At 0 hours, 1 h no patient require rescue analgesia as it was due to residual effects of spinal anaesthesia. At 2, 3, 4, 5 h the

ASA grade	Group L		Group T	
	No.	% age	No.	% age
I	25	83.33	23	76.67
II	5	16.67	7	23.33
Total	30	100.00	30	100.00

χ^2: 0.417, df: 1, *P*=0.519, ASA: American Society of Anesthesiologists



Group	Duration of analgesia	
	Mean	SD
L	10.000	1.9652
T	7.400	1.9757
P-value	0.001	



mean VAS score was non significant between two groups as due to effect of respective blocks. At 6,8,10 hours VAS score was significantly lower in group L than Group T. The prolonged effect of ilioinguinal/iliohypogastric nerve block can be explained as due to anatomical course of IIN/IHN nerve, use of ultrasound for performing blocks and direct perineural deliverance of the drug. Other factor that favoured was easier spread of local anesthetic in the deep inguinal ring and blocking the genital branch of genitofemoral nerve. These findings were consistent with the study conducted by Youfa Zhou in 2019.[11] They found that transverse abdominis plane block has significantly higher pain score at 6 and 8 hours post operatively. In 2019 YuluJinYongliangli *et al.*[12] conducted a study in which they found that VAS score was significantly lower in ilioinguinal /iliohypagastric block at 24 and 48 hrs after surgery. In our study total dose of rescue analgesia and

number of doses of rescue analgesia were comparable and statistically non significant.

CONCLUSION

We concluded that ilioinguinal/iliohypogastric nerve block with 0.25% levobupivacaine and injection fentanyl 1 μg/kg leads to prolonged duration of post-operative analgesia as compared to transverse abdominis plane block

LIMITATION

Limitation of our study was small sample size, only male patients of ASA I and ASA grade 2 was studied. We did not follow our patients beyond 24 hours so difference between two groups regarding incidence and severity of chronic post-surgical pain could not be compared.

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Original Article

A Study to Evaluate Development of Tuberculosis and its Correlation with CD4 + T Lymphocytes Count in Newly Diagnosed People Living with HIV AIDS Attending Tertiary Art Centre at Maharaja Yeshwantrao Hospital Indore

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Abstract

Background: Tuberculosis (TB) is the most common opportunistic infection among HIV-infected patients, who remain at high risk for TB throughout the course of their disease. In this study, we evaluated the development of TB and its correlation with CD4 + lymphocyte count in newly diagnosed People Living with HIV AIDS (PLHA).

Material and Methods: The present study was conducted at the Tertiary AntiRetroviral therapy center and Department of Medicine, Maharaja Yeshwantrao Hospital, Indore during the period January 2019 to July 2020. We had screened 1610 patients with PLHA. Of these 1610, 200 patients were diagnosed with TB. All these patients fulfilled the inclusion criteria and none of the exclusion criteria and those who were willing to provide their voluntary written informed consent were enrolled.

Results: Of 200 TB-HIV patients 75 (37.5%) had pulmonary TB and 125 (62.5%) had extrapulmonary involvement. Out of 125 cases of extrapulmonary TB in 57 (45.6%) patients there was Koch's abdomen, in 48 (38.4%) patients there was lymph node TB, in 10 (8%) patients there was pleural effusion, and in 10 (8%) patients tubercular meningitis was seen.

Conclusion: Our study supports the findings that as CD4+ T lymphocytes count decreases, the risk of development of TB is increases. Therefore screening the HIV/AIDS patients for co-infections, TB should be definitely included in the study.

Key words: Tuberculosis, Opportunistic infection, People living with HIV AIDS, Tubercular meningitis

INTRODUCTION

Tuberculosis (TB) is the most common opportunistic infection among HIV-infected patients, who remain at high risk for TB throughout the course of their disease.[1] TB is the most important cause of morbidity and mortality in People Living with HIV (PLHIV).[2] India is the third-highest HIV burden country in the world, with an adult prevalence of 0.22%. By numbers, India ranks 2nd in the world and accounts for about 9% of the global burden of HIV-associated TB.[3] PLHIV are 20–21 times at higher risk of developing TB. TB-HIV co-infection results in higher mortality rates and nearly 25% of all deaths among PLHA are due to TB. In India, about 110,000 people are estimated to be HIV-TB co-infected annually, with the national average for HIV prevalence among incident TB cases at 5%. The mortality in this group is very high and 9700 people die every year among TB/HIV co-infected patients.[4-6]

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The HIV virus damages the body's natural defences - the immune system and accelerates the speed at which TB progresses from a harmless infection to life-threatening condition. The estimated 10% activation of dormant TB infection over the life span of an infected person, is increased to 10% activation in 1 year, if HIV infection is superimposed TB is already the opportunistic infection that most frequently kills HIV-positive people. Even in HIV positive cases, TB can be cured if diagnosed in time and treated properly.[4,5]

To mitigate the effect of dual burden of HIV and TB, Revised National TB Control Programme and National AIDS Control Programme have developed a collaborative framework. Via Single window delivery of TB and HIV services is being successfully implemented for all PLHIV in the AntiRetroviral therapy (ART) centers, wherein intensified case-finding through screening all ART center attendees for TB, offering rapid molecular testing to symptomatic patients and providing anti- TB treatment.[4,5]

MATERIALS AND METHODS

This prospective and observational study was conducted at the Tertiary ART center and Department of Medicine, Maharaja Yeshwantrao (M.Y.) Hospital, Indore during the period January 2019 to July 2020. We had screened 1610 patients with PLHA. Of these 1610, 200 patients were diagnosed with TB.

Study Centre

Tertiary ART Center and Department of Medicine, M.Y. Hospital, Indore, Madhya Pradesh.

Study Design

Prospective observational study.

Methodology

The patient and/or his/her legally acceptable representative were explained about the study in detail including the procedures, risks/benefits, etc. After obtaining their verbal approval for participation in the study, a voluntary written informed consent was obtained from them for participation in the study. All the study-related procedures were carried out after obtaining the consent.

A detailed medical history including the presenting complains, history of any chronic medical illness, surgical history, history of drug treatment, family history of chronic medical illness or any familial surgical history were obtained. The personal history included diet, sleep, bowel, and bladder patterns.

The patient underwent general and systemic examinations. Following which blood samples were collected for routine laboratory investigations, which included CD+T lymphocyte counts.

Ethical Considerations

This study was approved by the institutional ethical committee and review board.

Statistical Analysis

The data were initially entered into the Microsoft Excel for analysis. Online statistical software such as GraphPad, and Epi Info. were used for calculating the p values. Comparison of means between the groups was done using Unpaired "*t*"-test and within the group was done using Paired "*t*"-test. Association between two non-parametric variables was done using the Pearson Chi-square test. $P < 0.05$ was taken as statistically significant. The final data were presented in the form of tables and graphs.

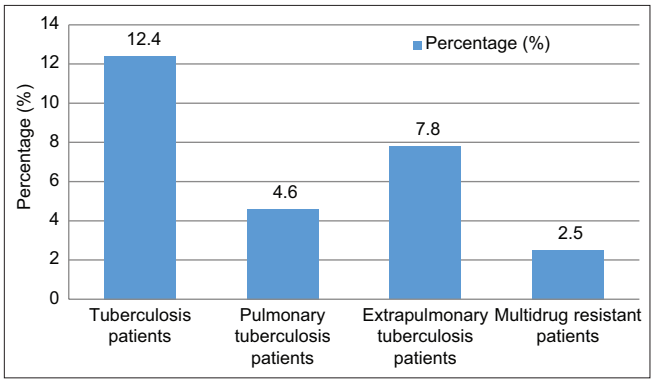
RESULTS

As shown in Table 1 and Graph 1, a total of 1610 patients were enrolled in this study. Of these 1610 patients, 200 (12.4%) patients had TB, out of those TB patients, 75 (4.6%) patients had pulmonary TB and 125 (7.8%) patients had extrapulmonary TB.

As shown in Table 2, in 57 (28.5%) patients there was Koch's abdomen, in 48 (24.0%) patients there was lymph node TB, in 10 (5.0%) patients there was pleural effusion,

Table 1: Distribution of patients

Category	No. of patients	Prevalence
Total PLHIV patients at tertiary ART centre and M.Y. Hospital, during the study period	1610	
Tuberculosis patients	200	12.4%
Pulmonary tuberculosis patients	75	4.6%
Extrapulmonary tuberculosis patients	125	7.8%



Graph 1: Bar diagram showing distribution of patients

in 75 (37.5%) patients pulmonary TB was seen and in 10 (5.0%) patients tubercular meningitis was seen.

Majority of the patients had pulmonary TB followed by Koch's abdomen and lymph node TB.

As shown in Table 3 and Graph 2, in 32 (16.0%) patients the CD4+ count was between 200 to 500, in 119 (59.5%) patients it was between 100 and 199, in 37 (18.5%) patients it was between 50 and 99 and in 12 (6.0%) patients it was <50. The mean CD4+ count in our study was 195.26 ± 104.59.

As shown in Table 4 and Graph 3, the mean CD4+ count in extrapulmonary TB was 195.75 ± 105.38 and in the pulmonary TB was 194.44 ± 103.96. The difference was found to be statistically not significant ($P = 0.932$), showing a comparable mean CD4+ count between the pulmonary and extrapulmonary TB patients.

As shown in Table 5 and Graph 4, the mean CD4+ count in Koch's abdomen was 136.79 ± 49.21, in lymph node it was 146.04 ± 62.92, in pleural effusion it was 170.80 ± 64.81, in pulmonary TB it was 155.11 ± 69.96 and in tubercular meningitis it was 69.90 ± 36.20. The comparison of mean CD4+ counts in relation to type of TB was found to be statistically significant (F value = 4.952, $P = 0.001$), showing that the mean CD4+ count across all the types of TB is varying.

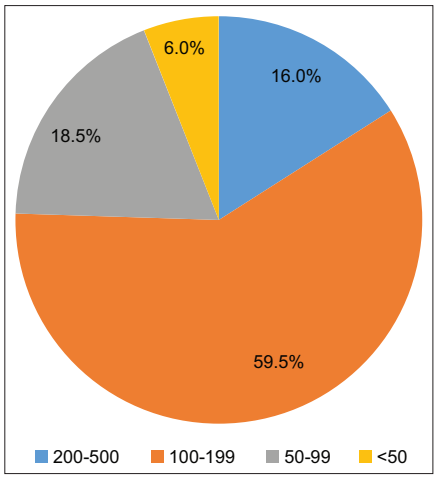
The CD4+ count was highest in pleural effusion and lowest in tubercular meningitis.

Table 2: Distribution of patients according to tuberculosis type

Tuberculosis type	Number	Percentage
Koch's abdomen	57	28.5
Lymph node	48	24.0
Pleural effusion	10	5.0
Pulmonary tuberculosis	75	37.5
Tubercular meningitis	10	5.0
Total	200	100.0

Table 3: Distribution of patients according to CD4+ count

CD4+ count	Number	Percentage
200–500	32	16.0
100–199	119	59.5
50–99	37	18.5
<50	12	6.0
Total	200	100.0



Graph 2: Pie diagram showing distribution according to CD4+ count

DISCUSSION

In 32 (16.0%) patients the CD4+ count was between 200 to 500, in 119 (59.5%) patients it was between 100 to 199, in

Table 4: Comparison of mean CD4+ count in relation to pulmonary and extrapulmonary tuberculosis

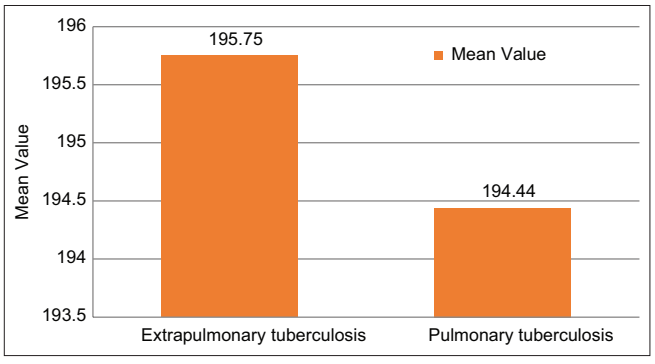
Group	No.	Mean±SD	*"t"*- value	*P* value
Extrapulmonary tuberculosis	125	195.75±105.38	0.086, df=198	0.932, NS
Pulmonary tuberculosis	75	194.44±103.96		

Unpaired "t"-test applied. *P*=0.932, Not significant

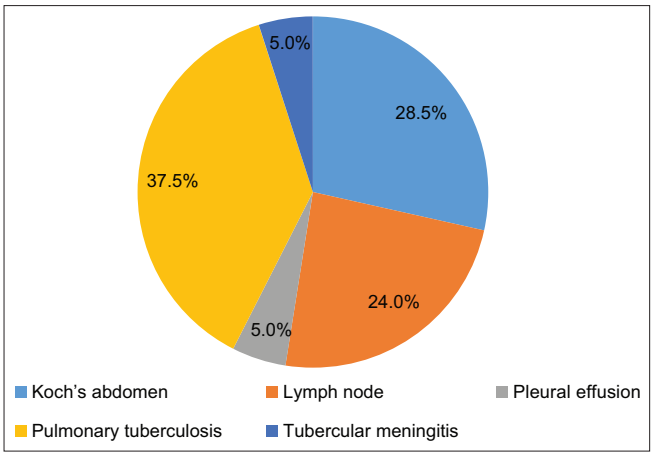
Table 5: Comparison of CD4+ counts in relation to type of tuberculosis

Type of Tuberculosis	Number	CD4+	F value	*P* value
Koch's abdomen	57	136.79±49.21	4.952	0.001*
Lymph node	48	146.04±62.92		
Pleural effusion	10	170.80±64.81		
Pulmonary tuberculosis	75	155.11±69.96		
Tubercular meningitis	10	69.90±36.20		

*Significantl level, *P* value < 0.05



Graph 3: Bar diagram showing comparison of mean CD4+ count between pulmonary and extrapulmonary tuberculosis



Graph 4: Pie diagram showing distribution according to type of tuberculosis

37 (18.5%) patients it was between 50–99 and in 12 (6.0%) patients it was <50. The mean CD4+ count in our study was 195.26 ± 104.59.

The mean CD4+ count in Koch's abdomen was 136.79 ± 49.21, in lymph node it was 146.04 ± 62.92, in pleural effusion it was 170.80 ± 64.81, in pulmonary TB it was 155.11 ± 69.96 and in tubercular meningitis it was 69.90 ± 36.20. The comparison of mean CD4+ counts in relation to type of TB was found to be statistically significant (F value = 4.952, $P = 0.001$), showing that the mean CD4+ count across all the types of TB is varying.

Leeds *et al.* (2012)[7] collected data from the medical records of patients with extrapulmonary TB. Of these 320 patients, 150 (48.1%) patients had HIV infection and 40% had concomitant pulmonary TB. They found in patients of HIV infection with low CD4+ counts (<100), CNS/meningeal and/or disseminated type of TB was the more common.

Dias *et al.* (2016)[8] included 112 patients to study the prevalence of extrapulmonary TB in HIV patients and to relate them to the immune status and final outcome. They found that the mean CD4+ count was lowest in the meningeal TB (31.4 ± 35.3/μl).

In our study also we found that in patients with tubercular meningitis the CD4+ counts were <100, which is comparable with the mean reported by Leeds *et al.* (2012).[7] Dias *et al.* (2016)[8] also reported lowest CD4 count in meningeal TB, which is comparable to our study, but we found higher CD4 count in our tubercular meningitis patients in comparison to Dias *et al.* (2016)[8] study.

In our study, the prevalence of pulmonary TB was 4.6% and extrapulmonary TB was seen in 7.8% of patients. According to National TB Elimination Programme Annual Report, 2020,[4] evidence has shown that the prevalence of TB in PLHA patients was approximately 5%, which is less in comparison to our study findings. Of the 200 TB patients, 75 (37.5%) patients had pulmonary TB; According to the WHO Index-TB Guidelines for Extrapulmonary TB in India, 2016[9] have reported a prevalence of 50–60% of pulmonary TB among patients with newly diagnosed TB in PLHA patients; which is comparatively low in our study population. The prevalence of EPTB in our study was 62.5%, while according to Index-TB guidelines have reported a prevalence of 40–50% of EPTB among patients with newly diagnosed TB in PLHA patients; which is lower than that reported in our study.

Dharmshale *et al.* (2012)[10] conducted a study on patients with HIV and non-HIV patients. They found 47.5% of HIV patients had extrapulmonary TB; which is lower than that reported in our study.

Dias *et al.* (2016),[8] Study done by Dias *et al.* (2016)[8] showed lymphatic involvement in 31.3% of patients, which is higher than that reported by our study and Pulmonary TB incidence is very high, i.e., 86.6%, which is lower in our study, i.e., 37.5%. The prevalence of pleural and meningitis was higher in the study.

CONCLUSION

We found that the prevalence of pulmonary TB is comparatively lower than the extrapulmonary TB in these patients. Our study supports the findings of various studies that while screening the HIV/AIDS patients for co-infections, TB should be definitely included in the study. As CD4+ T lymphocytes count decreases, the risk of developement of TB is increases.

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Original Article

A Study of Burden, Quality of Life assessment, Psychiatry Morbidity in Terms of Depression, Anxiety, and Stress in Caregivers of Patients with Intellectual Disability

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Abstract

Background: Psychiatric illnesses such as depression, adjustment disorders, and anxiety disorders are common in caregivers of the patients with Intellectual disability and are likely to reduce patient's quality of life (QOL).

Objectives: Study of Burden, QOL assessment, Psychiatry morbidity in terms of depression, anxiety, and stress in caregivers of patients with Intellectual Disability.

Materials and Methods: The relatives/caregivers of the patients to be involved in the study were assessed. Those meeting the inclusion criteria were further evaluated using Zarit Burden Interview, World Health Organization QOL -BREF, and Depression, Anxiety, and stress scale-21.

Results and Conclusion: The burden assessed as per scoring scales showed that higher the intellectual disability, more the burden severity was found in caregivers. Most of the caregivers were suffering from mild to moderate depressive symptoms, thus effecting their QOL. Routine assessment of burden and psychiatric morbidity in the caregivers will help to reduce their burden and thus help them care for their children more appropriately and efficiently.

Keywords: Intellectual disability, Depression, Burden, Stress

INTRODUCTION

Individuals suffering from intellectual disability have neurodevelopmental deficits having limitations in *intellectual functioning* and *adaptive behavior*. The above-mentioned disabilities have there origin and manifest before the age of 18 years and may be associated with other related problems including neurodevelopmental (e.g., autism spectrum disorders, and attention deficit hyperactivity disorder), some other psychiatric disorders (e.g., depression, and anxiety), neurological (e.g., infantile cerebral palsy), and medical conditions (e.g., meningitis). Intellectual functioning tested includes a wide range of mental activities such as the ability of logical reasoning and problem-solving, learning and verbal skills.[1]

Adaptive functioning encompasses three domains including the conceptual domain (language, knowledge, and memory), the social domain (empathy, social judgment, and rule-following ability), and the practical domain (self-care, organization, and daily living skills). It is estimated to range between 1–3%, with a male to female ratio of 1.6:1 in the Western world.[2] Its prevalence in developing countries is estimated to range from 10 to 15/1000 children among whom 85% have a mild intellectual disability. The etiology of intellectual disability mainly comprises of the causes related to genetic abnormalities and environmental exposure. Genetic abnormality includes single gene mutation, copy number variation, or chromosomal abnormality leading to inborn errors of metabolism, neurodevelopmental

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defect, and neurodegeneration. Environment exposure such as maternal exposure to toxin/infectious agents, uncontrolled maternal medical conditions, complications related to delivery, post-natal trauma, and exposure to various toxin/infectious agents. The commonest known preventable or environmental cause of intellectual disability is fetal alcohol syndrome, most common chromosomal cause is Down syndrome and the genetic cause being Fragile X syndrome. Intelligence quotient of 70 or below suggests intellectual disability diagnosis.[2]

It is further seen that the demand of the care givers of children with developmental disability especially intellectual in nature is much more than the other disabilities. These caregivers are usually the mothers, elderly or the un-employed members of the family. These people normally never planed to be caregivers but became accidentally with the need unavoidable. The caregivers are never prepared for this role and when given the same, finds It very demanding later on. Factors that contribute to poor health outcomes of the caregivers include the severity of the disability, child's behavior, child's temperament, low self-esteem, and poor social support.[3]

It is observed commonly that the parents suffer from different emotional and psychological problems if one child is disabled in family. Attitude of the society produces stress among family members. Even marital relationships suffer excessively due to guilt, shame, blame, and anxiety.[4]

A disabled child, regardless of the type of the disability, brings difficulties into the family members. It mainly includes mental health, financial situation, education, lifestyle changes, health relationships with the family and social environment, and the child's disability. Research studies point out that mother takes on a more active role.[5] When the child showed a high level of dysfunction with more frequent episodes of anxiety and depression, parents reported more psychiatric symptomatology. In such parents, social support is inversely related to anxiety and depression, whereas behaviors of their children are positively associated with these symptoms. Mothers experience more stress than fathers, higher caregiver burden, and a low sense of coherence.[6] This may be strenuous for the parents and put a major impact on their quality of life (QOL). Caring for disabled children can be a physically and mentally strenuous resulting in compromised QOL of the carers too. Even the carers need help to cope with the physical, mental, and emotional stress, they are bearing while caring for their loving children. It is also important to note that caring for a child with a disability does not equally affect all the families. There are families who cope well despite facing a lot of adversities. A number of factors that can affect the QOL of carers which include severity of the illness of the child, presence of behavioral problems, socioeconomic and education status of the family, low social support.[7]

The studies conducted earlier stated that the mean caregiver burden was minimal to moderate in all families. Children suffering from intellectual disability are regarded as a burden by their family members. Negative attitude of the parent leads to rejection of such disabled children. This puts adverse impact on the interactions within the family. Intellectual disabled children should be offered support by family members to cope with stressful situations and in their rehabilitation.[8,9]

Other Studies reported that stress is related to the severity of intellectual disability, being maximum in those children suffering with severe-to-profound retardation. Mothers perceived much more stress and burden in caring for their children than fathers. These studies also revealed that these caregivers also faced various kinds of challenges, such as psychological, social, and economic challenges other than poverty. Caregivers felt stressed and burdened. They suffered from sadness for various reasons including the task of giving care, worries about the future lives of their kids, and the cognitive and the behavioral changes of their children. They are even stressed because of inadequate social services for their children and the stigma attached to these disabilities.[8-10]

It is important to address stigma in cases of intellectual disability. Only few studies have been conducted in past specifically focusing on the caregiver burden and the impact on QOL of the family members rather than mental illness. Stigma associated with intellectual disability is present across all ethnic groups, although it appears to be increased among those from developing countries.[11,12] The aim of the present study conducted was to identify burden, assess QOL and psychiatric morbidity in terms of depression, anxiety, and stress in the caregivers of children with intellectual disability.

Aims and Objectives

1. To study the burden in caregivers of patients of Intellectual disability.
2. To study QOL of caregivers of patients of Intellectual disability.
3. To study psychiatric morbidity in terms of depression, anxiety, and stress.

MATERIALS AND METHODS

The study was conducted in the Department of Psychiatry, Government Medical College, Amritsar and Institute of Mental health Amritsar. A random sample of 50 relatives/ care givers of the patients of Intellectual disability who agreed to participate was informed about the precise aim of

the interview and a written informed consent was taken from them. The subjects of the study conducted were assessed using Zarit burden Scale, World Health Organization QOL-BREF (WHOQoL-BREF), and Depression, Anxiety, and stress scale-21 (DASS-21) questionnare. The study did not interfere in the treatment and management of the patients. Relatives/caregivers were reassured about the confidentiality of the information given by them. Data collected was analyzed through standard statistical methods.

Inclusion Criteria for Key Caregivers/Relatives

1. Identified current caregivers of patients should be aged more than 18 years.
2. Caring and living with patient for more than 1 year.
3. Not suffering from any chronic illness for the past 1 year (medical/psychiatric).
4. Agreed to give informed consent.

Exclusion Criteria

1. Caregivers who had a cognitive impairment or an intellectual disability.
2. Children and young people <18 years.
3. Caregivers not giving consent.
4. Uncooperative caregiver.

The study sample was assessed using following documents:

Self-Structured Sociodemographic Proforma

Zarit Burden interview[13]

It is a popular caregiver self report measure used by many aging agencies. The revised version contains 22 items and each item on interview is a statement which caregiver is asked to endorse using a 5- point scale.

WHOQOL-BREF[14]

WHOQOL is a QOL assessment developed by the WHOQOL Group with fifteen international field centers, simultaneously, in an attempt to develop a QOL assessment that would be applicable cross-culturally.

DASS-21 questionnare[15]

The Items DASS-21 is a set of three self-report scales designed to measure the emotionally states of depression, anxiety, and stress. Each of the three DASS-21 scales contains 7 items, divided into subscles with similar content.

Statistical Analysis

At the end of the study, the data was collected and analyzed using appropriate statistical methods.

RESULTS

Fifty caregivers of the patients suffering from intellectual disability were assessed. Of these 60% of the patients suffered from mild, 22% from the moderate, and 18% suffered from severe intellectual disability.

Intellectual disability

Severity	No of patients	percentage
Mild	30	60
Moderate	11	22
Severe	9	18
Profound	0	0

Zarit Burden Interview

Burden	No of caregivers (%)
Little/no burden	9
Mild-to-moderate	19 (38%)
Moderate-to-severe	22 (44%)
Severe	0

DASS-21 Questionnaire

	Depression	Anxiety	Stress
Mild-to-moderate	16 (32%)	12 (24%)	24 (48%)
Severe	4 (16%)	9 (18%)	9 (18%)

WHOQoL-BREF

Domains	Mean±SD
Physical health	13±1.52
Psychological	12±1.45
Social relation	11±1.55
Environment	9±1.21

Of the caregivers assessed, 22 (44%) had moderate-to-severe category of burden assessed by zarit burden interview, 19(38%) of the subjects suffered from mild to moderate degree of burden, and 9 (18%) had little to no caregiver burden which was almost similar to the results of the previous studies conducted.

The results showed that 40% of the caregivers suffered from depression assessed by DASS-21 scale out of which 32% suffered from mild to moderate degree of depression and 8% suffered from severe depression.

The results showed that 42% of the caregivers suffered from anxiety as assessed by DASS-21 scale out of which 24% suffered from mild to moderate degree of anxiety18% and suffered from severe anxiety issues.

The results showed that 60% of the caregivers suffered from stress as assessed by DASS-21 scale out of which 48% suffered from mild to moderate degree of stress and 12% suffered from severe stress issues.

The QOL of the caregivers was assessed using WHOQol-BREF scale which concluded that out of all the four domains of the scale mentioned maximum impact was seen

on psychological domain with a mean score of 13 ± 1.52, followed by physical domain (12 ±1.45), social domain (11 ± 1.55) and environmental domain (9 ± 1.21).

DISCUSSION AND CONCLUSION

The following study conducted had an aim to assess the burden, impact on QOL and psychiatric morbidity in terms of depression, anxiety, and stress in the family members of the intellectually disabled patients. Similar studies were also conducted in the past with same aim. The results of the present study concluded that the family members of such disabled patients had significant caregiver burden on them, maximally moderate-to-severe degree in intensity. Similar results were depicted by a study conducted in India in the year 2014–2015 by Bhatia *et al*.[16] A significant impact was seen on the QOL of the caregivers, affecting maximally the psychological domain as also seen in the studies conducted in the past. One such study conducted by Chou *et al*. in the year 2009 in China interpreted the similar results.[17] On applying DASS-21 on these subjects, it was found that the caregivers suffered from significant amount of depression and anxiety due to the underlying stress related to the worsening conditions of their disabled children, their loved ones, affecting further their interpersonal relations and other aspects of their lives mainly the social and environmental domains. It was clearly noticed that this impact on the caregivers was directly related to the severity of the intellectual disability of their children and the cognitive and behavioral changes seen in them.

The study conducted had its own limitations. The sample size was small, also the subjects of the study assessed were taken from the tertiary care centers which indirectly shifted the results slightly to the severe side as being a tertiary healthcare center more sick and patients with severe disability approach the present place of the conduction of the study.

A single Intellectual disabled child in the family, severity of their illness, societal attitude can put a major impact on the emotional and the psychological health of the primary caregivers of these patients. Awareness, better accessibility to the services for these patients along with psychosocial support of the other family members and society as a whole can help in positive adaptation.

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Original Article

Efficacy of Airway Exchange Catheter during Extubation in Patients Undergoing Major Head-and-Neck Surgeries

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Abstract

Background: Head-and-neck surgeries encompasses an expanded spectrum of procedures varying greatly in complexity, duration and complications thereby carrying considerable risk of post-operativelaryngo-pharyngeal edema and airway obstruction due to surgical manipulation. The aim of this study was to study the efficacy of airway exchange catheter (AEC) during extubation in patients undergoing major head-and-neck surgeries.

Material and Method: Clinical Observational study, enrolling 30 patients of either sex, aged 20–70 of the American Society of Anesthesiologist physical status I and II, scheduled for major head and neck surgeries. Cook's AEC (CAEC) was used in this study. Tolerability, number of patients desaturated with CAEC *in situ*, number of patients required reintubation over the catheter, ease of reintubation, and complications were assessed.

Result: It was observed 2 patients (6.67%) showed moderate tolerability and 1 patient (3.33%) showed poor tolerability. Four patients (13.33%) desaturated with catheter in situ out of which 1 patient (3.33%) required emergency reintubation after 4 h of tracheal extubation. Reintubation in this patient, was thought to be nearly impossible by direct laryngoscopy, was easily achieved over CAEC and none of the patient experienced any complication related to the catheter.

Conclusion: The study concluded that CAEC can act as life-saving device in patients with risk factors for difficult reintubation and loss of airway access due to surgical manipulation or anatomical changes.

Key words: Cook's airway exchange catheter, Head and neck surgeries, Extubation

INTRODUCTION

Head-and-neck surgery encompasses an expanded spectrum of procedures varying greatly in complexity, duration and complications, presenting unrivalled challenges for the anesthesiologist. Anesthesiologist needs to maintain airway patency, oxygenation, and ventilation in similar anatomical space in which surgeon operates, i.e., shared airways.

Extubation in such patients is extremely difficult as no one can predict adequacy of airway once endotracheal tube (ETT) has been removed though criteria used to predict successful extubation are generally satisfactory before extubation.[1] Planning for tracheal extubation is a critical component of successful airway management strategy when dealing with situations at increased risk for extubation failure and in patients with difficult airways and at risk of reintubation.[2]

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An extubation strategy should aim to maintain uninterrupted oxygen delivery to the patients lungs, avoiding airway stimulation and include a backup plan, that would permit ventilation and re-intubation with minimal difficulty and delay should extubation fail.[3] Head and neck surgeries carry considerable risk for post-operativelaryngo-pharyngeal edema and airway obstruction due to surgical manipulation, distorted airway anatomy and characteristics of surgery.[4] Re-establishing the airway in these patients can be extremely challenging and often result in considerable morbidity

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and mortality.[5] Hence, there should be a preformulate dextubation algorithm in such patients.

Airway exchange catheters (AEC) act as bridging devices to staged extubation trial as recommended in difficult airway society (DAS) guidelines. Cook's AEC (CAEC) plays a very important role in not only by securing the airway but also by providing continuous means of oxygen insufflation and also acting as conduit for tracheal reintubation if required.[6-10]

MATERIALS AND METHODS

After obtaining clearance from the ethical committee, we carried out a clinical observational study in 30 patients of ASA grade I and II in the age group 20–70 years posted for elective head and neck surgeries.

Proper pre-anesthetic check up was done and appropriate investigations were done. Patient was advised Tab Alprazolam 0.25 mg a night before and on the day of surgery with sip of water.

On arrival of patient in operation theater, 20G i/v cannula was secured, all the routine monitors were attached and baseline vitals were recorded. Following pre-medication with Inj. midazolam 1 mg, Inj. glycopyrrolate 0.2 mg and Inj. fentanyl 2mcg/kg, patient was preoxygenated for 3 minutes and induced with propofol 2 mg/kg. The trachea of patient intubated orally or nasally after attaining proper relaxation with Inj. scoline 1.5 mg/kg.

At the completion of surgery, Inj. myopyrrolate (neostigmine angglycopyrrolate) was given. Depending on complexity and characteristics of surgery, patients were transferred to ICU with a tube in situ, Patients who had undergone thyroidectomy were extubated on table over CAEC and were kept in post anesthesia care unit (PACU) for monitoring.

Technique of CAEC Insertion

Patients were extubated when they become conscious and had normal body temperature normal blood gases with inspired O2 concentration (FiO2) of 0.4, positive end-expiratory pressure less than 5 cm H20 and pressure support of <8 cm H20. Patients were given spontaneous breathing trial (SBT), i.e., CPAP and T-piece trial.

After sedating the patient with Inj. midazolam 2 mg, pharyngeal suctioning was done. CAEC was lubricated with lignocaine jelly and was inserted through ETT to the predetermined depth (not more than 26 cm orally) avoiding carinal irritation. Distal end of CAEC was connected to O2 supply with flow between 5 and 8 L/min and was fixed on cheek or forehead.

Patients were kept under observation in PACU or ICU and hemodynamic and ventilator parameters were observed and maintained for 15 min till 2 h, for 30 min till 4 h then hourly for 10 h, and 2 hourly thereafter.

Hemodynamic parameters (heart rate [HR], systolic blood pressure [SBP], diastolic blood pressure [DBP], mean arterial pressures [MAP]), ventilator parameters (SpO2, EtCO2), tolerability, need for reintubation, ease of reintubation, and complications were observed.

Statistical Analysis

The data from the present study was systematically collected and was analyzed to draw relevant conclusion. Sample size was calculated in consultation with statistician taking mainly the duration for which CAEC was need to be placed in situ, risk factors for difficult extubation and based on previous study to get power of study more than 85%. The continuous data were represented as standard deviation (mean ± SD). Number of patients and percentage of cases expressed discrete categorical data. The *P* value was calculated to evaluate level of significance. The $P > 0.05$ was considered non-significant, $P = 0.01$-0.05 was considered significant and $P < 0.001$ was highly significant. The results were then analyzed and compared to previous studies.

RESULTS

The distribution of sex, ASA grade, mean age, mean weight, mean duration of surgery, and mean duration of catheter kept in situ were observed.

Mean HR, Mean SBP, mean DBP, mean MAP, mean SpO2, and mean EtCO2 was observed before and after CAEC insertion and was found to be clinically insignificant with $P > 0.05$.

CAEC was kept for mean duration of 8.45 ± 8.59 h for maximum period of 24 h.

CAEC can be kept for 72 h.

It was observed that CAEC was well tolerated in 27 patients (90%), moderately tolerated in 2 patients (6.67%) for which patients were kept sedated and were kept under observation in ICU. Compliance of one patient was very poor and requested catheter removal after 15 min of insertion.

Four patients (13.33%) were desaturated of which three patients were managed with supplemental oxygen (1 with NRB and 2 with simple O2 mask).

One patient (3.33%) needed emergency reintubation after 4 h of extubation (had a history of difficult intubation during maxillectomy where patient was intubated following multiple attempts and use of video laryngoscope). Patient was easily reintubated over CAEC that would otherwise would had been difficult with direct laryngoscopy.

Seventeen patients (56.67%) could vocalize with indwelling catheter whereas 13 patients (43.33%) could not able to speak due to extensive surgery and altered anatomy.

No CAEC related complications such as esophageal misplacement, barotraumas, and pneumothorax were seen.

Demographic profile	
Mean age in years	43.53±12.09 years
Mean weight in kilogram	74.13±10.93 kg
Mean duration of surgery	181.67±88.79 min
Mean duration of catheter *in situ*	8.45±8.59 h
Sex distribution	Male=18 (60%)
	Female=12 (40%)
ASA grading	Grade 1=20 (66.67%)
	Grade 2=10 (33.33%)

Duration	Heart rate		*P*-value
	Mean	SD	
Before CAEC insertion	84.77	10.04	0.190 (NS)
After CAEC insertion	88.17	9.82	

Duration	Systolic blood pressure		*P*-value
	Mean	SD	
Before CAEC Insertion	126.33	8.09	0.184(NS)
After CAEC Insertion	128.83	6.22	

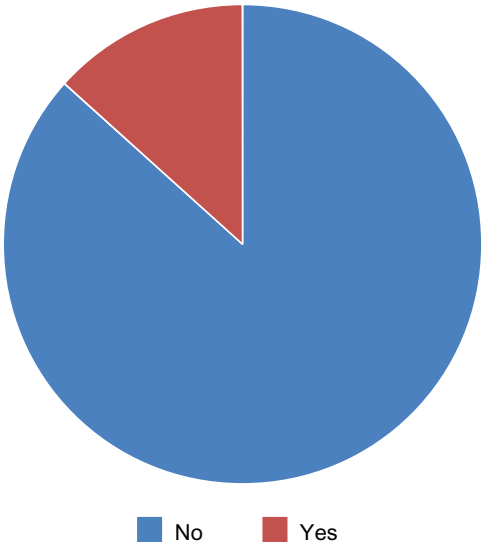
Duration	Diastolic blood pressure		*P*-value
	Mean	SD	
Before CAEC Insertion	80.53	6.08	0.093 (NS)
After CAEC Insertion	83.20	6.05	

Duration	Mean arterial pressure		*P*-value
	Mean	SD	
Before CAEC Insertion	97.80	6.40	0.299 (NS)
After CAEC Insertion	99.41	5.47	

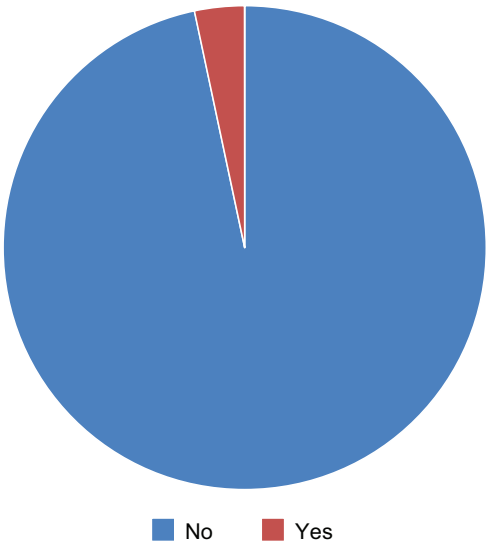
Duration	Saturation		*P* -value
	Mean	SD	
Before CAEC Insertion	99.12	1.02	0.499 (NS)
After CAEC Insertion	98.97	1.25	

Duration	ETCO2		*P*-value
	Mean	SD	
Before CAEC Insertion	35.60	1.73	0.186 (NS)
After CAEC Insertion	36.47	1.93	

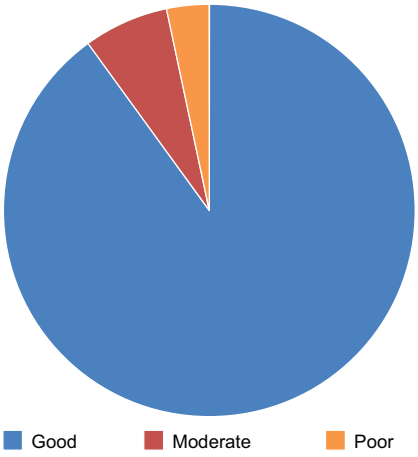
Desaturation	No. of cases	% age
No	26	86.67
Yes	4	13.33
Total	30	100.00



Reintubation	No. of cases	% age
No	29	96.67
Yes	1	3.33
Total	30	100.00



Tolerability	No. of cases	% age
Good	27	90.00
Moderate	2	6.67
Poor	1	3.33
Total	30	100.00



DISCUSSION

Tracheal extubation is a critical step during emergence from anesthesia.[11] It is not simply reversal of the process of intubation as conditions are often less favorable than at the start of process of intubation. At extubation, there is a transition from controlled to uncontrolled situation.

Extubation is a vulnerable time in patients undergoing head and neck surgeries. Head-and-neck surgeries carry considerable risk of post-operativelaryngo-pharyngeal oedema and airway obstruction due to surgical factors, hematoma, and anatomical changes. Reintubation may be very difficult or impossible through laryngoscopy in such patients. Even the bag mask ventilation may be difficult or impossible in such patients. A pre-established extubation plan with considerations made for the possible need for re-intubation is of utmost importance.

AEC, i.e., CAEC played very important role and offers several advantages:

- Providing method of continuous administration of oxygen
- Can be used as stlet for tracheal reintubation
- Provides a method of ventilating the patient.

In our study, it was observed CAEC was well tolerated in most of patients, two patients (6.67%) showed moderate tolerability, for which patients were kept sedated. Results were similar to study conducted by Dosemeci *et al.*[12]

One patient (3.33%) showed poor tolerability and requested removal 15 min following insertion. As patient was able to vocalize well and risk of developing respiratory distress appeared to be low airway exchange catheter was removed. Results were similar to study conducted by Loudermilk *et al.*

Four patients (13.33%) got desaturated with catheter in situ of which three patients were managed with supplemental oxygen in addition to oxygen insufflated through CAEC.

Results were similar to study conducted by Loudermilk *et al.*

One patient (3.33%) needed emergency reintubation, so patient was easily reintubated over CAEC on first attempt without any need for any other alternate method.

Results were similar to similar conducted by Dosemeci *et al.*

CONCLUSION

The use of CAEC is a life-saving method and a bridge to extubation in patients with a potential difficult airway. AEC is an efficient method of maintaining continuous access to the airway after extubation as it is well tolerated and offers a clinically valuable conduit for reintubation. It allows a safer trial of tracheal extubation and therefore can shorten the duration of reintubation.

Limitation

Sample size is small.

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Original Article

Comparative Evaluation of Normal Saline and Dextrose as Diluent of Local Anesthetic in Ultrasonography-Guided Supraclavicular Brachial Plexus Block

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Abstract

Background: Ultrasonography has revolutionized the field of regional anesthesia due to its various advantages over peripheral nerve stimulation techniques.

Materials and Methods: This prospective blinded controlled study was carried out in 60 patients of American Society of Anesthesiologists grade I and II undergoing elective upper limb surgery randomly allocated into 30 patients in each group. Each group received supraclavicular block. Group NS patients received 21 ml 0.5% Ropivacaine (Prepared by diluting 14 ml 0.75% Ropivacaine with 7 ml of normal saline) and group D5% patients received 21 ml 0.5% Ropivacaine (Prepared by diluting 14 ml 0.75% Ropivacaine with 7 ml of dextrose). The time to onset of sensory block and motor block, duration of sensory and motor block and duration of post-operative analgesia and any side effects were recorded for each patient.

Results: In this study, the meantime for onset of analgesia with normal saline group was 41.00 ± 2.74 min and 28.33 ± 2.42 min for the dextrose group. The $P = 0.0001$, which shows that there was clinical evidence that dilution with dextrose results in a faster onset time of analgesia compared to dilution with normal saline.

Conclusion: Our study suggests that decrease in onset time of analgesia when dextrose was used as a diluent instead of normal saline for ultrasound-guided supraclavicular brachial plexus block.

Key words: Dextrose, Normal saline, Ropivacaine, Ultrasonography

INTRODUCTION

Regional anesthesia has many advantages over general anesthesia such as decreased chances of aspiration, decreased chances of nausea vomiting, maintenance of patient's consciousness and protective airway reflexes, less chance of post-operative hypoxia and respiratory complications (bronchospasm, aspirations, hypoxia post-operative residual paralysis etc.).[1]

The modern history of regional anesthesia and local anesthesia begins with Carl Koller who demonstrated topical anesthesia of the eye with cocaine in 1884. Later in 1884, William Halsted used cocaine for intradermal infiltration and for peripheral nerve blocks using the open surgical technique, applying cocaine directly onto the nerve plexus. The landmark-based percutaneous approach of the supraclavicular block (SCB) was introduced into clinical practice in Germany by Diedrich Kulenkampff in 1911.[2,3]

In 1880 French physicists Pierre Curie and Paul Jacques Curie discovered the piezoelectric effect in certain

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crystals. Paul Langevin, a student of Pierre Curie, developed piezoelectric materials, which can generate and receive mechanical vibrations with high frequency (therefore ultrasound). During World War I, ultrasound was introduced in the navy as a means to detect enemy submarines. Diagnostic applications of ultrasound began through the collaboration of physicians and sonar (sound navigation ranging) engineers. In 1942 Karl Dussik, a neuropsychiatrist and his brother Friederich Dussik, a physicist described ultrasound as a medical diagnostic tool to visualize neoplastic tissues in the brain. The real-time B scanner was developed in 1965 and was first introduced in obstetrics. In 1976 the first ultrasound machines coupled with Doppler measurements were commercially available. With regard to regional anesthesia as early as 1978 La Grange *et al.* were the first anaesthesiologists to publish a case series report of ultrasound application for peripheral nerve blockade (PNB). With the advancement of technology in 1994 "Kapral *et al.*" first described ultrasound imaging of brachial plexus in supraclavicular position and needle insertion under ultrasound guidance.[4,5]

Rising popularity of ultrasound guidance for PNB is due to its various advantages over peripheral nerve stimulation (PNS) techniques. Principle benefit of ultrasound is its inherent ability to directly visualize anatomical structures such as peripheral nerves and tissue planes in real-time and additional benefit is the ability to reposition one's needle while assessing for adequate local anesthetic spread.[6,7]

The overall idea of pre-emptively scanning patient anatomy with Ultrasonography (USG) for neurovascular variations or abnormalities has been suggested as a means of improving patient safety by preventing block complications. So when compared to PNS guided nerve blocks, USG guided nerve blocks have been shown to require less time to perform, possess more rapid onset, longer duration of anesthesia and less risk of block failure, decrease risk of vascular puncture and improved quality of sensory block.[8-10]

The utilization of ultrasound in modern medicine is well established. This study evaluates and compare the quality of anesthesia and analgesia in patients undergoing upper limb surgeries under ultrasound-guided supraclavicular brachial plexus block (SCBPB) using inj. Ropivacaine with NS and inj. Ropivacaine with D5%.

MATERIALS AND METHODS

This prospective randomized casecontrol study was conducted at Netaji Subhash Chandra Bose Medical College and Hospital Jabalpur (Madhya Pradesh). After obtaining the Ethics Committee's approval, proper consent and thorough pre-anesthetic check-up of all 60 patients of either gender aged between 18–60 years and of American Society of Anesthesiologists (ASA) Class I and II, scheduled for elective upper-limb surgeries (arm, forearm, and hand). Patient was excluded from the study, who refused for surgery for trial, ASA physical status >III and have any medical problem such as history of allergy to local anesthetics, cardiac dysrhythmias, liver and renal dysfunctions, bleeding disorders, convulsions and have sensory neuropathy and motor deficit in the limb on which surgery was to be performed. Patient with or history of Diabetes Mellitus I and II and have severe systemic diseases such as asthma, chronic obstructive pulmonary disease and coronary artery diseases also be excluded from the study. Using computer-generated table of random numbers, patients were allocated into two groups of 30 each. Group NS- Patients received 14 mL of 0.75% inj. Ropivacaine and 7 ml of inj. Normal saline 0.9%. Group D5- Patients received 14 mL of 0.75% inj. Ropivacaine and 7ml of inj. dextrose 5%. Final volume and concentrations of local anesthetic solution in both groups were 0.5%, 21 ml Ropivacaine. After all standard preparations, patient entered the operating room placed them into a supine position in trolley/couch and routine monitoring devices was installed, i.e., Electrocardiography, Spo2, Non-invasive Blood Pressure and a patent I/V line. Preoperative antibiotic was given. I/V Midazolam 1mg was given to all patients before procedure as a premedication to reduce to relieve anxiety. Under all aseptic precaution, SCBPB was performed using a Sonoscape USG machine and a 13-6 MHz linear probe. In group NS and group D5%, drug were injected through 50 mm long, 22G insulated, short bevel needle (B Braun).

Patient Positioning

The patient is placed in a supine position with the head rotated away from the site to be blocked and the shoulder pulled down. The arm rests comfortably on the side while the wrist, if possible, is supinated [Figure 1]. The main landmarks for this USG guided block are behind the midpoint of the clavicle in the supraclavicular fossa region. Light premedication, for example., inj. Midazolam 1 mg is beneficial for patient comfort.

USG Guided Technique

Place a linear probe in the coronal oblique plane behind the midpoint of the clavicle in the supraclavicular fossa region [Figure 2]. Scan supraclavicular fossa to identify the subclavian artery and brachial plexus in short-axis view. The Brachial plexus will be visualized as a hypoechoic group of nerves, i.e., "Bunch of grape" appearance, located laterally and caudally to the prominent subclavian artery. Deep to the artery, the hyperechoic first rib is typically seen; however, the pleura is obscured by the rib's acoustic shadow [Figure 3]. After scanning and identifying the structures,

insert a 22 gauge 50 mm needle is in "In-plane" with USG beam toward the plexus and posterior to anterior direction, once at appropriate location local anesthetic solution will be administered slowly, incrementally using intermittent aspiration technique after negative aspiration ensuring expansion and adequate spread around the three sites of brachial plexus, a total of 21 ml LA is injected in three divided doses, i.e., 7 ml of 0.5% Ropivacaine injected in following three areas:-

1. Corner pocket area
2. Intercluster region
3. Supracluster area.

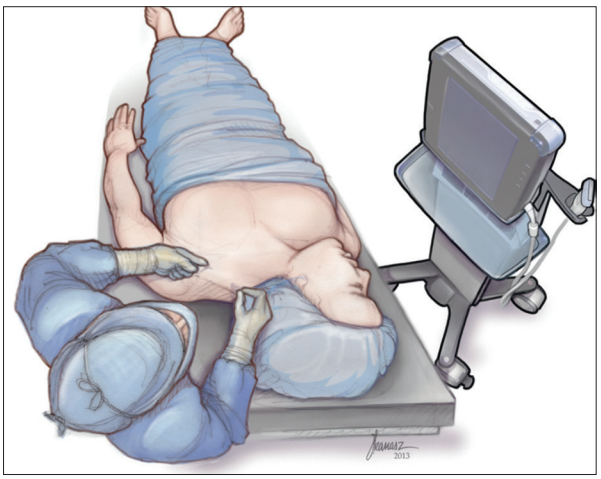


Figure 1: Patient position with the ultrasound machine for the supraclavicular block

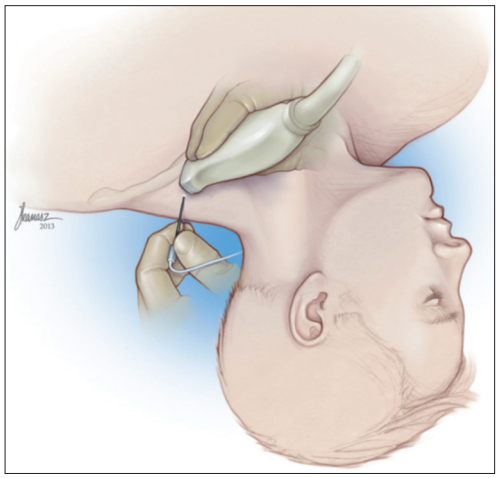


Figure 2: The probe is in the coronal oblique plane. Note the in-plane position of the needle with the direction of the needle from posterior to anterior

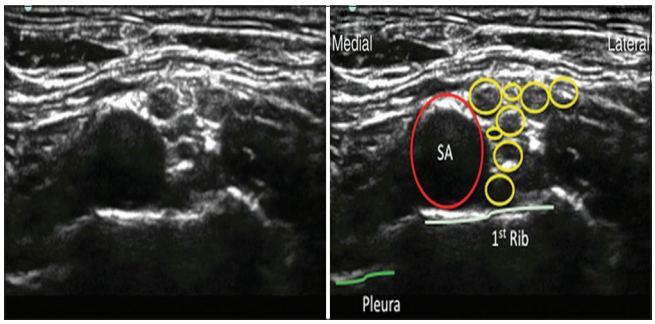


Figure 3: Ultrasonographic view of brachial plexus in supraclavicular approach

For abolishing tourniquet-related pain and discomfort in the upper-arm region, 5–7 ml 1% Lignocaine with adrenaline will be infiltrated subcutaneously in the medial aspect of arm at level of axillary fossa to block inter-costo-brachial nerve (T2 Block).

Parameters of Comparison

All patients were evaluated for the following parameters from the time of induction to 12 h. post induction-

1. The time to onset of sensory loss (Analgesia) and duration of sensory loss.
2. Evaluation of sensory and motor blockade up to 60 min or total block.
3. Post-operative analgesia.

Evaluation of Block

Assessment scales

- The sensory block was evaluated by a three-point scale for sensory block.
- The motor block was evaluated by three-point scale for motor block.
- Post-operative analgesia was evaluated by VAS score for pain at rest and at the movement of the limb at the proper interval in ward or post-op care unit.
- Result was noted and analyzed.

Three-point scale for sensory block

Score	Observation
2	Normal Sensation of pin prick
1	Analgesia (Less than normal pain to Pin Prick)
0	Anesthesia (Loss of Pin Prick sensation)

Sensory block evaluation site

Nerves	Sensory distribution for evaluation
Radial nerve	1st dorsal web space
Ulnar nerve	Median margin of the little finger
Median nerve	Lateral margin of the index finger
Musculocutaneous nerve	Lateral margin of the forearm

Three-point scale for motor block

Score	Observation
2	Full strength, normal movements
1	Some movements possible (Paresis)
0	Absence of movements (Total paresis)

Motor block evaluation sites

Nerves	Motor evaluation
Radial nerve	Loss of thumb abduction, finger, and wrist extension
Ulnar nerve	Loss of thumb adduction
Median nerve	Loss of thumb opposition
Musculocutaneous nerve	Loss of elbow flexion

Analgesia

Postoperative pain was assessed by verbal numeric rating scale (visual analog scale [VAS]) at 2 h, 4 h, 6 h, 8 h, 10 h, 12 h, 14h, 16, 20 h, and 24 h after surgery [Figure 4].

VAS score[11]

- 0 - no pain
- 1–3 - mild pain
- 4–7- moderate pain
- 8–10 - severe pain.

Data Analysis

Patients were monitored intra-operatively and all findings and observations were recorded on the patient proforma. The data of the present study was recorded/fed into the computers and after its proper validation, check for error, coding, and decoding was compiled. Appropriate univariate and bivariate analysis and use of Student's *t*-test. The VAS scores in two groups were analyzed using a non-parametric test. For the onset time of sensory blockade, the independent-t test was used. Individual nerve block times, total duration of block, total procedure time, and onset time for total paresis were also analyzed using the independent *t*-test. Data analysis was done using SPSS version 20 (SPSS Inc, Chicago, Illinois, USA). All means are expressed as mean ± standard deviation and the proportion as in percentage (%). The critical value for the significance of the results will be considered at 0.05 levels.

RESULTS

Mean age ± standard deviation of patients in group NS was 35.57 ± 11.98 years and in group D5 it was 39.37 ± 12.78 years. Mean age in both groups was comparable statistically. (P = 0.24). Mean weight (kg) of the patients in group NS and D5 was 68.73 ± 6.03 and 65.67 ± 6.48 respectively. Mean weight in both groups was statistically comparable (P= 0.063).

Table 1 shows the meantime for onset of analgesia in both the group. Normal saline group was 41.00 ± 2.74 min and 28.33 ± 2.42 min for the dextrose group. The P = 0.0001, which means difference between both the groups was statistically highly significant [Graph 1].

Tables 2-5 show the mean onset time of sensory block for median nerve, ulnar nerve, musculocutaneous nerve % radial nerve, respectively. The comparison between both groups was not statistically significant (P > 0.05) [Graphs 2-5].

Table 6 shows the duration of the sensory block (386.31 ± 4.78 min in NS group, 389.30 ± 8.27 min in D5 group, P = 0.096). The comparison between both groups was not statistically significant [Graph 6].

Table 7 shows post-operative mean vas score at different time intervals in both groups. The difference in mean vas

Table 1: Onset time of sensory block (in minutes)

Group	NS		D5		*P*
	Mean	SD	Mean	SD	
Time	41.00	2.74	28.33	2.42	0.0001

Table 2: Onset time of sensory block for median nerve (in minutes)

Group	NS		D5		*P*
	Mean	SD	Mean	SD	
Time	30.88	2.99	29.50	2.47	0.057

Table 3: Onset time of sensory block for ulnar nerve (in minutes)

Group	NS		D5		*P*
	Mean	SD	Mean	SD	
Time	34.00	2.55	32.77	2.54	0.0659

Table 4: Onset time of sensory block for musculocutaneous nerve (in minutes)

Group	NS		D5		*P*
	Mean	SD	Mean	SD	
Time	20.53	1.22	19.90	1.56	0.0859

Table 5: Onset time of sensory block for radial nerve (in minutes)

Group	NS		D5		*P*
	Mean	SD	Mean	SD	
Time	29.83	2.42	28.82	1.85	0.067

Table 6: Duration of sensory block (in minutes)

Group	NS		D5		*P*
	Mean	SD	Mean	SD	
Time	386.31	4.78	389.30	8.27	0.096

score in both groups was non-significant from 2 to 12 h post-operative period [Graph 7].

DISCUSSION

USG has revolutionized the field of regional anesthesia. The effective application of this technology requires understanding of two-dimensional anatomy, optimal imaging of the nerves and anatomical structures, accurate real-time needle guidance, and precise local anesthetic delivery. Principle benefit of ultrasound is inherent ability to directly visualization of anatomical structures like peripheral nerves and tissue planes in real-time and additional benefit is the ability to reposition one's needle in assessing for adequate local anesthetic spread. The overall idea of pre-emptively scanning patient anatomy with USG for neurovascular variations or abnormalities has been suggested as a means of improving patient safety by preventing block complications. So when compared to PNS guided nerve blocks, USG guided nerve blocks has been shown to require less time to perform, possess more rapid onset, longer duration of anesthesia and less risk of block failure, decrease risk of vascular puncture and improved quality of sensory block.[2-6] In our study block procedure time in both groups was not different between two groups.

In this study, the mean time for onset of analgesia with normal saline group was 41.00 ± 2.74 min and 28.33 ± 2.42 min for dextrose group. The $P = 0.0001$, these finding is similar to another study by Dhir *et al.*[12] They prospectively compared and evaluate block characteristics when local anesthetics drug was diluted with D5W and NS.

Table 7: Post-operative vas score

VAS score (at h)	NS group		D5 group		*P*
	Mean	SD	Mean	SD	
2	0.23	0.97	0.34	1.17	0.692
4	1.93	1.33	1.21	1.80	0.083
6	2.90	0.71	2.66	1.31	0.376
8	4.43	0.72	4.31	1.00	0.591
10	5.47	0.62	5.00	1.28	0.079
12	6.23	0.50	6.07	1.28	0.516

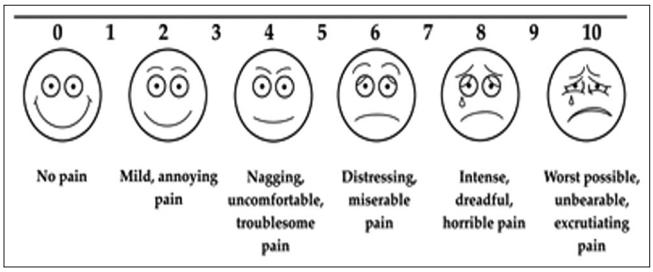
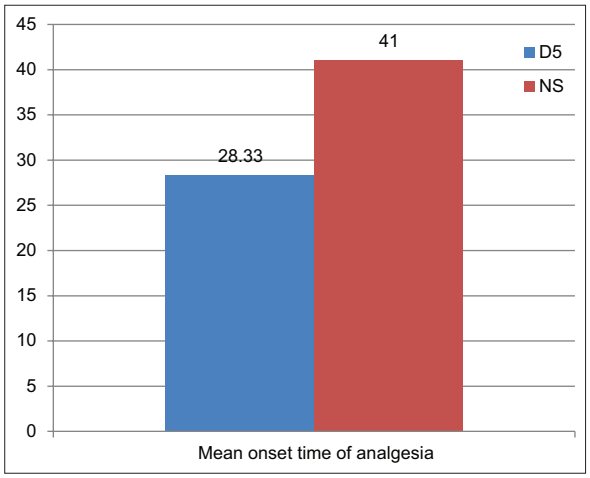
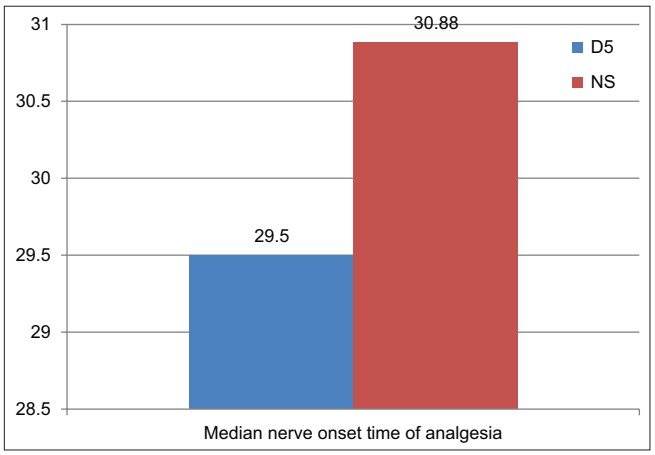


Figure 4: Visual analogue scale

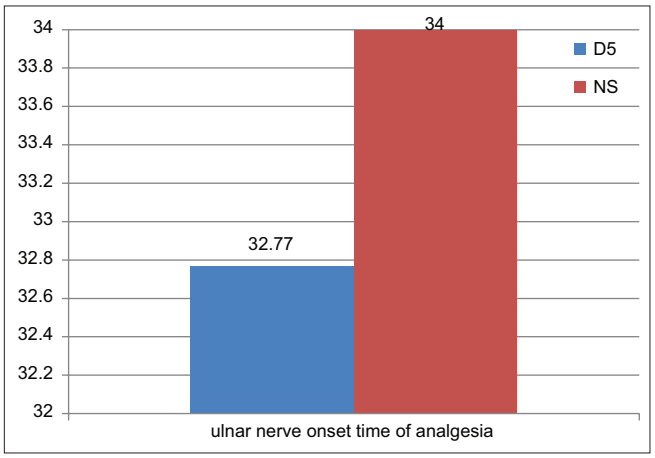
The mean time to complete the sensory block was 18.3 ± 6.1 min in the dextrose group and 22.5 ± 6.4 min in the saline group ($P < 0.001$, 95% confidence interval for mean difference 3.0-5.4 min). In their study, they concluded that dilution with 5% dextrose provides earlier onset of axillary brachial plexus block with Ropivacaine.



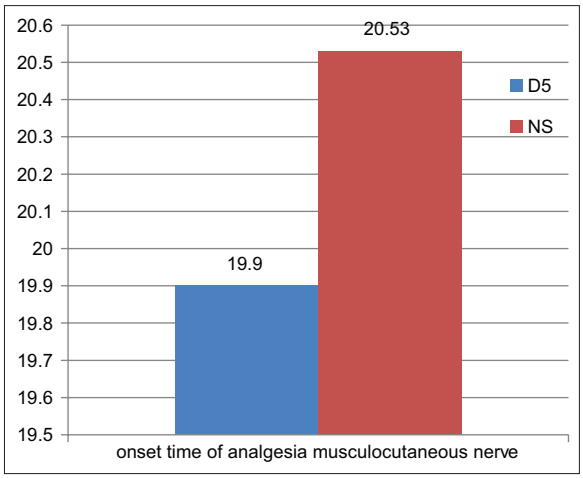
Graph 1: Mean onset time of analgesia



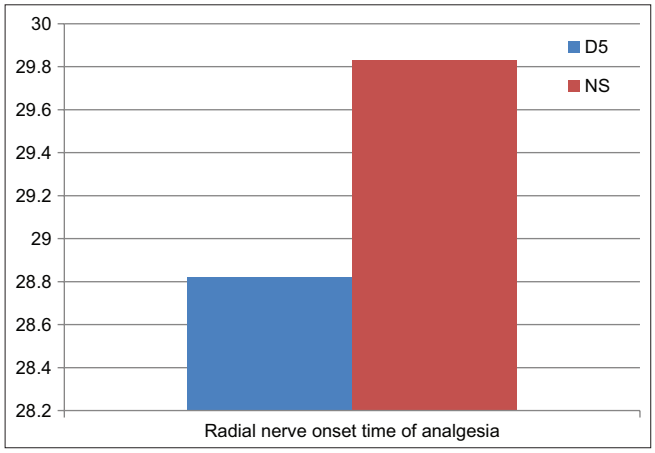
Graph 2: Median nerve onset time of analgesia



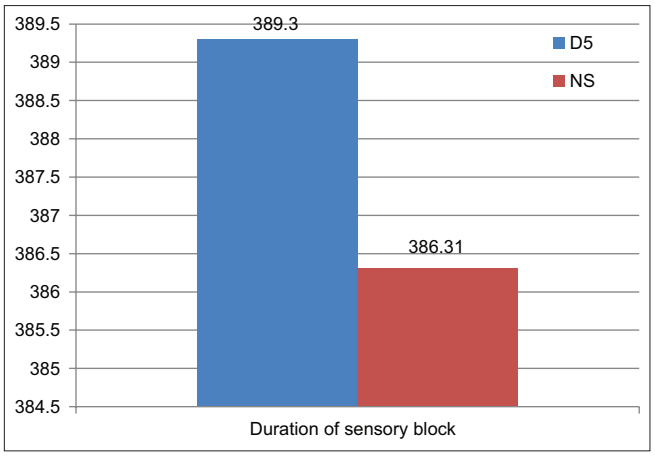
Graph 3: Ulnar nerve onset time of analgesia



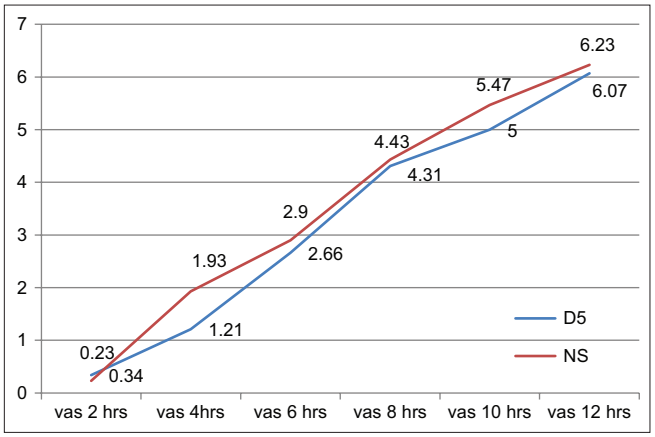
Graph 4: Onset time of analgesia musculocutaneous nerve



Graph 5: Radial nerve onset time of analgesia



Graph 6: Duration of sensory block



Graph 7: Post-operative vas score

In a study by Lim and Hasan,[13] a prospective, randomized comparison was made between 13.3 ml, 0.75% Ropivacaine diluted with either 6.7 ml normal saline or dextrose in upper extremity surgery via ultrasound-guided supraclavicular (SCB) nerve block. In their study, 50 patients scheduled for upper limb surgery were randomly assigned to receive supraclavicular plexus block with 0.75% Ropivacaine (diluted with either 5% dextrose or normal saline). They found meantime for onset of analgesia for the dextrose group was 37.6 ± 12.9 min while the meantime for the saline group was 45.2 ± 13.9 min with a $P = 0.05$.

The study of Shah *et al.*[14] also observed that the effect of 5% DW as diluent, in onset and duration of complete motor and sensory block as compared to normal saline, when given through supraclavicular approach of brachial plexus block. 5% Dextrose administered resulted in significant reduction in latency of onset of complete motor and sensory block with no significant increase in duration of block. Onset of complete sensory blockade for 5D and NS were 10.38 ± 3.14 and 18.10 ± 4.68 min respectively ($P < 0.0001$). Onset of complete motor blockade with 5DW and NS were 16.42 ± 4.23 and 22.36 ± 3.56, respectively ($P < 0.0001$). Duration of complete sensory block with 5D and NS groups was 193.12 ± 18.54 and 185.26 ± 19.89 respectively ($P = 0.1188$). Duration of complete motor block with 5D and NS was 217.32 ± 19.35 and 209.65 ± 21.48 ($P = 0.1516$). It is concluded that 5% DW produces a definite reduction in latency of complete sensory as well as motor blockade with no significant changes in the duration of motor and sensory block.

Perlas *et al.*[11] performed 510 USG guided SCB (50 inpatients, 460 outpatients) over 24 month period. Successful surgical anesthesia was achieved in 94.6% of patients after a single attempt, 2.8% required local anesthetic supplementation of a single peripheral nerve territory, and 2.6% received an unplanned general anesthetic. No cases of clinically symptomatic pneumothorax developed. Complications included symptomatic hemi-diaphragmatic paresis (1%), unintended vascular punctures (0.4%), and transient sensory deficits (0.4%). They concluded USG guided block is associated with a high rate of successful surgical anesthesia and a low rate of complications and thus may be a safe alternative for both inpatients and outpatients. Severe

underlying respiratory disease and coagulopathy should remain a contraindication for this brachial plexus approach.

Williams *et al.*[15] has done prospective study and assessed the quality, safety, and execution time of SCBPB using USG guided and neuro-stimulation guided combined and compared with anatomical landmarks guided neuro-stimulation. Eighty patients were randomized into two groups of 40, Group US (SCBPB guided in real-time by a 2D ultrasound image, with neuro-stimulator confirmation of correct needle position) and Group NS (SCBPB using the subclavian perivascular approach, also with neuro-stimulation). Blocks were performed using bupivacaine 0.5% and lidocaine2% (1:1 vol) with epinephrine (1:200,000) as the anaesthetic mixture. The onset of motor and sensory block for musculocutaneous, median, radial, and ulnar nerves was evaluated over a 30 min period. At 30 min 95% of patients in Group US and 85% of patients in Group NS had a partial or complete sensory block of all nerve territories ($P = 0.13$) and 55% of patients in Group US and 65% of patients in Group NS had a complete block of all nerve territories ($P = 0.25$). Surgical anesthesia without supplementation was achieved in 85% of patients in Group US and 78% of patients in Group NS ($P = 0.28$). No patient in Group US and 8% of patients in Group NS required general anesthesia ($P = 0.12$).

In our study meantime for onset of motor block could not be calculated, as a large number of patients (approx. 95%) did not have complete motor paralysis at the point of total loss of sensation to pinprick. This was predictable, as the total dose of Ropivacaine used in the study was lesser than usual dose so total motor blockade was not achieved in approx. 95% patients.

In this study, no differences were observed in post-operative analgesia using VAS scale and in the duration of sensory block (386.31 ± 4.78 min in NS group, 389.30 ± 8.27 min in D5 group, $P = 0.096$).

CONCLUSION

Our study concluded that Ropivacaine when diluted with dextrose shows faster onset time of analgesia compared to dilution with normal saline. Further studies are required to ascertain if the results are similar for different concentrations of other local anesthetics, and for other ultrasound-guided nerve blocks.

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Original Article

Association of Biochemical Abnormalities in Different Type of Neonatal Seizures

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Abstract

Introduction: Neonatal seizure is a common neurological problem in the neonatal period with a frequency of 1.5 to 14/1000 neonates.[1] Neonatal seizures have always been a topic of particular interest because of their universal occurrence. A varied number of conditions are capable of causing seizures in the neonatal period. The presence of a seizure does not constitute a diagnosis but is a symptom of an underlying central nervous system disorder due to systemic or biochemical disturbances. This study aims to study the various clinical types of seizures and the biochemical abnormalities associated with them.

Methods: This prospective study was conducted in the Department of Pediatrics, Government Headquaters Hospital, Ramanathapuram. Details of history, examination and investigations were recorded on predesigned proforma.

Results: Out of total 100 cases, 82(82%) cases had seizures during the first 3 days of life and hypoxic ischemic encephalopathy remains the main etiological factor in 32 (32%) cases. More than one metabolic abnormality was present in five cases. Hypoglycemia and hypomagnesemia were the most common abnormality in neonates having seizures.

Conclusion: A biochemical workup is necessary for all cases of neonatal seizures. The type of seizure does not give much information as to whether the seizures are purely metabolic or organic or about the type of biochemical abnormality.

Key words: Biochemical abnormalities, Etiology, Hypoglycemia, Neonatal seizure

INTRODUCTION

Neonatal seizure is a common neurological problem in the neonatal period with a frequency of 1.5 to 14/1000 neonates.[1] Neonatal seizures often indicate primary or secondary dysfunctions of the central nervous system.[2,3] The other common etiologies of neonatal seizures are intraventricular hemorrhage or intraparenchymal hemorrhage, meningitis, sepsis, or metabolic disorders. New animal research suggests that neonates may exhibit some neuroprotection from prolonged seizures, but brief, recurrent seizures can result in significant, permanent changes in the central nervous system, an increased risk of epilepsy, and long-term cognitive disabilities.[4] It is essential to determine the etiology of seizure at the earliest because it gives an opportunity to treat the seizure actively and promptly and avoid preventable morbidity, mortality, and sequelae associated with it.[1]

A seizure is the most frequent sign of neurologic dysfunction in the neonate. Since seizures may be the only sign of a central nervous system disorder, their recognition is important.[5] The neonate is at particular risk for the development of seizures because of metabolic, anoxic, structural, and infectious causes, although no causes can be identified in one-fourth cases. Clinical presentation of seizure, etiology, management, and diagnosis of seizure differ markedly to convulsions occurring in older children.[6]

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METHODS

This study was conducted in the neonatology unit, Department of Pediatrics, Government Headquaters Hospital, Ramanathapuram from February 2018 to January 2020. All neonates (1–28 days) with neonatal seizures admitted to onsite hospitals were included in the study. A detailed history was recorded in each case on a pretested

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proforma. Emphasis was laid on the age of occurrence of first seizure, duration of seizure, number of seizures, type of seizure, antenatal, natal, and post-natal risk factors which includes maternal drug addiction/withdrawal, maternal diabetes, prolonged rupture of membranes, Perinatal asphyxia, traumatic delivery, preterm, small for date, low birth weight baby, septicemia, meningitis, intracranial bleed, and hyperbilirubinemia. Seizures were classified according to Volpe's classification as subtle, multifocal clonic, focal clonic, generalized tonic, and myoclonic.[7] Detailed examination of neonate was done as per the proforma. Anthropometry was recorded and gestational age assessed according to new Ballard scoring system. As part of evaluation of cause of neonatal seizures, following investigations were ordered. Complete blood count, CRP, blood culture, random blood sugar, serum electrolytes, serum Ca^{+2}, serum Mg^{+2}, renal function tests. RBS< 40 mg/dl was diagnosed as hypoglycemia; total serum calcium <8.0 mg/dl was considered hypocalcemia, hypomagnesemia if $Mg^{+2}$was <1.5 mg/dl and hyponatremia if serum Na was less than 135 meq/L, if > 150 meq/L it was considered hypernatremia. If required, CSF analysis, neurosonogram, PT/aPTT, neuroimaging was done. The statistical operations were done through Statistical Presentation System Software (SPSS) for Windows, version 10.0 (SPSS, 1999. SPSS Inc.: New York).

RESULTS

During the study period, total number of deliveries was 1634, out of which 63 neonates developed seizures. Among the 628 neonates referred from outside, 37 of them developed seizures. Table 1 depicts the age-wise distribution of onset of neonatal seizures. Out of total 100 cases, 82 (82%) cases had seizures during the first 3 days of life. In the present study, 8 (8%) cases had seizures after 7 days of life which were mainly due to infections and metabolic causes. Fifty-two (82.53%) inborn neonates had day 1 seizures.

Table 2 shows the distribution of cases according to gender. Among outborn, out of 37 neonates, 25 (67.56%) were male and among inborn babies, 51 (80.95%) were male.

Table 3 shows the distribution of cases in relation to gestational age. Among outborn 31 (83.78%) were term and 6 (16.21%) were preterm. Among inborn babies 55 (87.31%) were term and 8 (12.69%) were preterm. Out of 86, term neonates 26 had hypoglycemia (30.23%) and among 14 preterm neonates, 6(42.85%) had hypoglycemia. Out of 86 term neonates, 15 (17.44%) had hyponatremia, two preterm inborn neonates with infection had hyponatremia. Four neonates had hyponatremia with primary metabolic disorders with no other associated comorbid states.

Table 1: Onset of seizures in neonates as per age

Onset of seizure	Neonates
Day 1	82
2–3 Days	4
4–7 Days	6
8–28 Days	8
Total	100

CC: 0.228; P<0.4

Table 2: Distribution of patients as per gender

Gender	Neonates (%)		Total (%)
	Out born	In born	
Male	25 (67.56)	51 (80.95)	76 (76)
Female	12 (32.43)	12 (19.04)	24 (24)
Total	37 (100)	63 (100)	100

CC=0.81; P<0.553

Table 3: Distribution of patients in relation to gestational age

Gestational age	Neonates (%)		Total (%)
	Out born	In born	
Term (≥37 weeks)	31 (83.78)	55 (87.31)	86 (86)
Pre term (<37 weeks)	6 (16.21)	8 (12.69)	14 (14)
Total	37 (100)	63 (100)	100 (100)

Out of 86 term neonates, 10 (11.62%) had hypocalcemia, among 14 preterm neonates 1 (7.14%) had hypocalcemia. Two term neonates had hypocalcemia as direct metabolic abnormality; whereas no preterm neonate had hypocalcemia in the primary metabolic group. Of 86 term neonates 27 (31.39%) had hypomagnesemia, among 14 preterm neonates two (14.28%) had hypomagnesemia. Among 86 term neonates 4 (4.65%) had Hypermagnesemia. Three neonates with Primary metabolic disorder had hypomagnesemia of these two neonates had hypocalcemia with hypomagnesemia. Table 4 depicts the distribution of neonates having metabolic seizures in accordance with biochemical profile and gestational age.

More than one metabolic abnormality was present in five cases. Hypoglycemia and hypomagnesemia were the most common abnormality in neonates having seizures. Four neonates had only hypocalcemia and these four neonates had late-onset hypocalcemia. Three neonates had hypocalcemia with hypomagnesemia. Table 5 highlights the concomitant metabolic abnormalities in cases of neonatal seizures with established etiologies such as hypoxic-ischemic encephalopathy (HIE), meningitis, IC bleed, and sepsis.

No neonates had hypercalcemia, hypernatremia, and hyperglycemia.

Some neonates had more than one metabolic abnormalities, hence will reflect in more than one row.

Table 6 depicts the distribution of cases with different types of seizure activity. The most common type of seizure noted in this study was subtle seizure seen in 25% of cases.

DISCUSSION

In the present study, out of 1634 babies born in the hospital during the study period, 63 (3.85%) had seizures. Of 628 neonates referred to this institution during the study period, 37 (5.89%) had neonatal seizures. The incidence of neonatal seizures as reported by various authors ranges from 0.2% to 1.4%. Keen[8] from Manchester and Brown *et al*.,[9] from Edinburgh, reported an incidence of 0.9% and 1.4%, respectively, which is slightly less than our study findings. Studies done by Brown[10] from Nigeria showed the same as being 1.2% and 0.8%, respectively, Goldberg and Sheely in 1983 from Melbourne,[11] reported an overall increase in the incidence of neonatal seizures from 2.6/1000 to 8.6/1000 live births from 1971 to 1980. The variability in the incidence of above author's observations might be due to different criteria in selection of babies that is; gestational age, weight, high-risk deliveries, and population-based studies. Eriksson and Zetterstrom in 1977 studied all full-term neonates, whereas Rose and Lombroso studied only full-term babies weighing 2500 g and more.[6,12] The present study observations are in contradiction to the findings of most of the investigations such as Bergman (0.6), Goldberg (0.6), Airede (0.8), Garg (0.2-0.8), and Keen (0.9).[1,8,13-15]

In the present study out of 100 neonates, 92 (92%) cases presented with seizures during the 1st week of life and 8 (8%) of the neonates had seizures after 7 days of life. Rose and Lombraso[6] from Boston reported incidence of 115 (77.66%) cases during the 1st week of life, 21 (14.09%) cases during 2nd week, and 13 (8.72%) after the 2nd week.

In the present study out of total 100 cases, 82 (82%) cases had seizures during the first 3 days of life and HIE remains the main etiological factor in 26 (26%) cases. In the present study 8 (8%) cases had seizures after 7 days of life which were mainly due to infections and metabolic causes. Calciolari *et al*.,[16] reported that 73.30% of cases had seizures during the first 2 days of life and Hypoxic-Ischemic-encephalopathy remains the main etiological factor in 87 (79.09%). A study by Kumar *et al*., from Varanasi, reported 16 cases of birth asphyxia and al, (100%) had seizures during the first 2 days of life.[1,15,17] In a similar study of 59 neonatal seizures by Sood *et al*., 32 (54.23%) cases had seizures during the first 3 days of life and Hypoxic-Ischemic-Encephalopathy remains the main etiological factor.[18]

In the present study, an overall male to female ratio of 3.16:1 was seen. Male babies usually get better care in this society and are brought for medical care more frequently than female babies; the male dominance observed in the present study may be partially because of this factor. In the present study, out of 100 neonates, 60% of cases had single seizure type. Focal clonic in 8 (8%) cases, multifocal clonic in 4% cases, generalized tonic in 6%, and myoclonic in 11% of the cases. Combined type of seizures was observed in 34% of cases. Calciolari *et al*.[16] from Washington, reported single seizure type in 50% of cases and combined type in 50%. Among the single type, subtle seizures were more common in 21% cases followed by multifocal clonic 15%,

Table 4: Distribution of neonates having metabolic seizures in accordance with biochemical profile and gestational age

Gestational age	No of neonates	Hypoglycemia	Hyponatrema	Hypocalcemia	Hypo-magnesemia	Hyper-magnesemia
Preterm	11	6	2	1	2	-
Term	82	26	15	10	27	4
Total	93	32	17	11	29	4

Table 5: Biochemical disturbances in neonates with seizures.

Etiology (*n*=100)	Neonates with metabolic abnormality	Hypo-glycemia	Hypo-calcemia	Hypo-magnesemia	Hyper-magnesemia	Hypo-natremia
Hypoxic ischemic encephalopathy (*n*=37)	26	13	7	11	2	3
IC Bleed (*n*=6)	6	0	1	3	0	2
Meningitis (*n*=4)	2	1	1	0	0	0
Metabolic (*n*=24)	24	9	7	9	2	2
Infection (*n*=25)	20	10	0	9	0	2

Table 6: Distribution of patients with different types of seizure activity

Type of seizure	Observation No (%)
Subtle	25 (25%)
Focal clonic	14
Multi focal clonic	8
Multi focal tonic	6
Focal myoclonic	6
General myoclonic	4
Subtle with focal clonic	14
Subtle with multi focal clonic	23
Total	100 00%)

7% had focal and 2% had myoclonic seizure activity. In another study done by Arvind *et al*., out of 59 neonates, 69.49% of cases had a single seizure type with subtle seizures being the most common in 27.11% of cases. Focal clonic were seen in 13.55% cases, multifocal clonic in 11.86% cases, generalized tonic in 3.39%, and myoclonic in 8.47% of the cases.[18] Combined type of seizures were observed in 30.51% of cases. All the three studies are quite similar in that subtle seizures were the commonest type of seizures in both single and combined types. However, these findings are in contrast to those observed by Airede[1] from Nigeria, this study showed single type of seizures in 91% of cases and combined type in 9%.1 Among single type seizure activity generalized tonic were seen in 51%, focal clonic 23%, and subtle in 16% of the neonates.

In the present study, overall biochemical disturbances were observed in 78 cases which constituted 78% of all the subjects. Of these 78 cases hypoglycemia was observed in 33 (33%) cases, hypomagnesemia 32 (32%), hyponatremia in 9 (9%) cases, hypocalcemia in 16 (16%) cases while hypermagnesemia, and hypokalemia were observed in 4% and 4% of the cases, respectively. Kumar *et al*.[17] studied 35 neonates for biochemical abnormalities in neonatal seizures. In 22 (62.8%) of their cases, hypocalcemia was detected in 7 (31.8%), hypoglycemia in 11 (50%), hypomagnesemia in 3 (13.63%) cases while hypermagnesemia, hyperphosphatemia, and hyponatremia were present in 4.54%, 13.63% and 5.45% of cases respectively. In a similar study of 59 neonatal seizures, overall biochemical abnormalities were observed in 29 (49.15%). Of these 29 cases hypocalcemia was observed in 15 (51.72%) cases, hypoglycemia in 12 (41.37%) cases, and hypomagnesemia in 4 (13.79%) cases while Hypermagnesemia, hyperphosphatemia, and hyponatremia were observed in 3.44%, 3.44%, and 17.25%, respectively.[18] In the present study, 33% of cases showed hypoglycemia which is comparable with the studies done by Calciolari *et al*.,[16] (38%), Kumar *et al*.,[17] (50%), and Arvind *et al*.,[18] (41.37%). The present study and the studies conducted by Kumar *et al*., and Arvind *et al*., showed one similarity in that the biochemical disturbances were seen in cases of hypoxic-ischemic-encephalopathy, intracranial bleed, infections, and metabolic disorders.[17,18] Calciolari *et al*., reported 8 cases of neonatal seizures with primary metabolic abnormalities, out of which 38% had hypoglycemia, 50% had hypocalcemia and 12.5% had hyponatremia. Rose AL from Boston observed hypocalcemia in 28 (20.4%) cases, followed by hypoglycemia in 7 (5.1%) cases.[6,16] In a study done by Kumar *et al*., on 35 neonates to determine the various biochemical abnormalities in neonatal seizures, primary metabolic disorders (nine cases) accounted for one-fourth of the cases of neonatal seizures, the most common being hypoglycemia, hypoglycemia with hypocalcemia, and hypocalcemia with hyperphosphatemia.[17] A similar study showed primary metabolic abnormalities in 10 (16.94%) cases out of 59 neonatal seizures the most common being hypocalcemia 7 (70%) followed by hypoglycemia 4 (40%).

In the present study of 100 neonatal seizures, 22 (22%) neonates showed primary metabolic abnormalities. Hypoglycemia 32 (32%) and hypomagnesemia 29 (29%) were the most common in neonates having primary metabolic seizures while hypocalcemia 11 (11%) as metabolic abnormality was detected, of which two neonates had late-onset hypocalcemia. Isolated hypoglycemia was observed in four cases of metabolic seizures; out of these one was preterm. More than one metabolic abnormality was observed in five cases. Among these, two neonates had hypocalcemia with hypomagnesemia, two neonates had hypoglycemia with hypomagnesemia, and one had hypoglycemia with hypocalcemia.

CONCLUSION

Biochemical abnormalities are common in neonatal seizures. There is a male predominance in this study. However, the study showed no significant difference in the pattern of biochemical abnormalities between the sexes. Isolated biochemical abnormalities without other co-morbid states which could account for the seizures are seen in 23%. Hypoglycemia and hypomagnesemia are the most common biochemical abnormalities accounting for seizures in this group. 51 (51%) of cases of neonatal seizures with identifiable etiology had biochemical abnormality. These abnormalities may significantly contribute to seizure activity and possibly correction of these abnormalities may play a significant role in seizure control. A biochemical workup is necessary for all cases of neonatal seizures.

The onset of seizures was most common during the first 3 days of life, 86 (86%) of which 37 (43.02%) was due to HIE, 25 (29.06%) due to infection, 24 (27.90%) due to metabolic causes. Hence, babies with a history of significant

birth asphyxia need to be closely watched and monitored for evidence of seizure activity. This is also of prognostic importance as, metabolic causes, once identified and treated have a good short-term outcome. HIE is associated with significant mortality and morbidity. Hence, neonates with seizures in the first 3 days of life, with normal biochemical parameters and no evidence of sepsis; etiology is most likely to be HIE.

Subtle seizures were the most common type of seizure observed in term and preterm neonates. The type of seizure does not give much information as to whether the seizures are purely metabolic or organic or about the type of biochemical abnormality.

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Original Article

A Pharmacovigilance Study of the Combination Therapies of Augmenting Drug Doses of 50 mg and 75 mg Remogliflozin with 500 mg Metformin among Type II Diabetics, Along Global Pharmacoepidemiology: An Appraisal of Rational Pharmacotherapeutics in Metabolic Medicine

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Abstract

Introduction: Diabetes mellitus type II is globally very common, yet neglected. Remogliflozin, a selective insulin-independent sodium glucose cotransporter subtype 2 inhibitor, inhibits reabsorption of renal glucose, lowers blood sugar, and causes glucosuria, in type II diabetes mellitus patients. Metformin, as a combination antidiabetic drug, lowers serum glucose levels, by the activation of 5' adenosine monophosphate-activated protein kinase.

Objectives: The objectives of this endocrinological rational pharmacotherapeutic study were the safety evaluation of augmenting doses in the combination therapies of 50 mg and then 75 mg remogliflozin with 500 mg metformin, in type II diabetes mellitus patients, in tertiary care medical college hospitals, along a global pharmacoepidemiological perspective.

Methods: A total of 150 new early moderate grade type II diabetes mellitus patients were prescribed oral metformin 500 mg once daily for 30 days. Then, diabetics uncontrolled with metformin were prescribed oral 50 mg remogliflozin with 500 mg metformin once daily, for 15 days; who were subsequently prescribed oral 75 mg remogliflozin with 500 mg metformin once daily for 15 days. The safety assessment, along with blood sugar and hemoglobin A1c levels and urine routine examination, on day 0, day 30, day 46, day 60, and further follow-up, was recorded and statistically analyzed.

Results: The adverse effects with the combination therapy of 50 mg remogliflozin with 500 mg metformin and then the combination therapy of 75 mg remogliflozin with 500 mg metformin were statistically non-significant; hence, both were safe and tolerable.

Conclusions: The combination therapy of 50 mg remogliflozin and 500 mg metformin and, then, the combination therapy of 75 mg remogliflozin and 500 mg metformin, were safe and tolerable.

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Key words: Biguanides, Metformin, Sodium glucose cotransporter subtype 2 inhibitors, Remogliflozin, Pharmacovigilance, Augmenting drug doses in combination therapies, Diabetology and metabolic medicine

INTRODUCTION

Diabetes mellitus type II is one of the most common, yet often neglected disease, that the world has witnessed in the recent times. The global incidence and prevalence of type 2 diabetes mellitus (T2DM) is on a perennial increase, with about one in 11 adults having diabetes mellitus and 90% among them being type 2 diabetic. According to the International Diabetes Federation, 425 million global population has diabetes mellitus, accounting for two-thirds of adults aged 20–64 years, and the proportion of deaths due to diabetes mellitus before the age of 60 years ranges from 36 to 73%. Diabetes mellitus has its highest prevalence in 10 countries, with almost 60% of the global disease burden, mostly distributed in China (114 million people), India (73 million people), and the USA (30 million people). Given its extensive occurrence, the management of diabetes mellitus through effective treatment interventions is of utmost significance in the field of clinical research.[1,2]

The diagnostic criteria of type II diabetes mellitus by the American Diabetes Association (ADA) include the following:

1. A fasting plasma glucose level of 126 mg/dl (7.0 mmol/L) or higher, or
2. A 2 h plasma glucose level of 200 mg/dl (11.1 mmol/L) or higher during a 75 g oral glucose tolerance test, or
3. A random plasma glucose of 200 mg/dl (11.1 mmol/L) or higher in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, or
4. A hemoglobin A1c (HbA1c) level of 6.5% (48 mmol/mol) or higher.[1,3]

With remogliflozin, a selective insulin-independent sodium glucose cotransporter subtype 2 (SGLT2) inhibitor, the management of type II diabetes mellitus has taken a quantum leap, producing antihyperglycemic activity in both diabetes mellitus type II and insulin-resistant patients, when given in monotherapy or in combination with metformin. Remogliflozin inhibits glucose reabsorption in the kidney, thus lowering blood sugar, and causing glucosuria. Clinical guidelines recommend SGLT2 inhibitors as one of the second-line pharmacological therapeutic approaches, following metformin failure or intolerance. SGLT2 inhibitors cause wider benefits like adequate glycemic control, significant improvements in HbA1c, insulin sensitivity and β-cell function, weight loss, blood pressure reduction, cardiovascular and renal protection by significantly increasing high-density lipoprotein cholesterol, decreasing low-density lipoprotein cholesterol, reducing albuminuria, and delaying the progression of nephropathy. The ADA and the European Association for the Study of Diabetes suggest the therapeutic use of SGLT2 inhibitors for patients with diabetic comorbidities such as cardiovascular disease (including heart failure and atherosclerotic cardiovascular disease) and chronic kidney disease.[1,4]

Metformin has considerable improved outcomes, as a combination antidiabetic drug, with pleotropic effects on glucose metabolism. Metformin inhibits hepatic gluconeogenesis in a substrate selective manner, through the transcription, allosteric, substrate availability, or redox mechanisms; and by metformin inhibition of complex I leading to reductions in hepatocellular energy charge and other downstream events (e.g., adenosine monophosphate-activated protein kinase [AMPK] activation, fructose 1,6-bisphosphatase inhibition, inhibition of glucagon signaling). It overcomes insulin resistance and lowers serum glucose levels, by the activation of 5' adenosine monophosphate (AMP) AMPK. Metformin alters the cellular redox balance, and the increased cytosolic redox state, due to the inhibition of glycerol-3-phosphate dehydrogenase by metformin. This is observed at clinically relevant concentrations and is the only proposed mechanism of action that predicts substrate selective (glycerol and lactate) inhibition of hepatic gluconeogenesis. Metformin is both effective and inexpensive, and may reduce the risk of cardiovascular events and death. It has beneficial effects on $HbA1_C$ and weight; and a well-established safety profile.[1,5,6]

The American Association of Clinical Endocrinologists guidelines for T2DM management suggest lifestyle therapy, medically assisted weight loss, and individual goals of achieving HbA1c level of ≤6.5%. The determining factors behind the choice of antidiabetic drugs are the different patient characteristics, such as glycemic index, weight, lifestyle, comorbidities, and undesirable side effects of pharmacotherapeutic management. The commonly associated side effects with oral antidiabetic agents are hypoglycemia, weight gain due to hyperinsulinemia, gastrointestinal symptoms, and hepatorenal toxicity. The critical effects under consideration for the clinical rationale of the antidiabetic drugs are their potential for hypoglycemia, weight gain, and long-term side effects. This augmentation of adverse effects demands a safer

antidiabetic agent. Therefore, this study was conducted as an endocrinological pharmacovigilance study to evaluate the safety involving the clinical therapeutic prescription of antidiabetic combination therapies, with the augmenting doses of remogliflozin: 50 mg remogliflozin and 500 mg metformin, which were subsequently followed by 75 mg remogliflozin and 500 mg metformin, once daily. The successful synergistic effects of these combination therapies and the better drug-dose combination regimens intend to decrease the occurrence of adverse effects, with increased safety and tolerability, thus benefiting the treatment of diabetes mellitus type II. A patient-centered approach was used to guide the choice of pharmacologic agents. The effects of the cardiovascular and renal comorbidities, efficacy, hypoglycemia risk, impact on weight, cost, risk for side effects, and patient preferences were also taken into consideration.[1,4-6]

Objectives

The objectives of this endocrinological rational pharmacotherapeutic study were the safety evaluation of the combination therapies of augmenting drug doses of 50 mg and then 75 mg remogliflozin with 500 mg metformin, in type II diabetes mellitus patients, in tertiary care medical college hospitals, along a global pharmacoepidemiological perspective.

METHODS

Ethical Approval

At first, the Institutional Ethics Committee clearance and approval was taken. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and Good Clinical Practices contained within the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH-E6), and in compliance with the global regulatory requirements. An informed consent was obtained from each patient.

Selection Criteria of the Study Participants

Inclusion criteria

The inclusion criteria were as follows: (i) Patients of any gender, (ii) patients within 35 and 60 years, (iii) patients of around 60 kg average body weight, (iv) patients presenting with new type II diabetes mellitus, of early moderate grade, (v) type II diabetes mellitus ADA diagnosis criteria, (vi) cooperative and conscious patients, (vii) patients willing to undergo all pre- and post-treatment investigations and willing to complete the entire course of treatment, (viii) patients who have given consent and are willing to go for a follow-up, (ix) patients not taking any previous antidiabetic drug, and (x) patients not taking any concomitant medication.

Exclusion criteria

The exclusion criteria were as follows: (i) Uncooperative or unconscious patients, (ii) patients below 35 and above 60 years, (iii) patients presenting with any grade other than early moderate grade of diabetes, (iv) patients with a history of hypersensitivity to any of the study drugs, (v) patients with high-risk diseases or comorbidities, (vi) cardiac, renal, or any other associated complications or comorbidities, (vii) any chronic disease intervening with the study data, (x) pregnant or lactating women, (xi) pediatric or geriatric patients, (xii) other associated medical illness or disorders, like urogenital tract infections, having impact on study results, and (xiii) female patients using hormonal contraceptives.

Study design

This was a global, multicenter, prospective, randomized, open-labeled study.

Study population

The study population was 150 new type II diabetes mellitus patients, of early moderate grade.

Place of study

The place of research study and the compilation of the study literature were the Departments of Pharmacology, Clinical Pharmacology, Molecular Pharmacology, Endocrinology, Diabetology and Metabolic Medicine, Pharmacovigilance, Rational Pharmacotherapeutics, Evidence Based Medicine, Clinical Medicine, Clinical Pathology and Pathology, in Mamata Medical College and Hospitals, Rama Medical College Hospital and Research Centre, Rama University, Dr. Moumita Hazra's Polyclinic and Diagnostic Centre, Hazra Nursing Home, Shri Ramkrishna Institute of Medical Sciences and Sanaka Hospitals, Hi-Tech Medical College and Hospital, K.D. Medical College Hospital and Research Center, Gouri Devi Institute of Medical Sciences and Hospital, J.J.M. Medical College and Hospitals, GIOSTAR IRM Institutes, Hospitals and Laboratories, and Mahuya Diagnostic Centre and Doctors' Chambers.

Study period

The study period, including the research study and the compilation of the study literature, was 5 months: June 2015 and from July 2021 to December 2021.

Study procedure

A total of 150 new type II diabetes mellitus patients, of early moderate grade, were prescribed oral metformin 500 mg (8.40 mg/kg), once daily, for 30 days. After 1 month, from these 150 patients, 50 diabetic patients uncontrolled with metformin, (i) who had achieved adequate glycemic control with metformin monotherapy, or (ii) who were lost to follow-up, or (iii) who had dropped

out due to adverse effects, or (iv) who had withdrawn voluntarily, were excluded from the study. The remaining 100 patients were prescribed oral 50 mg (0.84 mg/kg), remogliflozin once daily with 500 mg metformin once daily for 15 days; and were subsequently prescribed oral 75 mg (1.25 mg/kg) remogliflozin once daily with 500 mg metformin once daily for 15 days.

The patients' characteristics, diabetic symptoms assessment, patients' disease, and disease-related history were recorded with a pro forma. Then, thorough general physical examination and systemic examination were performed on the patients under study. The relevant blood, urine, and other investigations were done to confirm the progressing health status of the patients being treated.

The efficacy assessment was done, by recording the fasting and the post-prandial blood sugar level, HbA1c level, and urine routine examination findings including sugar and albumin levels and microscopy, (a) at baseline level on day 0; (b) after administering metformin monotherapy at day 30; (c) after administering the combination therapy at day 46; (d) after administering the combination therapy at day 60; and (d) further follow-up.

The safety assessment was done with an Adverse Event Case Report Form, by the monitoring of adverse drug reactions, such as hypoglycemia, weakness, gastrointestinal disturbances, abdominal pain, and upper respiratory tract infections, after metformin monotherapy, from day 0 to day 30. Then, the safety was assessed by monitoring any adverse reaction, such as genital mycotic infections, urinary tract infections, pyrexia, headache, dizziness, nausea, gastrointestinal disturbances, hypoglycemia, weakness, or abdominal pain, after the combination therapy of 50 mg remogliflozin once daily with 500 mg metformin once daily, from (i) day 30 to day 46; after the combination therapy of 75 mg remogliflozin once daily with 500 mg metformin once daily; from (i) day 46 to day 60; and (ii) further follow-up.

Statistical Analysis

At the study completion point, the observations recorded in this study, were statistically analyzed by Z-test, and test of significance with *P* values, with subsequent tabular representations.

RESULTS

The demographic characteristics of the patients, in this study, were comparable. Among 150 new type II diabetes mellitus patients, of early moderate grade, receiving metformin monotherapy for 1 month, 50 uncontrolled diabetic patients, (i) who had achieved adequate glycemic control with metformin monotherapy, or (ii) who were lost to follow-up, or (iii) who had dropped out due to adverse effects, or (iv) who had withdrawn voluntarily, were excluded from this study. The remaining 100 patients received 50 mg remogliflozin with metformin combination therapy, for 15 days, which was subsequently followed by the combination therapy of 75 mg remogliflozin with metformin, for 15 days. These patients had completed the study thoroughly, with no adverse effects related dropout patients, lost to follow-up patients, or voluntarily withdrawn patients.

The combination therapies of 50 mg or 75 mg of remogliflozin and metformin were observed to be safe, which had controlled type II diabetes mellitus among new patients, with significant decrease in the blood sugar levels and the HbA1c levels, within 2 months.

Table 1 depicts the occurrence of adverse effects with 50 mg remogliflozin and 500 mg metformin combination therapy. Table 2 depicts the occurrence of adverse effects with 75 mg remogliflozin and 500 mg metformin combination therapy.

There were no adverse effects observed with the combination therapy of 50 mg remogliflozin with 500 mg metformin and then, with the combination therapy of 75 mg remogliflozin with 500 mg metformin, which were statistically non-significant. The combination therapy of 50 mg remogliflozin with 500 mg metformin and, then, the combination therapy of 75 mg remogliflozin with 500 mg metformin were observed to be safe and tolerable.

DISCUSSION

Gliflozin drugs, the sodium-glucose cotransporter 2 inhibitors, are the newly developed class of oral

Table 1: The occurrence of adverse effects with 50 mg remogliflozin and 500 mg metformin combination therapy

Adverse effects	Number of patient occurrence	Z value	*P* value
Genital mycotic infections	0	-	Non-significant
Urinary tract infections	0	-	Non-significant
Pyrexia	0	-	Non-significant
Headache	0	-	Non-significant
Dizziness	0	-	Non-significant
Nausea	0	-	Non-significant
Gastrointestinal disturbances	0	-	Non-significant
Hypoglycemia	0	-	Non-significant
Weakness	0	-	Non-significant
Abdominal pain	0	-	Non-significant

Table 2: The occurrence of adverse effects with 75 mg remogliflozin and 500 mg metformin combination therapy

Adverse effects	Number of patient occurrence	Z value	*P* value
Genital mycotic infections	0	-	Non-significant
Urinary tract infections	0	-	Non-significant
Pyrexia	0	-	Non-significant
Headache	0	-	Non-significant
Dizziness	0	-	Non-significant
Nausea	0	-	Non-significant
Gastrointestinal disturbances	0	-	Non-significant
Hypoglycemia	0	-	Non-significant
Weakness	0	-	Non-significant
Abdominal pain	0	-	Non-significant

hypoglycemic agents used for the treatment of the type-II diabetes mellitus. This drug category was approved by the food and drug administration for the treatment of diabetes, and it has a very unique mechanism of action. The sodium-glucose transport (SGLT) proteins are the macromolecules causing reabsorption of the filtered glucose from the proximal convoluted tubule (PCT) part of the nephron. The significance lies in the fact that these proteins work independent of insulin. Probably, the SGLT proteins occur in the nephron and the large intestine. The two main types of SGLT proteins are SGLT 1 and SGLT 2. The SGLT 1 proteins occur in PCT of nephron as well as in the large intestine. The SGLT 2 proteins occur only at PCT part of the nephron. SGLT 1 has a higher affinity but low concentration (with 2:1 sodium-glucose cotransport ratio), thus causing only 10% of total glucose reabsorption; while, SGLT 2 has higher concentration (with 1:1 sodium-glucose cotransport ratio) with 90% of total glucose reabsorption. Selective inhibition of SGLT 2 transport proteins reduces reabsorption rate of glucose molecule resulting in an increase in the glucose excretion rate and reduction in the blood glucose concentration to 40–120 mg/dL, and this is beneficially effective for treating diabetes mellitus type II. The functions (rather than glucose absorption) of SGLT1 in the large intestine are presently under investigation, but it is observed that the inhibition of SGLT1 produces the intestinal complications like diarrhea, which disturbs the wellness of large intestine.

The clinical benefits of SGLT-2 inhibitors are improved glucose control, faster metabolic effect, weight loss, significant reduction in blood pressure, cardiovascular benefits, and reduced sympathetic overactivity.

Remogliflozin etabonate (RE), an oral prodrug of remogliflozin, is a selective SGLT2 inhibitor, having antihyperglycemic activity, which is used in the treatment of diabetes mellitus type 2. RE could be an effective oral adjunct to insulin for the treatment of type 1 diabetes. RE has a water solubility of 0.189 mg/ml, and it is a proposed drug for the treatment of non-alcoholic steatohepatitis and type 2 diabetes. RE significantly increases urinary glucose excretion and reduces plasma glucose concentration.[1,7]

Remogliflozin is administered in the prodrug form, that is, RE in an immediate release (IR) tablet formulation. Different doses of remogliflozin of 20 mg, 50 mg, 100 mg, 150 mg, 500 mg, and 1000 mg, with varying daily drug intake schedules, are being investigated.[1,8,9] After administration, RE is de-esterified by non-specific esterases present in the mucosal cells of the gastrointestinal tract and converted into its active form remogliflozin. RE is rapidly and almost completely absorbed, with an availability in the plasma within 10 min with a Tmax of 0.5–1 h. The administration with standard breakfast slightly delayed the Tmax by approximately 0.5–1.5 h; without any significant difference in the Cmax or area under curve relative to the fasting state. Hence, RE can be administered with or without food. The plasma protein binding of remogliflozin was around 65%. Either RE or remogliflozin was not preferentially distributed to blood cells, and there was no selective association of RE or its metabolites with melanin containing tissues. In the systemic circulation, remogliflozin is extensively metabolized, leading to N-dealkylation, O-dealkylation, oxidation, loss of glucose, and glucuronidation. *In vitro* studies have demonstrated that the primary enzyme involved in the CYP-based metabolism of remogliflozin is CYP34A, with a minor contribution from CYP2C19. Remogliflozin gets metabolized to two active metabolites, namely: GSK279782 and GSK333081. The major active metabolite GSK279782 has been shown to account for approximately 16–22% of the concentration of remogliflozin in circulation. The exposure of GSK333081 was found to be extremely low after single-dose studies and hence not considered clinically significant. Remogliflozin has multiple pathways of elimination, such as CYP and non-CYP pathways. The mean plasma elimination half-life of remogliflozin and GSK 279782 were around 1.5–1.9 h and 2.3–3.8 h, respectively, in healthy volunteers after a single dose of RE at 100 mg or 250 mg. In the same study, the mean plasma half-life of prodrug was mostly around 0.4–0.7 h. Metabolic products of RE are eliminated from the body through renal excretion. In several radiolabeled absorption, metabolic, and excretion studies, approximately 93% was excreted in the urine, with 11% of the dose being recovered as remogliflozin in urine; and the majority of drug-related material is eliminated through the urine as inactive glucuronide metabolites. On the evaluation of the inhibitory concentration of remogliflozin, it was demonstrated that Ki values were 12.4 and 4520 nmol/l for SGLT2 and SGLT1, respectively. This shows that remogliflozin is a selective inhibitor of SGLT2.[1,4]

The adverse effects of SGLT2 inhibitor drugs include diabetic ketoacidosis, bone fracture, urinary tract infection, genital fungal infection, foot and toe amputation, breast cancer, Leydig cell tumor, and bladder cancer.[1,7]

In this study, among 150 new type II diabetes mellitus patients, of early moderate grade, receiving metformin monotherapy for 1 month, 50 uncontrolled diabetic patients, (i) who had achieved adequate glycemic control with metformin monotherapy, or (ii) who were lost to follow-up, or (iii) who had dropped out due to adverse effects, or (iv) who had withdrawn voluntarily, were excluded from the study. The remaining 100 patients received 50 mg remogliflozin with 500 mg metformin combination therapy, for 15 days, and subsequently 75 mg remogliflozin with 500 mg metformin combination therapy, for 15 days. These patients had completed the study thoroughly, with no adverse effects related dropout patients, lost to follow-up patients, or voluntarily withdrawn patients. The demographic characteristics of the patients were comparable. The combination therapies of increasing doses of remogliflozin and metformin were observed to be safe, and they have controlled type II diabetes mellitus among new patients, with significant decrease in the blood sugar levels and the HbA1c levels, within 2 months. This supports the successful synergistic effect of these antidiabetic combination therapies, with a gradually increasing dose of remogliflozin. There were no adverse effects observed with the augmenting doses of combination therapies of 50 mg and then 75 mg of remogliflozin with 500 mg metformin, which were statistically non-significant. The combination therapies of 50 mg and then 75 mg remogliflozin with 500 mg metformin were observed to be safe and tolerable. The results showed a significant decrease in the occurrence of adverse effects associated with these combination therapies, which were quite beneficial in the treatment of diabetes mellitus type II patients.

A single-dose, dose-escalation study in healthy human volunteers and T2DM patients observed 24 h urine glucose excretion (UGE) to be 17.5–40.5 g and 66.6–112.6 g, respectively, in a dose-dependent manner. The UGE showed a dose-dependent increase in total UGE from 0 to 24 h in fasted and fed conditions. However, UGE increased less proportionally with an increase in dose from 150 mg to 500 mg, indicating a plateau effect, as observed with drugs of this class. Urinary glucose excretion was higher in patients with T2DM than in volunteers because of higher plasma glucose concentrations in patients. On correcting the UGE according to circulating plasma glucose concentrations and creatinine clearance, to estimate the percentage filtered glucose load, it was found to be similar in both healthy individuals and T2DM patients. Clinically significant increase in UGE and urine volumes was observed in 12-week dose-ranging (50–1000 mg) study in drug naïve T2DM patients. A dose ordered increase at 12 weeks from baseline was observed in UGE over 24 h ranging from 61 to 96 g/day. A similar dose-ordered increase at 12 weeks in urine volume was observed (~0.5 L/day). The key pharmacokinetic and pharmacodynamic studies that assisted the characterization of clinical profiles were also significant.[1,4]

Therefore, this study suffices its objective, amply assessing the globally relevant prescribing rationale of pharmacotherapeutic application in molecular medicine, along with the safety evaluation of the antidiabetic combination therapies with subsequent increase in drug doses of 50 mg, and then, 75 mg remogliflozin with 500 mg metformin, in type II diabetes mellitus patients, in tertiary care medical college hospitals. This type of stepwise increase in a single drug dose within a combination therapy potentiates the effective evidence-based selective pharmacotherapeutic response of the diabetic patients to gradual modification of the combination regimens; thereby also focusing on the minimization of adverse effects of antidiabetic drugs along with effective clinical responses, shown even with lowered doses of a single drug in the prescribed combination drug regimens.

CONCLUSIONS

This study established that the combination therapies consisting of the increasing doses of remogliflozin 50 mg and then 75 mg, along with 500 mg metformin, were safe and tolerable. This study would remain a significant landmark toward the determination of precisely adjusted dose schedules of antidiabetic singular drug regimen or combination drug regimens, each dose being specifically titrated in accordance with the investigative and evidence-based pharmacotherapeutic effectiveness and clinical response of the diabetic patient, emphasized further by the significant authentication of drug efficacy and safety.

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Original Article

Diagnostic Evaluation of Alvarado Score in Pre-operative Diagnosis of Acute Appendicitis

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Abstract

Introduction: Acute appendicitis is one of the most common surgically correctable acute abdomens presenting at emergency department worldwide. In spite of all advances in diagnostic modalities and surgical techniques, diagnosis remains difficult sometimes as a challenge and delayed decision making complicates this surgical disease. Alvarado scoring system is one of available scoring system for diagnosis of acute appendicitis, based on history, clinical examination, and laboratory investigations and easy to apply, helps in clinical decision regarding planning surgery and avoid negative laparotomies. The aim of the study was to evaluate diagnostic accuracy of Alvarado scoring system in pre-operative diagnosis of acute appendicitis and correlating with post-operative findings.

Methods: This study was conducted in 50 cases of suspected appendicitis admitted in Surgery Department, from January 2018 to December 2020 by adopting Alvarado scoring system. Results were recorded and analyzed.

Results: Out of 50 patients admitted with suspected acute appendicitis, number of cases operated suspecting acute appendicitis were 41 of which 39 were found to have acutely inflamed appendix. Results of Alvarado score of operated patients are as follows: 39 patients had score 7–10, and 4 patients had score 5–6, patients with Alvarado score <5 (17 pts) were managed conservatively.

Conclusions: The Alvarado scoring system is a simple and useful diagnostic tool for diagnosis of acute appendicitis with acceptable sensitivity and specificity and can be used with high degree of accuracy. Our findings suggest that patients presenting with abdominal pain and Alvarado scores >7 are more likely to have appendicitis.

Key words: Abdominal pain, Acute appendicitis, Alvarado score, Appendicitis

INTRODUCTION

Acute appendicitis is an inflammation of the appendix that occurs suddenly. It's the most prevalent kind of acute abdominal emergency that necessitates immediate surgical intervention. If early diagnosis fails, simple appendicitis may develop to perforation, resulting in increased morbidity and death; hence, surgeons have been more willing to operate when the diagnosis is likely rather than wait until it is confirmed. Despite more than a century of practice, the surgeon is still unable to make an accurate diagnosis.[1,2]

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When diagnosing a suspected case of acute appendicitis, the core essential concern is whether or not to operate if identified without increasing the likelihood of needless negative surgical procedures.[1]

Acute appendicitis is prevalent due to its unusual presentations, but diagnosis becomes more difficult when the symptoms coincide with those of other diseases, making diagnosis difficult, especially at an early stage of presentation.[3] The clinical examination's accuracy has been found to vary from 71% to 97%, and it varies substantially depending on the examiner's expertise.[4] Due to the serious repercussions of missing ruptured appendices, surgeons have typically accepted a 20% incidence of negative findings during appendicectomy and the removal of a normal appendix. Negative appendectomy (removal of a normal appendix in patients with other reasons of stomach discomfort) is said to occur between 20% and 30% of the time.[5,6]

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Alvarado developed a ten-point clinical scoring system, dubbed "Mantrels," in 1986 for the diagnosis of acute appendicitis based on symptoms, signs, and diagnostic tests in patients with suspected acute appendicitis.[7]

The Alvarado score facilitates risk classification in patients with abdominal discomfort by correlating the likelihood of appendicitis with recommendations for discharge, monitoring, or surgical intervention. When the risk of appendicitis is in the intermediate range, more investigations such as ultrasound and computed tomography scanning are required.[6,7]

Scoring methods are beneficial and accurate for differentiating acute appendicitis from nonspecific abdominal discomfort. Alvarado scoring system is one of many accessible scoring systems for acute appendicitis diagnosis. It is entirely based on history, clinical examination, and a few laboratory tests and is quite simple to administer.[8] Using an objective grading method such as the Alvarado system, it is possible to minimize the rate of negative appendicectomy to 0–5%. However, this method is not intended to take the place of clinical judgment. It assists in identifying acute appendicitis and determining whether or not to operate on a specific instance, hence minimizing the frequency of negative laparotomies. The present study aims at evaluating the efficacy of Alvarado scoring system in pre-operative diagnosis of acute appendicitis and correlating it with post-operative findings.

METHODS

This study was conducted on 50 patients presenting with symptoms and signs of acute appendicitis to the casualty over a period of 2 years from January 2018 to December 2020. Results were analyzed using Microsoft Excel software.

Inclusion Criteria

Patients with symptoms and signs of acute appendicitis in whom emergency appendicectomy was done; both the genders and all age groups were included in the study; patients who were willing to participate in study were included in this study.

Exclusion Criteria

Patients with appendicular mass, urinary calculus, gynecological causes of right iliac fossa (RIF) pain; patients who underwent elective/interval appendicectomy; patients who were not willing to participate in the study were excluded in this study.

Patients with clinical signs and symptoms suggestive of acute appendicitis such as abdominal pain, rebound tenderness, nausea, vomiting, or elevated temperature who met the inclusion criteria were admitted and after taking informed consent and initial assessment were subjected for detailed history taking, physical examination, routine laboratory investigations, and imaging. Then, they were evaluated using Alvarado scoring system as per the scores of all variables of the scoring system and the aggregate score was given for each patient [Table 1]. Based on the score patients were classified into three groups.

- Group 1: Score 7–10 was most likely acute appendicitis; these patients were taken up for emergency appendicectomy
- Group 2: Score 5–6 was possibly acute appendicitis. Patients in this group were admitted and kept under observation for a day with reassessment of the clinical findings and reapplication of the score. Some patients improved with conservative treatment which was shown by a decrease in score and were discharged with advice that they should revert back if symptoms persist, recur or increase in intensity
- Group 3: Score 1–4 was unlikely acute appendicitis: These patients, after giving initial symptomatic treatment, were discharged and sent home with the instructions to revert back if symptoms recur or worsen.

Decision for appendicectomy was made after the assessment of the patient depending on the Alvarado scoring system for patients with score of 7–10. All the patients were operated by open method (open appendicectomy). Intra operative findings were documented and definitive diagnosis of acute appendicitis was made based on histopathological examination of the appendicectomy specimen.

Finally, the reliability of Alvarado scoring system was assessed by calculating negative appendicectomy rate (the proportion of operated patients having normal appendix removed) and positive predictive value (the proportion of

Table 1: Alvarado scoring system

Variables	Score
Symptoms	
Migratory right iliac fossa pain	1
Anorexia	1
Nausea/vomiting	1
Signs	
Tenderness in right iliac fossa	2
Rebound tenderness in the right iliac fossa	1
Elevated temperature	1
Lab findings	
Leukocytosis	2
Shift to the left of neutrophils	1
Total	10

patients with a positive test result who actually have the disease).

RESULTS

One hundred patients were preoperatively diagnosed to have acute appendicitis were admitted and studied. Of the 50 cases that were admitted with suspicion of acute appendicitis, 41 cases were taken up for surgery based on the Alvarado scoring system while 8 cases with Alvarado score <5 and 1 case with palpable mass in RIF was kept under conservative management. Among the 41 cases that were operated 37 cases had acutely inflamed appendix. The percentage of inflamed appendix found on operation was 90.24%.

The age group in which acute appendicitis occurred commonly is between 11 and 30 years, that is, about 65%. Incidence is less in younger and older age group with peak incidence in second and third decade. Table 2 depicts the frequency of patients as per the symptoms.

Pain was the most common symptom seen almost in all of the patients (98%), followed by nausea and vomiting (80%), rebound tenderness (76%), and anorexia (64%).

Results of Alvarado Score

The patients were categorized into three groups, that is, male, female and children. Out of 100 cases studied 24 were male, 17 were female and 9 were children (<12 years).

Out of 24 male patients, 17 had a score of 7–10; 2 had a score of 5–6 and 4 patients had score <5; 1 patient had mass in RIF. Out of 17 female patients, 13 had a score of 7–10; 2 had a score of 5–6 and 2 patients had score of <5. About 9 children had a score between 7 and 10 and all the children were operated on [Table 3].

Among the 10 patients of score <6 and 1 patients with mass in RIF were observed in the hospital with conservative treatment and did not undergo surgery since they improved symptomatically. The patients with mass in RIF were advised for interval appendicectomy.

Operative Findings

A total of 41 patients were operated, out of which 19 were males; 13 were females; 9 were children. In the present study, the number of male patients (24) outnumbered females (17) approximately in the ratio of 1.41:1.

In male patients having score of 7–10; 15 patients had acute appendicitis; 1 patient had normal appendix and 1 patient had diseases in the form of ileal perforation and Meckel's diverticulitis.

Table 2: Distribution of patients as per the symptoms (variables of Alvarado scoring system) presented (*n*=100)

Clinical symptoms	Number of patients *n* (%)
Migratory RIF pain	20 (40)
Anorexia	32 (64)
Nausea and vomiting	40 (80)
Tenderness over RIF	49 (98)
Rebound tenderness RIF	38 (76)
Elevated temperature	32 (64)
Leukocytosis	31 (62)
Shift to left	23 (46)

RIF: Right iliac fossa

Table 3: Distribution of patients based on Alvarado score

Alvarado score	Number of patients *n* (%)
7–10	39
5–6	4
1–4	6

In female patients having score of 7–10; 10 had acute appendicitis; 1 patient had normal appendix and 1 patient had other diseases, out which 1 had pelvic inflammatory disease; 1 had twisted right ovarian cyst. All the 9 children who underwent appendicectomy had acute appendicitis.

DISCUSSION

In our study, the age range of our patients in this study was 9–60 years, with mean age of 24–25 years. Of all 41 patients operated, 26 patients (63.41%) were in the age group of 9–30 which is comparable to those found in Talukder and Siddiq[9] and Shrestha *et al*.[10] studies.

In this study, there was male preponderance (24 patients) as compared to females (17 patients) with a male to female ratio of 1.41:1 which is comparable to 1.27:1 in Subedi *et al*.[11] whereas it was 3.2:1 in Patra *et al*.[12]

In our study, the most common presenting symptom was pain (98%) followed by nausea/vomiting in 80% of the patients and rebound tenderness in 76%. The least common symptom seen was migratory RIF pain which was found in 40% cases. 62% of the patients had leukocytosis and 46% had shift to left. These findings were comparable to those of Lameris *et al*.[13] Subedi *et al*.[11] reported that 98% of patients with acute appendicitis presented with pain in peri-umbilical region migrating to RIF, but leukocytosis was seen in only 65% of cases which was comparable to present study. Merhi *et al*.[14] concluded that anorexia, neutrophils left shift and rebound tenderness are significantly correlated with a correct diagnosis of appendicitis.

In our study, 15 patients (38.46%) had a score of 7, only 3 of the patients had a score of 10 and none of the patients were seen with scores of 1 and 2. 83 patients (78%) were in score range of 7–10, 8% (4 patients) in 5–6 range and 12% (6 patients) were in 1–4 score range which was comparable to Singh *et al*.[15]

In this study, acute appendicitis (simple appendicitis) was confirmed intra-operatively in 34 (82.92%) patients. 3 (7.31%) had acute gangrenous appendicitis and 4 (9.75%) had perforated appendix. These findings were comparable to those reported by Dey *et al*.[16] Subedi *et al*.[11] found that the most common pre-operative finding was acutely inflamed appendix (84%) followed by perforated appendix (7.5%), gangrenous appendix (3.5%) and appendicular mass (1.5%). Shrestha *et al*.[10] observed that appendicitis accounted for 88.8%.

In our study, positive and negative appendicectomy rates overall were 90.24% and 9.76%, respectively which was comparable to other studies.[16] Bhattacharjee *et al*.[17] concluded that high Alvarado score was found to be a dependable aid both in the pre-operative diagnosis of acute appendicitis and in the reduction of negative appendicectomies in men and children but the same was not true for women who had a high false positive rate for acute appendicitis. In the present study, positive predictive value was 90.24% which was comparable to other studies.

CONCLUSIONS

In our study, the most common age group affected by appendicitis was identified to be 9–30 years which is 63.41% of study group. Out of 50 patients 39 patients had Alvarado score of 7–10 and were taken up for surgery. Males were affected more than the females (1.41:1), high Alvarado score was very much correlating with the intra operative findings among males and children than females. Acute appendicitis is the most common histological examination finding in our study group (82.94%). Hence, applying Alvarado scoring system improves diagnostic accuracy and reduces negative appendicectomy rate in majority of the patients and also help in anticipating possible complications. In our study, positive and negative appendicectomy rates overall were 90.24%% and 9.76%, respectively.

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Original Article

Study of Iron Deficiency Anemia and its Association with Cholelithiasis

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Abstract

Introduction: The incidence of gall stones is in increasing trend. The old axiom that a typical gall stone sufferer is a fat, fertile, female of 50, is only partially true, as the disease is found in women soon after their first delivery, in underweight and thin people. Hence, while searching for other parameters, iron deficiency was found to be a new parameter of interest in the etiology of gall stones.

Methods: Around 50 cases of cholelithiasis and 40 cases of anemia with low serum ferritin levels from October 2018 to September 2020 were studied. Serum iron was estimated by carbonyl metallo-immunoassay method. Serum cholesterol was estimated by the cholesterol oxidase-peroxidase (CHOD-POD) Enzymatic method. Biliary cholesterol was estimated after extraction of biliary lipids from bile from the gallbladder specimen of the patients by the method of Folch *et al*. which was followed by the procedure similar to the analysis of serum cholesterol by CHOD-POD enzymatic method. Fischer's Chi-square exact test was used as statistical method.

Results: It was observed that 70% of the group A, study group with cholelithiasis had normal serum ferritin levels, and 30% had low serum ferritin levels. It was observed that 95% had normal sonographic findings and 5% had cholelithiasis with normal ferritin levels in group B.

Conclusions: In our study, low serum ferritin levels with cholelithiasis was associated with raised bile cholesterol levels and so it can be concluded that low serum ferritin level is causing biliary stasis and hence leading to increase in the incidence of cholelithiasis.

Key words: Anemia, Cholelithiasis, Cholesterole, Gall stones

INTRODUCTION

Gallstone disease is a common clinical entity affecting the adult population of both sexes. The earliest known gallstone dates back to the 21st Egyptian dynasty discovered in the mummy of priestess of Amenen (1085-945 BC). There are also descriptions of stones in the biliary system in Greeks in the 5th century anno domini (AD), as well as Persians in the 10th century AD. Vesalius (1514-1564) established the teaching that gallstones were evidence of disease and he associated them with jaundice.[1,2]

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Open cholecystectomy first performed by Carl Langenbuch in 1882, has been the primary treatment for gallbladder disease has been the primary treatment of gallbladder disease through the early 1990s. In 1985, the first endoscopic cholecystectomy was performed by Erich Muhe of Boblingen, Germany.[3] Swedish epidemiologic study found that the incidence of gall stones was 1.39/100 person- years. In an Italian study, 20% of women had gall stones, and 14% of men had stones.[4]

The prevalence of gallstones varies widely in different parts of the world. In India it is estimated to be around 4%. An epidemiological study restricted to rail road workers showed that north Indians have 7 times higher incidence of gallstones as compared to south Indians.[5] Women are more likely to develop cholesterol gallstones than men, especially during their reproductive years, when the incidence of gallstones in women is 2–3 times that in men. The difference appears to be attributable

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mainly to estrogen, which increases biliary cholesterol secretion.[6]

Risk of developing gallstones increases with age. Gallstones are uncommon in children in the absence of congenital anomalies or hemolytic disorders. Beginning at puberty, the concentration of cholesterol in bile increases. After age 15 years, the prevalence of gallstones in the US women increases by about 1% per year; in men, the rate is less, about 0.5% per year. Gallstones continue to form throughout adult life, and the prevalence is greatest at advanced age. The incidence in women falls with menopause, but new stone formation in men and women continues at a rate of about 0.4% per year until late in life.

The old axiom that a typical gall stone sufferer is a fat, fertile, female of 50, is only partially true, as the disease is found in women soon after their first delivery and also in underweight and thin people. Hence, while searching for other parameters, iron deficiency was found to be a new parameter of interest in the etiology of gall stones.[7]

Other factors contributing to formation of gallstones impaired gallbladder function, supersaturated bile, cholesterol nucleating factors, absorption/enterohepatic circulation of bile acids.[8] Iron deficiency, that is, low serum ferritin levels has been shown to alter the activity of several hepatic enzymes, leading to increased gall bladder bile cholesterol saturation and promotion of cholesterol crystal formation.[9,10] Iron acts as a coenzyme for nitric oxide synthetase, which synthesizes nitric oxide and that is important for the maintenance of basal gall bladder tone and normal relaxation.[11,12] It was found that iron deficiency (low serum ferritin levels) resulted in altered motility of gall bladder and sphincter of Oddi, leading to biliary stasis and thus increased cholesterol crystal formation in the gall bladder bile.[13]

The present study was done to test the hypothesis that iron deficiency (low serum ferritin levels) is an etiological factor in the formation of gall stones.

METHODS

Study Design

This was a prospective study of minimum 90 patients of either sex admitted to our hospital (a tertiary level center) with cholelithiasis or anemia with low serum ferritin levels. The study was prospective, observational, and analytical study.

Selection of Patient

Inclusion criteria

Inclusion criteria were all patients with sonographic findings of cholelithiasis. All patients with low serum ferritin levels.

Exclusion criteria

Exclusion criteria were patients with empyema of gall bladder. Patients with mucocoele of the gall bladder, Immunocompromised patients and patients not willing for the study were excluded. The present study will comprise of 50 cases of cholelithiasis (group A) and 40 cases of anemia with low serum ferritin levels (group B) from October 2018 to September 2020. Detailed clinical history and examination of the 90 selected cases was done. Estimation and tabulation of the lipid profile, serum ferritin level and bile cholesterol in the 50 cases of cholelithiasis were done and the outcome was analyzed. 40 cases of anemia with low serum ferritin levels were studied and evaluated for the presence cholelithiasis and association with lipid profile.

As all cholelithiasis cases with low serum ferritin levels were not fit for surgery so to test the reverse hypothesis and to look for cholelithiasis in a known case of anemia with low serum ferritin levels these 40 cases were taken into our study. The study protocol was approved by the review board of our institute for ethical research.

Serum iron was estimated by carbonyl metallo-immunoassay method. The normal reference values for our laboratory were, for males (15–220 ug/dl) and for females (10–124 ug/dl), that is, males with serum ferritin <15 ug/dl and females with serum iron <10 ug/dl were labeled as anemic. Serum cholesterol was estimated by the cholesterol oxidase-peroxidase (CHOD-POD) enzymatic method.[14] Biliary cholesterol was estimated after extraction of biliary lipids from bile from the gallbladder specimen of the patients by the method of Folch *et al*., which was followed by the procedure similar to the analysis of serum cholesterol by CHOD-POD enzymatic method. The reference values were taken with respect to the standard reference values for our laboratory. For males and females, the normal range was 130–200 mg/dl.

For serum ferritin, serum lipid profile 5 ml of intra venous blood sample was drawn and sent to the laboratory for investigation and for the estimation of bile cholesterol if the operative procedure was open then bile was directly aspirated from the gall bladder after cholecystectomy and if the operative procedure was laparoscopic then bile was aspirated from one of the 5 mm ports.

RESULTS

In group A, it was observed that 72% of the study group were females and 28% were males. Cholelithiasis occurs most commonly in the age group 35–45 years. 68% of the group A study group with cholelithiasis had normal

Table 1: Ferritin levels in comparison to cholesterol

Variables	Normal (%)	High (%)	Total
Ferritin Group			
Normal	34 (68)	0 (0)	34
Low	16 (32)	2 (100)	18
Total	50	2	52

Chi-square (df)=6.5546 (1), $P<0.05$ (significant)

Table 2: Ferritin level in comparison to cholelithiasis

Variables	Cholethiasis (%)	Cholethiasis (%)	Total
Ferritin Group			
Normal	34 (66.03)	0 (0)	34
Low	19 (35.84)	37 (100)	56
Total	53	37	

Chi-square (df)=41.8531, $P<0.05$ (significant)

Table 3: Serum cholesterol (rows) versus biliary cholesterol (columns)

Cholesterol Group	Normal	Abnormal	Total
Normal	47 (94%)	0 (0%)	47
Low	3 (6%)	4 (100%)	7
Total	50	4	

Chi-square (df)=0.1273, $P>0.05$ (not significant)

serum ferritin levels and 32% had low serum ferritin levels. 94% had normal serum cholesterol levels and 6% had high serum cholesterol levels. 92% had normal bile cholesterol and 8% had high bile cholesterol. These 4% had low serum ferritin level and normal serum cholesterol levels. In group B, it was observed that 92.5% had normal sonographic findings and 7.5% had cholelithiasis with normal ferritin levels [Tables 1-3].

DISCUSSION

Recent studies have defined the role of trace elements (Fe, Ca, Zn, and Cu) and defective pH in the formation of gall stones. Iron deficiency, that is, low serum ferritin levels has been shown to alter the activity of several hepatic enzymes, leading to increased gall bladder bile cholesterol saturation and promotion of cholesterol crystal formation.[10,11] In our study, 90 cases constituted the study population. In group A, 50 cases of cholelithiasis were taken and in group B 40 cases of anemia with low serum ferritin levels were taken.

Group A

In our study, 50 cases of cholelithiasis 24% were male and 76% were females. Our findings correlated with the study done by Sarhan *et al.* in which 80% were female and 20% were males supporting the age-old axiom that gall stones are more common in the females.[6,15] 50% of the patients were in the 35–45 years age group.

In our study, out of 50 cases 34, that is, 68% had normal serum ferritin and 16, that is, 32% had low serum ferritin. In a study done by Muneesh *et al.*,[16] 52% had normal serum ferritin and 48% had low serum ferritin levels.

In our study, 47, that is, 94% had normal serum cholesterol and 3, that is, 6% had high serum cholesterol. In our study, there was no significant correlation between high serum cholesterol with cholelithiasis. Our findings correlated with the findings of the study done by Muneesh *et al.*[16] In a study done by Sarhan *et al.*,[15] also there was no significant difference in the serum cholesterol levels of the cholelithiasis patients with low serum ferritin levels and with cholelithiasis patients with normal serum ferritin levels.

In our study, 46, that is, 92% had normal biliary cholesterol and 4, that is, 8 % had high biliary cholesterol. The 4 patients with high biliary cholesterol had normal serum cholesterol and low serum ferritin levels. In a study done by Sahu *et al.* the mean bile cholesterol level in group A, that is, normal serum ferritin group was found to be 214.6 mg/dl and in group B, that is, low serum ferritin group was 375.3 mg/dl. The difference in values in both the groups was found to be statistically extremely significant ($P < 0.0001$).[17]

We would like to continue our study with a larger study group and taking some other factors into consideration like other trace elements. As all cases of cholelithiasis with anemia with low serum ferritin levels are not fit for surgery and are not operated, so 40 cases of anemia with low serum ferritin levels were taken and studied for the findings of cholelithiasis and in a way testing the reverse hypothesis.

Group B

In our study, of 40 cases only 3, that is, 7.5% of the study group had cholelithiasis. The serum cholesterol was normal in these 7.5% of the study group. Later on, these cases were operated and their bile cholesterol was also found out to be normal. Probably anemia, obesity, and sex hormones are independent risk factors operating for the causation of gallstones and if present together, they produce synergistic effects. The scope of this study can be further advanced in the field of enzymes controlling gallbladder tone, motility and relaxation and cofactors affecting these enzymes.

We would like to continue our study further with a larger study group. Many other studies are required related to this topic as both cholelithiasis and low serum ferritin are fairly common conditions prevalent in the general population. On combining group A and group B and cross tabulating

the results of our study, our findings were 66.07% of the cholelithiasis cases had normal serum ferritin and 35.84% of the cholelithiasis cases had low serum ferritin levels. Chi-square (df) = 41.8531, $P < 0.05$ (significant). Our findings correlated with the findings of the study done by Sarhan *et al.*,[15] 96% of the cholelithiasis cases had normal serum cholesterol and 4% had high serum cholesterol Chi-square (df) = 1.4948, $P > 0.05$ (not-significant). Our findings correlated with the findings of the study done by Muneesh *et al.*[16] *et al.* in a study done by Sarhan *et al.*[15] also there was no significant difference in the serum cholesterol levels of the cholelithiasis patients with low serum ferritin levels and with cholelithiasis patients with normal serum ferritin levels.[6] 92% of the cholelithiasis cases had normal bile cholesterol and 8% had high bile cholesterol. Chi-square (df) = 6.5546, $P < 0.05$ (significant). Chi-square (df) = 0.1273, $P > 0.05$ (not significant).

CONCLUSIONS

Based on our studies the following are the conclusions, cholelithiasis is more common in females than in males and the most common affected age group is 35–45 years. Low serum ferritin level is a significant factor in the formation of gallbladder stones. No significant correlation could be found with raised serum cholesterol and cholelithiasis. In our study, low serum ferritin levels with cholelithiasis was associated with raised bile cholesterol levels and so it can be concluded that low serum ferritin level is causing biliary stasis and hence leading to increase in the incidence of cholelithiasis.

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Original Article

Study of Respiratory Distress Syndrome Etiology in Neonates

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Abstract

Introduction: Respiratory distress (RD) is a medical emergency responsible for most of the admissions in neonatal intensive care units (NICUs) during neonatal period. It is a major contributor to neonatal morbidity and mortality and results from a variety of respiratory and non-respiratory etiology. It occurs in 0.96–12% of live births and responsible for about 20% of neonatal mortality. Aim of study is to find out the proportion of patients with different etiology of RD in neonates.

Methods: The present study is a prospective, descriptive study which was carried out at headquarters hospital. All the neonates with RD admitted in NICU admitted from April 2018 to March 2019 were selected for the present study. Detailed history including antenatal history, natal history, and postnatal history with thorough clinical examinations and investigations done in each case and were recorded in the performa.

Results: A total of 500 neonates were admitted and among them 375 were inborn (delivered in our hospitals) and 125 out-born (referred to our hospitals from outside). In inborn group, hyaline membrane disease was the most common cause (32%) of RD and in out-born congenital pneumonia/septicemia (34.4%). There was male preponderance in both inborn and out-born groups with male: female ratio 1.45:1 and 1.6:1 respectively.

Conclusions: Respiratory distress is one of the most common reasons an infant is admitted to the neonatal intensive care unit. The commonest causes of respiratory distress in this study was transient tachypnea of newborn (43.2%) followed by hyaline membrane disease (30.2%).

Key words: Etiology, Neonates, Respiratory distress, Respiratory distress, Syndrome

INTRODUCTION

Respiratory distress (RD) is a common medical emergency responsible for 30–40% of total admissions in the neonatal period.[1] RD is one of the major causes of mortality and morbidity among the newborns. It occurs in 0.90–12% of live births and responsible for about 20% of neonatal mortality.[1] There are many causes of RD in neonates these include[2] transient tachypnea of newborns (TTNB), septicemia, meconium aspiration syndrome (MAS), hyaline membrane disease (HMD), perinatal asphyxia, congenital or acquired pneumonia, Persistent pulmonary hypertension of the newborn, air leaks(Pneumothorax), congenital anomalies of upper airway (choanal atresia), gut (tracheoesophageal fistula, congenital diaphragmatic hernia) or lungs (lobar emphysema, congenital cystic adenomatoid malformation, cysts), cardiac shock or congenital heart disease (CHD), hematological causes (severe anemia, Polycythemia), neurological causes leading to hyperventilation like seizures and Metabolic causes like inborn errors of Metabolism.

Aim of this study is to find out the proportion of patients with different etiology of RD in neonates.

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METHODS

This is a prospective descriptive study, carried out at neonatal units in government headquaters hospital, Tamilnadu. 50 neonates with RD admitted in Neonates intensive care unit (NICU) both male and female, inborn (37) and out-born (13) were included in the study. Study

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was conducted for the period of 1 year April 2018 to March 2019.

Inclusion Criteria

- Neonates inborn or out-born admitted to the neonatology units with symptoms and/or signs of RD
- Age <28 days.

Exclusion Criteria

- RD settled in first 2 h after birth, in inborn neonates by correction of hypothermia, hypoglycemia and not needed admission to NICU were excluded from the study.

Detailed history including antenatal history, natal history, and postnatal history with thorough clinical examinations and investigations done in each case and were recorded in the performa. The diagnosis of respiratory problems was based on guidelines recommended by the National Neonatology Forum (National Neonatal-Perinatal Database 2002–2003).[3]

RD

Presence of at least two of the following criteria

- Respiratory rate >60/min
- Subcostal/intercostal recessions
- Expiratory grunt/groaning
- Flaring of alae nasi
- Central cyanosis in room air.

TTNB is diagnosed as RD in a term or borderline term or preterm neonate starting within 6 h after birth, often requiring supplemental oxygen, but recovering spontaneously within 3–4 days and showing characteristic X-ray changes, that is, Linear streaking at hilar and interlobar fluid.

HMD is diagnosed when following three criteria are present: (a) preterm neonates; (b) RD having onset within 6 h of birth; and (c) Amniotic fluid L/S ratio of <1.5, or negative gastric aspirate shake test, or skiagram of chest showing poor expansion with air bronchogram/ reticulogranular pattern/ground glass opacity.

MAS is diagnosed in the presence of at least two of the following: (1) meconium staining of the liquor or staining of nails or umbilical cord or skin; (2) RD soon after birth; and (3) Radiological evidence of aspiration pneumonitis (atelectasis or hyperinflation).

Congenital Pneumonia is diagnosed in the presence of RD with: (a) positive blood culture or (b) if any two of the following are present: (1) existing or predisposing factors characterized by one of the following (a) maternal fever (>38°c) (b) foul smelling liquor; (c) prolonged rupture of membrane (>18 h) (2) clinical picture of sepsis characterized by any of the following; (a) poor feeding, (b) lethargy, (c) poor reflexes, (d) hypo or hyperthermia, (e) abdominal distension; and (3) X-ray picture suggestive of pneumonia characterized by any of the following; nodular or coarse patchy infiltrates, diffuse haziness or granularity, air bronchogram, and lobar or sub lobar consolidation. (4) Positive septic screen.

Birth Asphyxia

Definition I

- Moderate birth asphyxia: Slow gasping breathing at 1-min of age
- Severe birth asphyxia: No breathing at 1-min of age.

Definition II

- Birth asphyxia: Apgar score of less than 7 at 1 min of age
- Moderate birth asphyxia: Apgar score between 4 and 6 at 1-min of age
- Severe birth asphyxia: Apgar score of 3 or less at 1-min of age.

Septicemia (Systemic Bacterial Infection)

Culture negative (clinical)

In an infant having clinical picture suggestive of septicemia, the presence of any one of the Following criteria is enough for assigning probable diagnosis of infection:

1. Existence of predisposing factors: Maternal fever or foul smelling liquor or prolonged Rupture of membranes (>18 h) or gastric polymorphs (>5 per high power field)
2. Positive septic screen: two of the four parameters - total leucocytes count (TLC) <5000/mm, band to total polymorph ratio of >0.2, absolute neutrophil count <1800, and micro ESR >10 mm 1st h
3. Radiological evidences of pneumonia.

Culture positive sepsis

In an infant having clinical picture suggestive of septicemia, pneumonia or meningitis along with either of the following.-isolation of pathogens from blood or Cerebrospinal fluid or urine or abscess (es) -pathological evidence of sepsis on autopsy.

Investigations

- X-ray chest anteroposterior view:
- Septic screening:
  i. TLC
  ii. Absolute neutrophil count
  iii. Immature to total neutrophil (I/T ratio)
  iv. C-reactive protein
- Blood culture and sensitivity.

RESULTS

Out of 50 neonates admitted, 37 were inborn (delivered in our hospitals) and 13 out-born (referred to our hospitals from outside). Sex wise distribution of neonates admitted in NICU with RD is shown in Table 1. There was male preponderance in both the groups (neonates born in hospital and outside the hospital).

The distribution of cases of RD based on the diagnosis is shown in Table 2. The most common cause of RD in neonates born in hospital was HMD (32%) and in neonates born outside the hospital, was congenital pneumonia/ septicemia (34.4%).

Table 1: Gender ratio of neonates and admitted in NICU respiratory distress

No of cases of respiratory distress	Male	Female	Total	Ratio
Inborn	22	15	37	1.46:1
Out born	8	5	13	1.60:1

NICU: Neonates intensive care unit

Table 2: Distribution of respiratory distress syndrome cases as per diagnosis

Disease	In born No. of cases (%)	Out born No. of cases (%)
HMD	11 (29.72)	3 (23.07)
Congenital pneumonia/Septicemia	9 (24.32)	4 (30.76)
Transient Tachypnea of Newborn	5 (13.51)	2 (15.38)
Meconium aspiration syndrome	4 (10.81)	1 (7.69)
Perinatal Asphyxia	3 (8.10)	1 (7.69)
Congenital heart disease	2 (5.4)	1 (7.69)
Surgical causes (TOF, CDH Diaphragmatic eventration)	2 (5.4)	0 (0)
Inborn error of metabolism	1 (2.7)	0 (0)
Aspiration pneumonia	0 (0)	1 (7.69)

CDH: Congenital diaphragmatic hernia, TOF: Tetralogy of Fallot

DISCUSSION

The sex ratio in the present study was 1.53:1 overall, with male predominance which is consistent with study conducted by Ali[4] (1.48:1). Male predominance was also shown by Hjalmarson[5] (1.7:1), Mishra[6] (1.5:1) and Malhotra *et al*.,[7] (1.08:1).

In our study, male predominance was 60% and preterm babies with RD constituted 54%. Overall, the most common cause of RD in our study was HMD (28%). The study done by Haque *et al*.,[8] showed that there was male predominance (64.6%) and most of babies admitted in NICU with RD were preterm babies (65.6%). The commonest causes of RD in this study was TTNB (43.2%) followed by HMD (30.2%).

Santosh *et al*.,[9] observed that out of 76 babies with RD, 35 (46%) babies had TTNB, 24 (31.5%) babies had RD syndrome (RDS), 19 (25%) had BA, 19(25%) babies had pneumonia and sepsis, 6 (7.8%) babies had MAS, 2 (2.6%) babies had pneumothorax, 1 (1.3%) neonates had CHD, 1 (1.3%) neonates had laryngomalacia.

Fedakar and Aydoğdu[10] reported that 20.4% cases with RD were premature, 64.4% were males and TTNB was the most common (76.7%) cause for admission in NICU followed by MAS (8.3%), RDS (HMD) (6.3%), birth asphyxia (3.8%), sepsis (2.1%), pneumonia (1.7%), multiple congenital anomalies (0.4%), inborn metabolic disease (0.4%), and aspiration pneumonia (0.4%).

Qian *et al*.,[11] study showed that most common of RD was HMD. Zaman *et al*.,[12] showed that TTNB was found to be the commonest (35.7%) cause of RD followed by HMD (25%). Mathur *et al*.,[13] found that pneumonia to be the most common cause (68.6%) of RD in neonates.

CONCLUSIONS

Respiratory distress is one of the most common reasons an infant is admitted to the neonatal intensive care unit. The commonest causes of respiratory distress in this study was transient tachypnea of newborn (43.2%) followed by hyaline membrane disease (30.2%). Learning to readily recognize respiratory distress in the newborn and understanding physiologic abnormalities associated with each of the various causes will guide optimal management.

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Original Article

Association between Blood Type and Severity in COVID-19

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Abstract

Background: Although respiratory failure is the most prevalent complication of coronavirus disease 2019 (COVID-19), renal and circulatory failure are also common in individuals who require critical care or die from the disease. Given the high morbidity and mortality associated with COVID-19 infection, scientists have been interested in gathering information about the traits that make people more vulnerable to the virus, as well as establishing what risk factors are linked to illness development and severity.

Aim: The goal of this study was to see whether there was a link between blood type and the severity of COVID-19, which was defined as intubation or death, as well as to see if there was any variation in testing positive for COVID-19 among blood types.

Methods: In this observational study done in Sree Balaji Hospital during the second COVID wave, adult patients who tested positive for COVID-19 were identified, and the effects of blood type on hospitalization and intubation were investigated.

Results: An increased risk of infection has been associated with blood group A: 144 (72%). Infection with COVID-19 was common in non-blood Group O people. Blood type A had the greatest death rate in our study, followed by blood Group B, and blood Group O had the lowest mortality rate.

Conclusion: In our study, COVID-19 was shown to be common in non-blood type O people, with a high incidence and severity. COVID-19 was not transmitted to those with blood group O. As a result, non-blood type O patients must be closely monitored to avoid Post-COVID complications.

Key words: ABO, Blood type, Intubation, Mortality, Non-blood type O

INTRODUCTION

COVID-19 infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread globally, impacting 30 million individuals. COVID-19 symptoms were weariness, fever, and a dry cough, which were invariably followed by myalgia, anorexia, dyspnea, and other symptoms.[1] COVID-19 is most commonly diagnosed as a lung infection, with symptoms ranging from flu-like symptoms to acute respiratory distress syndrome. The emergence of COVID-19 has created a public health danger, and governments are committing scientific and medical resources to combat the epidemic.[2] The virus has had various impacts on the worldwide population; individuals who are older and have comorbidities such as cardiovascular illness, diabetes, or pulmonary disease are more susceptible to severe disease. The emergence of COVID-19 has posed a public health danger, and governments are dedicating scientific and medical resources to combat the epidemic.[3]

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The ABO blood type system is frequently employed in clinical practice because it is the most well-examined erythrocyte antigen system and the most easily accessible factor in an individual's genetic makeup.[4] After Karl Landsteiner discovered the ABO blood group system in 1901, the link between the ABO blood group system and numerous disorders was not looked upon. The ABO blood type system has been linked to a variety of bacterial and viral infections.[5] Several research on COVID-19 in China

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and the United States recently identified links between ABO blood group and COVID-19 infection, severity, and death.[6] Polymorphisms in the ABO gene are reflected in the ABO blood type characteristic. This gene is linked to several other characteristics, including COVID-19 morbidity and mortality risk factors.

In addition to individual mutations, a non-O blood type was determined to be one of the most important genetic risk factors for venous thromboembolism in a 2012 meta-analysis. These circumstances apply to COVID-19 as well. The multiple connections between diseases and both blood type and COVID-19 lead to the conclusion that actual relationships between blood type and COVID-19 morbidity and death may exist. In addition, past research has found links between ABO blood types and a variety of illnesses and disease severity.[7] While blood types are inherited genetically, environmental variables can impact which blood types in a population are handed down to the next generation more frequently. The ABO blood type has been linked to viral infection susceptibility. The Norwalk virus and Hepatitis B, for example, have distinct blood group susceptibility. It was also discovered that those with blood type O were less likely to contract the SARS coronavirus.[6]

The major goal of our research was to look at the distribution of ABO blood types in COVID-19-infected hospitalized patients. The prevalence of severe COVID-19 infection in distinct ABO blood types and the need for mechanical ventilation in various blood types were also analyzed.

METHODOLOGY

This observational study consists of 200 adult men and women, who were diagnosed as COVID19 positive in the period between June 2020 and November 2020. The diagnosis of COVID-19 will be based on the results obtained by the real-time polymerase chain reaction. The subjects will be patients admitted under the COVID ward and intensive care unit at Sree Balaji Medical College and Hospital, Chennai. Every patients' blood group and typing will be determined during the admission. The patient will be observed for the period of the whole hospital stay till he gets discharged/deceased. The severity of the disease will be measured in terms of fall in saturation, the requirement of O2 support, the requirement of IV steroids, Heparin, NIV support, and intubation and mortality despite all measures. The patients having elevated CRP, LDH, and D-dimer will also be considered as severe. All the details will be entered in a master chart and data will be analyzed to find out the association of various blood groups with the severity of the SARS COVID-19 disease.

Inclusion Criteria

The inclusion criteria included COVID-19 positive of either sex, age 18 years or more.

Exclusion Criteria

The following subjects were excluded from the study: (a) Those under the age of 18, (b) individuals who are beyond 90 years old, and (c) those who refuse to participate in the research.

All patients were given a complete medical history, including the onset and duration of their symptoms. All of the patients had a chest high resolution computed tomography (HRCT) and an electrocardiogram (ECG). A complete blood image was taken. blood typing and grouping, renal function test, lactate dehydrogenase (LDH), serum electrolytes, C-reactive protein, serum ferritin, D-dimer, total bilirubin, alanine aminotransferase, prothrombin time, aspartate aminotransferase, and gamma-glutamyl transferase (GGT) are some of the tests performed. A commercial kit provided by Spinreact was used to quantify serum triglycerides, total cholesterol, and high-density lipoprotein (cholesterol), as well as low-density lipoprotein.

The glucose-oxidase method was used to measure fasting blood glucose. A commercial kit was used to quantify glycated hemoglobin A1C using a column chromatography technique. The outcome was determined photometrically using a photometer after the final evaluation (Reference range 5.1–6.4%).

Relevant laboratory and radiological investigations

Liver function tests (including GGT) and hepatic viral markers as required; prothrombin time, blood grouping and typing, fasting lipid profile, fasting plasma glucose, postprandial glucose, HbA1C, ultrasound abdomen and pelvis, renal function test, S. ferritin, S.LDH, C-reactive protein, D-dimer, ECG, and HRCT chest.

Study Period

A period of 3 months was from September 2020 to November 2020.

Study Design

This was a prospective observational study.

RESULTS

200 adult men and women, who were diagnosed as COVID-19 positive in the period from June 2020 to November 2020, were included in this study. Among them, 78 of them were identified with mild infection followed by 74, 48, and 122 patients with moderate, severe, and cases requiring oxygen support [Table 1].

Among the patients, 144 were reported with blood Group A followed by 34 of them with Group O, 14 and 8 of them B+, and AB blood groups, respectively[Table 2].

With respect to the severity of disease, 39 of them belonged to blood Group A+, followed by 3, 14, 22, and 12 with groups A-, B+, AB, and O [Table 3].

Among patients requiring mechanical ventilation, 8 belonged to blood Group A-, 6 to Group A+, and 3 in Groups B+ and AB each, followed by 1 in blood Group O [Table 4].

Table 1 : Comparison of severity of disease enlisted

Disease severity	Number of patients
Mild cases	78
Moderate cases	74
Severe cases	48
Cases requiring oxygen support	122
Total	200

Table 2: Impact of COVID-19 on blood groups

Blood group	Number of patients
A	144
O	34
B+	14
AB	8
Total	200

Table 3: Severity of COVID-19 among blood groups

Blood group	Number of patients
A+	39
A-	34
B+	14
AB	22
O	12

Table 4: Severity of COVID-19 among various blood groups requiring mechanical ventilation

Blood group	Number of patients
A+	6
A−	8
B+	3
AB	3
O	1

DISCUSSION

Given the severity of the present epidemic, a better knowledge of COVID-19 is critical. We looked into if blood type had anything to do with infection, intubation, or mortality. Overall, we discovered minor but persistent changes in risk between blood types. In the current study, we discovered that people with blood type A had a higher chance of contracting COVID-19, but people with blood type AB have a reduced risk. A possible link between ABO blood group and COVID-19 infection, severity, and death was previously documented in a systematic review with meta-analysis of the literature on the relationship between ABO blood group and COVID-19 infection, severity, and death.[5] However, according to another study by Mullins *et al.*,[8] blood type O had the highest occurrence, followed by blood type A. Nevertheless, the greater COVID-19 frequency in blood type O was most likely due to the higher blood type O prevalence in our region's population. This indicates that having a certain blood type does not make you more susceptible to COVID-19 infection.[8]

Individuals with blood groups A+, A-, and AB had a higher risk of COVID-19 severity, whereas those with blood Group O had a reduced risk.[9] Wu *et al.*[5] previously observed a reduced frequency of blood type O in COVID patients in his research. According to Zietz *et al.*,[7] types A and B were associated with a higher risk of an initial positive test than type O, whereas type AB (the rarest) was associated with a very slight risk reduction (0.2%). These findings support a previously established link between SARS-CoV-1 and O blood types being less frequent among SARS patients. Guillon *et al.*[10] postulated that lower sensitivity to blood type O was caused by anti-A antibodies interfering with the interaction of the SARS-CoV-1 spike protein with the cellular receptor for angiotensin-converting enzyme-2.

A mechanical ventilator is used in 21 of the 48 patients, with the highest number of patients belonging to the A- blood group. Our findings are also in line with Zhao *et al.*,[6] who found that non-O types have a higher risk of infection, and Ellinghaus *et al.*[11] who found that non-O types have a higher risk of infection but a lower risk of mechanical ventilation, though the authors note that the difference is not statistically significant at the 5% level. In contrast to Ellinghaus *et al.*,[11] we estimate a slightly greater risk of intubation for types B and AB compared to type O.

CONCLUSION

Our findings revealed that blood type A is more vulnerable to COVID-19 infection, whereas blood Group O is less susceptible; suggesting that more research into the relationship between ABO blood group and COVID-19 infection is warranted. Meanwhile, our findings imply that those with blood Group A should practice greater personal hygiene to reduce the risk of infection. Furthermore, a correlation between ABO blood group and severity, as well as the requirement of oxygen support, might validate

as a strategy that contributes to the better management of SARA-CoV-2.

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Original Article

Correlation of Intraocular Pressure with Visual Field Defects in Glaucoma Patients

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Abstract

Introduction: Glaucoma is a chronic, progressive optic neuropathy caused by a group of ocular conditions that damage the optic nerve with loss of visual function. The most common risk factor is raised intraocular pressure (IOP). Hence, the present study was performed to study the correlation of IOP with visual field (VF) defects in glaucoma.

Methodology: This is an observational, cross-sectional case series study. Patients diagnosed with glaucoma in the outpatient department of tertiary care hospitals were included in the study. In the present study, a total of 50 subjects with glaucoma were enrolled. IOP measurement, VF test, visual acuity assessment, and optic disc changes were measured during 1 year of the study.

Results: Of all patients, 42 (84%) patients were new diagnosed subjects. The majority of patients were found to be male, 39 (78%), compared to females 11 (22%). The majority of patients were observed with glaucoma suspects 23 (46%), whereas only 2 (4%) were observed with neovascular glaucoma. The majority of the patients, 41 (82 eyes), were observed with normal IOP, whereas 9 (18 eyes) patients were reported with increased IOP. A total of 68 eyes were found with glaucomatous optic nerve head changes, 26 eyes with the normal optic nerve. However, six eyes were also reported with vision loss in the present study. In the present study, maximum patients, 60%, were observed with normal VF followed by severe tubular vision/poor vision with 28% of patients. Whereas only 6% of patients were found with mild paracentral scotomas and moderate arcuate, respectively.

Conclusion: Raised IOP was one of the major risk factors leading to VF defects and complete vision loss in our society. Visual blindness was more prevalent in glaucoma patients who did not get anti-glaucoma therapy. The present awareness and knowledge should be enhanced through glaucoma awareness programs.

Key words: Glaucoma, Intraocular pressure, Angle closure, Optic neuropathy

INTRODUCTION

As elevated intraocular pressure (IOP) is a major risk factor in the development of glaucoma that can severely threaten our visual function, accurate IOP measurements are essential for the daily management of this disease.[1,2]

IOP, on the other hand, is a highly variable and dynamic parameter that is influenced by a variety of variables, including measurement parameters (such as the tonometer and examiner), ocular factors (such as corneal thickness, corneal hysteresis, and dehydration), and individual characteristics (such as accommodation, circadian cycle, body position, mental stress, and blood pressure).[3,4]

It is critical for ophthalmologists to understand IOP changes and their impact on clinical therapy and follow-up of glaucoma patients.[5,6] Visual field (VF) examination is an another critical component of the clinical evaluation of glaucoma or glaucoma suspects and is often performed concurrently with IOP readings. The cause of glaucomatous optic neuropathy is unknown. Numerous risk variables have been suggested, but the two most persistent seem to be IOP and age. Direct correlations between the extent of VF loss and the level of pretreatment IOP at presentation have been found to be weak for primary open-angle glaucoma (POAG).[5] This probably reflects the multiple interacting risk factors for damage that modifies the response of a particular nerve to a given IOP. At a certain IOP, the likelihood of getting glaucoma varies according to the

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type of glaucoma. In pseudoexfoliative glaucoma, which was previously assumed to be a more pressure-dependent condition, stronger relationships between VF defect (VFD) and IOP have been seen than in POAG. Primary angle-closure glaucoma (PACG) is likewise a more strictly pressure-dependent condition than POAG.[7,8]

A significant association between pre-treatment IOP and the quantity of VFD present may indicate how pressure dependent a disease is. This finding may provide credence to the notion that the pathogenic processes behind PACG are more pressure dependent. This may have consequences for prognosis and the need for clinical studies to determine if pressure reduction alone effectively halts the development of optic nerve damage and subsequent VFD.[9] Hence, the present study was carried out to assess the functional defects, namely, VFDs in correlation with IOP in glaucoma patients.

METHODOLOGY

Between December 2019 and November 2020, an observational, cross-sectional case series investigation was undertaken on patients presenting to the ophthalmology department of a tertiary care hospital. The research involved 50 participants who were diagnosed with glaucoma. Forty-two of the 50 participants were newly diagnosed with glaucoma in this research. Applanation tonometry was used to determine the patients' IOP, and automated perimetry was used to determine their VF. Glaucoma suspects constituted the majority of the glaucoma population. Severe VF abnormalities were more often seen in individuals with increased IOP and moderate-to-severe optic nerve head cupping. Blindness was prevalent in newly diagnosed glaucoma patients who had not begun therapy. Before the research began, authorization was obtained from the institutional ethics committee, and signed consent was obtained from all participants.

RESULTS

In the present study, a total of 50 subjects with glaucoma were enrolled, of which 42 (84%) patients were new diagnosed subjects. The majority of patients were male, 39 (78%), compared to females 11 (22%). The type of glaucoma was observed in all patients, and it was found that most of the patients were glaucoma suspects 23 (46%), followed by normal-tension glaucoma 13 (26%), and POAG with 6 (12%) patients. However, only 2 (4%) were observed with neovascular glaucoma [Table 1].

The IOP has measured in all patients both eyes, and it was found that the majority of the patients, 41 (82 eyes), were observed with normal IOP, whereas 9 (18 eyes) patients were reported with increased IOP [Figure 1].

The optic nerve integrity was examined in the present study; 68 eyes were found with glaucomatous optic nerve head changes, 26 eyes with the normal optic nerve. However, six eyes were also reported with vision loss in the present study [Table 2].

All 50 subjects were studied for any VFD, and it was observed that maximum patients 60% were observed with normal visual filed followed by severe tubular vision/poor vision with 28% of patients. Whereas only 6% of patients were found with mild paracentral scotomas and moderate arcuate, respectively. [Figure 2].

DISCUSSION

The present study was performed on 50 subjects with glaucoma, of which patients were found to be male 39 (78%).

Table 1: Observation of type of glaucoma in all enrolled patients

Type	Frequency	%
Normal-tension glaucoma	13	26.0
Glaucoma suspect	23	46.0
Primary open-angle glaucoma	6	12.0
Primary angle-closure glaucoma	6	12.0
Neovascular glaucoma	2	4.0

Table 2: Observation of optic nerve changes in all subjects eyes

Fundus changes	Eyes with normal IOP	Eyes with increased IOP
Glaucomatous optic nerve head changes	54	14
Normal optic nerve head	24	2
No view	4	2

IOP: Intraocular pressure

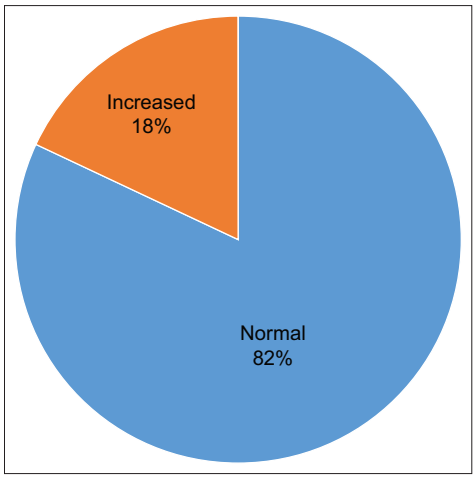

Figure 1: Observation of intraocular pressure in all participating subjects

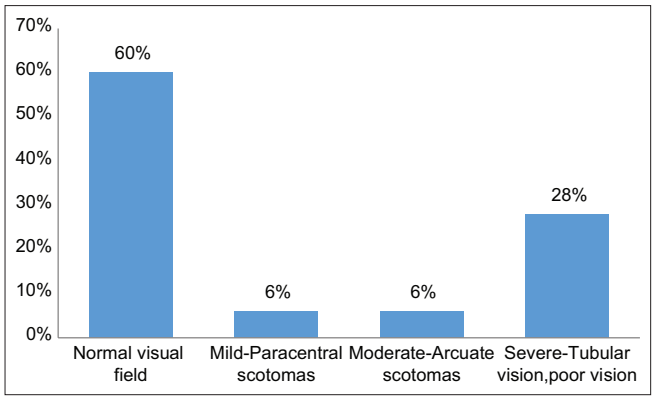

Figure 2: Observation of the visual field defect in all subjects

Similar observations were also reported by Gazzard *et al.* in their study with 71% of males. In contrast, Mengwei *et al.* reported 57% of male patients in their study.[10,11]

Our study observed that most of the patients were glaucoma suspect 46%, followed by normal-tension glaucoma 26% and POAG with 6 (12%). In contrast, only 2 (4%) were observed with neovascular glaucoma. Hollows and Graham, in their study, also recorded predominant glaucoma patients in their study.[12]

The measured IOP among all patients with both eyes revealed that most patients, 41 (82 eyes), were observed with normal IOP, whereas 9 (18 eyes) patients were reported with increased IOP. These findings in the present study are in confirmation of earlier reported studies.[13]

Regarding the optic nerve head cupping, among patients with normal IOP, 68 eyes were found with glaucomatous optic nerve head changes, of which 14 eyes were found with increased IOP. A total of 26 eyes were reported with the normal optic nerve, of which two eyes were found with increased IOP. However, in the present study, six eyes were also reported with vision loss, with two eyes having increased IOP. These findings showed that glaucomatous nerve head changes were common in eyes with normal IOP and increased IOP. These findings in the present study are in confirmation of the earlier reported studies.[14]

All 50 subjects were evaluated for any VFD, and it was found that most of the patients, 60%, were observed with normal VF followed by severe tubular vision/poor vision with 28% of patients. Whereas only 6% of patients were found with mild paracentral scotomas and moderate arcuate, respecitively. Foster *et al.* also reported similar findings in their study.[15]

CONCLUSION

Raised IOP was one of the major risk factors, leading to VFDs and complete vision loss in our society. Visual blindness was more common among the glaucoma patients who were not on anti-glaucoma treatment. The present awareness and knowledge should be enhanced through glaucoma awareness programs.

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