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Case Report

A Rare Case of Hepatic Tuberculosis in Cholangiocarcinoma

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Abstract

Tuberculosis (TB) is one of the oldest known infective bacterial diseases to mankind. Hepatic TB is an extremely rare form of extrapulmonary TB and can be seen as miliary TB, tubercular abscess, or portal hepatitis. Primary involvement of the liver in TB is rare due to the low tissue oxygen level, which makes the liver unfriendly for the propagation of the bacilli. Hepatic TB is observed in predominantly three forms, namely, (i) miliary hepatic TB, seen as a part of systemic tubercular infection, where small tubercular lesions can be seen diffusely distributed across the liver and where the patient remains almost asymptomatic from the hepatic perspective, (ii) primary TB of the liver without the involvement of other organs present as granulomatous hepatitis, and (iii) tubercular abscess and nodular TB. Hepatobiliary TB forms an important subgroup in TB cases. It requires a combination of imaging, histological, and microbiological procedures to define the diagnosis. The diagnosis is made by image-guided tissue acquisition.[1] Medical management is the key treatment of hepatic TB with an excellent prognosis. Hereby, we report a case of hepatic TB in a patient who was on treatment for cholangiocarcinoma.

Key words: Cholangiocarcinoma, Hepatic tuberculosis, Liver/spleen mass

INTRODUCTION

Although the prevalence of tuberculosis (TB) decreased quickly worldwide after the widespread use of anti-TB drugs in the 1940s, the incidence rates have increased in recent years due to government and patient complacency regarding the TB problem, inadequate public health measures, HIV coinfection, intravenous drug abuse, multidrug resistance, and an increased number of immunocompromised patients. Tuberculous involvement of the liver as a part of disseminated TB is seen in up to 50–80% of cases and with the increasing resurgence of TB, the incidence of hepatic TB has also been increasing.

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TB can affect any system or organ throughout the body. TB infection of the liver, also known as hepatic TB, is a manifestation of extrapulmonary infection with *Mycobacterium tuberculosis*.[1] Hepatic TB is uncommon clinically, clinicians in TB-endemic regions should have a high index of suspicion in patients presenting with hepatomegaly, fever, respiratory symptoms, and elevated liver enzymes and the main clinical manifestations our patient presented with are fever, hepatomegaly, splenomegaly, and abdominal distention.

CASE REPORT

A 61-year-old female patient who is a known case of cholangiocarcinoma, undergoing chemotherapy, presented with complaints of pain abdomen and fever for 7 days. Pain abdomen was aggravated on the right hypochondriac region, with sharp pain. Fever was high graded in nature and aggravated in the evenings. The previous history of weight loss was noted, along with decrease in appetite, nausea, and bloating. On examination, the patient was thin built, vitals stable on palpation, and the spleen was enlarged.

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PET scan report showed multiple ill-defined lesions in both lobes of the liver showing FDG uptake SUV-10. On further investigation, the CT-guided biopsy of liver showed coalescent small granuloma composed of epitheloid cells, Langhan's type giant cells with no atypical cells, and suggestive of granulomatous inflammation of Koch's etiology.

HISTOPATHOLOGY REPORT

HISTORY:
- Cholangio carcinoma.
- Multiple ill defined lesions in both lobes of liver showing FDG uptake SUV – 10.

SPECIMEN:
CT Guided Biopsy – Liver / Spleen mass.

GROSS :
Received six linear grey white / grey brown soft tissues bits measuring 0.2 – 1.5 cm.- A, B.

MICROSCOPIC EXAMINATION:
Sections show fragments of liver parenchyma with portal tracts and mild lymphocytic inf small tiny peri portal focus shows coalescent small granuloma composed of epithelioid langhan's type giant cells. There is no evidence of any atypical cells.

IMPRESSION:
FEATURES MAY BE SUGGESTIVE OF GRANULOMATOUS INFLAMMATION OF KOCH'S

Suggest to correlate with biopsy from other representative site and gene expert studies.

End of report

DISCUSSION

TB of the liver is uncommon and accounts for <1% of all tuberculous infections. It is rare due to low tissue oxygen tension in the liver, which is unfavorable for mycobacterial growth. Liver is a common site for granuloma formation due to its rich blood supply, lying at the distal end of portal circulation, and a large number of reticuloendothelial cells. A majority of granulomas are usually located near the portal tract and there is only mild perturbation of hepatic function, so most patients are minimally symptomatic or asymptomatic.[2] The disease may present at any age but is most commonly seen in young adults.

Primary hepatic TB may occur in the extremely rare congenital form, but it is usually secondary to miliary TB. However, our case had no previous history of TB. According to the Levine classification, our case likely represents hepatobiliary TB (HBTB) secondary to cholangiocarcinoma.

Levine classified TB as follows: (i) miliary TB; (ii) pulmonary TB with hepatic involvement; (iii) primary liver TB; (iv) focal tuberculoma or abscess; and (v) TB cholangitis.[3]

Tuberculous involvement of the liver as a part of disseminated TB is seen in up to 50–80% of cases, but localized HBTB is uncommonly described.[2] Among the cases of hepatic TB reported in the literature, the miliary form was common (79% of cases), with local hepatic TB accounting for only 21% of cases.[4]

Hepatic TB has many faces and the imaging manifestation can show considerable overlap with other relatively more frequent primary or secondary lesions of the liver. Isolated hepatic involvement by TB can especially be challenging to diagnose on imaging alone due to its largely non-specific imaging features.

The term HBTB refers to either isolated hepatic, biliary, or hepatobiliary involvement with other organ system involvement.[5] The liver is involved in Mtb in two major forms. The more common involvement of the liver in TB is as a part of a miliary or a disseminated disease. In such type of involvement, there may not be any specific signs or symptoms related to the liver except for the presence of hepatomegaly. Liver biopsy in such patients may show the presence of granulomas. The second form, seen less often, is a localized form of TB involving the liver and the biliary ducts. Localized HBTB may occur as the following: (i) localized solitary or multiple nodules, tuberculoma, and TB hepatic abscess without bile duct obstruction; (ii) bile ductal epithelium involvement producing inflammatory strictures resulting in obstructive jaundice; and (iii) enlarged lymph nodes at porta causing obstruction to the bile duct.[6] Obstructive jaundice is more common in those having biliary system involvement. In most patients, an increase in alkaline phosphatase, gamma-glutamyl transferase, and a mild rise in serum transaminases is evident.

This regimen cures more than 90% of patients with TB. The optimal duration of time to treat hepatic TB in patients diagnosed with cancer is 12 month regimen of ATT seems to be effective for most patients to avoid relapse. Patients will require monthly follow-ups with LFT. If LFT is normal, the treatment is to be continued as any other normal patient. Patients generally do not require any further surgical intervention after the completion of anti-TB therapy, but the surgical treatment of hepatic TB is usually required in cases of TB-related biliary compression leading to jaundice, portal hypertension, or biliary bleeding, or when the diagnosis is uncertain.

Glucocorticoids may have a role in the treatment of hepatic TB that does not respond appropriately to standard anti-TB therapy. There is insufficient controlled data to recommend the use of corticosteroids in all cases of hepatic TB, either in isolated hepatic TB or in complications of cornified/spread TB. However, if there are indications for surgery or challenging to diagnose, surgical procedures along with anti-tubercular drug therapy could be adopted.

CONCLUSION

Hepatic TB is usually associated with atypical clinical manifestations. In endemic countries and inappropriate clinical settings, an atypical imaging pattern of a hepatic lesion should prompt the radiologist to consider hepatic TB as one of the differential diagnoses. Image-guided fine-needle aspiration biopsy is the best diagnostic method so far for diagnosing hepatic TB. Although image-guided fine-needle aspiration biopsy is often required for a confirmatory diagnosis, in a low-resource setting, the presence of calcifications and the concurrent involvement of extrahepatic sites (spleen, lungs, and nodes) should prompt the possibility of HBTB.

Patients of HBTB often respond well to anti-TB treatment.

In this case, we must understand the importance of suspecting TB, especially in endemic countries, where CT reports show calcifications and nodules principally in immunocompromised patients, although they do not present with classical symptoms of TB. An early diagnosis and prompt treatment will prevent the further spread of infection, prevent complications, and increase the better outcomes for the patient.

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Case Report

An Interesting Case of Solitary Human Muscular Cysticercosis with Elastography Findings

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Abstract

Context: Cysticercosis is an infection caused by the larval form of the parasite *Taenia solium*. High-resolution ultrasonography was done on Mindray Resona 7 machine with linear probe at 12 MHz frequency and we diagnosed as cysticercosis with surrounding inflammation in the right adductor magnus muscle of thigh.

Case Report: A female patient in her 20's presented with a painful swelling on the inner aspect of her right thigh. On ultrasonography, there was a well-defined isolated cystic lesion of size 3.3 × 2.5 cm with a hyperechoic speck within in intramuscular plane of adductor magnus muscle. Shear wave elastography was also performed and muscular cysticercosis was confirmed. She was treated conservatively with albendazole and steroids, which led to complete resolution of the swelling.

Conclusion: Lesions in intramuscular plane can be diagnosed on high-resolution sonography combined with elastography confidently. This reduces the expenditure cost for the patient.

Key words: Cysticercosis, Elastography, High-resolution ultrasound, Intramuscular, Medical management, Non-invasive

INRODUCTION

Cysticercosis is very common in Indian communities with poor sanitary facilities and poor hygiene. It is also commonly seen in pork eaters. There are two-way a human can get infected, the first being by eating contaminated pork meat. Second is by eating food or water contaminated by feces containing eggs of tis parasite. History taking is crucial for every patient, as it could help us narrow down the differentials. Furthermore, since this disease is prevalent in India, we should be able to treat the patient with the least number of investigative methods. Here, we are trying to emphasize the importance of ultrasonography along with elastography is diagnosing neurocysticercosis as it is non-invasive and non-ionizing method.

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CASE DESCRIPTION

A female patient in her 20's, non-vegetarian, residing in a low socioeconomic status, presented clinically with a painful swelling in the inner aspect of her right upper thigh for the past 2 months. On clinical examination, her vitals were stable and on local examination, a swelling measuring 3 × 4 cm was noted in the upper posteromedial aspect of her right thigh. No discoloration of the skin or surrounding tissues noted. The swelling was soft and mildly tender on palpation. There was no associated neurological or ocular involvement.

Baseline blood investigations, renal and liver functions tests showed values within the normal range. As a part of radiological investigations, ultrasound (USG) of upper right thigh [Figure 1] was performed using MINDRAY RESONA 7 high end USG machine with linear transducer of 12 Mhz, which showed a well-defined hypoechoic area measuring 3.5 × 1.9 × 3 cm in the adductor magnus muscular plane of posteromedial aspect of the right inner thigh [Figure 2]. A well-defined cystic area [Figure 3] measuring 3.3 × 2.5 cm with hyperechoic speck [Figure 4] was seen within the lesion in the periphery. No peripheral or internal vascularity was noted. The lesion was seen placed along the muscle fibers of the adductor magnus muscle.

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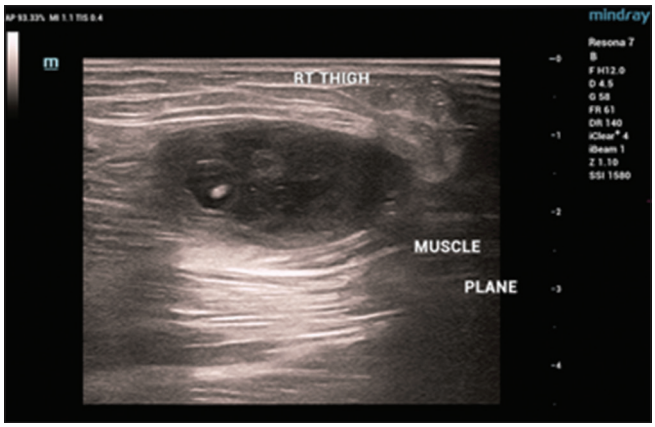

Figure 1: Encapsulated hypoechoic lesion with central echogenic nodule showing "cyst with dot sign" in the intramuscular plane

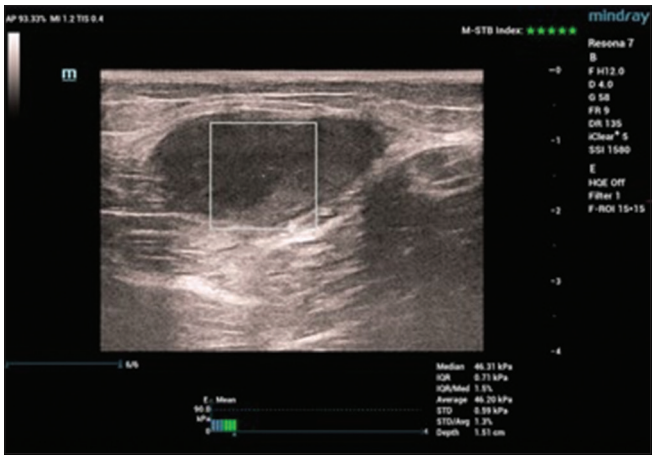

Figure 2: Elastography findings of the larger hypoechoic lesion

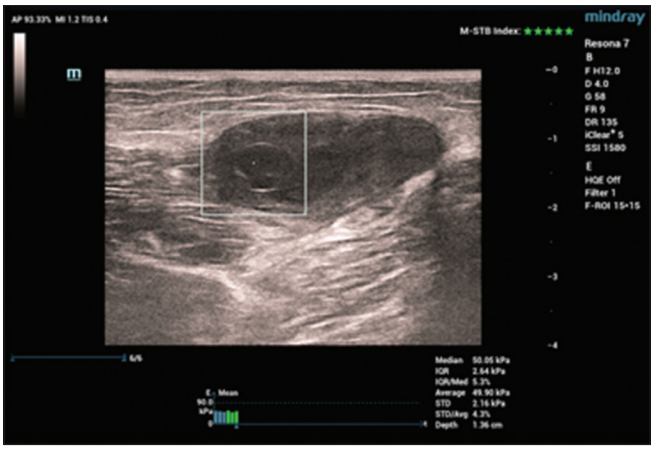

Figure 3: Elastography findings of the cystic lesion

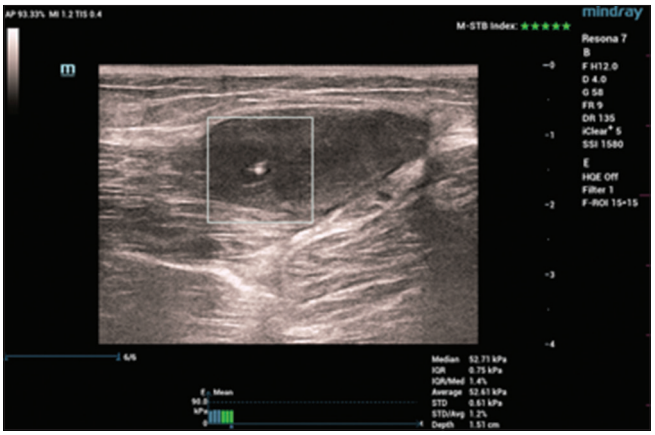

Figure 4: Elastography findings of the hyperechoic scolex

Table 1: Elastography findings comparison between hypoechoic lesion, cyst, scolex and adjacent muscle

STQ values	Hypoechoic lesion [Figure 2]	Cyst [Figure 3]	Scolex [Figure 4]	Muscle nearby
Median	46.31 kPa	50.05 kPa	52.71 kPa	35.8 kPA
IQR	0.71 kPa	2.64 kPa	0.75 kPa	2.14 kPa
IQR/MED (%)	1.5	5.3	1.4	6.0
Average	46.20 kPa	49.90 kPa	52.61 kPa	35.31 kPa
STD	0.59 kPa	2.16 kPa	0.61 kPa	1.78 kPa
STD/Avg (%)	1.3	4.3	1.2	5.0
Depth	1.51 cm	1.36 cm	1.51 cm	2.52 cm

Shear wave elastography (sound touch quantification [STQ]) was performed on this lesion. To weaken artificial stiffness, transducer was put on the surface of lesion vertically as gently as possible. Patients were asked to hold their breath for several seconds to acquire stable sound touch elastography (STE) images.

2D and 3D shear wave by supersonic mindray has come out with its unique STQ option which was used to analyze this lesion. We have used in this study STQ this tool which give us MEAN, MAX, MIN, SD, DEPTH OF ROI CENTRE, MEDIAN, IQR, IQR/MED, and AVERAGE of the selected region of interest. [Table 1] In view of location of the lesion in muscle and along the muscle fibers along with a small rounded cystic area containing speck of hyperechoic area in the center, diagnosis of cysticercosis of muscle plane in adductor muscle was made [Figure 1]. Now, we can safely say that the surrounding hypoechoic area is suggestive of the inflammatory change in the adjacent muscle, and the peripheral lesion placed within it was the encysted larvae, whereas the hyperechoic speck was the scolex of the parasite. Further, investigations were not necessary but if doubtful, biopsy would be confirmatory in such cases. However, due to financial affordability issues, we did not advise her such investigations.

Cysticercosis should always be kept as a differential diagnosis in all kinds of intramuscular or subcutaneous swellings in endemic regions. High-resolution ultrasonography has helped us in narrowing down our differential diagnosis. There are various differential diagnoses as listed below and how we ruled them out are described below:

1. Lipomas are hyperechoic lesions with no evidence of cystic changes
2. Neurofibromas are hypoechoic lesions adjacent to the nerve, which is proximally and distally visualized
3. Schwannoma is hypoechoic lesions seen eccentric to the nerve.

Fortunately, she responded well to medical treatment with tablet Albendazole 200 mg BD × 14 days and a course of steroids leading to complete resolution of the swelling. There was objective evidence of improvement with reduction in the pain and size of the swelling.

After 3 weeks of conservative treatment, on clinical follow-up, pain and tenderness had completely disappeared and patient was asymptomatic. On follow-up sonography, there was no evidence of phlegmon or cysticercosis in medial aspect of upper thigh. No appearance of new crops of cysticerci was noted.

DISCUSSION

Cysticercosis is an infection caused by the larval form of the tapeworm *Taenia solium*, from the cestode family. It is highly prevalent in India, Africa, China, and South America. However, due to increased travel and a mixture of immigrants, this disease is spreading to non-endemic parts of the world as well. This infection thrives in communities with poor sanitary facilities, overcrowding, poor personal hygiene, and places, where pigs are reared commonly.

Human beings are the definitive hosts and pigs are the intermediate hosts for the parasite *T, solium*. When the human being ingests contaminated water/food which contains the *T. solium* eggs or, when he is already infected with the gravid worm within the intestine (due to consumption of infected pork meat), the regurgitated eggs due to reverse peristalsis release oncopsheres within the small intestine which pierces and penetrates the mucosal wall using hooks and suckers, spread through blood stream to form encysted larvae in various parts of the body. This encysted larva from of the parasite is known as cysticercus cellulosae. As it ages the cyst becomes leaky, producing inflammatory reaction in the tissue surrounding it, and usually, the patient presents with symptoms in this stage.[1] In our case, the patient presented with a painful swelling in the inner aspect of her right thigh.

There are only few reported cases of the muscular cysticercosis diagnosed on USG.

In the muscular form, four types manifestations have been described.[2]

1. Myalgic type which has two subcategories
   a. The hyperechoic structure within the cystic lesion corresponds to the scolex. No inflammatory changes as the living parasite evades immune recognition
   b. Death of the larva causes the membrane to become leaky, causing inflammatory changes in the tissue surrounding it.
2. Abscess-like type: The next stage is when there is very minimal fluid within the partially collapse cysts and scolex is not seen within as it might have escaped from the cyst
3. Calcified cyst: Retracted cysts with calcified capsule and scolex is noted
4. Pseudo hypertrophic type: The cysticercosis cyst containing the scolex is noted within and irregular large collection of exudative fluid within the muscle.

Our case falls under the pseudo hypertrophic type of cysticercosis [Figure 1]. Usually, based on the three most common regions affected in the body, we have neurocysticercosis, ocular, and muscular cysticercosis.[3] The cysts are surrounded by a fibrous capsule except in the eye and ventricles of the brain. The larvae evoke a cellular reaction starting with infiltration of neutrophils, eosinophils, lymphocytes, plasma cells, and, at times, giant cells. This is followed by fibrosis and death of the larva with eventual calcification. The clinical features depend on the site affected.

Now let's discuss about elastography, which is an added advantage to the conventional USG.

Elastography in other words is known as palpation imaging. Over the past two decades, various elasticity imaging approaches have been introduced rampantly by radiologists because when combined with conventional USG techniques, this adds mechanical information of the tissue examined and helps in better diagnosis.

The most popular type of elastography was strain imaging for a long period of time, where higher strain corresponded to softer medium. However, the con was it varied according to the pressure used by the examiner. Hence, it took a rather long period of time to get accustomed to reliable images.

To overcome this limitation, shear wave elastography was introduced which helped in quantification of tissue stiffness. Just like palpation, elastography aims to characterize tissue stiffness. Physical palpation is replaced by point of shear wave quantification (VTQ by Siemens), 2d and 3d shear wave by supersonic mindray has come out with natural touch elastography and Mindray`s unique shear wave STE.

Shear wave elastography of mindray Resona 7 offers two imaging approaches: STE and STQ.[4]

STE technology will provide 2D color imaging of tissue stiffness information and display elastic distribution of the lesion.

The other approach on mindray Resona 7 is STQ which directly performs quantitative measurement on tissue stiffness in the ROI. This is a new approach to display real-time stiffness image of the region of interest, with better penetration and lesser noise. This uses ultrawide beam tracking imaging.

Based on the ultrawide beam tracking imaging platform, STE/STQ can reach a shear wave elastography speed of up to 10 KHz per frame, which allows super-fast detection of all necessary shear wave information in the ROI. Using better focused USG beams, STE/STQ boasts, in addition to an ultra-high frame rate, an excellent penetration capability, which ensures better elasticity images and measurement results.

We have used in this study STQ this tool give us MEAN, MAX, MIN, SD, DEPTH of ROI CENTRE, MEDIAN, IQR, IQR/MED, and AVERAGE of the selected region of interest. Elasticity bar given below easily evaluate the stability of STQ among multiple frames. Hence, we ask the patient to hold their thigh to have maximum stability of the images as possible. The height of each bar represents the mean value of young's modulus of whole ROI in each frame. Elastography has the advantages of real time 2-D shear wave, better penetration, more accurate quantification, lesser acoustic power for longer transducer life, and reduced radiation.

Normal relaxed muscle appears as an inhomogenous mosaic of intermediate or increased stiffness with scattered softer areas, especially at the periphery or near boundaries.

In inflammatory myopathies, USG elastography can show changes in muscle elasticity in correlation with elevated serum markers (increased stiffness due to fibrosis or as reduced stiffness, secondary to fatty infiltration).

The scolex will be harder as compared to the cyst or the lesion. As the elastography hardness increases, the firmness of the tissue increases.

Thinking about other radiological investigations, plain radiographs are not very helpful until the cysts have degenerated and calcify to become radio opaque. On the other hand, Computed tomography is only useful in neurocysticercosis but not much beneficial in the musculoskeletal cysticercosis.

High-resolution USG has become relatively inexpensive and is a readily available and reliable diagnostic modality for the diagnosis of intramuscular cysticercosis. There are many reports, in which cysticercosis had been accurately diagnosed by USG without the requirement of invasive techniques such as fineneedle aspiration cytology and biopsy. This is a huge achievement in the field of radiology.

Looking into the therapeutic options, waitful watching, surgical, or medical management is based on multiple factors, including symptoms and the location, number, stage, and size of cysts. Isolated solitary intramuscular cysticercosis requires no specific treatment unless it is symptomatic. Excision is the best method whenever possible. However, it may be required in case of intramuscular cysticercosis if there is neurovascular compromise due to growth of the cyst. Medical treatment should be considered if the site or number of the lesions makes surgical excision unfeasible. Concomitant intestinal taeniasis which is found in 25% of the cases should be investigated and treated as well. Antiparasitic therapy such as praziquantel and albendazole can be used to medically manage, and corticosteroids can be added to reduce the inflammatory reaction. Medical management can alone to be curative, such as in our patient. Praziquantel (50 mg/kg/day for 3 weeks) is considered the preferred treatment. Even albendazole (10–15 mg/kg/day for 2 weeks) can be effective as well.

Prophylactically, the critical thermal point of cysticercus is 56°C for 5 min; hence, we should not consume undercooked pork. Lifestyle changes, socioeconomic improvement, maintenance of clean personal habits and general sanitary measures, education to people about the disease, and anthelminthic therapy are important in reducing the prevalence of the *T. solium* larval diseases.

For control of cysticercosis, prevention of fecal contamination of soil, proper disposal of sewage, and avoidance of eating raw vegetables grown in polluted soil are useful measures.

Lots of recent publications and researched have shown the potential utility of the use of vaccines in pigs, but its widespread use is not yet a reality.[5]

Although solitary intramuscular cysticercosis is rare, the diagnosis should be kept in mind in patients presenting with an intramuscular or a subcutaneous mass, especially in endemic areas. USG and magnetic resonance imaging are useful non-invasive diagnostic modalities to clinch the diagnosis. Only symptomatic cysts require treatment. Both surgery and medical management have been found to yield good results, and thus, the treatment may be individualized.

CONCLUSION

High-resolution sonography, being non-invasive and non-ionizing, plays an important role in establishing the diagnosis in patients with muscular cysticercosis. Using elastography techniques, like in our case, of shear wave elastography, we can characterize tissue stiffness, complimenting B-mode imaging findings, which confirm the diagnosis of intramuscular cysticercosis. Therefore, we conclude that intramuscular cystic swellings can be diagnosed on high-resolution sonography along with great confidence without any need of FNAC/biopsy leading to easier management of the disease in patient at affordable rates. There is a huge scope in the future to apply elastography in various musculoskeletal studies to confirm B-mode USG findings.

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Review Article

Hydroxyzine for the Treatment of Patients with Pruritus: An Evidence-based Review

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Abstract

Pruritus is the most common skin symptom that is widely observed in many patients visiting dermatological clinics. It causes an unpleasant sensation on the skin and can sometimes impair patients' quality of life. Antihistamines, which are typically used to treat pruritus, can fail to reduce itching in some patients. Recent evidence has suggested that the use of first-generation anti-histamine hydroxyzine should be considered for treatment of pruritus due to its efficacy and safety. This has been shown to improve patients' quality of life. The current review discusses the efficacy of hydroxyzine in pruritus management and clinical expertise of different experts in dermatology on hydroxyzine use in patients with pruritus.

Key words: Anti-histamines, Dermatology, First generation, Hydroxyzine, Pruritus, Quality of life

INTRODUCTION

Itching, also known as pruritus, is an unpleasant sensation that causes a desire to scratch, which has an adverse effect on both psychological and physical aspects of a patient's life. It is the most common symptom of skin diseases, sometimes trifling or light and sometimes intolerable. In addition, it is one of the most common causes for patients to visit a dermatologist.[1,2] It can occur either continuously or intermittently. The site may be local or generalized. The free teleneuron, which is distributed in the outermost layers of the epidermis, is principally responsible for itch.

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The most common skin conditions that cause itching include eczema, urticaria, neurodermatitis, prurigo, and cutaneous pruritus.[1] In addition, systemic diseases such as cancer, inflammatory diseases, metabolic diseases, infections, neurologic disorders, endocrine disorders, and diseases of the nervous and endocrine systems can cause pruritus.[1]

The origin of itching is generally complex, and both internal and external causes can contribute to itching. The intrinsic factors that contribute to itch development are chronic infection, block of blood circulation, change of endocrine and metabolism, hereditary tendency to allergies, and so on, while extrinsic factors include inhaled substances, chemical materials, animal hair and fur skin, and so on.[1]

The current review discusses the concept of pruritus and the use of hydroxyzine in the treatment and management as per the expert opinions of 20 physicians.

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CLASSIFICATION OF PRURITUS

Pruritus is classified into five types: [1]

- Skin-derived pruritus
- Neuropathic pruritus
- Neurogenic pruritus
- Psychogenic pruritus
- Mixed pruritus

SKIN-DERIVED PRURITUS

This originates from the skin and results in irritation, dryness, or skin damage.

NEUROPATHIC PRURITUS

This is associated with the pathological alterations in the afferent pathway of sensory nerve fibers.

NEUROGENIC PRURITUS

The central nervous system is the source of neurogenic pruritus, in which itch is caused by the induction and transmission of mediators and receptors without causing nerve injury.

PSYCHOGENIC PRURITUS

It is a functional itch disorder caused by psychologic factors (some irritating factors, skin dryness, etc.) and psychiatric abnormalities.

MIXED PRURITUS

It is caused by multiple factors and is mediated by two or more mechanisms.

HYDROXYZINE

This is a first-generation anti-histamine that is used in treatment of pruritus. Sedative, anxiolytic, and antiemetic effects are all characteristic of this drug.[3] According to the Indian Consensus 2021, hydroxyzine is generally the first line of treatment for generalized pruritus.[4] The European guidelines on chronic pruritus recommends use of hydroxyzine as a first choice in treatment of pruritus due to its antipruritic, anxiolytic, and sedative properties.[4]

MECHANISM OF ACTION

Hypersensitivity and allergic responses are initiated by H1 histamine receptors. Antigen exposure causes basophils and mast cells to degranulate and produce histamine whenever a person is exposed to it. Histamine binds to H1 receptors and causes the release of proinflammatory mediators including interleukins, which aggravates the inflammatory response.[3]

- Hydroxyzine is a potent inverse agonist of H1 receptors.
- It reduces the production of the chemical mediator histamine from mast cells, which is involved in pruritus, by blocking the H1 receptors, reducing receptor activity, and blocking receptor function.
- Due to its off-target behavior, this medication can be used as a sedative and anxiolytic.
- It has a fast onset of action that occurs within 15 and 60 min and duration of action is 4–6 h.[3]

THERAPEUTIC EFFICACY OF HYDROXYZINE

Thomas *et al.*[5] evaluated the effectiveness of hydroxyzine in Indian patients (N = 400) with chronic pruritus. This was a prospective, observational, and patient-reported outcome (PRO) study that considered dermatology quality of life index (DLQI) as primary end point and secondary endpoint was improvement in 5-D itch scores.

The DLQI score significantly increased from the baseline by 2.70 (95% CI: 2.39–3.01) at 2 weeks and 10.86 (95% CI: 9.95–11.78) at 12 weeks [Table 1].

Over the course of the 12-week period, a significant (P < 0.0001) decrease in the mean 5-D itch score was noted.

In comparison to the baseline, the 5-D score significantly increased by 2.76 (95% CI: 2.48–3.05) at 2 weeks and 7.35 (95% CI: 6.88–7.83) at 12 weeks [Table 2].

Symptom Elimination

At some point during the study, 189 of 391 individuals had no symptoms with hydroxyzine overall. At 2, 4, and 8 weeks, the cumulative symptom elimination rates were 3.58% (n = 14), 46.04% (n = 180), and 48.34% (n = 189). No serious adverse events were reported in the study participants.

Table 1: Effect of treatment on DLQI scores over treatment period (Adapted from Thomas *et al.*)

Time point	*N*	DLQI score Mean±SD	*P* value (vs. baseline)
Baseline	391	11.78±5.45	
2 weeks	391	9.08±5.47	<0.0001
4 weeks	366	5.85±4.62	<0.0001
8 weeks	190	5.99±2.65	<0.0001
12 weeks	176	3.35±2.33	<0.0001

DLQI: Dermatology quality of life index

Table 2: Effect of treatment on 5-D itch scores over the treatment period (Adapted from Thomas *et al.*)

Time point	*n*	5-D score Mean±SD	*P* value (vs. baseline)
Baseline	391	15.44±2.94	
2 weeks	391	12.72±3.32	<0.0001
4 weeks	366	10.58±3.26	<0.0001
8 weeks	190	10.01±2.38	<0.0001
12 weeks	176	8.05±1.94	<0.0001

SD: Standard deviation

Table 3: Before and after treatment: Pruritic score in three groups

Drugs	Before	After	Difference
Cetrizine	38.2±4.8	24.8±3.1	−13.8±4.5
Doxepine	37.2±4.9	17.8±2.5	−17.8±4.0
Hydroxyzine	37.3±5.1	16.7±2.3	−20.6±2.6
P-value	0.854	0.057	0.061

Data was showed as mean±standard deviation (Adapted from Shohrati *et al.*)

This study concluded that hydroxyzine hydrochloride significantly improved pruritus ($P < 0.0001$) and quality of life in patients ($P < 0.0001$) and was well tolerated in patients with chronic pruritus at the end of 12 weeks treatment.

The effectiveness and safety of cetirizine, doxepin, and hydroxyzine in the treatment of chronic pruritus caused by Sulfur Mustard were compared by Shohrati *et al.*[6] This was a 4-week randomized double-blind study ($N = 75$).

For 4 weeks, patients received either cetirizine 10 mg, doxepin 10 mg, or hydroxyzine 25 mg/day.

The mean pre-treatment pruritic scores for the cetirizine, doxepine, and hydroxyzine groups were 38.2 ± 4.8, 37.2 ± 4.9, and 37.3 ± 5.1, respectively. Following therapy, the mean pruritic scores in the cetirizine, doxepine, and hydroxyzine groups were 24.8 ± 3.1, 17.8 ± 2.5, and 16.7 ± 2.3, respectively [Table 3]. Sedation was reported in all the treatment groups.

This study concluded that in treating the symptoms of patients with chronic pruritus, hydroxyzine 25 mg/day is as effective as doxepine 10 mg once daily, but more effective than cetirizine 10 mg once day.

CONCLUSIONS

- Hydroxyzine improves patients' quality of life, itch scores, and keeps pruritus under control.
- Improvement in symptoms can be observed in patients within a few days after the initiation of hydroxyzine therapy.
- Therefore, hydroxyzine should be considered as first-line treatment option in patients with pruritus.

EXPERT OPINION

Dr. Abha Diwan

In my routine clinical practice, I have seen that tinea, scabies, and urticaria are most common dermatological reasons for pruritus. Systemic diseases such as hepatitis, nephritis, and renal insufficiency are also associated with pruritus. I personally prefer hydroxyzine as a first-line therapy in pruritus management in such patients. One week after starting hydroxyzine therapy, it is possible to observe the improvement of pruritus symptoms. Improvement in 5D itch scores and DLQI scores (11–20 very large effect) is reported in these patients. Due to its antipruritic, anxiolytic, and sedative properties, it can be used as the first-line therapy in pruritus management.

Dr. Ankur Chauhan

Pruritus is commonly reported in 60% of dermatological outpatients. Dermatological causes such as eczema and scabies and non-dermatological causes such as renal causes, hepatic disorders, and hyperthyroidism are also associated with pruritus. It is also associated with complications such as sleep disturbances and stress. I personally prescribe Hydroxyzine as a first-line therapy in pruritus management due to its antipruritic, anxiolytic, and sedative properties. It is possible to see an improvement in pruritus symptoms 1 week after starting hydroxyzine medication. 5D itch scores and DLQI scores are used to measure itch scores and quality of life in these patients.

Dr. Mahendra Nagargoje

Usually, urticaria, scabies, and atopic dermatitis are most common dermatological reasons for pruritus. Furthermore, systemic diseases such as renal failure and hepatic encephalopathy are also associated with pruritus. I personally prescribe hydroxyzine as a first-line therapy in pruritus management. One week after beginning hydroxyzine therapy, improvement of pruritus symptoms is noted. Improvement in 5D itch scores and DLQI scores (11–20 very large effect) is observed in these patients. Hydroxyzine can be prescribed as first-line medication for managing pruritus due to its antipruritic, anxiolytic, and sedative effects.

Dr. Narendra Kumar Trivedi

Eczema and tinea are the most common dermatological causes of pruritus, as per what I see in my routine clinical practice. Systemic diseases such as fever and hepatitis are also associated with pruritus. I personally prescribe

hydroxyzine as a first-line therapy in pruritus management, and symptoms become better in approximately >10 days) after starting hydroxyzine. Improvement in itch scores (Visual analog scale-VAS) and DLQI scores (6–10 moderate effect) is reported in these patients. Due to its antipruritic, anxiolytic, and sedative actions, it is considered a first-line therapy for treating pruritus.

Dr. Senthil G

I observed that urticaria, eczema, and lichenification are most common dermatological reasons for pruritus. Systemic disease such as jaundice and renal failure is also associated with pruritus. I personally choose hydroxyzine as a first-line therapy in pruritus management due to its antipruritic, anxiolytic, and sedative properties. It is possible to see symptoms of pruritus improving within a week after starting hydroxyzine. Improvement in itch scores (5D) and DLQI scores (6–10 moderate effect) is observed in these patients.

Dr. Praveen Kumar Rathore

Scabies, tinea, and urticaria are the most common dermatological causes of pruritus, according to my usual clinical practice. Systemic diseases such as liver and kidney disorders are also associated with pruritus. I prescribe hydroxyzine as a first-line therapy in pruritus management. It is possible to see symptoms improvement (>10 days) after starting hydroxyzine medication. Improvement in itch scores (VAS) and DLQI scores (11–20 moderate effect) is observed in these patients. It is a first-line treatment for pruritus due to its antipruritic, anxiolytic, and sedative effects.

Dr. Dharani Durai

Usually scabies, eczema, and tinea corporis are the common causes for pruritus, in my clinical experience. Other systemic conditions such as thyroid, diabetes mellitus, and chronic renal failure are also linked with pruritus. I prescribe hydroxyzine as a first-line treatment option in my patients due to its antipruritic and sedative properties. Symptom improvement is observed in patients within 3–7 days after starting hydroxyzine. Improvement in itch scores (VAS) and DLQI scores (6–10 moderate effect) is also observed after hydroxyzine use.

Dr. Piyush Gupta

Urticaria, scabies, tinea, eczema, and xerosis are the most common dermatological causes of pruritus, as per my clinical expertise. Systemic condition like jaundice is associated with pruritus. I personally prescribe hydroxyzine as a first-line therapy for treatment in pruritus due to its antipruritic and anxiolytic properties. Symptom improvement is evident within a few days after starting hydroxyzine medication. Improvement in itch scores (5D) and patients' quality of life DLQI scores (11–20 very large effect) is evident in patients.

Dr. Pradeep Kumar

I observed that eczema and lichenification are frequent dermatological conditions for pruritus. Other systemic conditions like jaundice are associated with pruritus. Hydroxyzine is prescribed as a first-line therapy due to its antipruritic and sedative properties. It is possible to see symptoms of pruritus becoming better within a week after starting hydroxyzine medication. Reduction in itch scores (5D) and improvement in DLQI scores (6–10 moderate effect) is noticed.

Dr. Nilendu Sarma

Urticaria, eczema, and xerosis are the most common dermatological causes of pruritus, according to my clinical expertise. Systemic disease such as hepatic and kidney disorders is connected with pruritus. I personally choose hydroxyzine as a first-line therapy in pruritus management due to its antipruritic, anxiolytic, and anxiolytic properties. Symptom improvement is noticed within a few days after starting hydroxyzine medication. Itch scores (5D) minimization and DLQI scores improvement (11–20 very large effect) are evident in patients.

Dr. Punam Caplash

Urticaria, scabies, and tinea are the most common dermatological causes of pruritus. Non-dermatological conditions such as chronic kidney disease and jaundice are also associated with pruritus. I personally prescribe hydroxyzine as a first-line therapy in pruritus management due to its antipruritic and sedative properties. After taking hydroxyzine within a few days, it is possible to observe the improvement of pruritus symptoms. Improvement in itch scores (5D) and increased quality of life DLQI scores (6–10 moderate effect) is noticed in patients.

Dr. Ravi Shankar Dwivedi

In my routine clinical practice, atopic dermatitis, senile pruritus, and scabies are most common dermatological reasons for pruritus. Pruritus is also linked to systemic conditions such as chronic kidney disease and hepatitis C. Hydroxyzine is preferred drug for treatment due to its antipruritic, anxiolytic, and sedative properties. After taking hydroxyzine within a week, it is possible to observe the improvement of pruritus symptoms. Improvement in itch scores (VAS) and DLQI scores (6–10 moderate effect) is evident in patients after hydroxyzine use.

Dr. Swami Dass Mehta

Urticaria is the most common dermatological causes of pruritus, according to my clinical expertise. Pruritus is also linked to systemic conditions such as renal disease. I personally prescribe hydroxyzine as a first-line therapy in pruritus management due to its antipruritic, anxiolytic, and sedative properties. After taking hydroxyzine within a

day, symptomatic improvement is noticed. Improvement in itch scores (VAS) and DLQI scores (11–20 very large effect) is observed after hydroxyzine use.

Dr. Umesh Bhoi

I noticed that taenia, scabies, psoriasis, and eczema are common dermatological reasons for pruritus. Systemic disease such as diabetes mellitus, chronic renal failure, and hepatitis is also associated with pruritus. Hydroxyzine is commonly prescribed to treat pruritus due to its antipruritic, anxiolytic, and sedative effects. Symptom elimination and improvement were observed within 1–2 weeks, after starting hydroxyzine therapy. Improvement in itch scores (VAS) and DLQI scores (6–10 moderate effect) is noticed in patients after hydroxyzine use.

Dr. Sanjeev Aurangabadkar

Urticaria and eczema are the most common dermatological causes of pruritus. It is also linked to systemic conditions such as renal disease. I personally prescribe hydroxyzine as a first-line therapy in pruritus management due to its antipruritic, anxiolytic, and sedative properties. After taking hydroxyzine within a day, it is possible to observe the improvement of pruritus symptoms with a week. Improvement in itch scores (VAS) and patients' quality of life DLQI scores (11–20 very large effect) is noticed after hydroxyzine use.

Dr. Tapesh Sharma

Pruritus is commonly observed in dermatological outpatients. Dermatological causes such as anemia, hypothyroidism, and cholestasis and non-dermatological causes such as jaundice, anemia, and hypothyroidism are also associated with pruritus. I prescribe hydroxyzine as a first-line therapy in pruritus management due to its antipruritic, anxiolytic, and sedative properties. It is possible to see an improvement in pruritus symptoms within a week after starting hydroxyzine medication. 5D itch scores and DLQI scores (6–10 moderate effect) are improved in patients after hydroxyzine use.

Dr. Gautam Datta Gupta

Pruritus is a common dermatological complaint that affects about half of all patients who visit clinics. Dermatological causes such as eczema, scabies, and lichen planus and non-dermatological conditions such as hepatic and renal conditions are associated with pruritus. I personally treat patients with hydroxyzine for pruritus management due to its antipruritic and sedative properties. Symptom elimination is observed in patients within a week after treatment with hydroxyzine. After using hydroxyzine, an improvement in VAS scores and DLQI scores (11–20 very large effect) is noticed in patients.

Dr. Ganesh Sonawane

According to my clinical experience, urticaria is the most common dermatological reason for pruritus. Systemic disease such as chronic renal failure and hypothyroidism is also associated with pruritus. I prescribe hydroxyzine as a first-line therapy in pruritus management due to its antipruritic, anxiolytic, and sedative properties. After taking hydroxyzine within a week, symptom improvement is evident in patients. Improvement in itch scores (Eppendorf itch questionnaire – EIQ) and DLQI scores (11–20 very large effect) is observed after hydroxyzine use.

Dr. Rajashekar ML

Atopic dermatitis is the most common dermatological causes of pruritus, according to my clinical expertise. Pruritus is also linked to systemic conditions such as liver and kidney diseases. Hydroxyzine is considered as a first-line therapy in pruritus management due to its antipruritic, anxiolytic, and sedative properties. After taking hydroxyzine within a week, an improvement in pruritus symptoms is noticed. Improvement in itch scores (VAS) and DLQI scores (6–10 moderate effect) is observed in patients after hydroxyzine use.

Dr. Bhumesh Kumar

Pruritus is commonly observed in dermatological outpatients. Dermatological causes such as atopic dermatitis, tinea, and xerosis and non-dermatological causes such as renal causes, hepatic disorders, and hyperthyroidism are also associated with pruritus. It is also associated with complications such as sleep disturbances and stress. I prescribe hydroxyzine as a first-line therapy in pruritus management due to its antipruritic, anxiolytic, and sedative properties. It is possible to see an improvement in pruritus symptoms 1 week after starting hydroxyzine medication. Improvement in 5D itch scores and DLQI scores is noticed in patients after hydroxyzine use.

Dr. Manjoor Ahmed Seikh

Pruritus is a common complaint among dermatological patients. Dermatological causes such as atopic dermatitis and taenia infections are associated with pruritus. I prescribe hydroxyzine as a first-line therapy in pruritus management due to its antipruritic, anxiolytic, and sedative properties. It is considered to be very safe, and improvement in symptoms is observed within 2 weeks after starting hydroxyzine therapy. Improvement in symptom elimination (5-D itch scores) and improvement in quality-of-life scores (DLQI) is noticed in patients after hydroxyzine use.

Dr. Tamal Chakroborty

Pruritus is commonly observed in dermatological outpatients. Dermatological causes such as atopic

dermatitis and xerosis and systemic conditions such as renal causes and hepatic disorders are also associated with pruritus. I choose to prescribe hydroxyzine as a first-line therapy in pruritus management due to its antipruritic, anxiolytic, and sedative properties. Symptom improvement is evident within a week after starting hydroxyzine medication. 5D itch scores and DLQI scores are improved in patients after hydroxyzine use.

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Original Article

Association of Cerebroplacental and Cerebrouterine Ratio with Fetal Outcome in Kashmiri Pregnant Women with Hypertension

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Abstract

Background: Doppler velocimetry is a non-invasive technique that evaluates abnormal fetal hemodynamics that take place in response to changes in placental resistance. Doppler studies of multiple fetoplacental are used to predict adverse perinatal outcome and assisting in optimal time of delivery. Cerebroplacental ratio (CPR) is calculated as the absolute ratio between the Doppler pulsatility indices of fetal middle cerebral artery (MCA) and umbilical artery (UA) or as the ratio between the corresponding multiples of the median for gestational age. CPR is reflective of fetal hypoxia and acidemia, and therefore prediction of perinatal jeopardy. A low CPR in a hypertensive pregnancy is associated with an increased risk of induction of labor, emergency cesarean section and poor perinatal outcome. CRP ratio is an established predictor of unfavorable pregnancy outcomes, while cerebrouterine (CU) ratio is fairly new ratio of vascular impedance between MCA and uterine arteries.

Objectives: The objective of the study was to study CPR as predictor of adverse fetal outcome in pregnant women with hypertension from 34 weeks of gestation, and, to evaluate the role of middle cerebral to UA blood velocity waveforms and fetal outcome in terms of fetal growth restriction, mode of delivery, neonatal intensive care unit (NICU) admission, APGAR at 5min.

Methods: This prospective study was conducted in the Postgraduate Department of Obstetrics and Gynaecology of GMC Srinagar associated Lalla Ded Hospital over a period of 1½ year. During this period on an average around 400 patients attended the outpatient department on daily basis, 50432 patients were admitted in our hospital, 34,293 deliveries were conducted. All pregnant women from 34 weeks of gestation with CPR done within 1 week of delivery, admitted or referred to Lalla Ded Hospital. The scan in these women was done within 1 week of delivery considered. CPR value was obtained from the scan. CPR is ratio of pulsatility index of the MCA by the UA pulsatility index.

Results: We observed a statistically significant correlation between abnormal CPR with caesarean section ($P < 0.001$), abnormal CPR and low for gestational age ($P < 0.001$), abnormal CPR and APGAR at 1 min ($P < 0.001$), and APGAR score at 5 min ($P < 0.001$), abnormal CPR and NICU admission. ($P < 0.001$) abnormal CPR and neonatal death was also significant ($P < 0.0008$). We observed a statistically significant association between Abnormal CU with low for gestational age ($P < 0.001$), between abnormal CU ratio and APGAR SCORE at 1 min ($P < 0.001$) and APGAR score at 5 min ($P < 0.001$), abnormal CU and NICU admission ($P < 0.001$), between abnormal CU ratio and neonatal death.($P < 0.0004$). CP ratio had higher specificity and PPV and lower sensitivity than CU ratio in predicting abnormal fetal outcome. CRU ratio had higher sensitivity and NPV and lower specificity than CP ratio in predicting abnormal fetal outcome.

Conclusion: Fetal Doppler plays a crucial role in monitoring the redistribution of blood in the fetus and the placental circulation. CPR and CUR assesses parameters on both placental side and also the fetal response.

Key words: Cerebroplacental ratio, Cerebrouterine ratio, Dopper velocimetry, Pulsality index

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INTRODUCTION

Hypertension peculiar to pregnancy (preeclampsia and gestational hypertension) is a specific syndrome characterized by reduced organ perfusion secondary to vasospasm and endothelial pathology.[1] The earliest pathology is impaired conversion of spiral arteries to

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uteroplacental arteries. As the second wave of infiltration of trophoblasts into the myometrial segments of the spiral arteries is inhibited, the blood supply to fetus is reduced.[2,3] The progression of pregnancy is marked by a number of changes and adaptations in the maternal, placental and fetal vasculatures. An inability to adapt to these changes results in the development of abnormal vascular resistance patterns, which might consecutively lead to the compromise of fetal well-being and ultimately IUGR.[4] As placental insufficiency occurs, several changes occur in fetal circulation due to fetal hypoxia which activates a number of defense mechanisms, such as modification of fetal heart rate, increase in blood pressure and redistribution of blood to the heart, brain, and adrenal glands. Low oxygen partial pressure (pO_2) leads to cerebral vasodilation and a fall in vascular resistance, which results in a decrease in middle cerebral artery (MCA) resistance index values. This is seen as Brain Sparing effect on Doppler.[5]

Accurate assessment of the fetal condition in high risk pregnancies is important if perinatal mortality, and morbidity and also unwarranted intervention in pregnancy and labor are to be reduced. Doppler ultrasound of the uteroplacental fetal circulation offers the potential to study the functional and hence physiological changes in these circulations and may help identify circulatory problems that underlie placental insufficiency and chronic fetal hypoxia.[6] The objective of fetal Doppler is to detect any hemodynamic changes at the earliest and to assess the placental dysfunction and the consequences of this on fetal growth and well-being,[6] Umbilical artery (UA) and MCA Doppler ultrasound clearly depict the information about placental resistance and the changes in the fetal hemodynamics in response to it. UA Doppler reflects the maldevelopment of the placental tertiary stem villi which increases the placental resistance.[1]

Doppler velocimetry is a non-invasive technique that evaluates abnormal fetal hemodynamics that take place in response to changes in placental resistance. Doppler studies of multiple feto-placental vessels can be used to predict adverse perinatal outcome and assisting in optimal time of delivery.[7] Cerebroplacental ratio (CPR) is calculated as the absolute ratio between the Doppler pulsatility indices (PIs) of fetal MCA and UA or as the ratio between the corresponding multiples of the median for gestational age. CPR is reflective of fetal hypoxia and acidemia, and therefore prediction of perinatal jeopardy.[1,8] A low CPR in a hypertensive pregnancy is associated with an increased risk of induction of labor, emergency cesarean section, and poor perinatal outcome. CRP ratio is an established predictor of unfavorable pregnancy outcomes, while cerebrouterine (CU) ratio is fairly new ratio of vascular impedance between MCA and uterine arteries.[6,8] CPR should be considered as an assessment tool in fetuses undergoing third-trimester ultrasound examination, irrespective of the findings of the individual UA and MCA measurements. The brain sparing phenomenon is considered as an adaptive mechanism of the fetus which is activated to protect the fetal brain in adverse conditions. Velocimetry of the uterine artery has been reported by some authors to be more accurate than is that of the UA or fetal MCA in the prediction of adverse outcome. The ratio of vascular impedance between the fetal MCA and uterine

Table 1: Patient characteristics

	Number	Percentage
Age (years)		
<20	15	2.0
20–24	209	27.9
25–29	423	56.4
30–34	57	7.6
≥35	46	6.1
Mean±SD (Range)=28.1±4.78 (18–37 years)		
Parity		
Primigravida	514	68.5
Multigravida	236	31.5
Gestational age		
<37 Weeks	348	46.4
≥37 Weeks	402	53.6
Mean±SD=37.2±3.91		
Socioeconomic status		
Upper	5	0.7
Upper middle	62	8.3
Lower middle	210	28.0
Upper lower	297	39.6
Lower	176	23.5
Mode of delivery		
NVD	343	45.7
LSCS	407	54.3
Fetal Outcome		
Live birth	730	97.3
Still birth	20	2.7
Apgar score at 1 min		
<7	207	28.4
≥7	523	71.6
Apgar score at 5 min		
<7	169	23.2
≥7	561	76.8
Birth weight		
SGA	181	24.8
AGA	549	75.2
NICU admission		
Yes	178	24.4
No	552	75.6
Neonatal mortality		
Yes	63	8.6
No	667	91.4
Cerebroplacental ratio		
Normal	507	67.6
Abnormal	243	32.4
Cerebrouterine ratio		
Normal	443	59.1
Abnormal	307	40.9

NVD: Normal vaginal delivery, LSCS: Lower segment cesarean section, NICU: Neonatal intensive care unit, SGA: Small for gestational age, AGA: Appropriate for gestational age

arteries has not yet been evaluated. Uterine artery Doppler might be expected to reflect placental perfusion, while umbilical Doppler reflects placental pathology. Uterine artery Doppler might be expected to reflect placental perfusion, while umbilical Doppler reflects placental pathology, therefore the CU ratio (CU Ratio) could have a better predictive value for unfavorable outcome.[9-11]

Aims and Objectives

Aim

The aim of the study was to study CPR as predictor of adverse fetal outcome in pregnant women with hypertension from 34 weeks of gestation.

Objectives

Tobjective of the study was to evaluate the role of middle cerebral to UA blood velocity waveforms and fetal outcome in terms of fetal growth restriction, mode of delivery, NICU admission, and APGAR at 5 min.

MATERIALS AND METHODS

This prospective study was conducted in the Post Graduate department of Obstetrics and Gynaecology of GMC Srinagar associated Lalla Ded Hospital over a period of one and a half year. During this period on an average around 400 patients attended the outpatient department on daily basis, 50,432 patients were admitted in our hospital, 34,293 deliveries were conducted. All pregnant women from 34 weeks of gestation with CPR done within 1 week of delivery, admitted or referred to Lalla Ded Hospital.

Inclusion Criteria

The following criteria were included in the study:

1. Women delivering singleton babies
2. Women who are willing to participate in the study from 34 weeks of gestation
3. All pregnant women with gestational hypertension.

Exclusion Criteria

The following criteria were excluded from the study:

1. Women who are not willing to participate in the study
2. Multiple pregnancies
3. Fetal congenital anomalies
4. Intrauterine death.

Methodology

This study was conducted in the Department of Obstetrics and Gynecology at Government Lalla Ded Hospital, Srinagar. A semi-constructed questionnaire was used to collect all relevant obstetric information (maternal age, parity, gestational age at delivery, presence, or absence of medical diseases,). Pregnant women with gestational age (34 weeks onwards) were included in the study. The scan in these women was done within 1 week of delivery considered. CPR value was obtained from the scan. CPR is ratio of pulsatility index of the MCA by the UA pulsatility index. CPR = MCA PI/UA PI.

After taking informed written consent, the recruited patients were subjected to detailed history taking and examination, routine laboratory tests as CBC, liver, and kidney function tests. Ultrasonographic scanning was done trans-abdominally using ultrasound machine equipped with 3.5 Mhz convex probe to evaluate fetal weight, biometry, and Doppler studies. SIEMENS ACUSON X 300 USG machine was used for obtaining the ultrasonogram of the patients. Umblical Artery (Um A), MCA, Uterine Artery (Ut A) was examined by Color Doppler ultrasound and Pulsed wave Doppler a single cutoff value of 1.0 for all cases. Above this value, Doppler velocimetry was considered normal and below it, abnormal. Using this cutoff value, the study population was divided into two groups - those with a normal ratio (>1.0) and those with an abnormal ratio (<1.0). Adverse fetal outcome was analyzed by above mentioned statistical method in terms of emergency cesarean section for fetal distress, low birth weight, Apgar at 5 min, NICU admission, and Neonatal death.

Chi-square test was employed for determining association of CPR and CUR with fetal outcome, in terms of still birth, birth weight, APGAR score at 1 min, APGAR score at 5 min, NICU admission, and neonatal death. Further diagnostic accuracy (Sensitivity, Specificity, PPV, and NPV) of CPR and CUR was also obtained. $P < 0.05$ was considered statistically significant.

RESULTS

The mean maternal age at presentation was 28.1 (±4.78) years with the range from 18 to 37 years. Maximum number of cases was seen between the age group of 25 and 29 years (56.4 %), followed by 20–24 years (27.9%). About 7.6% of the patients were between 30 and 34 years and 6.1% of the patients belonged to age ≥35–37 and 2% belonged to age group <20 years. About 68.5% were primigravida and 31.5% were multigravida. The parity distribution is shown in Tables 1 and 2. The gestational age was between

Table 2: Association of cerebroplacental ratio with mode of delivery

Mode of delivery	Abnormal CPR		Normal CPR		*P*-value
	No.	%age	No.	%age	
NVD	79	32.5	264	52.1	<0.001*
LSCS	164	67.5	243	47.9	
Total	243	100	507	100	

NVD: Normal vaginal delivery, LSCS: Lower segment cesarean section, CPR: Cerebroplacental ratio

Table 3: Association of cerebrouterine ratio with mode of delivery

Mode of delivery	Abnormal CPR		Normal CPR		*P*-value
	No.	%age	No.	%age	
NVD	87	28.3	256	57.8	<0.001*
LSCS	220	71.7	187	42.2	
Total	307	100	443	100	

NVD: Normal vaginal delivery, LSCS: Lower segment cesarean section, CPR: Cerebroplacental ratio

Table 4: Association of cerebroplacental ratio with fetal outcome

Fetal outcome	Abnormal CPR		Normal CPR		*P*-value
	No.	%age	No.	%age	
Still birth					
Yes	20	8.2	0	0.0	<0.001*
No	223	91.8	507	100	
SGA					
Yes	128	57.4	53	10.5	<0.001*
No	95	42.6	454	89.5	
1 min Apgar score					
<7	131	58.7	76	15.0	<0.001*
≥7	92	41.3	431	85.0	
5 min Apgar score					
<7	109	48.9	60	11.8	<0.001*
≥7	114	51.1	447	88.2	
NICU admission					
Yes	90	40.4	88	17.4	<0.001*
No	133	59.6	419	82.6	
Neonatal death					
Yes	31	13.9	32	6.3	0.0008*
No	192	86.1	475	93.7	

NICU: Neonatal intensive care unit, SGA: Small for gestational age, CPR: Cerebroplacental ratio

Table 5: Association of cerebrouterine ratio with fetal outcome

Fetal outcome	Abnormal CPR		Normal CPR		*P*-value
	No.	%age	No.	%age	
Still birth					
Yes	20	6.5	0	0.0	<0.001*
No	287	93.5	443	100	
SGA					
Yes	145	50.5	36	8.1	<0.001*
No	142	49.5	407	91.9	
1 min APGAR score					
<7	160	55.7	47	10.6	<0.001*
≥7	127	44.3	396	89.4	
5 min APGAR score					
<7	128	44.6	41	9.3	<0.001*
≥7	159	55.4	402	90.7	
NICU admission					
Yes	107	37.3	71	16.0	<0.001*
No	180	62.7	372	84.0	
Neonatal death					
Yes	38	13.2	25	5.6	0.0004*
No	249	86.8	418	94.4	

NICU: Neonatal intensive care unit, SGA: Small for gestational age, CPR: Cerebroplacental ratio

34 and 37 weeks in 348 deliveries and 402 deliveries were equal to or above 37 weeks. The mean gestational age was 37.2 ± 3.91. Majority of patients belonged to upper lower (39.6%), followed by lower middle (28%). The least number of cases belonged to upper socioeconomic class (0.7%).

Among 750 patients, majority 407 (54.3%) delivered by cesarean section and rest 343 (45.7%) delivered vaginally. About 97.3% of babies were live births, but the rest (2.7%) were still born who could not be resuscitated at birth. The 1 min APGAR score was <7 in only 28.4% while the rest had a score of 7 ≥7 (71.6). The 5 min APGAR score was <7 in only 23.2% while the rest had a score of 7 ≥7 (76.8%). Majority of the babies (75.2%) were average for gestational age; however, 24.8% were small for gestational age. Although 24.4% babies required NICU care, 75.6% did not require any NICU Admission. About 8.6% case study neonates expired. 507 (67.6%) had normal CPR, while rest 243 (32.4%) had abnormal CPR. 443 (59.1%) had normal CUR, while rest 307 (40.9%) had abnormal CUR.

Among 750 patients with abnormal CPR 67.5% had cesarean Section while rest 32.5% delivered vaginally. Among patients with Normal CUR 52.1% delivered vaginally while rest 47.9% had cesarean section. Among 750 patients with abnormal CUR 71.7% had cesarean section while rest 28.3% delivered vaginally. Among patients with normal CUR 57.8% delivered vaginally while rest 42.2% had cesarean section. About 8.2% had still-birth, 57.4% were small for gestational age, 58.7% had APGAR score <7 at 1 min, 48.9% had APGAR score, 7 at 5 min, 40.4 required NICU admission, and 13.9% neonates died. While those with normal CPR, the difference was statistically significantly for all of the above parameters. About 6.5% had stillbirth, 505.5% were small for gestational age, 55.7% had APAGAR SCORE <7 at 1 min, 44.6% had APGAR SCORE, 7 at 5 min, 37.3% required NICU admission, and 13.2% neonates died while those with normal CUR the difference was statistically significant for all of the above parameters. CP ratio had 60.4% sensitivity, 81.3% specificity, positive predictive value 56.1%, negative predictive value 73.8% and 75.3% diagnostic accuracy with statistically significant positive correlation, to predict abnormal fetal outcome. CU ratio had 68.6% sensitivity and 72.3% specificity, positive predictive value 49.5%, negative predictive value 85.3 and diagnostic accuracy of 71.2% to predict abnormal fetal outcome [Tables 3-5].

DISCUSSION

The study was held in Postgraduate Department of Obstetrics and Gynaecology, Lal Ded hospital, an associated

Hospital of GMC, Srinagar, during the period between (December 2019 and October 2021.) This study included 750 pregnant women who fulfilled the inclusion criteria. Pregnant females with age group from 18 to 37 years were included in the study and the mean patient age was 28.1 with maximum number of cases seen between the age group of 25–29 years (56.4%), followed by 20–24 years (27.9%). About 7.6% of the patients were between 30 and 35 years and 6.1% of the patients were 35–37 years 2% of the patients belonged to <20 years of age. In a study conducted by Mallick *et al*.,[12] the most common age group of the expectant mothers was 26–30 years, with 201 women (40.9%), followed by 21–25 years as seen in 176 (35.8%). 69 women (14.02%) were 31–35-years-old and 34 (6.91%) were over 35 years of age. 12 women were between 15 and 20 years of age, with most of them being 18 or 19 years. Lakhute *et al*.[13] reported the mean age among their study population as 22.31 ± 2.93 years.

Our study had maximum number of primigravida (68.5%). Primigravida is considered to have a higher risk for gestational hypertension. Konwar *et al*.[14] in their study also had maximum cases (68%) in primigravida which is comparable to our study. 46.4% patients between 34 and 37 weeks and 53.6% were equal to or above 37 weeks. In a study conducted by Mallick *et al*.[12] 10.6% were <34 weeks, 29.1% of the patients between 34 and 36 weeks and 60.4% of the patients were >37 weeks. Konwar *et al*.[14] in their study had 6% patients between 30 and 34 weeks, 24% between >34 and 37 weeks 70% >37–40 weeks. Our study had majority of patients belonging to the upper lower (39.6%), followed by lower middle socioeconomic group (28%) and the least number of cases belonging to upper socioeconomic class (0.7%). In a Study conducted by Lakhute *et al*.[13] 45% were from low class, 33% were from middle class, and 11% from upper middle class and thus concluded that socio-economic status to be an important risk factor associated with gestational hypertension. 407 (54.3%) delivered by cesarean section and rest 343 (45.7%) delivered vaginally. About 97.3% were live birth, but (2.7%) were fresh still-born who could not be resuscitated at birth. Muti *et al*.[15] observed 94.4% live birth and 5.45 still birth, and Adiga *et al*.[16] reported 95% live births and 5% still birth rate. APGAR score at 1 min was <7 in only 28.4% while it was >7 (71.6%). Muti *et al*.[15] in her study observed Apgar score of < in 8.9% and >7 in 91.1% babies. In terms of APGAR score at 5 min, 23.2% had APGAR score <7 and 76.8% had score >7. Muti *et al*.[15] in her study had 8.1% with APGAR score <7 and 91.9% with APGAR Score >7.

Majority of the babies (75.2%) were average for gestational age, however (24.8%) were small for gestational age. Lakhute *et al*.[13] found 21.2% and Mallick *et al*.[12] found 20.9% were SGA. About 24.4% babies required NICU admission and 75.6% did not require any NICU Admission. Mallick *et al*.[12] in her study reported 23.4% babies who required NICU admission. About 8.6% neonates expired in the early neonatal period. Shahinaj *et al*.[17] has also reported a neonatal mortality of 5.96% in their study. Normal CPR was observed in 67.6% fetuses, while as 32.4% fetuses had abnormal CPR. El-Guindy *et al*.[18] in his study also reported that 34.1% fetuses had abnormal CPR and 65.9% had normal CPR. Eser *et al*.[19] in their study reported 22% fetuses to have abnormal CPR. In our study, 59.1% fetuses had normal CUR, while as 40.95% had abnormal CUR. El-Guindy *et al*.[18] in his study reported 62% neonates to have normal CUR. In our study with abnormal CPR, the mode of delivery in women with abnormal CPR was LSCS in 67.5% and vaginal delivery in 32.5%. Similar finding of LSCS rate of 62.5% and vaginal delivery in 37.5% has been reported by Shahinaj *et al*.[17] In our study with Abnormal CUR mode of delivery in 28.3% was normal vaginal delivery and caesarean section in 71.7%. Eser *et al*.[19] reported 88.46% cesarean section in patients with abnormal CUR and vaginal delivery in only (11.54%). In our study of neonates with abnormal CPR, still birth rate was 8.2%. This is much less than that reported by Shahinaj *et al*.[17] who observed 17% still -births in their study. Patil *et al*.[20] observed 7.8% still birth in their study.

In neonates with abnormal CPR SGA were seen in 57.4% as per our study. This is similar to Shahinaj *et al*.[17] who reported (52.4%) babies with abnormal CPR who were small for gestational age. Sirico *et al*.[21] also observed SGA in 45.2% babies. Among abnormal CPR in our study, 58.7% babies had APGAR score <7 at 1 min and 48.9% had <7 APGAR score at 5 min. Mariam *et al*. in patients with abnormal CPR reported that 36% patients had <7 APGAR at 1 min and Shahinaj *et al*.[17] reported 61.9% babies had <7 APGAR at 5 min while El-Guindy *et al*.[18] reported APGAR SCORE<7 at 5 min in 59.5% babies. In our study, 40.4% neonates with abnormal CPR required NICU admission. About 77% babies with abnormal CPR required NICU care as reported by El-Guindy *et al*.[18] and Shahinaj[17] 77.6%. We observed neonatal death rate in 13.9% babies with abnormal CPR. This is similar to Shahinaj *et al*.[17] who reported neonatal death as 13.6% neonates with abnormal CPR. Among babies with abnormal CUR, 6.5% had still as per our study. Kanika *et al*.[22] reported 9.09% still birth in babies with abnormal CUR. In women with abnormal CUR, small for gestational age babies was found in 50.5%. Kanika *et al*.[22] reported 65 (22%) neonates with SGA in women with abnormal CUR. However, Adiga *et al*.[16] reported only 47.4% babies with SGA in women with abnormal CUR.

Among abnormal CUR in our study, 55.7% neonates had <7 APGAR score at 1 min and 44.6% had <7 APGAR score at 5 min. Kanika *et al*.[22] reported that 58.8% babies had <7 APGAR at 1 min and 41.1% babies had

<7 APGAR at 5 min in their study of women with abnormal CUR. El-Guindy *et al*.[18] reported that (68.2%) babies had APGAR <7 at 1 min, and (55.1%) babies had APGAR <7 at 5 min. Among babies with abnormal CUR in our study, 37.3% required NICU admission. Kanika *et al*.[22] reported 50% NICU admission in babies having abnormal CUR. Adiga *et al*.[16] reported 31.6% NICU admission. In our study among abnormal CUR, neonatal death rate was 13.2%. El-Guindy *et al*.[18] reported 14% neonatal death rate in babies with abnormal CUR. In the present study CP ratio had 60.4% sensitivity, 81.3% specificity, positive predictive value 56.1%, negative predictive value 73.8%, and 75.3% diagnostic accuracy with statistically significant positive correlation, to predict abnormal fetal outcome. Comparison of our results of the sensitivity, specificity, positive predictive value, and negative predictive value of MCA/UA ratio with those of the study of Gramellini *et al*.,[23] Shahinaj *et al*.,[17] El-Guindy *et al*.[18] In our study with CU ratio had 68.6% sensitivity and 72.3% specificity, positive predictive value 49.5%, negative predictive value 85.3 and diagnostic accuracy of 71.2% to predict abnormal fetal outcome. Comparison of our results of the sensitivity, specificity, positive predictive value, and negative predictive value of MCA/UA ratio with those of the study of Adiga *et al*.,[16] El-Guindy *et al*.[18]

CONCLUSION

Hypertensive disorders of pregnancy have a significant impact on the fetal outcome. Fetal Dopplerplays a crucial role in monitoring the redistribution of blood in the fetus and the placental circulation. CPR and CUR assesses parameters on both placental side and also the fetal response. They help us to identify fetuses who are at higher risk of adverse perinatal outcomes and hence intensive monitoring during labor can be done for such fetuses. This is of great help in a high risk place with high case load like our hospital, as it identifies fetuses at potential risk during labor. CUR can be used as a complementary test.

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Original Article

Comparative Evaluation of Quality of Obturation between Two Obturation Techniques in Pulpectomy of Lower Primary Molars – An *In Vivo* Study

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Abstract

Aim: The aim of this study was to compare and evaluate the quality of obturation between hand held lentulo spirals and slow speed motor-driven lentulo spirals used obturation techniques in pulpectomy of lower primary molars.

Materials and Methods: The study was carried out among 136 children aged 4–7 years with pulpally involved mandibular primary molars requiring single visit pulpectomy who reported to the outpatient wing, Department of Pediatric and Preventive Dentistry, Government Dental College, Kottayam, satisfying the inclusion and exclusion criteria. Subjects were recruited consecutively into two groups with 68 children in each. Group I (obturation was done with handheld lentulo spirals technique) and Group II (obturation was done with slow speed motor – driven lentulo spirals technique). The parameters quality of obturation which, in turn, includes extent of apical seal, presence, or absence of voids was evaluated. The data were analyzed with Independent *t*-test and Chi-square test. Level of significance for the study was set as $P < 0.05$.

Results: Statistical analysis by Chi-square test showed that there is statistically significant difference regarding the quality of obturation between the groups with respect to apical seal and presence or absence of voids.

Conclusion: Powered lentulo spirals with a slow speed handpiece produced more ideal obturation compared to hand held lentulo spirals. Hence, the traditional lentulo spirals itself can be a better alternative option to newer costly, technique sensitive obturation techniques for an ideal obturation of the primary teeth.

Key words: Handheld-lentulo spirals, Obturation, Pulpectomy, Slow speed motor-driven lentulo spirals

INTRODUCTION

Maintaining the integrity of the primary teeth in the oral cavity is one of the major goals of pediatric dentistry. The primary dentition plays a key role in the child's growth and development, not only in terms of speech, chewing, appearance and the prevention of bad habits but also in the guidance and eruption of permanent teeth. The dental caries left untreated will progress to involve the pulp resulting in the early loss of the primary teeth. The best space maintainer in both primary and mixed dentition is the primary tooth itself, not only due to the clinical crown but also due to the presence of roots and periodontium that guides the eruption of the succedaneous permanent tooth.

Pulpectomy treatment is one option for maintaining primary teeth diagnosed with pulpal tissue inflammation involving radicular or non-vital pulp until normal exfoliation.[1] As per UK National Clinical Guidelines in Pediatric Dentistry, the rationale involved in pulpectomy procedure is to remove irreversibly inflamed or necrotic radicular pulp tissue and gently clean the root canal system. This is followed by obturating the root canals with a filling material that will resorb at the same rate as the primary tooth, which would

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be resorbed as time progress if accidentally extruded through the apex.[2]

Endodontic therapy of primary teeth is dependent on the factors such as unpredictable root canal anatomy of the primary teeth, deposition of secondary dentin, physiological resorption causing changes in anatomical forms of the root canals, and tortuosity of the root canals. An ideal filling technique should satisfy complete filling of the canal without overfill and with minimal or no voids. The most commonly used obturation techniques in the primary teeth includes amalgam pluggers, local anesthetic syringe, reamers, paper points, endodontic pressure syringe, handheld lentulo spiral, lentulo spiral mounted in a slow speed handpiece, mechanical syringe, cotton pellets, Jiffy tube, endodontic pluggers, endofiles, tuberculin syringe, and recently the NaviTip™.[3-8]

Lentulo spirals were advocated by Kopel.[9] It is the most traditional and commonly used instrument as the root canal paste carrier which is used in obturation of the primary teeth as hand held instrument or poer driven with a slow speed hand piece. According to the best of the researcher's knowledge, none of the obturation techniques available have been found to be ideal for obturation of root canals in the primary teeth. Several recent methods of obturation techniques in the primary teeth have found to show limitation in quality of obturation in various aspects, but considering the ease of use, handling and cost concerns, the traditional lentulo spirals can be a better option that can be used routinely in clinical practice than going in for advanced, technique sensitive and costly obturation techniques. Most of the studies about lentulospiral obturation techniques are *in vitro* comparisons and the quality of obturation is assessed by conventional radiography, digital radiography, and even cone-beam computed tomography. *In vitro* evaluation of root canal obturation methods in the primary teeth has reported the use of the lentulo spirals mounted in a slow-speed hand piece in filling of straight and curved canals of the primary teeth to be superior. However, there are a few research studies on *in vivo* clinical evaluation of obturation technique using two mode of usage of lentulo spirals. Hence, this present *in vivo* study was planned to assess the quality of obturation between hand held lentulo spirals and slow-speed motor-driven lentulo spirals as obturation technique in the primary teeth.

MATERIALS AND METHODS

The study was conducted in the Department of Pediatric and Preventive Dentistry, government dental college, Kottayam, Kerala. Evaluation of the study was done by the Ethical Committee of the Institute and Ethical Committee approval was taken before the study. Informed consent was taken from all the parents after explaining them the entire procedure in detail, before starting the treatment.

Sample size is calculated by the formula:[10,11]

$$n = \frac{Z^2_{1-\alpha/2}\left[P_1\left(1-P_1\right) + P_2\left(1-P_2\right)\right]}{\left(d2\right)2}$$

$$n = \frac{\left(1.96\right)2\left[\begin{matrix}0.15\left(1-0.15\right) + \\ 0.65\left(1-0.65\right)\end{matrix}\right]}{\left(0.1\right)2} = 136$$

Based on the inclusion and exclusion criteria, 136 patients indicated for pulpectomy were selected in the study. Pulpectomy was performed in all teeth indicated for pulp therapy. Based on technique of obturation, patients were divided into two groups by consecutive sampling:

- Group I: 68 teeth obturated with handheld lentulo spirals
- Group II: 68 teeth obturated with slow-speed motor-driven lentulo spirals.

Primary molars with signs of irreversible pulpitis, with adequate bone support with at least two-third of intact root length, no gingival swelling or presence of sinus tract, and no purulent exudates expressed from the gingival margin were included in the study. Whereas, grossly decayed teeth which cannot be restored. Any pathologic signs of external or internal resorption. Children with underlying systemic diseases and with special health-care needs. Children exhibiting lack of co-operative behavior. Teeth with anatomic variations were excluded from the study.

Clinical Procedure

A standard pre-operative radiograph was taken using digital radiography. Access to the pulp was obtained by round bur and barbed broach was used to remove it. The working length of the canal was established 1 mm short of radiographic apex. Biomechanical preparation of root canal was done and the canal was irrigated using saline and dried using paper points. Obturation of the tooth was then done using either handheld lentulo spirals or slow-speed motor-driven lentulo spirals and the teeth were divided in groups I and II, respectively.

Obturation with Handheld Lentulo spiral

A 21 mm hand held lentulo spiral was used to deliver the zinc oxide eugenol into root canals. Predetermined canal length was positioned with a stopper. Lentulo spirals was coated with the zinc oxide eugenol mix and inserted into

canal with clockwise rotation, accompanied by vibratory motion to allow material in to apex and then withdraw from the canal, while simultaneously continuing the clockwise rotation.

Obturation with slow Speed Motor-driven Lentulo spiral

A 21 mm lentulo spiral mounted in slow speed hand piece (1000 rpm) was used to deliver the zinc oxide eugenol into root canals. A rubber stopper was used to keep lentulo spirals 1 mm short of predetermined working length. The lentulo spirals were adjusted in clockwise rotation initially to pick up the freshly mixed creamy mix of zinc oxide eugenol. After insertion in to the canal, it was operated in counter clockwise rotation and withdrawn from the canal while still rotating.

The process was repeated in the both groups until the canal orifices appeared to be filled visibly. Final restoration was done with a glass-ionomer cement.

Assessment of Obturation Techniques

The comparison among the two techniques was determined radiographically by evaluating quality of obturation and voids in the obturated canals, based on the following criteria given by Sandrian and Coll (1996)[12]

a. Apical seal
   - Under filling (score1): All the canals were filled more than 2 mm short of radiographic apex
   - Optimal filling (score2): One or more of canals having obturation material ending at radiographic apex or up to 2 mm short of radiographic apex
   - Over filling (score 3): Any canal showing obturation beyond radiographic apex

b. Obturated canals were assessed for presence or absence of voids.

Apical seal was evaluated in millimeters from the apical end of the canal filling material and to the radiographic apex and categorized as score 1, score 2, and score 3. The highest score is considered as overall quality of obturation for individual tooth.

Statistical Analysis

Data collected were statistically analyzed using SPSS 18 software. Quantitative data (Age) were compared by mean and standard deviation with independent sample *t*-test. Qualitative data (Gender, Apical seal, and Voids) were compared by frequency and proportion with Chi-square test.

RESULTS

A total of 136 healthy children (65 males and 71 females) in the age group of 4–7 years with a mean age of 5.48 ± 0.950 in Group I and 5.66 ± 0.932 years in Group II participated in our study.

No statistical significant difference was noted between the groups with respect to the age ($P = 0.276$) and gender ($P = 0.479$) [Figures 1 and 2]. This indicates that there was an equal distribution of the participants between both the groups. Thus, both groups were balanced with respect to age and gender [Tables 1 and 2].

In Group I, the overall obturation of the canals was under filling in 16 cases (23.5%), optimum filling in 46 cases (67.6%), and over filling in 6 cases (8.8%) and in Group II, the obturation of canals was under filling in three cases (4.4%), optimum filling in 50 cases (73.5%), and over filling in 15 cases (22.1%) [Table 3].

The root canals were optimum filled in 46 and 50 cases in Group I and Group II, respectively, which is more than 70.6% of total obturations with Group II showing

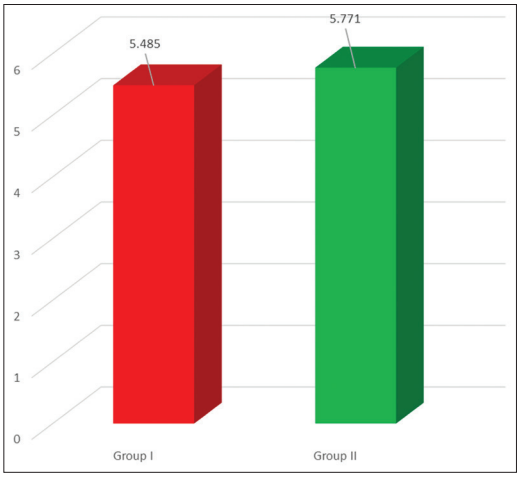

Figure 1: Bar diagram showing age-wise distribution in the study groups

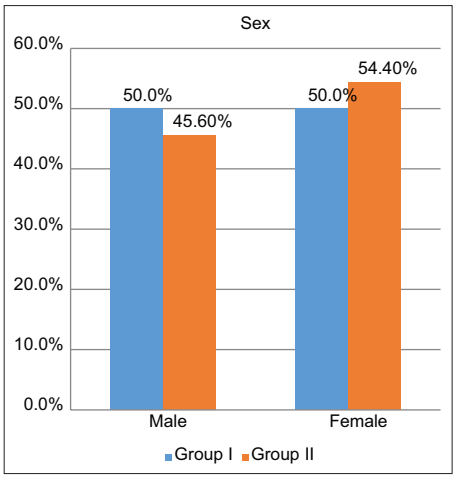

Figure 2: Bar diagram showing gender-wise distribution in the study groups

more number of optimally filled root canals which are about 73.5% [Figure 3]. Hence, a statistically significant difference was found between Group I and Group II with regard to apical seal in both canals of lower primary molars ($P = 0.002$) with Chi-square test [Table 3].

Table 1: Age-wise distribution in the study groups

Groups	*n*	Mean age	SD	t	*P*-value
Group I	68	5.485	0.9501	1.09	0.276
Group II	68	5.662	0.9322		

Table 2: Gender-wise distribution in the study groups

Groups	Sex		Total	χ^2	*P*-value
	Male	Female			
Group I				1.47	0.479
Count	34	34	68		
%	50.0	50.0	100.0		
Group II					
Count	31	37	68		
%	45.6	54.4	100.0		
Total					
Count	65	71	136		
%	47.8	52.2	100.0		

Table 3: Comparison of apical seal in obturation of two study groups

Groups	Apical seal			Total	χ^2	*P*-value
	Under filling	Optimum filling	Over filling			
Group I					12.91	0.002
Count	16	46	6	68		
%	23.5	67.6	8.8	100.0		
Group II						
Count	3	50	15	68		
%	4.4	73.5	22.1	100.0		
Total						
Count	19	96	21	136		
%	14.0	70.6	15.4	100.0		

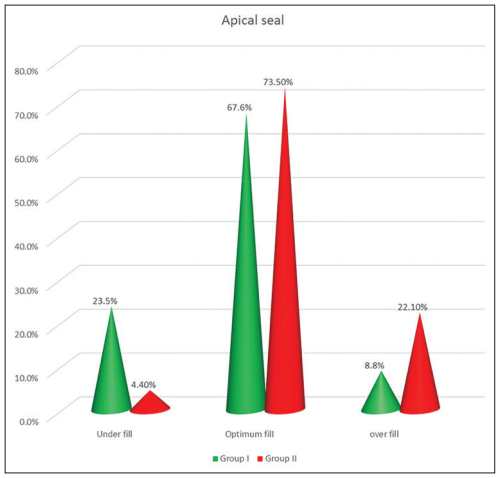

Figure 3: Bar diagram showing percentage distribution of under filled, optimum filled, and over filled cases of apical seal in obturation of two study groups

In Group I, absence of voids was in 34 cases (50.0%) and the presence of voids was in 34 cases (50.0%). Whereas in Group II, absence of voids was in 61 cases (89.7%) and presence of voids in seven cases (10.3%) in root canals, respectively, [Figure 4] so Group II showed less number of voids than Group I [Table 4].

Considering both groups, voids were present in only 41cases (30.1%) and absence of voids was noted in 95 cases (69.9%). Hence, a statistically significant difference was found between Group I and Group II with regard to the voids in canal obturation of lower primary molars ($P = 0.000$) which was calculated using Chi-square test [Table 4].

DISCUSSION

In the present study, the mean age (years) of the children was 5.57, which was similar to the study reported by Omar and Salama.[3] Out of 136 children, there were 47.8% of male patients and 52.2% of female (52.2%) patients. Hence, the gender imbalance has no effect on the procedure and results of root canal obturation. This was in agreement with study by Gandhi *et al*.[10] and Chandrasekhar *et al*.[11]

In our study, there were 73.5% of cases showing optimum filling with slow speed motor-driven obturation technique (Group II) after the procedure, whereas 67.6% cases showed optimum filling with the handheld lentulo spiral obturation technique (Group I) which was statistically significant. This findings are accordance with the study by Singh *et al*.[13] that motor-driven lentulo spirals produced best optimum filled obturation compared to handheld lentulo spirals technique and the study by Gandhi *et al*.[10] which showed that handheld lentulo spirals produced more number of underfilled canals compared to disposable syringes and past inject.

A previous study by Pandranki *et al*.[14] also revealed that motor-driven lentulo spiral was superior to tuberculin and endodontic pressure syringe in the obturation of the primary root canals. The flexibility of the lentulo spiral was contributed to these findings. A study by Staehle *et al*.[6] also reported that motor-driven lentulo spiral system revealed significantly better results when compared to hand instruments.

In our study, the underfilled obturation of 23.5% was seen with handheld lentulo spirals (Group I) and of 4.4% with motor-driven lentulo spirals technique, respectively. Similar findings were reported in a study by Gandhi *et al*.,[10] which

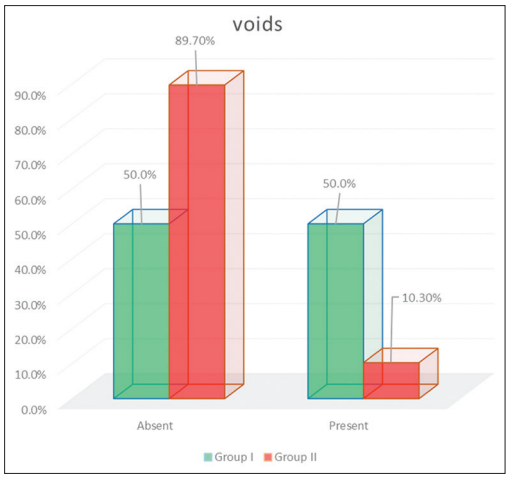

Figure 4: Bar diagram showing presence or absence of voids in obturation of two study groups

Table 4: Comparison of voids in obturation of two study groups

Groups	Voids		Total	χ^2	*P*-value
	Absent	Present			
Group I					
Count	34	34	68	25.45	0.000
%	50.0	50.0	100.0		
Group II					
Count	61	7	68		
%	89.7	10.3	100.0		
Total					
Count	95	41	136		
%	69.9	30.1	100.0		

showed 10% underfilled canals with handheld lentulo spirals when compared to past inject technique and a study by Sengupta *et al*.[15] reported a 30% of underfilled canals with motordriven lentulo spirals when compared to reamer technique.

The present study showed overfilled canals of 22.1% cases with motor-driven lentulo spirals and of 8.8% cases with handheld lentulo spirals, respectively. This was accordance with the study by Vashista *et al*.,[16] which reported 20% of overfilled obturation with handheld lentulo spirals compared to pressure syringe technique and a systematic review and meta-analysis by Aminabadi *et al*.[17] reported that 23.3% of overfilled obturation with motor-driven lentulo spirals. Hence, overfilled obturation is one of disadvantages with lentulo spiral obturation technique.

In the present study, the presence of voids in the root canal filling was also assessed radiographically following obturation. About 50.0% of cases showed voids with the handheld lentulo spirals in the obturation, whereas only 10.3% cases showed voids with the motor-driven lentulo spirals technique. The two techniques showed a significant difference regarding voids in the obturation. This result was in agreement with the previous study by Singh *et al*.[13] which stated that the handheld lentulo spirals produced more number of voids in obturation of the primary teeth than reamer technique and motor-driven lentulo spirals technique. A contradictory study by Walia *et al*.[18] showed that voids are inevitable and were present with both handheld lentulo spirals and motor-driven lentulo spirals techniques.

According to newer research, optimal fillings of the root canals of the primary teeth are easily achieved with past inject. Past inject paste carrier is a specifically designed device and works similarly to the lentulo spiral. However, study by Chandrasekhar *et al*.[11] concluded that lentulo spirals was superior in quality of obturation compared to past inject technique. Hence, lentulo spirals can act as substitute for cost effective obturation technique when compared to newer methods which produced better results as per several literatures.

The present investigation and findings of the study were limited to lower primary molars, the morphology of root canals of first and second primary mandibular molars are entirely different, and this may affect the quality of obturation which is not mentioned separately in this study. Quality of obturation was assessed as overall status of the primary molars; but it was not mentioned specifically whether it was in mesiobuccal, mesiolingual or distobuccal, or distolingual root canals.

CONCLUSION

We, thereby, conclude that within the limits imposed by the conditions used in the present study, both the hand held and slow speed motor-driven lentulo spirals technique could be effectively used for obturation in primary dentition. Considering apical seal and voids, the use of slow speed motor-driven lentulo spirals produced better quality of obturation as compared to handheld lentulo spirals. Being a clinical comparative study, based on the quality of evidence generated by comparing two traditional treatment techniques (handheld lentulo spirals and slow speed motor-driven lentulo spirals technique), this could be an alternative to newer costly techniques as quality of obturation which is an important clinical factor in pulpectomy procedure.

Limitations of the Study

The present study is based on the comparison between two different obturation techniques in the primary lower molars. The morphology of root canals of first and second primary mandibular molars is entirely different and this may affect the quality of obturation which is not mentioned separately in this study.

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Original Article

Comparative Study on the Effect of Pre-pregnant Body Mass Index on the Occurrence of Preeclampsia in a Tertiary Health-care Setup

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Abstract

Introduction: Association between maternal body mass index (BMI) and preeclampsia had been established by many a foreign study. A high number of maternal deaths in low-income countries is due to preeclampsia; therefore, both prevention of preeclampsia is exteremely important to bring down maternal mortality. Hence, we decided to find out the association between pre-pregnancy BMI and preeclampsia in our study.

Aim: The aim of the study was to compare the BMI between normotensive and preeclamptic women and to correlate it to occurrence of preeclampsia.

Materials and Methods: This was a case–control study conducted in the Department of Obstetrics and Gynecology, Government Kilpauk Medical College and Hospital, Chennai, Tamil Nadu, India. A total of 60 age-matched pregnant women were enrolled for the study. Out of the 60 women, 30 normal healthy pregnant women formed the control group, while another 30 preeclamptic patients formed the case group. All the patients underwent detailed history taking and clinical examination. Pre-pregnancy weight was self-reported during the first prenatal care visit. Calculation of BMI was done using Quetelet index formula, BMI was calculated as weight (kg) divided by the square of height (m), that is, BMI = Weight (kg)/Height (m^2).

Results: Mean BMI for preeclamptic women is 24.7 while that of normotensive women is 21, t-test for equality for means was 7.371, $P = 0.000$. Hence, BMI is statistically significant between two groups.

Conclusion: Increased BMI was seen in preeclamptic women, while BMI was less is normotensive women on comparison. Maintenance of pre-pregnant BMI in the lower normal values would help a long way in preventing preeclampsia.

Key words: Normotensive pregnancy, Preeclampsia, Pre-pregnancy body mass index

INTRODUCTION

Preeclampsia is a serious complication affecting 2–8% of all pregnancies. Globally, more than 287,000 women die each year due to pregnancy related causes,[1] of which 10–15% are estimated to be due to preeclampsia. The etiology of preeclampsia remains unclear, but mechanisms related to the placenta, genes, immune response, insulin resistance, and maternal vascular disease are suggested to contribute.[2-5] Established risk factors for preeclampsia include nulliparity, advanced maternal age, overweight/obesity, chronic hypertension, diabetes, previous preeclampsia, family history of preeclampsia, long time since previous pregnancy, and multiple pregnancy.[6] Obesity has been associated with a 2–4-fold increased risk of preeclampsia in different populations and is a leading identified attributable risk for this disorder. The risk of preeclampsia has been shown to increase with an increasing body mass index (BMI), with the lowest prevalence among underweight women.[7-12]

Researchers believe that preeclampsia is a multifactorial disease and propose several risk factors for it, including a history of preeclampsia, low and high maternal age, diabetes, chronic hypertension, null parity, birth intervals, history of abortion, high BMI value, twin pregnancy, fetal sex, migraine, and maternal RH.[6,13-15]

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Some studies have referred to obesity as a risk factor for preeclampsia and showed that the relationship between maternal weight and preeclampsia is a progressive risk and varies from 4.3% in women with a BMI <19.8 Kg/m^2, up to 13.3% for women with a BMI ≥35 kg/m^2.[16]

High BMI is an important risk factor for both preeclampsia[17,18] and cardiovascular disease[19,20] Obesity prevalence is increasing at an alarming rate in both high- and low-income countries.[21]

Maternal obesity and insulin resistance are believed to be important risk factors for the development of placental endothelial dysfunction and preeclampsia.[22,23] Because an elevated BMI (BMI; weight [kg] per height squared [m^2]) is a major component of dysmetabolic syndrome, as well as an important risk factor for preeclampsia and other complications of pregnancy,[7] a more precise estimate of the association between maternal pre-pregnancy BMI and preeclampsia is needed.

Aims and Objectives

The aim of the study was to compare the BMI between normotensive and preeclamptic women and correlate it to occurrence of preeclampsia.

MATERIALS AND METHODS

This was a case–control study carried out in the Department of Obstetrics and Gynecology, Government Kilpauk Medical College and Hospital, Chennai, Tamil Nadu, India, after obtaining approval from the Institutional Ethics Committee. A total of 60 age-matched pregnant women were enrolled for the study. Out of the 60 women, 30 normal healthy pregnant women formed the control group, while another 30 preeclamptic patients formed the case group. All the patients underwent detailed history taking and clinical examination.

BMI: Pre-pregnancy weight was self-reported during the first prenatal care visit. Calculation of BMI was done using Quetelet index formula, BMI was calculated as weight (kg) divided by the square of height (m), that is, BMI = Weight (kg)/Height (m^2). Measurement of height: Using stadiometer height was measured in all individuals in meters. Measurement of weight: Using standard spring type weighing scale, weight was measured in all subjects in kilograms.

Inclusion Criteria

Cases

Cases include

The following criteria were included in the study:

1. Pregnant women with BP ≥140/90 mmHg (previously normotensive women) on at least two occasions 6 h apart
2. Gestational age 28–40 weeks (sure of gestational age by last menstrual period or ultrasonography in the 1st or early 2nd trimester).

Controls

Controls include healthy pregnant normotensive women of gestational age of 28–40 weeks.

Exclusion Criteria

Subjects with the following diseases or disorders were excluded from the study: Chronic hypertension, gestational diabetes mellitus type 1 and 2 diabetes mellitus, connective tissue disorders, multiple pregnancy, liver diseases, severe anemia, smoking, obesity, and pregnancy with antiphospholipid syndrome.

OBSERVATION AND RESULTS

As shown in Table 1, among preeclamptic women, in the age group up to 25 years, there were 6 women and, above 26 years, there were 24 women. Among normotensive women, up to 25 years, there were 8 women and, above 26 years, there were 22 women. This is depicted in Figure 1. As shown in Table 2, Pearson Chi-square value 0.373, P = 0.542. Hence, maternal age is not statistically significant. Normotensive and preeclampsia subjects are, therefore, matched by maternal age.

As shown in Table 3, mean BMI for preeclamptic women is 24.7 and that of normotensive women is 21, this is depicted in Figure 2, t-test for equality for means 7.371, P = 0.000. Hence, BMI is statistically significant between two groups.

Table 1: Age matching of cases and controls

			PREECLAMPSIA		
			NO	YES	Total
AGE GROUP	UP TO 25 YEARS	Count	8	6	14
		% within PREECLAMPSIA	26.7%	20.0%	23.3%
		% of Total	13.3%	10.0%	23.3%
	26 YEARS & ABOVE	Count	22	24	46
		% within PREECLAMPSIA	73.3%	80.0%	76.7%
		% of Total	36.7%	40.0%	76.7%
	Total	Count	30	30	60
		% within PREECLAMPSIA	100.0%	100.0%	100.0%
		% of Total	50.0%	50.0%	100.0%

Table 2: Chi-square test – age matching

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.373[a]	1	.542		
Continuity Correction[b]	.093	1	.760		
Likelihood Ratio	.374	1	.541		
Fisher's Exact Test				.761	.381
Linear-by-Linear Association	.366	1	.545		
No of Valid Cases	60				

Table 3: Mean body mass index of cases and controls

PRE ECL AMP SIA	N	Mean	Std. Deviation	Std. Error Mean	P
PRE PREG BMI YES	30	24.713	2.4710	.4511	
NO	30	21.020	1.1941	.2180	0.000

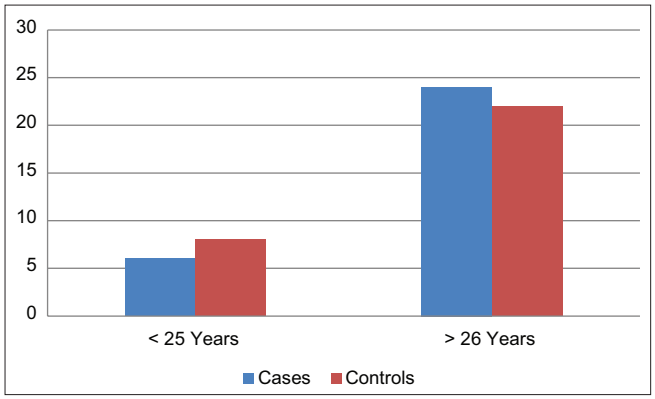

Figure 1: Age matching of cases and controls

As shown in Table 4 and in Figure 3, the area under the receiver operating characteristic curve is 0.918889, $P < 0.0001$. Hence, BMI is a statistically significant variable to predict preeclampsia.

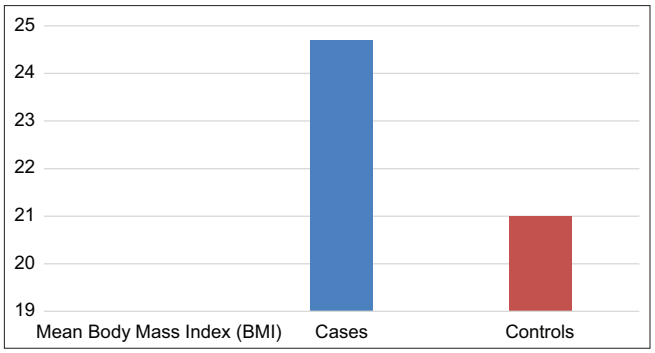

Figure 2: Mean body mass index of cases and controls

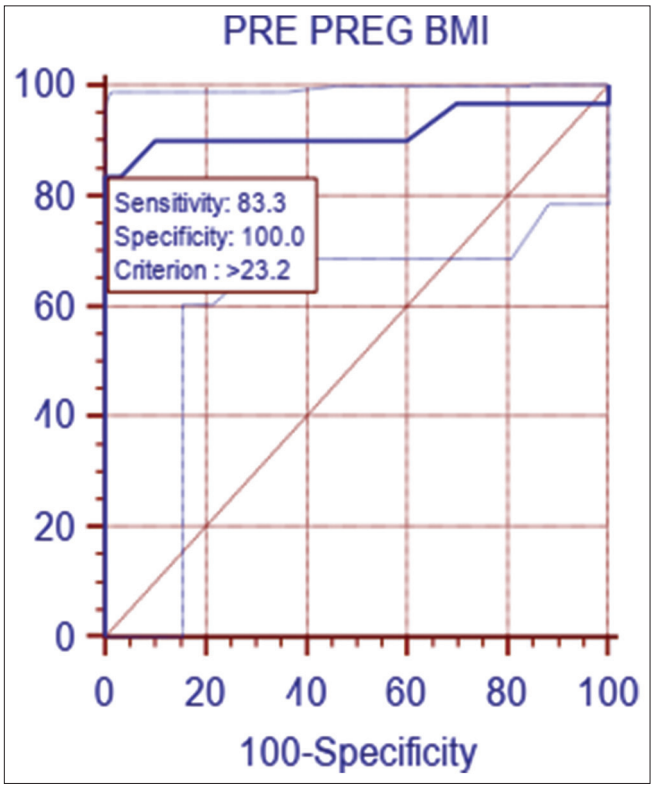

Figure 3: Receiver operating characteristic curve for mean body mass index in relation to preeclampsia

DISCUSSION

Obesity increases the risk of all "forms" of preeclampsia. Thus, the risk of severe and mild preeclampsia[18] and preeclampsia occurring in the early and late gestation[24] is greater in obese and overweight women. The relationship that obesity increases the risk of preeclampsia has been reported for several populations around the world indicating that this is not a phenomenon limited to western societies[25-27] It is also evident that this relationship is not limited to obese and overweight women, because increases in BMI in the normal range are also associated with an increased risk of preeclampsia.[10] The likelihood suggested by this, that fat mass is important, is supported by findings that weight loss reduces preeclampsia risk.[28,29]

Table 4: Area under the receiver operating characteristic curve

Variable	PRE_PREG_BMI PRE PREG BMI	
Classification variable	PREECLAMPSIA	
Sample size		60
Positive group :	PREECLAMPSIA = 1	30
Negative group :	PREECLAMPSIA = 0	30
Disease prevalence (%)	unknown	
Area under the ROC curve (AUC)		
Area under the ROC curve (AUC)	0.918889	
Standard Error[a]	0.0437	
95% Confidence interval[b]	0.819016 to 0.973660	
z statistic	9.588	
Significance level P (Area=0.5)	<0.0001	
Youden index		
Youden index J	0.8333	
Associated criterion	>23.2	

In our study, 60 patients were included after fulfilling the inclusion and exclusion criteria. Thirty patients had preeclampsia and 30 patients had normal pregnancy. The average gestational age of preeclamptic women was 36.03 weeks and normal pregnant was 35.70 weeks. There was no statistical difference in the gestational age in both the groups. In our study, we found out that BMI of normotensive pregnant individuals was 21 while that of preeclamptic women was 24.7. This difference is found to be statistically significant. Our findings were similar to a study done by Shao *et al.*[30] which also revealed that preeclampsia was more common in individuals with higher pre-pregnancy BMI.

A study done by AbdAllah *et al.*[31] also showed that the incidence of preeclamptic toxemia was higher in cases of raised levels of BMI which is similar to our findings that higher BMI had more risk of preeclampsia.

In a nationwide Swedish study by Sohlberg *et al.*,[32] similar to our findings, there was evidence to find an association between a high BMI and preeclampsia of all severities, but especially with the milder forms of preeclampsia. Nonetheless, the association between a high BMI and preeclampsia was established.

CONCLUSION

Our results were consistent with findings of many such previous studies. We conclude that higher pre-pregnant BMI, even though in the higher normal level, is a major risk factor for development of preeclampsia. Maintaining a lower normal pre-pregnant BMI would go a long way in preventing occurrence of preeclampsia. However, the sample size is small. Hence, our findings recommend an elaborate study with a large study population in the future.

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Original Article

Torch Infection among Females with Bad Obstetric History and its Association with Adverse Reproductive Outcomes in Current Pregnancy

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Abstract

Background: Maternal infections such as TORCH infections, syphilis, chlamydial infections, gonorrhea, and asymptomatic bacteriuria play a critical role in pregnancy wastage and their occurrence in patients with bad obstetric history (BOH) or a complicated pregnancy is a significant risk factor. At the same time, they contribute among the preventable factor. With immunoglobulin G antibody confirmed before pregnancy, there is no risk for a congenitally infected fetus. Congenital toxoplasmosis is suspected when sonography reveals findings such as hydrocephaly, intracranial, or hepatic calcifications, ascites, placental thickening, hyperechoic bowel, and growth restriction.

Objective: The aim of the study was to know the prevalence of TORCH infections in females with BOH and to find the association of TORCH infections with adverse pregnancy outcome.

Methods: Detailed clinical history, physical examination, and conventional laboratory investigations were conducted as per hospital protocol. History of any febrile illness or infections during previous pregnancies was also noted. All baseline investigations were done such as hemogram, kidney function test, liver function test, blood group, Rh type, coagulogram, urine analysis, blood sugar, thyroid stimulating hormone, triple serology, Venereal Disease Research Laboratory, antiphospholipid antibodies, antinuclear antibodies, anticardiolipin antibodies, Triple test, and TORCH test and was done in all patients included in the study. Ultrasonography obstetrics was done. ELISA is the most cost effective test to diagnose TORCH infections. 3–5 ml of blood sample was collected under aseptic precautions allowed to clot and centrifuged at 3000 rpm for 5 min.

Results: Out of 74 women studied, 63 were found to have TORCH infection of which 34 (54%) were aged between 31 and 35 years, 21 (33.3%) belonged to the age group of 36–40 years while only 8 (12.7%) women aged <30 years. History of the previous abortion was seen in 53 (84.1%) women with TORCH infection against 8 (72.7%) who did not have TORCH infection. The previous history of intrauterine death was observed in 10 (15.9%) women with torch infection against 1 (9.1%) women without any TORCH infection. The previous history of congenital anomaly was observed in 5 (7.9%) patients who had TORCH infection. The previous history of pre-term delivery was observed in 20 (31.7%) women with TORCH infection against only 3 (27.3%) who did not have any TORCH infection.

Conclusion: The present study demonstrates a strong association between the infectious agents (Toxoplasma, Rubella, and Cytomegalovirus) and BOH in women especially among young aged women.

Key words: Chlamydial infections, Gonorrhoea, Intrauterine death, Rubella, TORCH, Toxoplasma

INTRODUCTION

Pregnancy loss is a frustrating and challenging problem for couples and clinicians alike.[1] It is well realized that at least 12–15% of all recognized conceptions end in miscarriage and pre-clinical pregnancy loss rate is still higher - 22–30%.[2] The TORCH infections (Toxoplasmosis [TO], R- Rubella, C-Cytomegalovirus [CMV], and H-Herpes Simplex Virus [HSV]) can lead to severe fetal anomalies or even fetal loss. They are a group of viral, bacterial, and protozoan infections that gain access to the fetal bloodstream transplacental through the chorionic villi. Hematogenous transmission may occur at any time during gestation or occasionally at the time of delivery through maternal-to-fetal transfusion.[3] The ability of the

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fetus to resist infectious organisms is limited and the fetal immune system is unable to prevent the dissemination of infectious organisms to various tissues.[4] Early diagnosis and appropriate intervention will help in proper management of these cases.[5] The prevalence of TORCH infections varies from one geographical area to another.[6] In India, due to lack of national screening program, there are no baseline serological data regarding the presence of an antibody in TORCH infection during pregnancy.[7] Bad obstetric history (BOH) implies previous unfavorable fetal outcome in terms of two or more consecutive spontaneous abortion or history of intrauterine fetal death or intrauterine growth restriction or early neonatal deaths or congenital anomalies.[8,9]

Maternal infections such as TORCH infections, syphilis, chlamydial infections, gonorrhea, asymptomatic bacteriuria play a critical role in pregnancy wastage and their occurrence in patients with BOH or a complicated pregnancy is a significant risk factor. At the same time, they contribute among the preventable factor.[10,11] With immunoglobulin (Ig)G antibody confirmed before pregnancy, there is no risk for a congenitally infected fetus. The American College of Obstetricians and Gynecologists (2017) does not recommend prenatal screening for TO in areas of low prevalence, including the United States. Screening should be performed in immuno-compromised pregnant women, including those with HIV infection. In areas of high TO, the prevalence, for example, France and Austria-routine screening has resulted in diminished congenital disease.[12,13] Congenital *TO* is suspected when sonography reveals findings such as hydrocephaly, intracranial or hepatic calcifications, ascites, placental thickening, hyperechoic bowel, and growth restriction. Prenatal diagnosis of congenital TO is performed using PCR amplification of toxoplasma DNA in amniotic fluid.[14,15] The sensitivity of PCR varies with gestational age and is lowest before 18 weeks.[16]

CMV[17]

This DNA herpes virus eventually infects most humans. CMV is the most common perinatal infection in the developed world. There may be intrauterine or intrapartum infection or neonatal from breast feeding. Transplacental fetal infection is more likely during the first half of pregnancy. Maternal immunity does not prevent recurrences and maternal antibodies do not prevent fetal infection. Some seropositive women can also be reinfected with symptomatic congenital disease. Most infections are asymptomatic but 15% of infected adults have mononucleosis such as syndrome (fever, pharyngitis, lymphadenopathy, and polyarthritis). Immunocompromised women may develop myocarditis, pneumonitis, hepatitis, retinitis, gastroenteritis, or meningoenchephalitis.

HSV[18]

Two types of HSV have been distinguished based on immunological as well as clinical differences. Type 1 HSV accounts for the majority of non-genital herpetic infections, and Type 2 HSV is recovered almost exclusively from the genital the tract and is usually transmitted by sexual contact. More than half of the new cases of genital herpes in adolescents and young adults are now found to be caused by HSV-1 infection.[19] There is a large amount of DNA sequence homology between the two viruses, and prior infection with one type attenuates a primary infection with the other type. Approximately 70% of neonatal HSV cases are due to HSV-2 and 30% due to HSV-1.

Most primary and first-episode infections in early pregnancy are not associated with an increased rate of spontaneous abortion or stillbirth and there are no increased adverse fetal or neonatal effects after first trimester exposure. Late pregnancy primary infection results in an increased incidence of pre-term labor. Neonatal infection is acquired in three ways: Intrauterine (5%), peripartum (85%), or postnatal (10%).[20] The fetus becomes infected by virus shed from the cervix or lower genital tract. The virus either invades the uterus following membrane rupture or contacts the fetus at delivery.

Aims and Objectives

The objectives of the study are as follows:

1. To know the prevalence of TORCH infections in females with BOH
2. To know the specific TORCH infection that is more prevalent in Kashmiri women
3. To find the association of TORCH infections with adverse pregnancy outcome.

MATERIALS AND METHODS

The study entitled "Torch infection among females with BOH and its association with adverse reproductive outcomes in current pregnancy" was a prospective and cohort study that was conducted in the postgraduate Department of Gynaecology and Obstetrics, Lalla Ded hospital, Government Medical College, Srinagar, over a period of 1 ½ year after obtaining clearance from the Institutional ethical Committee and written informed consent from the patient.

Inclusion Criteria

Pregnant women with history of the previous unfavorable pregnancy outcome in terms of 2 or more consecutive spontaneous abortion, intra uterine fetal death, IUGR, congenital anomalies, in the age group of 19–36 years attending the antenatal clinic were taken for study.

Exclusion Criteria

Pregnant women with BOH of the same age group (19–36 years) attending the antenatal clinic with comorbidities which can contribute to BOH excluded, for example, (1) pregnancy-induced hypertension or chronic hypertension, (2) diabetes (Type 2 diabetes or gestational diabetes), (3) Rh incompatibility, (4) cervical incompetence, (5) antepartum hemorrhage (5a) placenta previa, (5b) abruptio placenta, and (6) syphilis.

Methodology

Detailed clinical history, physical examination, and conventional laboratory investigations were conducted as per hospital protocol. A preformed questionnaire was completed regarding parity of the patient, history of the previous abortions, gestational age at the time of abortions, history of IUGR or previous intrauterine death (IUD) or congenital malformations and type of congenital malformations or pre-term deliveries, mode of delivery and duration between pregnancies. History of any febrile illness or infections during previous pregnancies was also noted. All baseline investigations were done such as hemogram, kidney function test, liver function test, blood group, Rh type, coagulogram, urine analysis, blood sugar, thyroid stimulating hormone, triple serology, Venereal Disease Research Laboratory, antiphospholipid antibodies, antinuclear antibodies, anticardiolipin antibodies, triple test and TORCH test and was done in all patients included in the study. Ultrasonography obstetrics was done. Patients were followed till culmination of pregnancy which may be: Abortion, pre-term delivery, intrauterine death, still birth, or term delivery. Mode of delivery was noted in terms of vaginal delivery, instrumental delivery, or cesarean section and babies were followed in neonatal period. ELISA is the most cost-effective test to diagnose TORCH infections. 3–5 ml of blood sample was collected under aseptic precautions allowed to clot and centrifuged at 3000 rpm for 5 min. The serum samples were stored in small screw capped vials at 20°C. The samples were then tested for the presence of IgG and IgM antibodies against TO gondii, Rubella virus, CMV, and HSV using ELISA kits as per the kit instructions.

The recorded data were compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were express as Mean ± SD and categorical variables were summarized as frequencies and percentages. Graphically, the data were presented by bar and pie diagrams. Chi-square test or Fisher's exact, whichever appropriate, was employed for establishing association between various parameters. $P < 0.05$ was considered statistically significant. All *P*-values were two tailed.

RESULTS

In this study, a total of 74 patients were studied aged between 28 and 40 years. Majority of the patients, that is, 39 (52.7%) belonged to the age group of 31–35 years, 26 (35.1%) patients aged between 36 and 40 years, and 9 (12.2%) aged <30 years with a mean age of 34.5+3.12 years. Majority of the women were gravida 3 ($n = 36$), gravida 4 ($n = 18$), and >gravida 6 ($n = 11$) while 9 (12.2%) were gravida 5. History of the previous abortion was obtained from 63 (85.1%) women and the previous history of IUD in 11 (14.9%) the previous history of congenital anomaly in the baby were obtained from 5 (6.8%) women. Twenty-three (31.1%) women gave history of the previous pre-term delivery causing early neonatal death. Majority of women were found to have CMV, that is, 62 (83.8%) followed by rubella in 59 (79.7%), TO in 22 (29.7%) whereas herpes was observed in 5 (6.8%) patients. The prevalence of torch infection TO was observed in 4 (5.4%) patients with IgM positivity compared to 20 (27%) patients with IgG positivity. Rubella was observed in 4 (5.4%) women with IgM positivity against 58 (78.4%) women with IgG positivity. 7 (9.5%) women with CMV were positive for IgM against 61 (82.4%) women who were positive for IgG. Heperes was seen in 2 (2.7%) women with IgM positivity compared to 4 (5.4%) women with IgG positivity.

Out of 74 women studied, 63 were found to have torch infection of which 34 (54%) were aged between 31 and 35 years, 21 (33.3%) belonged to the age group of 36–40 years while only 8 (12.7%) women aged <30 years. When association of TORCH infection with age was observed, the difference was found to be statistically insignificant with p 0.733. Of the 63 women with torch infection, 29 (46%) were gravida 3, 16 (25.4%) were gravida 4, 10 (15.9%) were >gravida 6, and 8 (12.7%) women were gravida 5. The difference observed was statistically insignificant ($P = 0.756$). History of the previous abortion was seen in 53 (84.1%) women with TORCH infection against 8 (72.7%) who did not have TORCH infection. The previous history of IUD was observed in 10 (15.9%) women with torch infection against 1 (9.1%) women without any TORCH infection. The previous history of congenital anomaly was observed in 5 (7.9%) patients who had torch infection. The previous history of pre-term delivery was observed in 20 (31.7%) women with torch infection against only 3 (27.3%) who did not have any torch infection. Of the 74 studied women, term pregnancy was observed in 39 (52.7%) patients, 18 (24.3%) preterm, 10 (13.5%) had IUD, 5 (6.8%) had abortion while 2 (2.7%) delivered anomalous baby. Association of torch infection with pregnancy outcome was observed and found to be statistically significant with $P = 0.036$. Term pregnancy

Table 1: Age distribution of study patients

Patient characteristics	Number	Percentage
Age (years)		
≤30	9	12.2
31–35	39	52.7
36–40	26	35.1
Mean±SD (Range)=34.5±3.12 (28–40)		
Gravidity		
Gravida 3	36	48.6
Gravida 4	18	24.3
Gravida 5	9	12.2
≥Gravida 6	11	14.9
Obstetric history		
Previous history of abortion	63	85.1
Previous history of IUD	11	14.9
Previous history of congenital anomaly	5	6.8
Previous history of preterm delivery causing early neonatal death	23	31.1
TORCH infection		
Toxoplasmosis	22	29.7
Rubella	59	79.7
Cytomegalovirus	62	83.8
Herpes	5	6.8

IUD: Intrauterine death

Table 2: Prevalence of torch infections as per type of antibody among study patients

Type of torch infections	IgM		IgG	
	No.	% age	No.	% age
Toxoplasmosis	4	5.4	20	27.0
Rubella	4	5.4	58	78.4
Cytomegalovirus	7	9.5	61	82.4
Herpes	2	2.7	4	5.4

Table 3: Association of torch infections with age and gravidity in study patients

Patient characteristics	Torch infection		No torch infection		*P*-value
	No.	% age	No.	% age	
Age (years)					
≤30	8	12.7	1	9.1	0.733
31–35	34	54.0	5	45.5	
36–40	21	33.3	5	45.5	
Gravidity					
Gravida 3	29	46.0	7	63.6	0.756
Gravida 4	16	25.4	2	18.2	
Gravida 5	8	12.7	1	9.1	
≥Gravida 6	10	15.9	1	9.1	

was the outcome of 30 (47.6%) patients of TORCH infection, pre-term in 17 (27%) patients, IUD in 7 (14.3%) patients, abortion in 5 (7.9%) patients while as 2 (3.2%) with TORCH infection delivered anomalous baby. Of the 63 patients with TORCH infection, 30 (47.6%) had normal pregnancy outcome while of the 11 patients with no TORCH infection, 9 (81.8%) had normal pregnancy. The association between pregnancy outcome and TORCH infection was observed to statistically significant with *P* = 0.036. RR (95% CI) = 2.9 (0.804–10.32) [Tables 1-5].

Table 4: Association of torch infections with obstetric history

Obstetric history	Torch infection		No torch infection		*P*-value
	No.	% age	No.	% age	
Previous history of abortion					
Yes	53	84.1	8	72.7	0.359
No	10	15.9	3	27.3	
Previous history of IUD					
Yes	10	15.9	1	9.1	0.901
No	53	84.1	10	90.9	
Previous history of congenital anomaly					
Yes	5	7.9	0	0.0	0.752
No	58	92.1	11	100	
Previous history of preterm delivery					
Yes	20	31.7	3	27.3	0.767
No	43	68.3	8	72.7	

IUD: Intrauterine death

Table 5: Association of torch infections with pregnancy outcome

Pregnancy outcome	Torch infection		No torch infection		*P*-value
	No.	% age	No.	% age	
Normal	30	47.6	9	81.8	0.036*
Abnormal	33	52.4	2	18.2	
RR (95% CI)=2.9 (0.804–10.32)					
Term	30	47.6	9	81.8	
Preterm	17	27.0	1	9.1	
IUD	9	14.3	1	9.1	
Abortion	5	7.9	0	0.0	
Anomalous baby	2	3.2	0	0.0	

IUD: Intrauterine death, *Statistically Significant

DISCUSSION

History of the previous abortion was obtained from 63 (85.1%) women and the previous history of IUD in 11 (14.9%) and the previous history of congenital anomaly was obtained from 5 (6.8%) women. Twenty-three (31.1%) women gave history of previous preterm delivery causing early neonatal death. Singh M *et al*., (2016)[20] did a study on 260 pregnant women in in which still births (17.4% vs. 3.8%; *P*=0.006), congenital abnormalities (8.7% vs. 0.5%; *P*=0.002), and abortions (17.4% vs. 2.7%; *P*=0.001) were more common in those positive for IgM antibodies compared to seronegatives. The IgG seropositives also showed adverse effects of abortion (31.4%), IUD (7.0%) congenital malformations (3.5%), and still birth (1.2%) in 37 out of the 86 cases (Bhatia M and Harle S, 2013)[21].

In the present study, majority of women were found to have Cytomegalovirus, that is, 62 (83.8%) followed by Rubella

in 59 (79.7%), Toxoplasmosis in 22 (29.7%) while Herpes was observed in 5 (6.8%) patients. Manjunathachar HV *et al*., (2020)[22] found Rubella as the most prevalent infection (46.5%) followed by HSV 1 and 2 (41%), CMV (34.7%), and toxoplasmosis (6.3%). Tiwari S *et al*., (2016)[23] conducted a study on 63 women admitted in obstetrics and gynecology ward with abortion as adverse pregnancy event in current pregnancy. Evidence of TORCH infection was seen in 66.7% of women positive for serum IgM antibodies. Maximum percentage was for HSV infection (30.10%) followed by rubella (14.2%), CMV (12.6%), and toxoplasma (9.5%). In the present study, the prevalence of TORCH infection Toxoplasmosis was observed in 4 (5.4%) patients with IgM positivity compared to 20 (27%) patients with IgG positivity. Rubella was observed in 4 (5.4%) women with IgM positivity against 58 (78.4%) women with IgG positivity. Seven (9.5%) women with cytomegalovirus were positive for IgM against 61 (82.4%) women who were positive for IgG. Heperes was seen in 2 (2.7%) women with IgM positivity compared to 4 (5.4%) women with IgG positivity. In a study by Turbadkar D *et al*., (2003)[24], IgM antibodies were positive in 40 (10.52%) for Toxoplasma, 102 (26.8%) for Rubella, 32 (8.42%) for CMV. IgG antibodies were positive in 160 (42.10%) for Toxoplasma, 233 (61.3%) for Rubella, 346 (91.05%) for CMV. Based on the IgM positivity, Rubella is the most prevalent infection (46.5%) followed by HSV 1 and 2 (41%), CMV (34.7%), and TO (6.3%) in high-risk pregnant women having rash or any clinical signs. On the whole, the highest IgG seropositivity was recorded against CMV (88.6%), followed by Rubella (86.8%), HSV 1 and 2 (28.4%), and TO (15.2%) [Manjunathachar *et al*.,[22]

In India, the reported seroprevalence rate of TO is up to 80% (Nissapatorn *et al*., 2011;[25] Shrivastava *et al*., 2014).[26] In the present study, 15.2% and 6.3% pregnant women showed anti-toxoplasma IgG and IgM antibodies, respectively, whereas Shrivastava *et al*.[26] reported 9.37% and 29.68% toxoplasma IgG and IgM antibodies, respectively, in pregnant women from Indore, Madhya Pradesh. The seroprevalence of TO in different countries ranges between 7.7% and 76.7%.[25,27,28] The varying prevalence status between the geographical regions may be due to climate variability, hygiene and sanitization practices, and life standards of the people.[25-28] TO is a completely treatable infection in pregnancy with antibiotic therapy; hence, early antenatal detection and prompt treatment of infection may prevent the fetal complications. Out of 74 women studied, 63 were found to have TORCH infection of which 34 (54%) were aged between 31 and 35 years, 21 (33.3%) belonged to the age group of 36–40 years while only 8 (12.7%) women aged <30 years. When association of torch infection with age was observed, the difference was found to be statistically insignificant with $P = 0.733$. Tiwari *et al*.[23] conducted a study on 63 women admitted in obstetrics and gynecology ward with abortion as adverse pregnancy event in current pregnancy. When analyzed with respect to. age groups, in age group <20 years (18–20 years), toxoplasma IgM was found to be present in 5% suggestive of acute infection. In age group 21–25 years, toxoplasma IgM was 13.3% in age 26–30 years, IgM was 7.6%. Statistical analysis of the same has given the $P = 1.000$ (Fischer's exact test). It is a significant finding that the age group bears no relevance to IgM seropositivity if it is considered as evidence of infection responsible for adverse reproductive outcome. Similar findings have been reported by very few workers but one study by Mohammed *et al*.,[29] has very clearly shown that there is no relationship of IgM antibodies evidence in cases of abortion when TO is considered as an underlying cause 4. In an Indian study of Kaur *et al*.,[11] IgM antibodies were reported as 11.2% 5 while other studies across India, especially by Dar *et al*.[30] reported it in the range 0.7–3.1%.6 A relatively higher rate of resistance against the adverse effects of Toxoplasma infection appears to be due to improving environmental conditions and better personal habits, hygiene, and overall improving life styles of the people.

Tiwari *et al*.[23] conducted a study on 63 women. In age group <20 years, rubella IgM was found to be 5%, in 21–25 years age group, it was 20% while in age group 26–30 years, it was 15.3%. *P* value, in both the groups, is <0.05. It reflects that IgM serology status is very important as an evidence of primary Rubella infection in pregnancy. Primary Rubella infection has been reported as 4.5% by Yasodhra[31] while Surpam *et al*.[32] have reported IgM seropositivity 4.66%. Erstwhile, in Indian context, seropositivity has been reported in the range 4–17.7%. WHO estimates, across the globe, that more than 1 lakh children are born with congenital rubella syndrome each year, most of them in developing countries (Vijayalakshmi *et al*., 2004).[33] Nearly 10–20% women in child bearing age are susceptible to Rubella and primary Rubella virus infection during pregnancy may cause fetal damage. Tiwari *et al*.,[23] also observed that in the age group <20 years, IgM seropositivity was 10% in group 21–25 years, it was 20% in age group 26–30 years, none was positive for IgM. On statistical analysis, *P* value is border line insignificant (0.055). IgM Seropositivity has been reported to be in the range 3–12.9 (Hossain *et al*., 1986;[34] Seth *et al*., 1971[35]). Primary CMV infection in pregnancy has a higher incidence of symptomatic congenital infection and fetal loss (Turbadkar *et al*., 2003).[25] Demonstration of IgM antibodies is indicative of primary infection (Padmavathy *et al*., 2013).[36] The transmission of CMV infection to fetus occurs in 40% of the cases with primary infection and results in the delivery of 10–15% symptomatic and 85–90% asymptomatic congenital-infected newborns (Singh *et al*., 2009).[37]

CONCLUSION

TORCH series infection is one of the important causes of abnormal pregnancy outcomes. It is absolutely necessary to screen TORCH infection for women who had the histories of abnormal pregnancies to prevent birth defects and perinatal complications. TORCH testing being costly investigation cannot be done in all patient on antenatal care; therefore, selected patients with bad obstetric must be tested for TORCH. Knowledge of TORCH infection will help the clinician appropriately counsel mothers on preventive measures to avoid these infections and will aid in counseling parents on the potential for adverse fetal outcomes when these infections are present.

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Original Article

A Study of Sensorineural Hearing Loss in Patients with Chronic Suppurative Otitis Media

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Abstract

Introduction: Chronic suppurative otitis media (CSOM) is the most infectious disease that leads to hearing loss, mainly conductive type, but some studies have also found sensorineural component in such patients.

Aims and Objectives: The aim is to study the incidence of age, sex, nature of discharge, type of perforation in CSOM patients on development of sensorineural hearing loss (SNHL), and to determine the association between CSOM and SNHL.

Materials and Methods: The prospective study was carried out on 100 patients presented in Department of ENT, SMHS Hospital, Government Medical College, Srinagar, J and K from January 2018 to December 2018. The patients presented with complaints of recurrent ear discharge.

Results: In the present study, the incidence of SNHL was found in 19% of patients. Incidence of SNHL increases with age, that is, 36.84% in patients of age group 51–60 years developed SNHL. SNHL was also found to be predominant in males (51.21%) as compared to females (48.78%). In the present study, purulent ear discharge had more predisposition to develop SNHL.

Conclusion: There were relation and association between age, sex, nature of ear discharge, and type of disease in CSOM patients of SNHL.

Key words: Chronic suppurative otitis media, Ear discharge, Mixed hearing loss, Sensorineural hearing loss

INTRODUCTION

Chronic suppurative otitis media (CSOM) is the chronic inflammation of the middle ear fossa with discharge through perforated tympanic membrane.[1] CSOM leads to hearing loss. Hearing loss leads to impaired development of language and speech skills in case of children. Hearing loss may also cause poor quality of life in adults.[2,3] Chronic otitis media causes permanent perforation of drum membrane. CSOM is of two types: Suppurative otitis media and cholesteatoma.[4] It has been found that toxins in CSOM can cause damage to cochlea so it can also cause sensoneural hearing loss.[5] Hence, this study was planned to assess clinically the incidence with respect to sex of patient, duration of discharge and disease, and type of perforation on development of sensorineural hearing loss (SNHL) in CSOM patients.

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MATERIALS AND METHODS

The present study was carried out in outpatient department (OPD) of otorhinolaryngology (ENT) of SMHS Hospital, Government Medical College, Srinagar, J and K. It was a cross-sectional study and was carried out during the study period from January 2018 to December 2018. One hundred patients were selected during study period based on inclusion and exclusion criteria.

Inclusion Criteria

All CSOM patients with history of recurrent discharge from ear are the main inclusion criteria coming to ENT OPD and patients with tuning fork test, ABC decreased.

Exclusion Criteria

Patients in whom hearing loss could be attributed to reasons other than CSOM such as patients who are below 12 years

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are excluded to eliminate the possibility of inaccuracy of audiological testing because of non-cooperative attitude of children. Patients with age above 55 years were also excluded from the study because of high incidence of presbyacusis in this age group, history of previous ontological surgery, familial hearing loss, prolonged exposure to noise, and head trauma were excluded from the study.

History Taking and Examination

A proforma of ENT examination was filled for each patient and documented. Consent of all patients was taken for clinical examination and required investigation.

Special Investigation

Pure tone audiometry was performed by calibrated audiometer in a sound proof room. Pure tone air threshold (AC) and pure tone bone conduction threshold audiometry were done. The hearing of the patient was assessed by pure tone audiogram, type, and degree of hearing loss recorded.

OBSERVATION AND RESULTS

Age

In patients of age <20 years, SNHL is prevalent in 5.26%. The incidence of SNHL among patients of age group of 21–30 years was 10.52% whereas it was 15.78% in 31–40 years. However, it was found that the incidence was highest in age group of 41–56 and 51–60 years which was 31.57% and 36.84%, respectively [Table 1].

Sex

Among the total number of 100 patients, 50 were males and 50 were females. The incidence of SNHL in females was 44.44% where as in males, it was 55.55% [Table 2].

Nature of Ear Discharge

The SNHL in patients with mucoid ear discharge was 17.64%. Among the patients with mucopurulent ear discharge, SNHL was found in 35.29%. In patients with purulent discharge, SNHL was 47.05% [Table 3].

Type of Disease

Among 100 patients, in pars flaccida perforation, SNHL was 37.59% and in pars tensa perforation, SNHL was 62.59% [Table 4].

Table 1: Age distribution

Pure tone audiometry	Age group (year)					
	<20	21–30	31–40	41–50	51–60	Total
SNHL (%)	1 (5.26)	2 (10.52)	3 (15.78)	6 (31.57)	7 (36.84)	19 (100)
MHL	4	8	14	25	30	81
Total						100

MHL: Mixed hearing loss, SNHL: Sensorineural hearing loss

Table 2: Sex distribution

Pure tone audiometry	Sex		Total
	Male	Female	
SNHL (%)	10 (55.55)	8 (44.44)	18 (100)
MHL (%)	40 (48.78)	42 (51.22)	82 (100)
Total			100

MHL: Mixed hearing loss, SNHL: Sensorineural hearing loss

Table 3: Nature of discharge

Pure tone audiometry	Nature of discharge			Total
	Mucoid	Mucopurulent	Purulent	
SNHL (%)	3 (17.64)	6 (35.29)	8 (47.05)	17
MHL	22	36	25	83
Total				100

MHL: Mixed hearing loss, SNHL: Sensorineural hearing loss

Table 4: Type of disease

Pure tone audiometry type	Type of disease		Total
	Pars flaccida perforation	Pars tense perforation	
SNHL (%)	6 (37.5)	10 (62.5)	16
MHL	14	70	84
Total			100

MHL: Mixed hearing loss, SNHL: Sensorineural hearing loss

DISCUSSION

CSOM is one of the most common otological conditions encountered in ENT OPD. It is one of the major cause of conductive hearing loss.

In the present study, the incidence of SNHL in CSOM was highest in age group of 51–60 years (35.29%). There was increase of SNHL with age. In a study conducted by Azevedo *et al*.[6] and Vartiainen and Vartiainen,[7] there is also increase in incidence of SNHL in CSOM patients with older age.

In the present study, the distribution of SNHL in CSOM patients was 44.44% in females and 55.55% in males. In a study conducted by Mohsin *et al*.,[8] it was found that the SNHL was higher in males than females.

In our study, it was found that the purulent ear discharge is more prone to develop SNHL (47.05%) than mucopurulent (35.29%) and mucoid (17.64%). This result was not supported by studies of Levine *et al*.[9] and Mohsin *et al*.[8]

In the present study, patients with pars flaccida perforation developed less SNHL (37.59%) than patients with pars tensa perforation (62.59%). The results were supported by MacAndie and O'Reilly.[10]

CONCLUSION

There was increase in incidence of SNHL in CSOM patients. The risk of disease is more in patients with increasing age and the longer duration of disease. Early detection and management can limit SNHL in these patients. The risk of SNHL is more in patients with active stage disease with chronic otorrhea more in males. Hence, we can conclude that there is an association between CSOM and SNHL. Our study was done on small group of population so for better understanding the study should be carried out in large group of population.

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Original Article

Evaluation of Quality of Life, Pharmacoeconomics, and Cardiovascular Risk in patients of Type 2 Diabetes Mellitus: A Prospective and Observational Study

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Abstract

Background: Diabetes mellitus (DM) is a chronic, metabolic disorder characterized by elevated levels of blood glucose, negatively affecting multiple body organs and quality of life (QoL).

Objectives: The objectives of the study were to evaluate QoL and cardiovascular risk in patients of Type 2 diabetes using Modified Diabetes QoL (MDQoL17) questionnaire and United Kingdom Prospective Diabetes Study Risk Engine (UKPDS-RE) respectively, and to evaluate pharmacoeconomics in the same patients.

Materials and Methods: A prospective observational study was carried out for 18 months after approval from the Institutional Review Board. Patients of either sex, 18 years and above, attending the medicine outpatient department were included in the study.

Results: Out of 311 patients, 194 (62.38%) were male and 117 (37.62%) were female. The mean age was 58.31 ± 10.63 years. The mean MDQoL-17 scores (68.75 ± 15.65) showed the QoL to be moderately affected, with male patients having better QoL scores (73.04 ± 14.31) as compared to female patients (61. 65 ± 15.24). Average income for 3 months was ₹71,981.81 ± 67,145.00. Average total cost was ₹5876.15 ± 3139.81; average direct cost was ₹5600.93 ± 2944.56; and average indirect cost was ₹275.22 ± 195.25 for 3 months. Out of 311 total patients; 77 patients were eligible for UKPDS-RE. Among these 77 patients, 31 (40.26%) had <15% risk (low); 31 (40.26%) had ≥15 - <30% risk (medium); and 15 (19.48%) had highest risk for developing coronary heart disease (CHD) in next 10 years. Biguanide + sulfonylurea combination was found most commonly prescribed antidiabetic drug also least expensive and cost effective in QoL score >70. Male patient had higher risk of developing CHD compared to female. Patients who had habit of smoking, hemoglobin A1c >8%, and HDL cholesterol >40 mg/dl were at higher risk of developing CHD.

Conclusion: QoL is moderately affected in DM. It predisposes to cardiovascular disease. It adds to the economic burden of the patient.

Key words: MDQoL17, Pharmacoeconomics, Quality of life, Type 2 diabetes mellitus, UKPDS-RE

INTRODUCTION

Diabetes mellitus (DM) is a chronic, metabolic disease which is marked by elevated levels of blood glucose, which over time leads to significant damage of multiple organs such as the heart, blood vessels, eyes, kidneys, and nerves. The World Health Organization has projected that 300 million people would suffer from diabetes by the year 2025.

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The quality of life (QoL) assessment is essential because it is a powerful tool to predict an individual's capacity to manage the disease and maintain long-term health and well-being.[1] QoL collectively includes measurement of physical and psychological state; level of person's independence, social life, and personal belief. It is important to assess QoL in chronic conditions at regular intervals.[2]

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As diabetes is a lifelong condition, it is an expensive aliment for a large fraction of people in a developing country like India.[3] The diabetic health-care cost is increasing throughout the world. Pharmacoeconomic (PE) analysis is one means of minimizing this expenditure.

Assessment of cardiovascular risk in individuals with Type 2 DM (T2DM) is important because in these patients, there is a 2-fold increased risk for cardiovascular disease (CVD) and it is the principal cause of death in T2DM patients.[4]

MATERIALS AND METHODS

This prospective, observational study began after obtaining approval from the Institutional Review Board. It was carried out for a period of 18 months at a tertiary care teaching hospital.

Patients fulfilling the inclusion criteria such as those aged 18 years or older; of either gender; attending medicine outpatient department (OPD) and diagnosed with T2DM and willing to give their written informed consent were included in our study. Patients having Type 1 DM or gestational diabetes and those with major psychiatric disorders were excluded from the study. The demographic details, history of diabetes and comorbidity details and prescription details in terms of drugs prescribed, their dose route, and frequency were entered in the case record form.

QoL Assessment

All patients were subjected to Modified Diabetes QoL (MDQoL17) questionnaire. It contains 17 diabetic-specific questions and eight concepts for physical and social functioning, role limitations due to personal and emotional problems, psychological impact of disease, energy/fatigue, bodily pain, and general health perceptions. The score ranges between 0 and 100, 0 being the minimum and 100 being the maximum score. QoL score >70 indicates mildly affected QoL. QoL score between 50 and 70 indicates moderately affected QoL. Score <50 indicates severely affected QoL.[5,6]

PE Assessment

Cost of drugs was calculated from patient's original bills. The following PE parameters were evaluated. Costs calculated were in terms of Indian Rupees for a 3-month period.

Cost of illness

Cost of illness was calculated as direct and indirect cost.

Direct medical cost included cost of drugs, cost of investigations, and cost of treating complications due to DM. Non-medical direct cost included transportation cost. Indirect cost included loss of productivity in terms of hours and wage loss. The wage loss of the accompanying person was also considered. This was calculated by consulting the patient or his/her relative.

Cost minimization analysis (CMA)

Based on the calculation of cost of illness, CMA was done. Patients were categorized into one, two, three, four, and five drug regimens based on the number of antidiabetic drugs (ADDs) they received. Comparison was done within each category among regimens having the same outcome in terms of QoL scores.

Cost-effectiveness analysis

Cost of treatment and resulting effect (outcome in terms of QoL score) ratio was evaluated for this analysis. Average cost-effectiveness ratio (ACER) and incremental cost-effectiveness ratio (ICER) also calculated. ICER is a measure of willingness to pay value for outcome of interest. It helps policymakers for optimum resource allocation.

- ACER = Total Cost of treatment/Resulting effect (outcome) (QoL Score)
- ICER = Total Cost of treatment A - Total Cost of treatment B/Resulting effect of treatment, A (QoL Score) - Resulting effect of treatment B (QoL Score).

Cardiovascular Risk Assessment

Cardiovascular risk assessment for men and women was done by the United Kingdom Prospective Diabetes Study Risk Engine (UKPDS-RE) version 2 which was calculated based on age, sex, ethnicity, smoking status, presence or absence of atrial fibrillation, and levels of hemoglobin A1c (HbA1c), systolic blood pressure, total cholesterol, and HDL cholesterol levels. This Risk Engine calculates a 10-year cardiovascular risk as a percentage.[7]

The inclusion and exclusion criteria for the UKPDS analysis were followed by 2018 American Diabetes Association Standards of Diabetes Care.

The risk was interpreted as individuals having a risk of stroke and coronary heart disease (CHD). A value <15% was considered mild risk for stroke and CHD; values ≥15% and <30% were considered as medium risk for stroke and CHD; and a value of ≥30% was considered as a high risk for stroke and CHD.

Statistical analysis was carried out using Statistical Package for the Social Sciences (IBM® SPSS) Version 23 and Microsoft Excel 2016.

QoL was compared in mentioned sociodemographic parameters with unpaired *t*-test and one-way ANOVA test, with $P < 0.05$ being considered statistically significant. For PE analysis, patients were divided into different

categories based on numbers of ADD prescribed. The mean direct, indirect, and total cost of treatment were calculated for different categories for a 3-month period. Difference between different regimens was compared with Kruskal–Wallis test on application of *post hoc* test, with $P < 0.05$ considered statistically significant.

RESULTS

A total of 311 patients were enrolled in the study conforming to the inclusion criteria. Of the total 194 males, most belonged to 41–60 years age groups (34.08%). Of the total 117 females, most were in the 61–80 age range (19.29%). Age and gender distribution is shown in Table 1.

QoL Analysis

MDQoL-17 score of 311 patients was 68.75 ± 15.65 (Mean ± SD). The association between the QoL scores and various demographic characteristics is shown in Table 2.

Table 1: Age and gender distribution of patients

Age range (years)	Gender distribution		Total
	Male	Female	
	n (%)	*n* (%)	*n* (%)
21–40	11 (3.54)	2 (0.64)	13 (4.18)
41–60	106 (34.08)	52 (16.72)	158 (50.80)
61–80	75 (24.12)	60 (19.29)	135 (43.41)
≥81	2 (0.64)	3 (0.96)	5 (1.60)
Total	194 (62.38)	117 (37.62)	311
Mean±SD	57.2±10.77	60.16±10.16	58.31±10.63

Male patients had a better QoL score (73.04 ± 14.31) compared to female patients (61.65 ± 15.24). With increase in age, a decrease QoL score was observed. All covariate factors of patients and their respective QoL scores (Mean ± SD) with p value are described in Table 2.

Out of 311 patients; 158 (50.80%) patients had mean QoL score >70 indicating mildly affected QoL and 120 (38.59%) had mean QoL score between 50 and 70 indicating moderately affected QoL. Only 33 (10.61%) patients had QoL score < 50 (poor QoL) [Figure 1].

PE Analysis

About 24.12% of patients were retired or on pensions and 15.76% of female patients were housewives. The mean income for 3 months was ₹71,981.81 ± 67,145.00 (Mean ± SD). The total cost for 3 months was ₹5876.15 ± 3139.81 (Mean ± SD). About 5.22% of average income was the expenditure on diabetes health care per patient. Out of the total direct cost, the antidiabetic drug cost was ₹3215.52 ± 1682.60, concomitant drug cost was ₹1465.31 ± 848.81, laboratory expense was ₹668.09 ± 295.93, consultation charges were ₹50.31 ± 4, and transportation cost was ₹202 ± 113.22 for a period of 3 months. Direct and indirect costs are summarized in Table 3.

Patient Categories Based on the Number of ADD Prescribed

Out of the total 311 patients, 12 (3.86%) were prescribed a single ADD, majority of the patients 153 (49.20%) were prescribed combination of two ADD. Patients also received

Table 2: Association of QoL scores with various demographics characteristics of diabetic patients (Total, *n*=311)

Covariate factors	Number of patients (*n*)	QoL scores (Mean±SD)	*P*-values
Gender	Male (194)	73.04±14.31	*t*=6.635
	Female (117)	61. 65±15.24	**P*<0.01
Age	≤50 years (90)	77.64±14.04	*t*=6.844
	>50 years (221)	65.14±14.83	**P*<0.001
Duration of diabetes mellitus	≤10 years (225)	72.83±14.37	*t*=8.089
	>10 years (86)	58.44±13.10	**P*<0.001
Diabetic complications	Present (80)	58.03±12.00	*t*=8.663
	Absent (231)	73.76±14.62	**P*<0.001
Patients diabetic medication	Insulin (7)	5.46±13.81	*t*=50.888
	Oral ADD (209)	73.89±14.25	**P*<0.001
	Insulin+oral ADD (95)	58.84±11.78	
No. of diabetic medication	Up to 2 medicine (165)	73. 07±15.70	*t*=5.294
	>2 medicine (146)	64.24±13.43	**P*<001
BMI	<18.5 (1)	62.35	*t*=2.734
	18.5–24.9 (58)	66.45±14.90	P=0.0665
	25–29.9 (170)	70.65±14.61	
	≥30 (82)	66.52±17.86	
HbA1C	5.7–6.5 (27)	66.50±15.21	*t*=35.020
	6.6–8 (188)	73. 87±14.91	**P*<0.001
	>8 (96)	59.07±12.24	

Independent *t*-test, one-way ANOVA test applied and **P*<0.05 was considered statistically significant

three drugs, four drugs, and five drugs combinations of ADD, as summarized in Figure 2 and Table 4.

CMA and ACER

In single-drug regimens, the QoL scores in patients receiving metformin alone (MDQoL score 62.65 ± 7.80) and insulin alone (MDQoL score 45.46 ± 4.20) were not in the same range hence PE comparison could not be done.

Among the two ADD combinations, Biguanide + Sulfonylurea was found to be least expensive (₹2147.30 ± 544.15) and most cost effective in the MDQoL score range of >70. Biguanide + Insulin was found least expensive (₹3260.23 ± 578.25) most cost effective (56.64) in moderately affected QoL score range (MDQoL score between 50 and 70).

In three ADD combinations, Biguanide + Sulfonylurea +Acarbose was the least expensive (₹2882.09 ± 560.18) and more cost effective in MDQoL score 50–70 while Biguanide + Sulfonylurea + Thiazolidinedione was the least expensive (₹3147 ± 304.05) and most cost effective in MDQoL score range >70.

In four ADD combinations, Biguanide + Sulfonylurea + DPP4 Inhibitor + Acarbose was the least expensive (₹3955 ± 660.47) and most cost effective in MDQoL score range between 50 and 70.

In five ADD combinations, Biguanide + Sulfonylurea + DPP4 Inhibitor + Acarbose + Insulin was the least expensive (₹14314 ± 165.14) and most cost effective in MDQoL score range between 50 and 70.

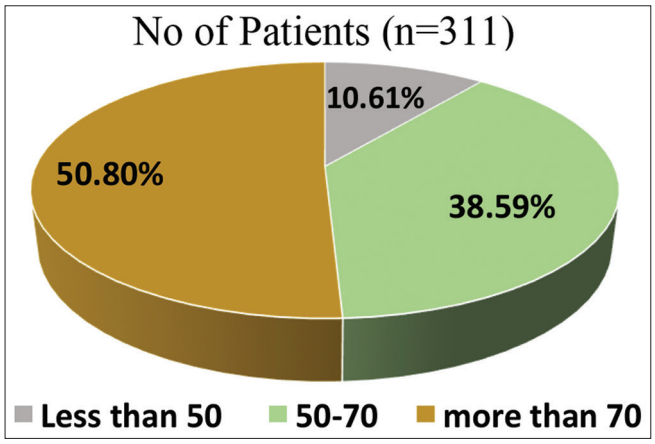

Figure 1: Assessment of QoL of diabetic patients based on MDQoL-17

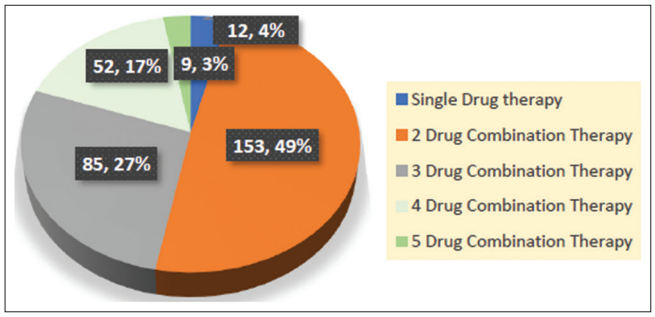

Figure 2: Percentage of patients receiving various ADD combinations

Table 3: Direct and indirect cost in ₹ for a 3-month period (*n*=311)

Direct cost	Indian rupees (Mean±SD)
Drug cost	3215.52±1682.60
Concomitant drug cost	1465.31±848.81
Investigation cost	668.09±295.93
Consultation cost	50.31±4.00
Transportation cost	202±113.22
Total	5600.93±2944.56
Indirect cost	**Indian rupees (Mean±SD)**
Wage loss of patient/ accompanying person	₹275.22±195.25
Time loss	5.34 h

ICER

In study of two ADD combination therapies, ICER was highest with Biguanide + DPP4I as compared to other two drug regimens in the same QoL score range.

In study of three ADD combination therapies for regimen, ICER was found to be the highest in Biguanide + Sulfonylurea + Acarbose as compared to other three drug combinations in the MDQoL score range 50–70. ICER was found to be highest with regimen of Biguanide + Sulfonylurea + Thiazolidinedione as compared to other three-drug regimens in the MDQoL score range >70.

In study of four antidiabetic drugs combination therapy, ICER was highest with Biguanide + Sulfonylurea+ Thiazolidinedione + Insulin as compared to other four-drug regimens.

In study of five antidiabetic drugs combination therapy, ICER was highest Biguanide + Sulfonylurea + DPP4I + Acarbose + Insulin as compared to the second five-drug regimen.

Cardiovascular Risk Assessment

Out of the total 311 patients, only 77 patients were eligible for cardiovascular risk assessment by the UKPDS risk engine based on the inclusion and exclusion criteria of this engine. Hence, the data of these 77 patients were entered in the UKPDS software for assessment. Of these 77 patients, 51 (66.23%) were male and 26 (33.77%) were female. The mean age of the patients was 58.38 ± 10.42 years.

Table 4: Drug regimens prescribed in various categories

Parameters	Parameters
Single-drug regimens:	Four-drug regimens:
• Biguanide	• Biguanide+Sulfonylurea+Dpp4i+Acarbose
• Insulin	• Biguanide+Sulfonylurea+Dpp4i+Thiazolidinedione
Two-drug regimens:	• Biguanide+Sulfonylurea+Acarbose+Insulin
• Biguanide+Sulfonylurea	• Biguanide+Sulfonylurea+DPP4I+Insulin
• Biguanide+DPP4I	• Biguanide+Sulfonylurea+Thiazolidinedione+Insulin
• Biguanide+Acarbose	• Biguanide+DPP4I+Acarbose+Insulin
• Biguanide+Thiazolidinedione	Five drug regimens:
• Biguanide+Insulin	• Biguanide+Sulfonylurea+DPP4I+Acarbose+Insulin
• Acarbose+Insulin	• Biguanide+Sulfonylurea+DPP4I+Thiazolidinedione+Insulin
Three-drug regimens:	
• Biguanide+Sulfonylurea+Acarbose	
• Biguanide+Sulfonylurea+DPP4I	
• Biguanide+DPP4I+Acarbose	
• Biguanide+DPP4I+Thiazolidinedione	
• Biguanide+Sulfonylurea+Thiazolidinedione	
• Biguanide+Sulfonylurea+Insulin	
• Biguanide+DPP4I+Insulin	

DPP4I: Dipeptidyl peptidase IV inhibitor

Of these 77 patients; 31 (40.26%) patients had low (<15%), another 31 (40.26%) patients had medium (≥15-<30%), and 15 (19.48%) patients had high risk for developing CHD.

Of the same 77 patients; 61 (79.22%) patients had low (<15%); 9 (7.79%) patients had medium (≥15–<30%); and 10 (12.99%) patients had high risk for developing stroke.

The risk of CHD in relation to the various parameters such as age, sex, duration of disease, coexistence of hypertension, HbA1c levels, BMI, HDL cholesterol, and smoking is given in Table 5.

DISCUSSION

In our literature search, we found that very few studies had been carried out in our country evaluating PE s in T2DM. This prompted us to evaluate PEs in T2DM. QoL is also an important aspect of diabetic care and CHD is commonly associated with diabetes; hence, we decided to study these aspects as well. Although diet and exercise along with lifestyle modifications remain the mainstay of diabetes management, regular treatment with the proper antidiabetic medication is essential to delay the anticipated long-term complications of this disease.

A total of 311 patients diagnosed with T2DM were enrolled in the study. We found middle-aged patients, in the age range 41–60 years to be more affected by T2DM. The mean age of patients in our study was 58.31 ± 10.63 years. This is similar to studies done by Singh *et al*., Adibe *et al*., and John *et al*. who reported the mean age of 54.96 ± 0.57, 54.3 ± 13, and 51±10.12 years, respectively.[8-10]

Table 5: Distribution of UKPDS score for coronary heart disease with various demographics characteristics of diabetic patients (*n*=77)

Covariate factor	UKPDS risk score for coronary heart disease		
	Low risk <15%, *n* (%)	Medium risk ≥15-<30%, *n* (%)	High risk ≥30%, *n* (%)
Gender			
Male (51)	20 (39.21)	19 (37.25)	12 (23.53)
Female (26)	11 (42.31)	12 (46.13)	3 (11.54)
Age			
≤50 years (21)	20 (95.24)	1 (4.76)	-
>50 years (56)	11 (19.64)	27 (48.21)	18 (32.14)
Duration of DM			
≤10 years (55)	28 (50.90)	20 (36.36)	7 (12.72)
>10 years (22)	2 (9.09)	12 (54.54)	8 (36.36)
Hypertension			
Present (55)	16 (29.09)	26 (47.27)	13 (23.64)
Absent (22)	15 (68.18)	5 (22.73)	2 (9.09)
Smoking			
Yes (65)	25 (38.46)	27 (41.53)	13 (20)
No (12)	7 (58.33)	3 (25)	2 (16.66)
HbA1c			
≤8 mg% (39)	22 (56.41)	15 (38.46)	2 (5.13)
>8 mg% (38)	9 (23.68)	16 (42.10)	13 (34.21)
HDL cholesterol			
≤40 mg/dl (24)	6 (25)	13 (54.16)	4 (16.67)
>40 mg/dl (53)	25 (47.16)	8 (15.38)	19 (35.85)

QoL

As diabetes is a chronic progressive disease, it has a negative impact on patients' QoL. In our study, we found the overall QoL to be moderately affected (68.75 ± 15.65). In 158 (50.80%), it was mildly affected, in 120 (38.59%), it was moderately affected, and in 33 (10.61%), it was severely affected. A study done by Gautam *et al*. (2009), assessed QoL using Short-Form 36 also showed that diabetes had an adverse effect on the QoL.[11]

We evaluated the QoL in relation to various factors such as age, gender, duration of disease, presence or absence of diabetic complications, number and type of antidiabetic medications, BMI, and HbA1c. We observed that with increasing age, in female sex, with duration of disease >10 years, the presence of diabetic complications, and a higher value of HbA1c and with greater number of antidiabetic medications, there was a significantly greater negative impact on QoL ($P < 0.05$). Diabetes being a chronic progressive condition, drugs do not halt the disease progress so it is logical to assume that in a patient with long-standing disease and poor control of diabetes reflected in higher HbA1c levels, there would be a greater negative impact on the QoL. Furthermore, patients receiving greater number of antidiabetic medications are assumed to have more severe disease as compared to patients receiving lesser number of antidiabetic medications, so their QoL is more significantly affected. In case of patients on a single medication, we had patients on biguanide alone and insulin alone. The QoL in patients on metformin alone was significantly better than those on insulin alone. It is logical to assume that patients on metformin alone would have a mild disease and those on only insulin would have a severe form of the disease hence the difference in QoL. However, it is not clear why the QoL should be significantly more affected in the female sex as compared to the male sex as we found in our study. Similar observations in relation to age, duration of disease, and presence of diabetic complications and QoL scores were seen in studies done by Ali *et al*., Glasgow *et al*., and Prajapati *et al*.[6,12,13]

PE Analysis

India is home to the second highest number of adults living with diabetes worldwide, after China. However, India spends less than 3% of the global total ($23 billion) cost on diabetes.[14]

In the present study, the cost calculation was done for an average period of 3 months. The reason behind 3-month cost calculation was that patients were called for follow-up every 3 months and reported earlier only if they faced any health issue related to DM.

In our study, 24.12% of patients were retired/pensioner and 15.76% of female patients were housewives. The total cost of treatment was ₹5876.15 ± 3139.81. Total direct cost was found to be ₹5600.93 ± 3944.56. Bifurcating the total direct cost, we observed that the antidiabetic drug cost was ₹3215.52 ± 1682.60, concomitant drug cost was ₹1465.31 ± 848.81, laboratory expense was ₹668.09 ± 295.93, consultation charges were ₹50.31 ± 4, and transportation cost was ₹202 ± 113.22 of 3 months. Indirect cost was ₹275.22±195; found including wage loss of patient and/or accompanying person and time loss was 5.34 h of 3 months. We found one Indian study on PEs of T2DM done by Bagle *et al*.[15] This study showed annual direct medical cost as ₹26,522.76 and indirect medical cost as ₹5838.51. If we extrapolate our 3 monthly direct cost to 1 year, it is slightly less as compared to this study. While all other expenses like laboratory charges, consultation charges, transportation charges were higher compared to our study.[15]

As a single ADD prescribed metformin was found to be least expensive and most cost effective which was seen in study by Gayathri *et al*.[16]

In 49.20% of T2DM patients prescribed two ADD combination therapies, we observed that Biguanide + Sulfonylurea combination was least expensive (₹2147.30 ± 544.15) and most cost effective in QoL score range of >70. In a study done by Gayathri *et al*. on PE evaluation of T2DM, it was observed that a combination of Biguanide + Thiazolidinedione in two ADD combinations was associated with lowest annual cost.[16]

We observed that in three ADD combination, Biguanide + Sulfonylurea +Acarbose combination was least expensive (₹ 2882.09 ± 560.18) and most cost effective on application of ACER and ICER in moderately affected QoL range (50–70) while Biguanide + Sulfonylurea + Thiazolidinedione among score ranges >70.

In four ADD combinations, Biguanide + Sulfonylurea + DPP4I +Acarbose combination was found to be most cost effective in our study, while Biguanide + Sulfonylurea + Acarbose + Insulin regimen was also found to be most cost effective in four ADD combinations in study by Gayathri *et al*.[16] In our study of five ADD combination therapies, incremental ICER was found to be highest in Biguanide + Sulfonylurea + DPP4I + Acarbose + Insulin.

Cardiovascular Risk Analysis

The UKPDS-RE is a risk model used only for diabetes patients. The UKPDS-RE version 2.0 was used to identify T2DM persons at increased risk for stroke and coronary events.

In our study out of the 77 patients who were assessed for cardiovascular risk, 15 (19.48%) patients were identified having a high 10-year risk for CHD and 10 (12.99%) patients were identified having a high risk for stroke. We found one Indian study done by Shivakumar *et al*. done to evaluate the long-term cardiovascular events using UKPDS risk engine in metabolic syndrome. They enrolled 567 patients and there was absolute risk of 3.79% (95% confidence interval) for CHD and 7.91% risk for stroke for 10 years.[17]

In a study by Seon *et al*., the 10-year CHD risk and 10-year stroke risk were 14.92% and 4.03%, respectively, using the UKPDS-RE. The 10-year CHD risk was similar to our study while stroke risk was found higher in our study.[18]

Ethnicity is an important factor in the assessment of cardiovascular risk. Cardiovascular risk assessment in one ethnic population cannot be extrapolated to other ethnic populations.[19] We came across one Indian study done in Chennai where age, hypertension, duration of diabetes, HbA1c levels, and smoking all these parameters were significantly associated with cardiovascular risk.[20] Although direct comparison of our study with this study was difficult because the sample size of this study as compared to ours was very large; we also observed an increase in cardiovascular risk with increase in age, duration of disease, smoking, HbA1c levels, and presence of hypertension in our study.

Limitation

As this was a single-point contact study and patients were called for OPD visit every 3 months, we have evaluated PE s in terms of 3 months. Extrapolating this 3-month data to 1 year would have affected the accuracy of results. Out of 311 patients, only 77 patients were eligible for evaluation of risk; hence, the sample size for cardiovascular risk assessment was small.

CONCLUSION

QoL measure gives a more direct measure of the impact of diabetes on daily life and is particularly relevant in physical functioning, role limitations due to physical health, social functioning, and overall general health.

QoL is moderately affected in DM. It predisposes to CVD. It also impacts the economic burden of the patient. To reduce it, we can promote manufacturing of good quality cheaper antidiabetic generic drugs.

Patient education and lifestyle measures are extremely important in the management of this condition.

Our study is a small step in the evaluation of PEs of DM which is very relevant in the current times considering the prevalence of the disease. Assessment of cardiovascular risk is also relevant as majority of patients of DM die due to cardiovascular complications.

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ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

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Original Article

Fetomaternal Outcome in Viral Hepatitis in Pregnancy – A Tertiary Care Hospital-based Study

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Abstract

Background: The most common viral agents causing hepatitis in pregnancy are hepatitis A virus, hepatitis B virus, hepatitis C (non-A and non-B hepatitis virus), hepatitis E, hepatitis G, and Epstein-Barr virus. Delta agent hepatitis has also received increasing attention as a cause of hepatitis. Various authors have reported findings ranging from no difference in fetal/maternal outcome to nearly universal fatality. Interestingly, these different types of outcome are peculiar to certain geographical areas. Jaundice complicates 3–5% of pregnancies and is one of the important causes of maternal and neonatal morbidity and mortality worldwide. It is responsible for 10% of maternal deaths.

Objective: The aim of the study was to study the maternal and fetal outcome in viral hepatitis in pregnancy.

Materials and Methods: After admission, all patients had a thorough history and clinical examination. The period of gestation was calculated on the basis of last menstrual period and early ultrasound which ever was available. The blood sample was collected and was sent for biochemical studies for liver function test, coagulation profile, and serological tests for Immunoglobulin (Ig)M anti-hepatitis A virus, Hepatitis B surface antigen, IgM anti-Hepatitis E virus, and IgM anti-hepatitis C virus using commercially available ELISA kits.

Results: Indications for caesarean section were acute fetal distress in 23 (54.8%) and the other indications included oligohydramnios, color Doppler changes, cephalopelvic disproportion, non-progression of labor, intra uterine growth restriction, macrosomia, and malpresentation were seen in 6 (14.3%), 3 (7.1%), 3 (7.1%), 2 (4.8%), 2 (4.8%), 2 (4.8%), and 1 (2.4%) women, respectively. Thrombocytopenia was observed in 14 (3.33%) women and postpartum hemorrhage and hypoglycemia in 3 (7.1%) patients each. Normal birth weight was observed in 65 (97%) patients while as 2 (3%) babies were overweight. The mean birth weight was 2.73 ± 1.26 kg. There were 42 (62.7%) patients with 1 min Apgar >7 compared to 49 (73.1%) at 5 min Apgar score >7 days. Fetal outcomes such as NICU admission were observed in 16 (38.1%) NICU admission, low birth weight in 7 (16.7%), and 2 (4.8%) intrauterine deaths.

Conclusion: In the case of women with very high viremia, a non-negligible proportion of newborns can acquire the infection (probably through in utero transmission) despite the use of passive/active prophylaxis. For this reason, antiviral treatment in the third trimester can be considered for those women. The choice of antiviral should be restricted to those drugs considered safe in this setting.

Key words: Hepatitis, Macrosomia, Oligohydramnios, Thrombocytopenia

INTRODUCTION

Pregnancy is a physiological phenomenon for most women. During pregnancy, there is a progressive anatomical, physiological, and biochemical change not only confined to the genital organs but also to all the systems of the body. This is principally a phenomenon of maternal adaptation to the increasing demands of the growing fetus. However, pregnancy can be met by various comorbidities and complications, infections being one of them.[1] Six different forms of viral hepatitis have now been defined. Each type of viral hepatitis has its own concerns. The most common viral agents causing hepatitis in pregnancy are hepatitis A virus, hepatitis B virus (HBV), hepatitis C (non-A and non-B hepatitis virus), hepatitis E, hepatitis G, and Epstein-Barr virus. Delta agent hepatitis has also received increasing attention as a cause of hepatitis.

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Viral hepatitis in pregnancy has incited a lot of debate and discussion all throughout the world. Various authors[2,3] have reported findings ranging from no difference in fetal/maternal outcome to nearly universal fatality. Interestingly, these different types of outcome are peculiar to certain geographical areas. For example, there was no increased maternal mortality due to Hepatitis E infection in pregnancy in the reports from South India[4] and Egypt,[5] but a significantly higher rate of mortality has been reported from North India.[6] This is despite the fact that all these geographical areas are endemic for hepatitis E infection.[7] Viral hepatitis is the most common cause of jaundice in pregnancy. Jaundice is defined as a clinical manifestation of hyperbilirubinemia which consists of deposition of bile pigments in the skin, resulting in yellowish staining of the skin and mucous membrane. Normal serum bilirubin level is <1 mg/dl. Clinical jaundice is manifested if serum bilirubin level >2 mg/dl. Jaundice complicates 3–5% of pregnancies and is one of the important causes of maternal and neonatal morbidity and mortality worldwide. It is responsible for 10% of maternal deaths.[8]

Acute hepatitis A is self-limiting disease. Its prognosis in pregnancy is same as that in non-pregnant patient.

Hepatitis B[9]

Hepatitis B is caused by a small DNA virus. The intact virus is termed the Dane particle. Hepatitis B surface antigen (HBsAg) is present on the surface of the virus and also circulates freely in the serum in spherical and filamentous forms. The middle portion of the Dane particle contains hepatitis B core antigen (HBcAg). The core antigen is present in hepatocytes and does not circulate in the serum. Hepatitis B e antigen (HBeAg) is encoded by the same portion of the viral genome that codes for the core antigen. The presence of HBeAg indicates an extremely high viral inoculum and active virus replication. The incubation period of hepatitis B is 6 weeks to 6 months. Hepatitis B is transmitted by parenteral and sexual contact.

Hepatitis C[9]

Hepatitis C virus (HCV) (previously termed non-A and non-B hepatitis) is a single-stranded RNA. The principal risk factor for acquiring HCV is the same as for hepatitis B. Specific tests: it is confirmed by identifying the antibody to HCV. Hepatitis C viral RNA can be detected by polymerase chain reaction assay of serum soon after infection as well as in chronic disease.

Hepatitis D[9]

Hepatitis D requires HBV for replication and expression and so occurs only in people already infected with hepatitis B. In acute hepatitis B, once HBsAg clears the bloodstream, so does hepatitis D. Vertical transmission of hepatitis D virus has been documented. Transmission is uncommon, however, because the measures used to prevent perinatal infection with HBV are almost uniformly effective in preventing infection by hepatitis D.

Hepatitis E[9]

Hepatitis E infection during pregnancy and in the third trimester is associated with more severe infection and might lead to fulminant hepatic failure and maternal death. In outbreaks of waterborne hepatitis E in India and Asia, the case-fatality rate is 1–2% and up to 10–20% in pregnant women. Mortality rates among pregnant women, especially those infected in the third trimester, have ranged between 15% and 25%, much higher that men and non-pregnant women. It has got high incidence of abortion, fetal death, and still birth.[10]

Hepatitis G[9]

Hepatitis G infection is more likely in people already infected with hepatitis B or C or who have a history of intravenous drug use and HIV. Vertical transmission is high and hepatitis G probably does not cause chronic active hepatitis or cirrhosis.

Aims and Objectives

The aim of the study was to study the maternal and fetal outcome in viral hepatitis in pregnancy.

MATERIALS AND METHODS

The study entitled viral hepatitis in pregnancy – Study of its effect on maternal and fetal outcome was a prospective and observational study conducted in the Postgraduate Department of Gynecology and Obstetrics, Lalla Ded Hospital, Government Medical College Srinagar over a period of one and a half year after obtaining clearance from the Institutional Ethical Committee and written informed consent from the patient.

Inclusion Criteria

All pregnant women with positive serology for viral hepatitis at any gestational age and those who are willing to participate were enrolled in the study.

Exclusion Criteria

Patients with chronic liver disease, jaundice with negative serology, HELLP syndrome, acute fatty liver, intra hepatic cholestasis, drug-induced jaundice, pregnancy with hypertension, pregnancy with diabetes, multiple pregnancy, antepartum hemorrhage, and previous cesarean section(s) were excluded from the study.

Methodology

After admission, all patients had a thorough history and clinical examination. The period of gestation was calculated on the basis of last menstrual period and early

Table 1: Various parameters

Patient characteristics	Number	Percentage
Age in years		
25–29	36	53.7
30–34	23	34.3
≥35	8	11.9
Total	67	100
Mean±SD (Range)=30.3±3.64 (26-45)		
Gravidity		
Primigravida	20	29.9
Gravida 2	26	38.8
Gravida 3	13	19.4
≥Gravida 4	8	11.9
Icterus		
Present	10	14.9
Absent	57	85.1
Edema		
Present	8	11.9
Absent	59	88.1
Icterus liver span		
Present	5	7.5
Absent	62	92.5
Status of Liver Function		
Normal	47	70.1
Deranged	20	29.9
Hepatitis Serology		
Hepatitis B	33	49.3
Hepatitis C	32	47.8
Hepatitis A	1	1.5
Hepatitis E	1	1.5
Liver morphology on USG		
Hepatomegaly	4	6.0
Liver atrophy	2	3.0
Normal hepatobiliary system	61	91.0
Gestational age at delivery		
<37 Weeks	12	17.9
≥37 Weeks	55	82.1
Mean±SD=37.2±1.87		
Mode of delivery		
Normal delivery	25	37.3
Cesarean section	42	62.7

Table 2: Indications for cesarean section, maternal, and fetal complications

Patient characteristics	Number	Percentage
Indications for LSCS		
Acute fetal distress	23	54.8
Oligohydramnios	6	14.3
Color Doppler changes	3	7.1
Cephalopelvic disproportion	3	7.1
Non-progression of labor	2	4.8
Intra uterine growth restriction	2	4.8
Macrosomia	2	4.8
Malpresentation	1	2.4
Maternal complications		
Thrombocytopenia	14	33.3
Postpartum hemorrhage	3	7.1
Hypoglycemia	3	7.1
Birth weight (kg)		
<2.5 Kg	7	10.4
2.5–3.5 Kg	58	86.6
>3.5 Kg	2	3.0
Fetal complications		
Low birth weight	7	16.7
NICU admission	16	38.1
Intra-uterine Death	2	4.8

Table 3: Apgar score at 1 and 5 min among study neonates

Apgar score	Number	Percentage
1 Min		
<7	25	37.3
≥7	42	62.7
5 Min		
<7	18	26.9
≥7	49	73.1

ultrasound which ever was available. The blood sample was collected and was sent for biochemical studies for liver function test, coagulation profile, and serological tests for Immunoglobulin (Ig)M anti-HAV, HBs antigen, IgM anti-HEV, and IgM anti-HCV using commercially available ELISA kits. The recorded data were compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean ± SD and categorical variables were summarized as frequencies and percentages. Graphically, the data were presented by bar and pie diagrams.

RESULTS

In our study, patient's age in our study ranged between 26 and 45 years with a mean age of 30.3 ± 3.64. Majority of patients age ranged between 25 and 29 years 53.7% (*n* = 36). 26 (38.8%) in our study were gravida 2 followed by 20 (29.9%) primigravida, 13 (19.4%) were gravida 3, and 8 (11.9%) were >gravida 4. Icterus was observed in 10 (14.9%) at presentation. Edema at presentation was observed in 8 (11.9%) patient. Increased liver span was seen in 5 (7.5%) patients. Liver function test was deranged in 20 (29.9%) patients in our study. There were 33 (49.3%) hepatitis B, 32 (47.8%) hepatitis C patients while 1 (1.5%) each had hepatitis A and hepatitis E. On ultrasonography, 61 (91%) patients had normal hepatobiliary system, in 4 (6%) patients findings were suggestive of hepatomegaly while 2 (3%) had liver atrophy. Gestational age at delivery was >37 weeks in majority of patients, that is, 55 (82.1%) while <37 weeks gestation was seen in 12 (17.9%) patients. Majority of women delivered through cesarean section, that is, 42 (62.7%) while normal delivery was seen in 25 (37.3%) patients.

Indications for cesarean section were acute fetal distress in 23 (54.8%) and the other indications included oligohydramnios, color Doppler changes, cephalopelvic disproportion, non-progression of labor, intra uterine growth

restriction, macrosomia, and malpresentation were seen in 6 (14.3%), 3 (7.1%), 3 (7.1%), 2 (4.8%), 2 (4.8%), 2 (4.8%), and 1 (2.4%) women, respectively. Thrombocytopenia was observed in 14 (3.33%) women and postpartum hemorrhage and hypoglycemia in 3 (7.1%) patients each. Normal birth weight was observed in 65 (97%) patients while as 2 (3%) babies were overweight. The mean birth weight was 2.73 ± 1.26 kg. There were 42 (62.7%) patients with 1 min Apgar >7 compared to 49 (73.1%) at 5 min Apgar score >7 days. Fetal outcomes such as NICU admission were observed in 16 (38.1%) NICU admission, low birth weight in 7 (16.7%), and 2 (4.8%) intra-uterine deaths [Tables 1-3].

DISCUSSION

Acute viral hepatitis is the most common form of liver disease worldwide and it frequently affects women of childbearing age, either as an acute infection or as a chronic disease.[11] It is still a major public health concern of developing countries such as India, despite improving socioeconomic condition, sanitation, and health awareness.[12] HEV infection occurring in young adults is a known phenomenon with a predisposition to pregnant women.[13] A total of 67 pregnant females were included in this study with serology positive for viral hepatitis. Patient's age in our study ranged between 26 and 45 years with a mean age of 30.3 ± 3.64. Majority of patients age ranged between 25 and 29 years 53.7% (n = 36). Similar age group was affected (25–29 years) in a study conducted by Chandni *et al*., (2021).[14] Same age group was reported by Jethwa *et al*. (2016)[11] (46%) and by Terrault NA *et al*. (2017)[15] (50.7%) in their respective studies. In our study, 26 (38.8%) patients were gravida 2 followed by 20 (29.9%) primigravida, 13 (19.4%) were gravida 3, and 8 (11.9%) were >gravida 4. Similar reports were reported by Chandni *et al*., (2021).[14] In their study, majority of women were primigravida (40.45%) followed by gravida 2 (35.39%). Elsheikh *et al*. (2007)[16] conducted a study where maximum patients were second gravida.

In our study, most common clinical presentation was icterus. It was noticed in 10 (14.9%), 8 (11.9%) had edema, and 5 (7.5%) had increased liver span. About 100% of patients had icterus at the time of admission (Choudhary *et al*., 2017)[17] similar observations were also confirmed by Prasad *et al*., (2016).[18] In the present study, deranged LFT was observed in 20 (29.9%) patients. Desai *et al*., (2020)[19] did a study in which 29 patients (58%) had SGOT and SGPT < 200 IU/L. Thirteen patients (26%) had SGOT and SGPT between 200 and 500 IU/L. Eight patients (16%) had SGOT and SGPT more than 500 IU/L and all of them were the cases of viral hepatitis. In our study, 33 (49.3%) had hepatitis B, 32 (47.8%) had hepatitis C, and 1 (1.5%) each hepatitis A and hepatitis E. Hepatitis B infection was responsible for maximum cases of viral infection contributing to (106) 92.9% in a study done by Chaitra *et al*., (2019).[20] Similar results was noted in the study conducted by Shukla *et al*. (2011),[21] whereas the study conducted by Jaiswal *et al*., (2001)[22] and Aziz *et al*., (1997)[23] reported the commonest virus to be hepatitis E. On ultrasonography, hepatomegaly was found in 4 (6%) patients and liver atrophy in 2 (3%) patients while majority 61 (91%) had normal hepatobiliary system. Hepatomegaly was also confirmed in 18.96% in a study by Choudhary *et al*., (2017),[17] 20% by Desai *et al*., (2020).[19]

In our study, gestational age at delivery in 55 (82.1%) women was >37 weeks, full-term gestation was also observed by Chandni *et al*., (2021)[14] in 44.9% against pre-term in 55.1% patient. About 52% of women had pre-term delivery and rest 48% had term delivery in a study by Desai *et al*., (2020).[19] Another study by Patil *et al*., (2017),[24] majority of patients were in the third trimester of pregnancy (82%) with mean gestational age at presentation of symptoms that was 34.44 + 6.28 weeks. Out of 67 patients, 42 (62.7%) women delivered through cesarean section in our study while 25 (37.3%) had normal vaginal deliveries. Maternal outcome and complications were analyzed in terms of mode of delivery, 43 (37.7%) patients delivered vaginally, whereas 71 (62.2%) underwent cesarean section in a study by Chaitra *et al*., (2019).[20] Acute in indications for cesarean section women, 42 women include acute fetal distress in 23 (54.8%). Acute fetal distress was observed in 38.3% pregnant women in a study conducted by Yang *et al*. (2002).[25] The main reason was chorion angioipathy induced by hepatitis B infection of placenta. Prasad *et al*., (2016)[18] conducted a study of hepatitis E in pregnancy in which 14% of women underwent LSCS for fetal distress and severe oligohydramnios, oligohydramnios in 6 (14.3%), color Doppler changes and cephalopelvic disproportion in 3 (7.1%) patients each, non-progression of labor, IUGR, and macrosomia in 2 (4.8%) patients while 1 (2.4%) patients had malpresentation. Oligohydramnios was observed in 11.2% of women in a study by Sujatha and Konda (2019).[26] Maternal complications such as thrombocytopenia were observed in 14 (33.3%) and postpartum hemorrhage and hypoglycemia in 3 (7.1%) patients each. Monteith *et al*., (2014)[27] conducted a study in which prevalence of thrombocytopenia was 10.3%. Sujatha and Konda (2019)[26] conducted a study on 93 hepatitis B-positive women in which postpartum hemorrhage was observed in 16.1%. Normal birth weight (2.5–3.5 kg) was seen in 58 (86.6%) newborns, 7 (10.4%) were low birth (<2.5 kg) while 2 (3%) were overweight (>3.5 kg). The mean birth weight was 2.73 ± 1.26 kg. Majority of the LBW cases (16%) were due to prematurity and all of them had NICU admissions (Sujatha A and Konda S, 2019).[26] Low birth weight was also observed in 7.6 and 8.3% by Kumar *et al*. (2004)[6] and Medhat *et al*. (1993),[28] respectively.

There were 42 (62.7%) patients with 1 min Apgar >7 compared to 49 (73.1%) at 5 min Apgar score >7 days. Cui *et al*., (2016)[29] conducted a study in which majority of women (488) had Apgar at 7 min with a mean Apgar score of 9.90 ± 0.53 at 5 min. Fetal outcomes such as NICU admission were observed in 16 (38.1%) NICU admission, low birth weight in 7 (16.7%), and 2 (4.8%) intra-uterine deaths. Chandni *et al*., (2021)[14] conducted a study in which low birth weight (25.33%) formed the bulk of NICU admission (54%) while IUD was seen in 10.11% of women which is similar to the results reported by Jethwa *et al*., (2016)[11] in their study (25% of low birth weight and 33.3% of NICU admission).

CONCLUSION

Identification of HBV-positive pregnant women remains the most effective way to prevent HBV transmission to newborns thanks to a very effective passive/active prophylaxis at birth. However, in the case of women with very high viremia, a non-negligible proportion of newborns can acquire the infection (probably through in utero transmission) despite the use of passive/active prophylaxis. For this reason, antiviral treatment in the third trimester can be considered for those women. The choice of antiviral should be restricted to those drugs considered safe in this setting. Decisions regarding the time of eventual discontinuation should consider the stage and activity of liver disease and of infection, taking into account also the risk of postpartum hepatitis flare. Breastfeeding is not contraindicated for HBV patients. However, it is not recommended for women taking antiviral drugs. Finally, there is no clear evidence that ECS reduces the risk of mother-to-child transmission compared to vaginal delivery. Urgent redressal of issues pertaining to sanitation and provision for clean drinking water for citizens of India is the need of the hour as HEV is fecooral in transmission.

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Original Article

A Prospective Observational Study to Determine a Correlation between Foot Length and Gestational Maturity in Neonates Born at a Tertiary Care Hospital in South India

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Abstract

Background: Accurate assessment of gestation maturity is not possible in all newborn babies especially when they are sick and when intensive care support is needed. The aim was to study correlation of foot length (FL) and other anthropometric measurement with gestational maturity in neonates.

Materials and Methods: Prospective observational study was done in 1000 babies born at Kovai Medical Center and Hospital, Coimbatore, Tamil Nadu, India, from October 2019 to May 2020. FL at birth was measured using sliding caliper from the posterior most prominence of foot to the tip of the longest toe on right foot. Gestational assessment was done using modified Ballard's scoring on day 1. Linear regression analysis was done to investigate the relation of FL to gestational age (GA), birth weight (BW), head circumference (HC), chest circumference (CC), and crown heel length (CHL).

Results: About 52.2% were male and 47.8% were female babies. Of the 1000 newborns, preterm babies were 209 (20.9%), term babies were 775 (77.5%), and post-term babies were 16 (1.6%). The mean FL was 7.43 cm with a range of 4.30–8.79 cm. FL correlated significantly ($P < 0.05$) with GA, BW, HC, CC, and CHL in preterm small for GA (SGA), preterm appropriate for GA (AGA), preterm large for GA (LGA), term AGA, and term LGA. The correlation coefficient of FL with GA was maximum in preterm SGA (r = 0.934) and preterm AGA groups (r = 0.902), followed by preterm LGA (r = 0.832), term AGA (r = 0.341), and term LGA (r = 0.246). In term SGA, FL correlated with BW, HC, and CHL but not with GA and CC, while in post-term AGA, FL only correlated with BW.

Conclusions: FL correlated significantly with GA and other anthropometric parameters in preterm babies and in term AGA and LGA babies.

Key words: Birth weight, Crown heel length, Foot length, Gestational age

INTRODUCTION

Neonatal period is the most vulnerable period of life.[1] Although the global number of newborn deaths declined from 5 million in 1990 to 2.4 million in 2019, children face the greatest risk of death in their first 28 days.[2] The main causes for neonatal deaths are prematurity, low-birth-weight (LBW), infections, asphyxia, and birth trauma, accounting for 80% of neonatal deaths.[1]

Prematurity is a major determinant of neonatal survival.[3] Globally, about one-sixth of all newborns are BW (<2500 g), which is single most important underlying risk factor for neonatal deaths.[4-6] Only about half of the newborns are weighed at birth and further for a smaller proportion of them the gestational age (GA) is known.[4,7] Identifying these LBW and preterm babies and referring them to higher centers for effective interventions will help in decreasing neonatal mortality and morbidity.[1]

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Conventionally, GA is calculated by Naegele's formula and antenatal ultra-sonography (USG), or using Ballard Scoring in neonates. In rural settings with low literacy levels, application of Naegele's formula and non-availability of antenatal USG check-up are limiting factors. Application of ballard scoring requires the expertise of a pediatrician who may not be available in remote area. Moreover, it cannot be used in asphyxiated neonates.

All these factors thus underline the importance of early identification and reference to higher center of preterm babies at the rural setup, where most of the deliveries are conducted at home by untrained relatives, traditional birth attendants, and dais having no proper neonatal medical care facilities.[8]

Parameters such as BW, crown-heel length (CHL), and head circumference (HC) are commonly used as predictors of growth and maturity in neonates. Anthropometric measurements such as BW and length are significantly affected by changes in water, carbohydrate, fat, protein, and mineral levels. Although HC reflects brain growth, the effect of head sparing during malnutrition may result in an underestimation of growth restriction.[9]

The identification and evaluation of low-cost tools to accurately identify small newborns in primary healthcare and community settings have been ranked as the number one research priority to reduce global mortality from prematurity and LBW.[10] Since decades, attempts have been made to find an alternative for GA assessment in newborns. These alternative measurements should be reliable, have a close correlation with GA, can be performed even by inexperienced medical personnel and have very little intra- and inter-observer variability.[8]

New born foot length (FL) is an easy, quick, and efficient measurement for preterm, critically ill newborns. This measurement technique is not influenced by either subcutaneous fat or biological sex.[11] It has also been stated that FL is the least affected anthropometric measurement in intra uterine growth restricted babies.[9] FL is one such parameter which can be measured easily in preterm and sick neonates without disturbing the baby.[8]

The foot of the new born is usually readily accessible for measurement, even in incubators.[12]

This study is being done to find a correlation between FL, gestational maturity, and other anthropometric measurements.

Aims and Objectives

The aim of the study was to a prospective observational study to determine a correlation between FL and gestational maturity in neonates born at a tertiary care hospital in South India.

1. To study the correlation of FL and GA among preterm, term, and post-term neonates
2. To study the correlation between FL and other variables (BW, GA, HC, chest circumference [CC], and CHL) among small for GA (SGA), appropriate for GA (AGA), and large for GA (LGA) newborns
3. To study whether FL can be used as a proxy measurement to BW and GA assessment in newborns
4. To study whether FL correlates with the GA assessment using new ballard score (NBS) and with that using last menstrual period (LMP) method and with ultrasound assessment.

MATERIALS AND METHODS

Study Design

This was a prospective observational study.

Study Area

This study was conducted at the Department of Paediatrics, Kovai Medical Center and Hospital, Coimbatore.

Study Period

The study period was from October 2019 to May 2020.

Inclusion Criteria

All live newborns of different GAs born at Kovai Medical center and hospital, Coimbatore within 72 hours of birth were included in the study.

Exclusion Criteria

Babies who were having skeletal deformities of the foot, foot edema, who had perinatal asphyxia, who are more than 72 hours of age, who are born elsewhere, having major congenital anomalies, whose mother is unaware of LMP or when USG is not available, and in whose parents refused to provide informed consent were excluded from the study.

Study Details/Methodology

The study was started after getting institutional scientific and ethical committee clearance. 1000 live newborn babies satisfying the inclusion criteria were recruited for the study.

Parents were approached following the birth of their child, and the study was explained in their local language. Patient information sheet was also provided. Following written informed consent (or for those illiterate, a witnessed thumb print was provided), a data collection form was completed by interview with the parent/guardian and a review of the medical records. Consent material also was made available in the local language. The date of LMP was sourced from the mother to estimate expected date of delivery and GA

of the newborn. Medical records were reviewed for early ultrasound findings and estimated date of delivery. If these were not recorded, the information was requested from the mother.

Data were collected using standard pro forma meeting the objectives of the study

a. GA assessment was done using modified NBS
b. FL was being measured using sliding which is having an accuracy of a millimeter. FL was measured from posterior most prominence of foot to the tip of the longest toe of the right foot
c. HC and CC were measured using flexible, non-stretchable fiber measuring tape as per standard protocol
d. CHL was measured using a standard infantometer using an assistant's help
e. Weight of the baby was measured using electronic weighing scale with an accuracy of ±10 g. All the dress of baby was removed before weighing.

Babies were grouped into preterm, term, and post-term categories. Babies <37 weeks of gestation were counted in the preterm group. Babies ≥42 weeks of gestation were counted in the post-term age group. All the three groups of babies were categorized into SGA, AGA, and LGA groups. This classification was done using Lubchenco intrauterine growth curve.

Statistical Analysis

Data entry was done in Microsoft Excel spread sheet and the statistical analysis was carried out using the SPSS software version 20.0 for windows. Descriptive analysis was done to exhibit the frequency of observations, mean, and standard deviation. Chi-square analysis was used to test the significant association on target variable by substantial variable. ANOVA was used to test the significant difference between three or more groups on selected variables. Regression analysis was used for estimating relationship between a dependent variable and one or more independent variables. $P < 0.05$ was considered as statistically significant.

RESULTS

The study included 1000 newborns of which 522 (52.2%) were male and 478 (47.8%) were females. Out of 1000 babies, 775 (77.5%) were term, out of which 13 (1.3%) were term SGA, 700 (70%) were term AGA, and 62 (6.2%) were term LGA babies. A total of 209 (20.9%) were preterm, of which 35 (3.5%) were preterm SGA, 166 (16.6%) were preterm AGA, and 8 (0.8%) were preterm LGA babies. A total of 16 babies were post-term, of which 15 (1.5%) were post term AGA and 1 (0.1%) was post term LGA. There were no babies in post-term SGA group.

Of the 1000 neonates studied, the mean FL was 7.43 cm with a range of 4.30–8.79 cm and standard deviation of 0.59. The preterm SGA, AGA, and LGA had a mean FL of 6.03, 6.78 and 7.63 cm, respectively. The mean FL for term SGA, AGA, and LGA were 7.04, 7.61, and 8.02 cm, respectively. The mean FL for post-term AGA and LGA were 7.60 and 8.48 cm, respectively [Table 1].

Overall mean HC was 33.43 cm. The minimum and maximum HC of preterm neonates were 24 cm and 35.5 cm, term neonates was 30.5 cm and 36 cm and for post-term neonates was 33.5 cm and 35 cm, respectively. The mean HC of pre-term SGA, AGA, and LGA was 29.23 cm, 31.51 cm, and 33.94 cm, while for term SGA, AGA, and LGA was 32.77 cm, 33.98 cm, and 34.76 cm, and it was 34.07 cm in post-term AGA and 34.5 in post-term LGA group, respectively [Table 1].

Minimum and maximum CC in preterm babies were 23 cm and 33.5 cm, term was 30 cm and 34.5 cm and post-term was 31 cm and 34 cm. Mean CC in pre-term SGA, AGA, and LGA group was 27.80 cm, 30.05 cm, and 32.31 cm, while for term SGA, AGA, and LGA babies was 31.12 cm, 32.40 cm, and 33.22 cm and the values where 32.43 cm and 33.50 cm in post-term AGA and post-term LGA groups, respectively. Overall, mean CC was 31.88 cm [Table 1].

Preterm babies had a maximum CHL of 52 cm and minimum of 33 cm, for term it was 53 cm and 45 cm and for post-term 52 cm and 49 cm, respectively. The mean CHL of preterm SGA, AGA, and LGA was 42.27 cm, 46.30 cm, and 50.38 cm, for term SGA, AGA, and LGA was 48.38 cm, 50.24 cm, and 51.71 cm, while in post-term AGA and LGA it was 50.47 cm and 52 cm, respectively. Overall mean CHL was 49.38 cm [Table 1].

In the study group, 801 (80.1%) babies had normal BW, 140 (14%) were low BW, 27 (2.7%) very low BW (VLBW), and 13 (1.3%) extreme low BW while 19 (1.9%) had macrosomia. Mean BW of babies in the study was 2898.76 grams. Lowest and highest BW recorded were 500 g and 4590 g, respectively [Table 1].

FL correlated with GA, BW, HC, CC, and CHL in preterm SGA, preterm AGA, preterm LGA, term AGA, and term LGA babies. In term SGA babies, FL correlated with BW, HC, and with CHL only and in post-term AGA babies, FL only correlated with BW. The correlation coefficient of FL with GA was maximum in preterm SGA ($r = 0.934$) and pre-term AGA groups ($r = 0.902$) followed by pre-term LGA ($r = 0.832$), term AGA ($r = 0.341$), and term LGA ($r = 0.246$) [Tables 2 and 3, Figures 1-7].

Table 1: General data from the study

	No	FL (cm)		HC (cm)		CC (cm)		CHL (cm)		BW (grams)	
		Range	Mean±SD	Range	Mean±SD	Range	Mean±SD	Range	Mean±SD	Range	Mean±SD
Pre-term SGA	35	4.3–7.33	6.03±0.80	24–33	29.23±2.83	23–32	27.80±2.79	33–50	42.27±4.47	500–2100	1529.71±498.97
Pre-term AGA	166	4.5–8	6.78±0.77	24–34.5	31.51±2.67	23–33	30.05±2.68	34–51	46.30±4.24	680–3260	2163.07±620.59
Pre-term LGA	8	6.9–8.09	7.63±0.48	32–35.5	33.94±1.08	31–33.5	32.31±0.96	48–52	50.38±1.41	2160–4030	3288.75±628.80
Term SGA	13	6.6–7.46	7.04±0.22	31.5–33.5	32.77±0.53	30–32.5	31.12±0.74	45–49	48.38±1.19	2010–2460	2266.92±154.40
Term AGA	700	6.57–8.5	7.61±0.24	30.5–36	33.98±0.57	30–34	32.40±0.84	45–53	50.24±0.87	2200–3800	3054.96±309.27
Term LGA	62	7.38–8.79	8.02±0.27	33.5–35.5	34.76±0.48	31–34.5	33.22±0.87	50–53	51.71±1.01	3470–4590	3891.13±246.43
Post-term AGA	15	7.12–8	7.60±0.25	33.5–35	34.07±0.32	31–34	32.43±0.94	49–52	50.47±0.92	2680–3650	3080±296.33
Post-term LGA	1	8.48–8.48	8.48	34.5–34.5	34.5	33.5–33.5	33.50	52–52	52	4450–4450	4450
Total	1000	4.3–8.79	7.43±0.59	24–36	33.45±1.81	23–34.5	31.88±1.86	33–53	49.38±2.92	500–4590	2898.76±625

SGA: Small for gestational age, AGA: Appropriate for gestational age, LGA: Large for gestational age, FL: Foot length, HC: Head circumference, CC: Chest circumference, CHL: Crown heel length, BW: Birth weight

Table 2: Correlation of FL with GA,BW,HC,CC and CHL in various gestational age groups

	Pre-term SGA		Pre-term AGA		Pre-term LGA		Term SGA		Term AGA		Term LGA		Post term AGA	
	r-value	*P*-value	r-value	*P*-value	r-value	*P* -value	r-value	*P* -value	r-value	*P*-value	r-value	*P*-value	r-value	*P*-value
GA	0.934	<0.001	0.902	<0.001	0.832	0.010	–0.120	0.696	0.341	<0.001	0.246	0.049	–	–
BW	0.970	<0.001	0.954	<0.001	0.980	<0.001	0.595	0.032	0.719	<0.001	0.560	<0.001	0.819	<0.001
HC	0.952	<0.001	0.961	<0.001	0.922	0.001	0.555	0.049	0.620	<0.001	0.594	<0.001	0.490	0.064
CC	0.944	<0.001	0.932	<0.001	0.815	0.014	0.210	0.492	0.328	<0.001	0.413	0.001	0.149	0.595
CHL	0.933	<0.001	0.941	<0.001	0.936	0.001	0.800	0.001	0.617	<0.001	0.533	<0.001	0.376	0.168

GA: Gestational age, BW: Birth weight, HC: Head circumference, CC: Chest circumference, CHL: Crown heel length, SGA: Small for GA, AGA: Appropriate for gestational age, LGA: Large for gestational age

Table 3: Relationship of GA with BW and FL

Gestation (number)	Birth weight (g)			Foot length (cm)		
	Min	Max	Mean±SD	Min	Max	Mean±SD
24–25 (1)	500	500	500±0	4.3	4.3	4.3±0
26–27 (8)	610	1000	785±118.92	4.5	4.99	4.71±0.17
28–29 (12)	750	1210	1006.67±181.34	4.82	6.01	5.54±0.48
30–31 (19)	860	1750	1336.84±283.43	4.6	6.4	5.69±0.54
32–33 (27)	1220	2160	1617.41±264.02	5.6	6.93	6.24±0.37
34–35 (52)	1500	3480	2190.96±402.89	5.77	7.7	6.86±0.39
36–37 (142)	1900	4030	2689.15±410.89	6.6	8.4	7.34±0.33
38–39 (457)	2010	4080	3032.06±351.08	6.57	8.79	7.58±0.26
40–41 (264)	2400	4590	3294.20±395.79	6.87	8.5	7.74±0.27
42–43 (18)	2680	4450	3184.44±429.86	7.12	8.48	7.67±0.31
Total (1000)	500	4590	2898.76±625	4.3	8.79	7.43±0.59
P-value			<0.001			<0.001

FL of the baby was found to have significant relationship with GA as follows; GA by LMP: 81.5%, GA by USG: 85.8%, and GA by Ballard: 83.1% [Table 4].

DISCUSSION

The early identification of low BW/preterm babies is an important prerequisite of any initiative to reduce neonatal mortality. There are various measurements in newborns to assess growth. Some of the routine measurements done at birth are HC, CC, CHL, and BW. In many developing countries including India, the equipment required to measure them will not be available in rural or tribal settings or the babies will be sick and minimum handling will be needed to get the maximum information about the anthropometry of the baby. In such cases, FL is an easy tool which can be measured even in sick neonates and requires less handling and is less disturbing to the neonate.

The present study was done to find correlation between FL, gestational maturity/GA, and other anthropometric measurements in neonates, so that FL can be used as a proxy measurement for estimation of GA and BW.

In our study on 1000 neonates, 52.2% (522) were males and 47.8% (478) were females. This was comparable to the study by Gavhane *et al*.[12] where males were 52.5% (420) and females were 47.5% (380) out of 800 newborns studied.

The BW of 1000 neonates ranged from 500 to 4590 g with a mean BW of 2898.76 g, comparable to a study done by Rakkappan and Kuppusamy,[13] where the median BW of 1000 babies was 2700 g with a BW range of 500–4250 g.

In our study, out of 1000 babies studied 18% (180) were low BW of which 1.3% (13) were extremely low birth weight, 2.7% (27) were very low birth weight, and 14% (140) were LBW. In a study done by Gavhane *et al*.,[12] 25.4% (203) constituted LBW out of 800 neonates.

Among 1000 neonates in our study, term AGA, SGA, and LGA were 70% (700), 1.3% (13), and 6.2% (62); preterm

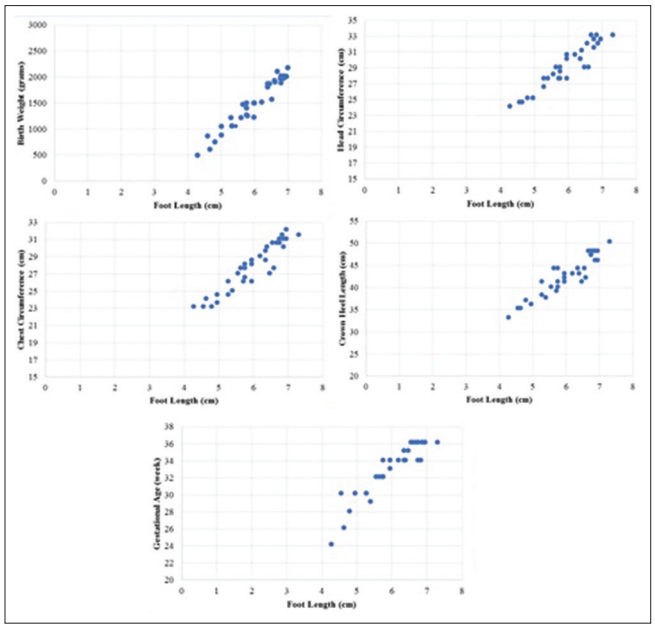

Figure 1: Correlation between foot length and other variables for pre-term small for gestational age

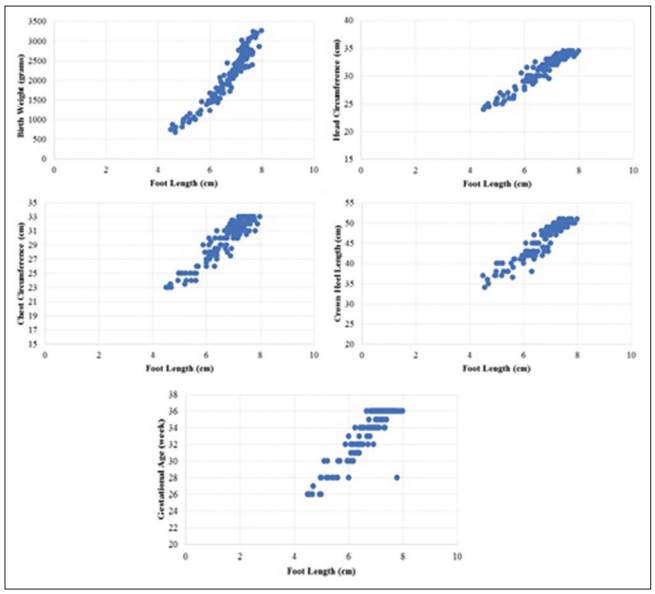

Figure 2: Correlation between foot length and other variables for pre-term appropriate gestational age

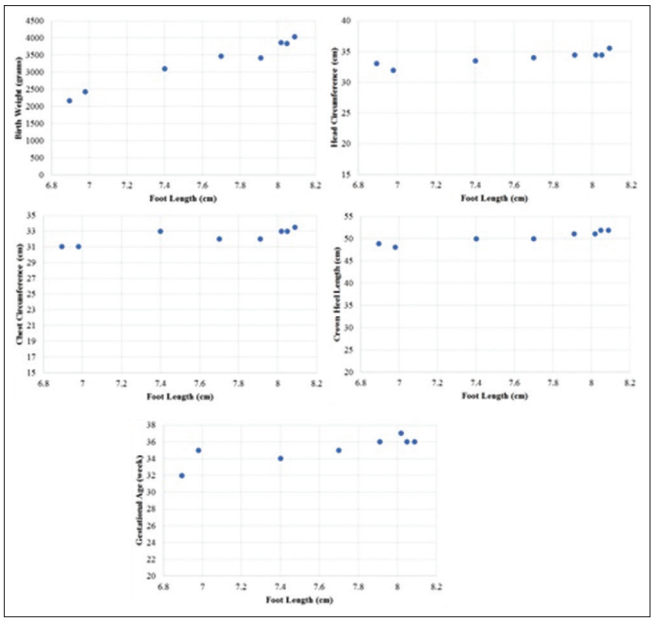

Figure 3: Correlation between foot length and other variables for pre-term large gestational age

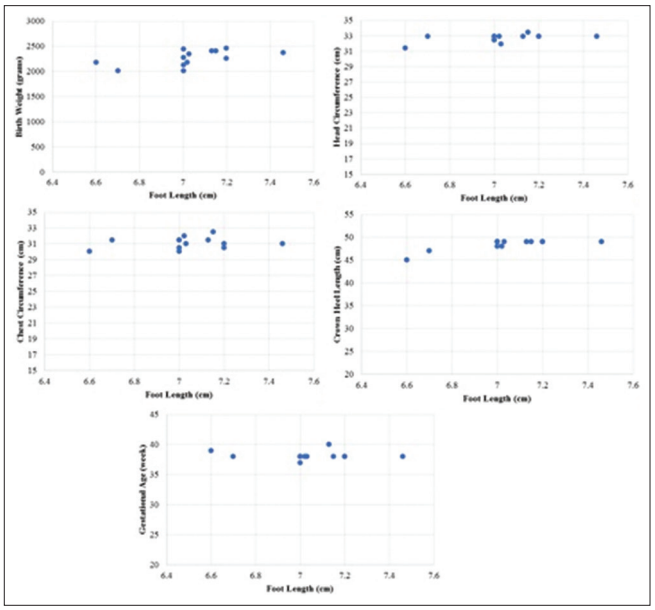

Figure 4: Correlation between foot length and other variables for term small for gestational age

AGA, SGA, and LGA were 16.6% (166), 3.5% (35), and 0.8% (8); and post-term AGA and LGA were 1.5% (15) and 0.1% (1), respectively. There were no babies in post-term SGA group. Out of 1000 neonates, Rakkappan and Kuppusamy[13] study showed 75.7% (757) term AGA, 5.1% (51) term SGA, and 0.6% (6) term LGA babies; pre-term AGA and SGA were 9.4% (94) and 9.2% (92), respectively.

Our FL findings [Table 2] were comparable to the study done by Gavhane *et al*.[12] which showed that the FL of preterm neonates ranged from 4.5 to 7.8 cm with the mean FL of 6.1571 cm and 6.6964 cm for preterm SGA and AGA, respectively. The FL of term neonates ranged from 5.4 to 8.7 cm with a mean FL of 7.0471 cm, 7.5703 cm for term SGA, and AGA respectively and the FL for post-term neonates ranged from 6.7 to 8.8 cm, with a mean FL of 7.5688 cm, 8.0170 cm for post-term SGA and AGA, respectively.

Rakkappan and Kuppusamy[13] in their study showed mean HC of preterm neonates as 29.18 ± 2.12, term neonates

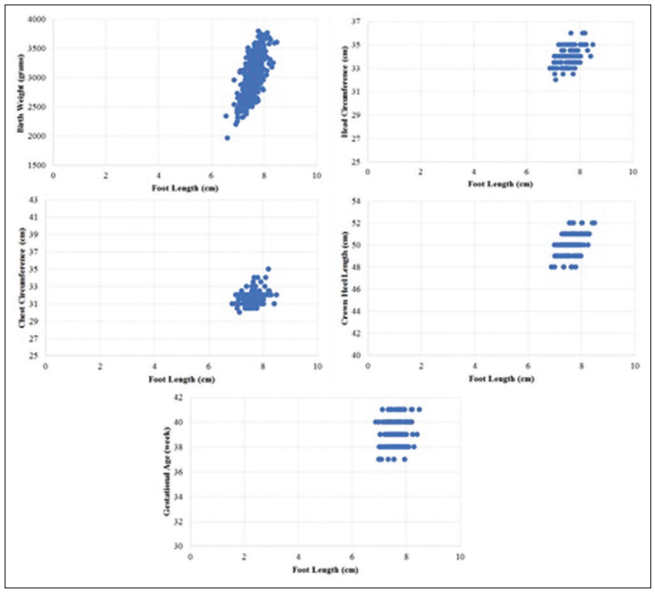

Figure 5: Correlation between foot length and other variables for term appropriate gestational age

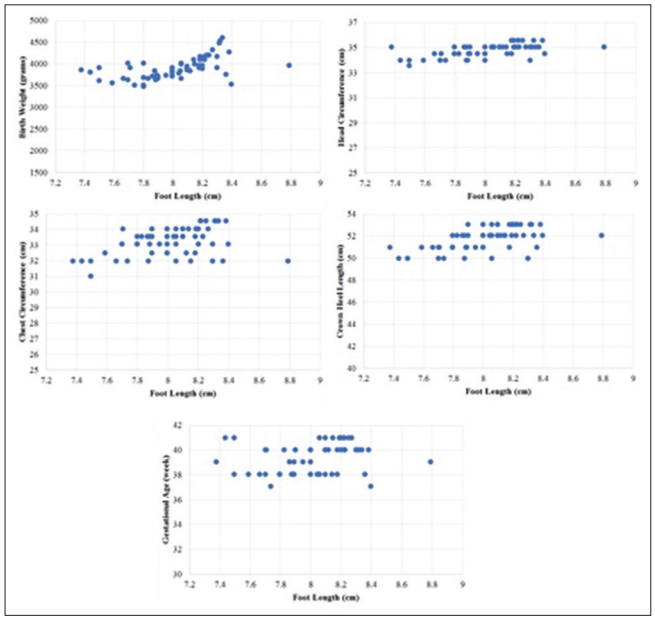

Figure 6: Correlation between foot length and other variables for term large gestational age

as 32.33 ± 0.97 which was comparable to our HC findings [Table 2]. Gupta *et al*.[14] in their study showed that mean CC of preterm SGA and AGA was 26 cm and 28.5 cm, while of term AGA, SGA, and LGA were 31.18 cm, 29.8 cm, and 34.43 cm and of post-term AGA and SGA were 32.55 cm and 31 cm, respectively, similar to our findings [Table 2]. CHL in our study [Table 2] were comparable to the findings in the study done by Gohil *et al*.[15] which showed a mean CHL of 42.7 ± 2.08 cm for preterm babies, 46.21 ± 1.23 cm for term SGA, and 48.36 ± 3.13 cm for term AGA babies, respectively.

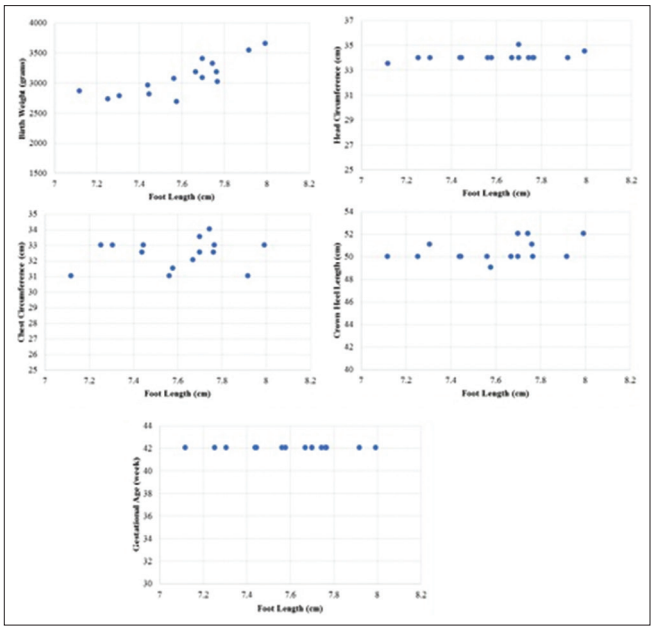

Figure 7: Correlation between foot length and other variables for post-term appropriate gestational age

Table 4: Regression analysis results of relationship between foot length and gestational age assessment by various methods

Gestational age	Foot length		
	R-value	R2-value	*P*-value
LMP	0.815	0.663	<0.001
USG	0.858	0.736	<0.001
Ballard	0.831	0.691	<0.001

LMP: Last menstrual period, USG: Ultra-sonography

FL correlated with GA, BW, HC, CC, and CHL in preterm SGA, pre-term AGA, pre-term LGA, term AGA, and term LGA babies. These results were comparable to studies done by Sateesha *et al*.,[16] Gavhane *et al*.,[12] and Saroj *et al*.[17]

CONCLUSIONS

FL correlated significantly with GA and other anthropometric parameters such as BW, HC, CC, and CHL in most of the GA groups.

FL is a simple, quick, cheap, effective, readily accessible, and a reliable anthropometric measurement which can be used as a proxy measurement to GA assessment/gestational maturity and BW especially in sick and pre-term neonates receiving intensive care.

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Original Article

Management of Acute Coronary Syndrome in COVID-19 Patients – A Single-Center Study

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Abstract

Introduction: In coronavirus disease 2019 (COVID-19) pandemic, many patients suffered acute coronary syndrome (ACS) which includes ST-segment elevation myocardial infarction (STEMI), non-STEMI (NSTEMI), unstable angina, and sudden cardiac death. There is increased risk of acute myocardial infarction with newly diagnosed COVID-19 compared to non-infective controls.

Purpose: The purpose of the study was to study the incidence of ACS in COVID-19 patients admitted from April 2021 to March 2022 to compare outcome with ACS cases in non-COVID intensive care unit (ICU) of same center and to come out with guidelines for the management of ACS with COVID-19 to reduce mortality in centers without dedicated COVID Cath Labs.

Materials and Methods: Population of the study comprises adult patients presenting to COVID wards with COVID 19 and ACS and patients with ACS without COVID of the same hospital for the period of April 2021–March 2022.

Results: We had 62 ACS cases, who were COVID-19 positive. Among them, 37 cases were STEMI, 20 cases of Unstable Angina and 5 cases of NSTEMI. 33 patients in COVID wards were lysed, no STEMI patients underwent primary PCI and PIT. In the same period, we had 1541 ACS patients admitted in Coronary Care Unit (Non-COVID wards). Among them, 1496 cases were STEMI, 24 cases had Unstable Angina and 21 cases had NSTEMI. Among those 1541 ACS cases, 1125 patients underwent thrombolysis, 86 patients underwent primary PCI and 112 patients underwent PIT. Among 62 ACS cases in COVID wards, there were 10 STEMI deaths, 3 Unstable Angina deaths and 1 NSTEMI death. Among 1541 ACS cases in Non-COVID wards, 231 STEMI deaths and no death in Unstable Angina and NSTEMI.

Conclusion: Role of thrombolytic therapy alone in COVID STEMI in reducing mortality is non-inferior to PPCI and pharmacoinvasive PCI in non-COVID STEMI. Mortality in COVID STEMI is also because of severe COVID infection. Incidence of unstable angina is higher in COVID patients.

Key words: Acute coronary syndrome, Coronavirus disease 2019, Non-COVID, Thrombolysis

INTRODUCTION

In the coronavirus disease 2019 (COVID-19) pandemic,[1] patients suffered from acute coronary syndrome (ACS) which includes ST-segment elevation myocardial infarction (STEMI), non-STEMI (NSTEMI), unstable angina, and sudden cardiac death.

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Acute myocardial injury in COVID-19 patients[2] has multiple mechanisms, myocardial ischemia caused by systemic hypoxia, in setting of severe acute respiratory distress syndrome, multiple thrombosis, coronary spasm, systemic inflammatory response due to cytokine storm, and vasculitis like vessel damage is likely triggers that lead to rupture of atherosclerotic plaque. Systemic Inflammation leads to activation of cytokines initiating rupture of pre-existing atherosclerotic plaque. There is imbalance between myocardial oxygen demand and supply due to respiratory failure, tachyarrhythmia and sepsis. COVID-19 patients have increased thrombotic tendency due to endothelial damage, dehydration and increased cytokines. All these contribute to the increased risk for Acute Coronary Syndrome.

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The clinical peculiarities of ACS in COVID-19 patients[3] are that the clinical picture of ACS is masked by course of the infectious disease itself.[4] The diagnosis of ACS may be delayed and medical personnel should focus on entire complex of clinical manifestations and examination data such as electrocardiograph (ECG), echocardiography, and enzyme levels and other imaging modalities.

In COVID wards, health-care providers were doing duties in shifts for 6 h with strict PPEs. All health-care providers were instructed to treat ACS cases using telemedicine[5] in most of the centers. There was confusion in diagnosing ACS cases due to ST, T changes associated with COVID which affected multiple systems. Even after diagnosis, the management options are limited due to non-availability of dedicated Cath Labs. Thrombolytic therapy with streptokinase is preferred modality in such circumstances. The survival rate following thrombolytic therapy is comparable with invasive strategy. In many cases, Covid dominates ACS patient has to fight with two major killer diseases.[6] The survival depends on the multiple factors such as immune status, comorbid conditions, and availability of management strategies. Individualized, COVID cardiac team approach is needed for every patient.

MATERIALS AND METHODS

Study Population

It comprises adult patients presenting to COVID wards with ACS. Patients with COVID having chest pain, dyspnea, palpitation confirmed myocardial infarction (MI) by universal definition of MI through enzymes, ECG, and echo were included in the study. The demographic profile ACS patients admitted in COVID wards and their management and in-hospital mortality were collected. Non-COVID ACS data were collected for same period, and compared the in-hospital mortality.

Study Period

During COVID-19 pandemic, between April 2021 and March 2022 (second wave).

Statistical Analyses of the Data

Statistical analyses of the data are conducted using the software IBM SPSS 20.0 version. Statistical inference was derived using Chi-square test.

Inclusion Criteria

- Patients present with ACS – STEMI, NSTEMI, and unstable angina
- Patients presenting with acute MI as diagnosed by electrocardiogram defined as new ST elevation at the J point in at least 2 contiguous leads ≥2 mm in men or ≥1.5 mm in women in leads V2–V3 and/or of ≥1 mm in other contiguous chest or limb leads admitted in the COVID wards
  - With real-time reverse transcription-polymerase chain reaction (RT-PCR) test positivity
  - With or without pneumonia ground-glass opacity (GGO) by computed tomography (CT) chest
  - COVID pneumonia by CT chest GGO with or without RT-PCR positivity
- Patients of age equal to or >18 years of both sexes.

Exclusion Criteria

- All non-COVID patients with ACS
- Patients with pseudo-infarctions (*).

(*)There have been reports of myocardial injury occurring in patients who have tested positive for COVID-19 with evidence of troponin leak and elevation, and these patients may initially present with a pseudo-infarct pattern in ECG. Other conditions for pseudo-infarctions are given below:

(1) Acute pericarditis, (2) myocarditis, (3) early repolarization pattern, (4) hyperkalemia, (5) Brugada pattern, (6) Ebstein anomaly, (7) epsilon wave in arrhythmogenic right ventricular dysplasia, (8) Osborn wave of hyperthermia, (9) in the left ventricular hypertrophy, in hypertrophic cardiomyopathy (HCM), (10) acute pancreatitis, (11) intracranial hemorrhage, (12) subdural hematoma, (13) in pulmonary emphysema, patients with pneumothorax and pulmonary embolism, (14) myocardial fibrosis in patients with dilated cardiomyopathy, progressive muscular dystrophy, Friedreich's ataxia, scleroderma, amyloidosis, and primary and metastatic tumors of the heart, (15) QS deflections are often seen in the right precordial leads in patients with complete left bundle branch block in the absence of myocardial infarction, and (16) the delta waves in Wolff-Parkinson-White syndrome.

RESULTS AND ANALYSIS

COVID ACS

During COVID pandemic 2nd wave, between April 2021 and March 2022,[7] there were 18,104 admissions in COVID ward. Out of them, 62 cases were admitted with ACS (0.34%). Among the 18,104 cases [Table 1], there were 427 deaths (2.36%). Among 62 cases of COVID ACS, 37

Table 1: The no. of patients admitted and no. of mortality in COVID wards

COVID	No. of patients
IP	18,104
Death	427

COVID: Coronavirus disease

cases (60%) were STEMI, 20 cases were Unstable Angina (32%) and 5 cases were NSTEMI (8%) [Chart 1]. Out of 62 COVID ACS cases, 14 cases died (22.6%). In-hospital mortality of COVID ACS patients comes as 0.08%, that is, 8 patients per 10,000 cases died due to COVID ACS. In-hospital mortality of STEMI, NSTEMI, and unstable angina for the admitted (18,104) cases is 0.06%, 0.006%, and 0.02% [Table 2], respectively. In-hospital mortality of STEMI, NSTEMI, and unstable angina among 427 deaths was 2.3% [*n*-10], 0.2% [*n*-1], and 0.7% [*n*-3], respectively. COVID disease was either in the form of seropositivity or COVID pneumonia with or without seropositivity. Male: female ratio for COVID ACS was 0.73:0.27 (45 male + 17 female). There were no female cases with ACS below 50 years with COVID-19.[8] Incidence of ACS is highest among 60–69 years with COVID.

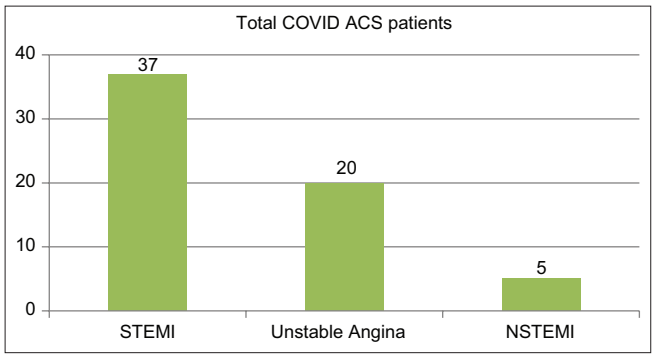


Chart 1: The total no. of COVID ACS patients which includes STEMI, unstable angina, and NSTEMI

Table 2: The no. of COVID ACS patients and their mortality among COVID In-patients (18,104 cases)

COVID ACS	ICU	In % (for 18,104 cases)	Death	In % (for 18,104 cases)
STEMI	37	0.2	10	0.06
NSTEMI	5	0.03	1	0.02
Unstable angina	20	0.1	3	0.006
Total	62	0.34	14	0.08

STEMI: ST-segment elevation myocardial infarction, NSTEMI: Non-STEMI, ICU: Intensive care unit, ACS: Acute coronary syndrome, COVID: Coronavirus disease

Table 3: The percentage of COVID ACS patients with comorbidities

Comorbidities	No. of patients (In %)
DM	35.5
HTN	27.4
CKD	1.6
Obesity	2.5
Dyslipidemia	5
Smoking	24.2
Alcoholism	17.8
Sedentary lifestyle	15
Anxiety and stress	5
Depression	1

ACS: Acute coronary syndrome, COVID: Coronavirus disease, DM: Diabetes mellitus, HTN: Hypertension, CKD: Chronic kidney disease

Comorbid conditions in ACS patients [Table 3] were diabetes mellitus (DM) – 35.5%, hypertension (HT) – 27.4%, and chronic kidney disease – 1.6%. About 2.5% were obese with body mass index ≥30%. Smoking was a risk factor in 24.2% of male cases. About 17.8% were alcoholics. Sedentary lifestyle was present in 15% of cases. Anxiety, depression, and stress were present in 5% of cases. Dyslipidemia was present in 5% of cases.

It is observed that in-hospital mortality of COVID ACS cases had increased with comorbid conditions [Table 4]. Half of them were diabetic. About 28.6% of them had HT and current smoking history. In-hospital stay of death cases was analyzed. Half of them (7 out of 14) died within 24 h. Mostly death occurred between 2 PM and 8 PM (50%) followed by 2 AM and 8 AM (42.9%). Overall death occurred in the age group between 60 and 69 years [Chart 2]. Mortality is high in males than females. COVID ACS in-hospital mortality is high (14 out of 62, i.e., 22.6%), when compared to non-COVID ACS in-hospital mortality in the same period of time. According to vaccination status among 62 COVID ACS patients, 9 had 1st dose, 21 had 2nd dose, and 32 were not vaccinated [Table 5].

Table 4: The co-morbidities and COVID-related conditions of COVID ACS patients who have died

Comorbidities and COVID-related conditions	Total (%)
Comorbidities	
DM	7 (50)
HTN	4 (28.6)
Smoking	4 (28.6)
CT – chest findings (in involvement)	
Mild	4 (28.6)
Moderate	4 (28.6)
Severe	6 (42.9)
In-hospital stay	
<12 h	3 (21.4)
12–24 h	1 (7.1)
24–48 h	2 (14.3)
Time of death	
8 am–2 pm	1 (7.1)
2 am–8 pm	7 (50)
8 am–2 am	0 (0)
2 am–8 am	6 (42.9)

CT: Computed tomography

Table 5: The vaccination status of COVID ACS patients

Vaccination	No. of patients
1st dose	9
2nd dose	21
Not vaccinated	32
Total	62

ACS: Acute coronary syndrome, COVID: Coronavirus disease

Non-COVID ACS

In coronary care unit, 1541 cases were admitted with ACS [Table 6]. STEMI, NSTEMI, and unstable angina were 1496 (97%), 21 (1.36%), and 24 (1.56%), respectively. Out of 1541 cases of ACS, 231 (15.4%) cases died due to MI complications. The in-hospital mortality of STEMI, NSTEMI, and unstable angina was 15.4% (231 cases), 0%, and 0%, respectively. Management in non-COVID ACS cases includes primary percutaneous coronary intervention (PPCI), thrombolysis, and pharmacoinvasive therapy (PIT). In spite of all three modalities of therapy, the in-hospital mortality is high due to STEMI (15.4%) alone.

COVID STEMI

STEMI[9] occurred between the age group of 50 and 59 years (9 males + 4 females) followed by 60–69 years (10 males + 2 females) [Chart 3]. Median delay for STEMI cases was between 6 h and 12 h in majority of cases (15 cases) [Chart 4]. Out of 37 STEMI cases, 28 were male and 9 were female with male: female ratio of 0.76:0.24. Among 37 STEMI cases, [Chart 5] 25 received thrombolytic therapy with streptokinase (SK), eight cases were referred after lysis for further management. Four cases were not lysed because of late arrival to hospital. Late arrival in the pandemic situation is multifunctional like fear of acquiring severe infection and silent myocardial infarction due to atypical symptoms such as shortness of breath and palpitation.

Two cases were received in cardiogenic shock. Among them, one had anterior wall myocardial infarction (AWMI) and another had inferior wall myocardial infarction (IWMI).

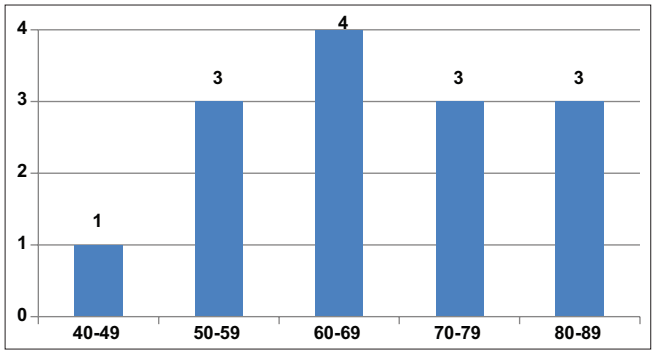


Chart 2: The mortality of COVID ACS patients according to their age group

AWMI case was lysed with SK and IWMI case was not lysed because of late arrival (>48 h). All STEMI cases were thrombolysed if they come in 12 h–24 h. Others were heparinized using low-molecular-weight heparin (LMWH) (enoxaparin 40 mg twice a day).

Since there is no dedicated COVID Cath Lab, we treated all STEMI cases with pharmacotherapy only. Only one patient underwent percutaneous transluminal coronary angioplasty (at private hospital) elsewhere following thrombolysis in our center (pharmacoinvasive PCI). Primary PCI could not be done as we mentioned already about lack of dedicated COVID Cath Lab [Table 7].

During lysis in COVID ICU, one patient developed ventricular tachycardia (VT) and another had ventricular fibrillation (VF). Both cases were direct current cardioverted. Among STEMI cases, nine patients had severe lung involvement with GGO of > 50% of lung fields with CORADS 5. Out of 37 STEMI, 10 cases died [Male-7 and Female-3]. The in-hospital mortality rate was higher with severe lung involvement. In-hospital mortality of COVID STEMI cases (27%) is high and overestimated, because six cases died of severe COVID pneumonia *per se*.

Non-COVID STEMI

Among 1496 non-COVID STEMI cases, [Table 7] thrombolysis was done to 1125 cases (75%), PPCI was done to 86 cases (5.7%), and PIT was offered to 112 cases (7.5%). Out of 1496 STEMI cases in non-COVID ICU, 231 deaths (in-hospital mortality – 15.4%). In spite of all three modalities of therapy, the in-hospital mortality was high (15.4%) in non-COVID STEMI when comparing with in-hospital mortality of COVID STEMI cases (27%).

COVID NSTEMI

Among 62 ACS cases, five cases – three males and two females had NSTEMI [Chart 6]. Four cases were between 50 and 60 years; one case was between 70 and 80 years. Diabetes and HT were the risk factors among NSTEMI cases. All NSTEMI were heparinized. One patient died due to severe COVID pneumonia. In-hospital mortality rate is high (one out of five) (i.e., 20%) in comparison with in-hospital mortality rate among NSTEMI cases admitted in non-COVID ICU (0 out of 25) (i.e., 0%) [Table 6].

Table 6: The total number of ACS patients in COVID and non-COVID ICUs and their death rate

Types of ACS	Total patients		Death		Death rate (in %)	
	COVID ICU	Non-COVID ICU	COVID ICU	Non-COVID ICU	COVID ICU	Non-COVID ICU
STEMI	37	1496	10	231	27	15.4
NSTEMI	5	21	1	0	20	0
Unstable angina	20	24	3	0	15	0
Total	62	1541	14	231	22.6	15

STEMI: ST-segment elevation myocardial infarction, NSTEMI: Non-STEMI, ICU: Intensive care unit, ACS: Acute coronary syndrome

Non-COVID NSTEMI

Non-COVID NSTEMI cases were 21 out of 1541 cases (1.4%). They were given heparin and guideline directed medical therapy followed by invasive therapy, that is, coronary artery angiography (CAG) and procedures. There were no deaths in non-COVID NSTEMI cases.

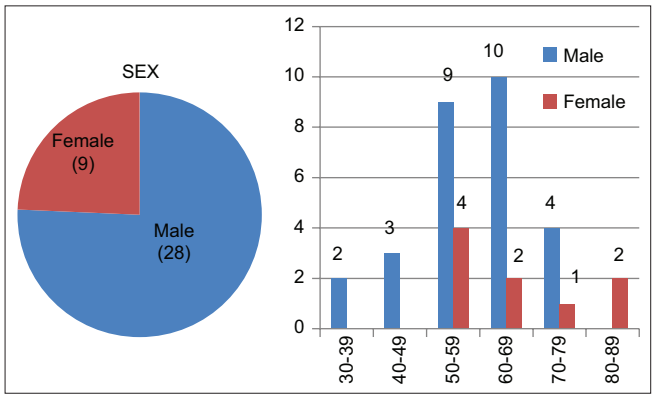


Chart 3: The number of STEMI patients in COVID wards according to sex and age criteria

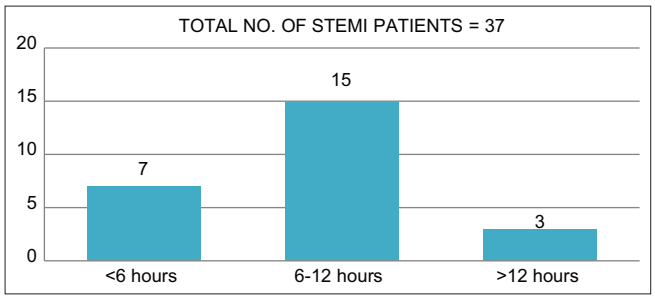


Chart 4: The duration of median delay for the COVID STEMI patients

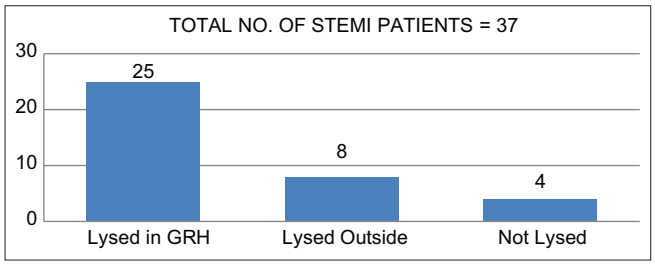


Chart 5: The thrombolysis status of STEMI patients in COVID

Table 7: The no. of STEMI patients undergone lysed, PPCI, and PIT in COVID and non-COVID wards

No. of STEMI	Management methods	No. of cases and (%)
COVID wards (37)	LYSED	37 (100)
	PPCI	0 (0)
	PIT	1 (2.7)*
Non-COVID wards (1496)	LYSED	1125 (75.2)
	PPCI	86 (5.75)
	PIT	112 (7.5)

(*) One patient underwent PIT privately, STEMI: ST-segment elevation myocardial infarction, PPCI: Primary percutaneous coronary intervention, PIT: Pharmacoinvasive therapy, STEMI: ST-segment elevation myocardial infarction

COVID Unstable Angina

There were 20 unstable angina cases, [Chart 7] 14 males and 6 females (male: female ratio – 7:3). Highest incidence occurred between 50 and 59 years of age. ST and T with changes were present in all cases and troponin levels were elevated in 50% of the cases. Typical angina with ST and T changes with elevated troponin levels was treated as unstable angina [Figure 1]. Those with diffuse ST and T changes [Figure 2] were categorized as myopericarditis, and they were followed up with echo, serial ECGs, and troponin. Cardiac magnetic resonance imaging would have thrown light to diagnose acute myocarditis and myopericarditis [Figure 3]. Eleven such cases were diagnosed in the same duration of our study.

All unstable angina cases were treated with LMWH (enoxaparin 40 mg IV twice a day). There were 3 deaths (15%) among unstable angina patients with COVID. This indicates that severe COVID contributed for increased in-hospital mortality in unstable angina.

Non-COVID Unstable Angina

Non-COVID unstable angina cases were 24 out of 1541 cases (1.6%) [Table 6]. They were managed with heparin-based therapy followed by invasive therapy, that is, CAG and procedures. There were no deaths in non-COVID unstable angina cases.

DISCUSSION

Since severe acute respiratory syndrome coronavirus 2 is a novel virus, there were no proper guidelines from randomized controlled clinical trials and studies to give[10] management protocols for ACS patients with COVID-19.[11] Many private hospitals were closed and there was shortage of workforce of doctors and staffs, since they were diverted to work in COVID wards in shift basis. Since there is no dedicated Cath Lab, primary PCI and pharmacoinvasive PCI could not be offered to COVID ACS patients. Many of them came late with evolved MI with poor left ventricle (LV) function. In these circumstances, we offered all STEMI cases (who were fit to receive thrombolytic therapy) thrombolysis with SK. All NSTEMI and unstable angina cases were treated with conservative medical therapy [Table 8]. LMWH was given intravenously 40 mg twice a day dose to have adequate anti coagulation without producing major bleeding. Aspirin (150 mg), Clopilet (75 mg), and Atorvastatin (80 mg) were given to all ACS cases unless contraindicated. Angiotensin-converting enzymes, angiotensin receptor blockers, and beta-blockers were avoided in some cases due to respiratory

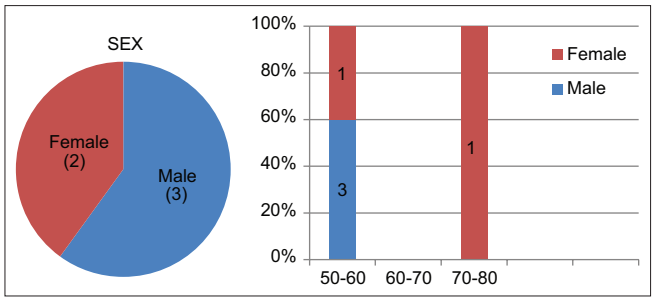


Chart 6: The number NSTEMI patients in COVID wards according to sex and age criteria

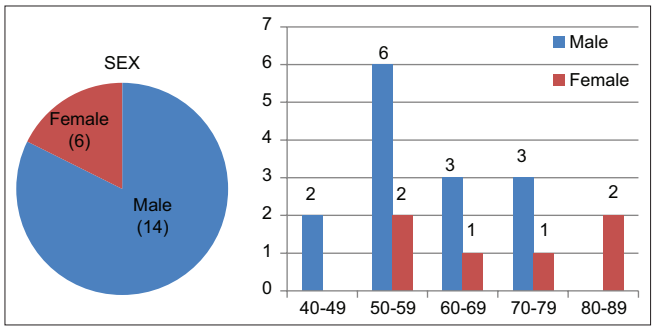


Chart 7: The number of unstable angina patients in COVID wards according to sex and age criteria

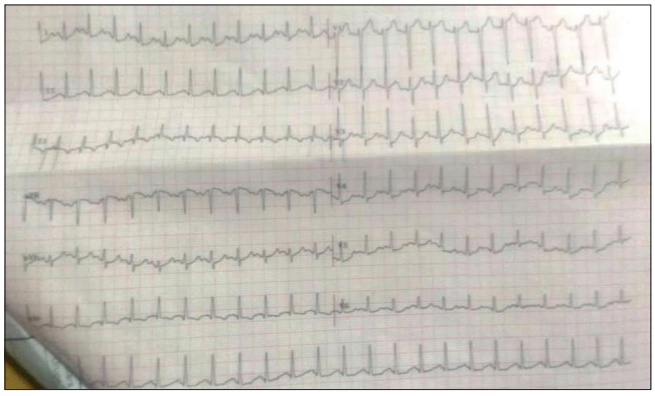


Figure 1: The ECG of COVID ACS patient with sinus tachycardia with ST depression

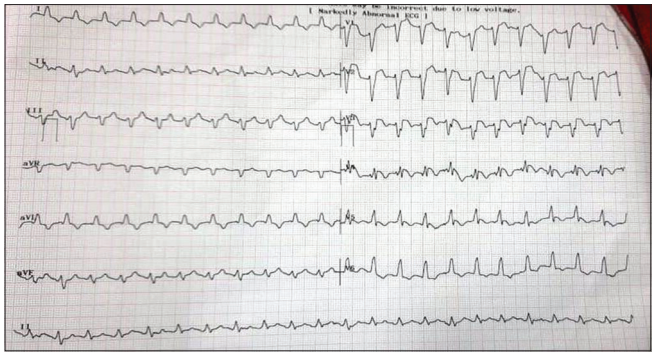


Figure 2: The ECG of COVID ACS patient with rheumatoid arthritis showing ST changes and 1st degree AV block

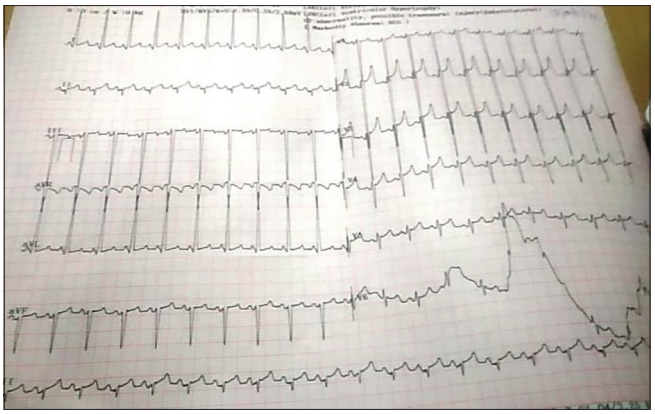


Figure 3: The ECG of a patient with myopericarditis

Table 8: The medical management protocol for COVID ACS patients

STEMI	NSTEMI	Unstable angina
Streptokinase	Heparin	Heparin
Heparin	Aspirin	Aspirin
Aspirin	Clopidogrel	Clopidogrel
Clopidogrel	Atorvastatin	Atorvastatin
Atorvastatin	Beta-blockers*	Beta-blockers*
ACE inhibitors*	ACE inhibitors*	ACE inhibitors*
Beta-blockers*		

(*) Used depending on the risk benefit ratio of the cases, STEMI: ST-segment elevation myocardial infarction, NSTEMI: Non-STEMI

distress due to severe lung involvement. Ivabradine used to reduce heart rate in sinus tachycardia [Figure 4] cases and also as a part of anti-failure management. Furosemide used with caution to avoid dehydration and electrolyte loss. Angiotensin receptor neprilysin inhibitor and sodium-glucose cotransporter-2 inhibitors were not used. Other management as per standard guidelines of ACS was followed. The outcome compared with non-COVID ACS cases who were admitted in the same period. In spite of interventional therapy, there is not much difference in the mortality rate comparing to thrombolytic therapy alone. Patients with MI and COVID died not only because of MI but also because of severe lung involvement.

During lysis, two cases developed VT and one had VF as reperfusion arrhythmia. Both were managed with electrical cardio version followed by amiodarone infusion for 12–24 h. All safety precautions as per COVID protocol were followed in the view of safety of patient as well as health-care providers. Inotropes (noradrenaline infusions) were used for two cardiogenic shock cases. Intra-aortic balloon pump, extracorporeal membrane oxygenation, and LV assist devices were not used because of unavailability. One young male (38 years) with AWMI had AWMI in COVID ward. He was lysed and referred to private hospital for further evaluation because he

Table 9: The COVID-related conditions for the COVID ACS patients

COVID-related conditions	Status	STEMI	NSTEMI	Unstable angina
RT-PCR	+ve	29	3	15
	-ve	6	1	4
	Not done	2	1	1
CT – Chest lung involvement	Mild (<15%, CORADS – 5)	11	2	6
	Moderate (15–50%, CORADS – 5)	17	2	10
	Severe (>50%, CORADS – 5)	9	1	4
O_2 management	Room air	11	2	1
	Face mask	9	1	7
	NRM	8	2	8
	NIV – CPAP	4	-	3
	Mechanical invasive ventilator	3	-	1
	HFNO	2	-	-

RT-PCR: Reverse transcription-polymerase chain reaction, CT: Computed tomography, ACS: Acute coronary syndrome, COVID: Coronavirus disease

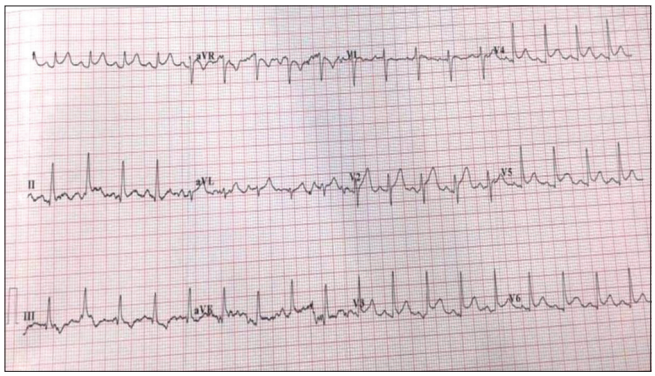
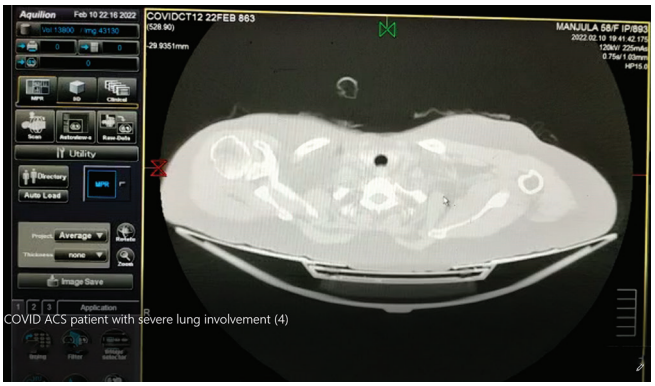


Figure 4: The ECG of COVID ACS patient with diffused ST elevation



Video 1: The CT cine video of COVID ACS patient with severe lung involvement (GGO – 90%)

wanted to go for it. We followed him; he was subjected to CT CAG and CAG. The left anterior descending artery showed 90% lesion which was stented. All other 61 cases were given only medical management. Role of bedside echo by point-of-care ultrasound[12] was useful to arrive at final diagnosis. Screening echo showed massive PE in one case and pulmonary embolism in another case. Both dealt accordingly. Both cases were having atypical angina and ST and T changes with tachycardia in the ECG. Pulmonary embolism patient was lysed with alteplase but he succumbed due to >95% lung involvement. Massive PE case survived after echo-guided pericardiocentesis. Three cases were COVID tested positive and one patient had severe lung involvement [Video 1]. Many (47 out of 62) were tested RT-PCR positive. Fourteen out of 62 cases had severe lung involvement. One case needed mechanical ventilation; other cases treated with continuous positive airway pressure (three cases), non-rebreather mask (eight cases), and facemask (seven cases) [Table 9].

Outcome

It is observed that there is little difference in in-hospital mortality between COVID ACS cases and non-COVID ACS cases. Out of 62 ACS cases with COVID-19, in-hospital mortality rate was 22.6%.[13] Out of 1541 ACS cases without COVID, in-hospital mortality rate was 15.4%. Half of them had DM as risk factor. In-hospital mortality rate is higher in males than females.[14] STEMI group shows higher deaths between ages 60 and 69 years. Most deaths (57%) occurred within 24 h.

Limitations of Study

In-hospital mortality may not represent true long-term outcomes that were not assessed in our study. Details on guideline directed medical therapy, duration of hospital stay, and risk factors for mortality such as arrhythmias have not been included in the study. Our study may not reflect the true population incidence of MI due to transport issues and referral bias.

CONCLUSION

In COVID pandemic, ACS patients seek medical attention and care after a period of delay due to fear of acquiring infection[15] and other social causes. There was dilemma in diagnosing[16] and classifying them as STEMI, NSTEMI, and unstable angina because of many mimickers. Even after diagnosis of ACS with COVID, there is difficulty in managing them with invasive strategy. There is high incidence

of unstable angina in COVID ACS when comparing to non-COVID ACS. In our Study, there were no female ACS patients with COVID-19 below 50 years.Thrombolytic therapy alone saved 85% of COVID ACS cases.[17] The in-hospital mortality in COVID ACS is not only due to MI[18] but also due to severe COVID pneumonia. The in-hospital mortality in COVID ACS treated with mild-to-moderate COVID pneumonia is comparable with non-COVID ACS treated with invasive strategy.

ETHICAL APPROVAL

This study was approved by the Institutional Ethics Committee.

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Original Article

Study of Patients Presenting with Complaint of Headache in ENT Outpatient Department: A Prospective Study

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Abstract

Introduction: Headache is perhaps one of the most common symptoms in medical practice. In most of the cases, headaches are not harmful, but in some cases, they can show symptoms of meningitis, stroke, brain tumor, or subarachnoid hemorrhage.

Aims and Objectives: The aims of this study were as follows: (1) To study the common age and gender distribution of headache. (2) To find out triggering and relieving factor. (3) To categorize different types of headache cases coming to an ENT specialist. (4) To find out frequency of sinus disease causing headache.

Methods: A total of 150 patients were selected randomly, attending ENT department with history of headache. A ready questionnaire was used to record the data of patients. Patients coming with different form of neuralgic pain were excluded from the study.

Results: The patients in the age group of 21–30 were experiencing more head ache. Women suffer more than men do from headache. Stress was found to be the triggering factor, whereas medication and good sleep were found to be relieving factor. Tension type headache followed by migraine were the most common cause among primary headache. A good number of patients 72 (48%) were having existing ENT-related problems.

Conclusion: The study showed the challenges of patients experiencing headache and approaching the ENT department to determine the exact cause of headache and get satisfactory treatment. A group of doctors consisting of ENT specialist, neurologist, ophthalmologist, psychiatrists, and psychologist can bring many benefits to remove or cut short the victims sufferings.

Key words: Headache, Migraine, Primary headache, Secondary headache, Sinus headache, Tension type headache

INTRODUCTION

Headache is one of the most common symptoms in medical practice. Headache is defined as pain or any unpleasant sensation in the region of cranial vault above the orbitomeatal line. The international classification of headache disorders classified headache into two principal types – primary headache and secondary headache. Primary headache is the one, in which research scientists have failed to reach any specific causes. Secondary headache is attributed to innumerable reasons and can be caused by any physical disorder or discomfort. The primary headaches include migraine, tension type headache (TTH), cluster headache, and other trigeminal autonomic cephalalgias.[1]

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It is hard to find out a human being who had never experienced headache in life time. However, consultation with the physician is done very seldom. Therefore, the true incidence of headache remains unknown. In general, the primary headache disorders constitute nearly 98% of all headaches, with TTH and migraine being the most prevalent.[2] TTH affects 60–80% of the population, while migraine has a prevalence of 11–15%.[3,4] However, a number of patients come to the ENT specialist with a headache claiming to have "sinus trouble," but, in reality, only few patients have headache of nasal or sinus

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headache and headache due to refractive errors that are very commonly misdiagnosed as "sinus headache" and are investigated and treated for the same which increases the economic burden on the patients.[5-9]

The diagnosis of the underlying cause of headache depends mainly on an accurate history taking. History must reveal the true characteristic of headache, for example, onset whether sudden or gradual, length of suffering whether recent or old, periodicity whether episodic or chronic, triggering factors, for example, stress, nasal blockage, nasal cold, any particular food, insomnia, excessive sleep, and weather change, relieving factors, for example, good sleep, vomiting, and medication, complaints in relation to ENT head and neck region, for example, nasal obstruction, nasal cold, earache, pain on opening the mouth, toothache, and dysphagia, and complaints in relation to eyes, for example, blurring of vision, pain in eye; h/o any head injury, h/o vascular disease, metabolic disorder, or OTC drug taken for headache.[10]

A complete physical and neurological examination should be done. In majority of cases, investigations are not required to reach a diagnosis.[11]

The prevalence of headache in ENT patients and its subsequent changes of misdiagonosis is high. Hence, this study was aimed to analyze the incidence of headache in ENT department patients and various triggering and relieving factors for headache.

Aims and Objectives

This aims of this study were as follows:

1. To find out the common age and gender distribution of headache
2. To find out the triggering and relieving factors of headache
3. To categorize different types of headache cases coming to ENT specialist
4. To find out the frequency of sinus disease causing headache.

METHODS

A total of 150 patients were selected randomly, attending ENT outpatient department of SMHS Hospital GMC Srinagar, J and K from June 2018 to 2019. A patient approaching with complaint of headache with history of recurrent episode was included in the study. Patients coming with different forms of neuralgic pain in head neck region such as TM joint neuralgia, glossopharyngeal neuralgia, or atypical facial pain were excluded.

A questionnaire sheet was given to each patient who was filled by the patient after having thorough conversation for 15–20 min with the patient. For every case, the characteristics of headache, symptoms associated with it, triggering factors, relieving factors, and complaints related to ENT Head – Neck region or Eye or CNS were noted carefully. Any previous history of head injury and present or past medical disorders was also documented in the ready sheet. A thorough and complete ENT head – neck and neurological examinations was done. The main purpose of majority of the patients to see an ENT specialist was the fear of having sinus disease, so an X-ray PNS occipitomeatal view was advised to all patients either to exclude sinus disease or prove sinus disease when history was suggestive.

RESULTS

For the study, a total 150 cases of headache were selected randomly.

DISCUSSION

The purpose of this study was to find out the age and sexual criteria of headache cases which come to ENT specialist. The age range was divided into five groups ranging from 11 to 60 years [Table 1]. The prevalence of headache in our study was maximum in age group of 21–30 years (35.33%), and thereafter, the prevalence declined which was similar with the study conducted by Tepper *et al*., Alberca *et al*., and Bahra *et al*.[12-14]

In this study, majority of patients were female (67.33%) than male (32.66%) in every age group [Table 1] which is similar with the study conducted by Bahra *et al*. and Manzoni *et al*.[15,16]

In present study, stress (14.66%) was the major triggering factor responsible for headache, followed by nasal cold (12%) and insomnia (11.33%) [Table 2]. Stress is also mentioned as the principal factor triggering headache in different studies conducted on headache.[17,18] However, the most common attributions of headache remains unrealized (16.6%).

Other factors which were discovered in our study that trigger headache include nasal blockage (8%), sunlight

Table 1: Age and gender distribution (*n*=150)

Age in years	Male patient (%)	Female patients (%)	Number of patients	Percentage
11–20	15 (10)	26 (17.33)	41	27.33
21–30	15 (10)	38 (25)	53	35.33
31–40	12 (18)	22 (14.66)	34	22.66
41–50	05 (3.33)	11 (7.3)	16	10.66
51–60	02 (1.33)	04 (2.6)	06	04

Table 2: Factors triggering headache

Triggering factor	Times mentioned	Percentage
Stress	22	14.66
Nasal cold	18	12
Insomnia	17	11.33
Nasal block	12	8
Sunlight	11	7.3
Long journey	08	5.3
Excessive talking	06	4
Excessive sound	05	3.3
Looking downward	04	2.6
Looking upward	04	8
Miscellaneous	14	9.3
Not realized	25	16.6

Table 3: Factors relieving headache

Relieving factors	Times mentioned	Percentage
Medication	48	21.33
Good sleep	32	21.33
Vomiting	10	6.6
Relieved spontaneously	09	6
Not relieved by anything	04	2.6
Not recognized	35	23.33

Table 4: Single clinical diagnosis (*n*=150)

Headache type	No of patients	Percentage
TTH	64	42.66
Migraine	52	34.66
Cluster headache	13	8.6
Paroxysmal hemicrania	7	4.6
Sinusitis	7	4.6
H/O head injury	7	4.6

TTH: Tension type headache

Table 5: ENT problem along with primary headache (*n*=150)

Cause of headache	Number of patients	Percentage
TTH+DNS	20	13.33
Migraine+DNS	15	10
Migraine+Sinusitis	08	5.3
TTH+Sinusitis	12	8
TTH+Nasal polyp	02	1.3
TTH+Nasal allergy	05	3.33
Migraine+Nasal allergy	08	5.3

TTH: Tension type headache

(7.3%), long journey (5.3%), excessive talking (4%), excessive sound (3.3%), looking downward (2.6%), looking upward (8%), and miscellaneous (9.3%).

Among the relieving factors [Table 3], medication 48 (21.33%) was found to be highest relieving factor, followed by good sleep 32 (21.32%) and vomiting 10 (6.6%). Medication was also noted to be the main relieving factor of headache in study conducted by Goadsby and Lipton, Aromaa *et al*.[17,18]

Table 6: Significant ENT problem in headache patients (*n*=150)

ENT problem	Present (%)	Absent (%)
No. of patients	72 (48)	78 (52)

Table 7: Referral required for further management (*n*=150)

Name of discipline	Number of patients	Percentage
Neuromedicine	02	01.67
Ophthalmology	04	03.33
Psychiatry	01	00.84
Physical medicine	01	00.84
ENT surgery	15	12.50

Sinusitis is the common cause of headache worldwide affecting millions of individuals, but only 7 (4.6%) cases of headache were truly seen diagnostic of sinus headache following the criteria of his [Tables 4 and 5]. Among the primary headache, most common cause on our study was TTH (42.66%), migraine (34.66%), cluster headache (8.6%), paroxysmal hemicranias, sinusitis, and h/o head injury (4.6%). This is similar with the study conducted by Goadsby and Lipton, Aromaa *et al*.[17,18]

In our study, a number of cases 72 (48%) had a coexisting significant ENT problem along with primary headache explaining the reason why headache is thought to be sinus in origin [Table 6].

For further evaluation, we had refer 2 (1.67%) cases to neurophysician, 4 (3.33%) cases to ophthalmologist, 1 (0.84%) cases to psychiatrists, and 1 (0.84%) cases to physical medicine. Fifteen (12.5%) cases, however, require surgical treatment in nose and paranasal region [Table 7].

CONCLUSION

Headache is nearly a universal human experience. The lifetime experience of headache is estimated to be at least 90%. Most of the patients either suffer from vascular or muscular headache diagnosed by medical practitioner or self-diagnosed as sinus headache. Thus, majority of cases can be treated by the primary care physicians or generalist with a correct clinical diagnosis without any special investigation. Therefore, a group of doctors consisting of ENT specialist, neurologist, ophthalmologists, psychiatrists, and psychologist can bring many benefits to remove or decrease the suffering of headache patients.

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Original Article

Prevalence of Cerebral Microbleeds in Patients Undergoing MRI Brain for Suspicious Neurological Symptoms

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Abstract

Aim: The aim is to estimate the prevalence of cerebral microbleeds (CMBs) in patients undergoing magnetic resonance imaging (MRI) brain for suspicious neurological symptoms.

Materials and Methods: This was a cross-sectional observational study of 200 patients (≥50 years of age) undergoing MRI brain. MRI examinations were assessed for the presence of CMBs, ischemic cerebrovascular disease, and intracerebral hemorrhage. Patients with contraindications for MRI examination, head trauma, intracranial space occupying lesion, and central nervous system infection were excluded for the study.

Results: Mean age of the study subjects was 63 years. Overall, the prevalence of CMBs was found to be 26%. The prevalence of CMBs among males was 26.1% and the prevalence among females was 25.8%. The prevalence of CMBs in patients having suffered from intracerebral hemorrhage was 72.7% and the prevalence in patients with ischemic cerebrovascular disease was 35.5%. Deep and infratentorial microbleeds were found in 86.5% of the study subjects while as 13.5% had microbleeds in strictly lobar distribution.

Conclusion: CMBs are considered as markers of small vessel pathology. The frequency of CMBs varies by population. The prevalence of CMBs is lowest in healthy individuals, intermediate in patients with ischemic cerebrovascular disease, and highest in patients with intracerebral hemorrhage.

Key words: Cerebral microbleeds, MRI brain, Neurological symptoms, Prevalence

INTRODUCTION

Cerebral microbleeds (CMBs) are small hypointense focii with maximum size of up to 5 mm or even up to 10 mm detected using susceptibility weighted imaging (SWI) magnetic resonance imaging (MRI).[1-5] CMBs are tiny deposits of blood degradation products (mainly hemosiderin) contained within macrophages and lying in close spatial relationship with structurally abnormal vessels. Hemosiderin is a strong paramagnetic material allowing its detection when a magnetic field is applied.[6] This phenomenon is called susceptibility effect and is the basis of T2*-GRE imaging.[7] Most sensitive sequence to detect CMBs is SWI.[8] CMBs act as markers of small vessel disease. Specific topographic patterns of CMBs are thought to be representative of particular underlying vasculopathies mainly hypertensive vasculopathy and cerebral amyloid angiopathy. CMBs are also a common finding in other populations, even in healthy elderly individuals. In the differential diagnosis of CMBs, other causes of signal loss on GRE sequences have to be considered which include vascular flow voids, calcium or iron deposits in basal ganglia, cerebral cavernous malformations, and head trauma.

CMBs may be categorized into one of the three locations: lobar (cortical gray and subcortical or periventricular white matter), deep (deep gray matter matter: basal ganglia and thalamus and white matter of corpus callosum, and internal and external capsule), and infratentorial (brainstem cerebellum). CMBs are strongly predictive of mortality.

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Deep and infratentorial microbleeds are associated with cardiovascular mortality, while as lobar microbleeds are associated with stroke related mortality.[9] CMBs can also cause gait disturbances and cognitive impairment.[10]

MATERIALS AND METHODS

This was a cross-sectional study which was undertaken by the Department of Radiodiagnosis and Imaging, Government Medical College, Srinagar, with the aim to estimate the prevalence of CMBs in patients undergoing MRI brain for suspicious neurological symptoms (headache, dizziness, vertigo, numbness, syncope, and subjective memory impairment). The study was carried out over a period of 18 months (2020–2021). The study included 200 patients. The Ethics Committee approved this study and the study was carried out after explaining the study details and taking written informed consent from the patients. Patients aged ≥50 years were included in the study. Patients with contraindications for MRI, brain trauma, acute central nervous system infection, and intracranial space-occupying lesion were excluded for the study.

MRI examination was done on 3 Tesla equipment. For brain, following sequences and slice thickness were obtained: (i) T1-weighted axial sequence-3 mm, (ii) T2-weighted axial sequence-3 mm, (iii) fluid-attenuated inversion recovery axial sequence-4 mm, (iv) diffusion-weighted imaging (DWI) sequence-5 mm, and (v) SWI sequence.

The SWI sequence used in our study was a 3-dimensional, T2*-weighted, and gradient recalled echo sequence with a high resolution used for microbleed detection. The parameters of SWI were as follows: TR/TE 28/20 ms, flip angle 15®, matrix 448 × 364, number of excitations 1, field of view 18.68 × 23.0 cm, and slice thickness 2.0 mm.

On MRI brain, patients were assessed for the presence of CMBs. MRI examination was also evaluated for the presence of white matter hyperintensities, lacunar infarcts, large vessel infarcts, and intracerebral hemorrhage.

Statistical Analysis

The recorded data were compiled and entered in a spread sheet (Microsoft Excel) and then exported to data editor of SPSS version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as mean ± SD and categorical variables were summarised as frequencies and percentages.

RESULTS AND DISCUSSION [TABLES 1-6 AND FIGURES 1-3]

This study included 200 patients undergoing MRI brain for suspicious neurological symptoms. Mean age of the study

Table 1: Prevalence of microbleeds in the study subjects

Microbleeds	Number	Prevalence (%)
Present	52	26
Absent	148	74
Total	200	100

Total number of study subjects=200. Number of subjects detected with CMBs=52. Overall prevalence of CMBs=26%

Table 2: Prevalence of microbleeds as per gender

Gender	Microbleeds		No Microbleeds		*P*-value
	No.	%age	No.	%age	
Male	29	26.1	82	73.9	0.964
Female	23	25.8	66	74.2	
Total	52	26.0	148	74.0	

Out of 200 study subjects, 111 were male and 89 were female. Prevalence of CMBs in males=26.1%. Prevalence of microbleeds in females=25.8%

Table 3: Prevalence of microbleeds in patients with ischemic cerebrovascular disease

Microbleeds	Number of patients with ischemic cerebrovascular disease	Prevalence (%)
Present	11	35.5
Absent	20	64.5
Total	31	100

Number of patients with ischemic cerebrovascular disease=31. Patients with ischemic cerebrovascular disease having CMBs=11. Prevalence of microbleeds among patients of ischemic cerebrovascular disease=35.5%

Table 4: Prevalence of microbleeds in patients with intracerebral hemorrhage

Microbleeds	Number of patients with intracerebral hemorrhage	Prevalence (%)
Present	8	72.7
Absent	3	27.3
Total	11	100

Number of patients with intracerebral hemorrhage among study subjects=11. Number of patients with intracerebral hemorrhage having CMBs=8. Prevalence of microbleeds among patients of intracerebral hemorrhage=72.7%

Table 5: Prevalence of microbleeds in healthy patients

Microbleeds	Number	Prevalence (%)
Present	33	20.9
Absent	125	79.1
Total	158	100

Prevalence of CMBs among healthy study subjects=20.9%

Table 6: Distribution/location of microbleeds

Location	Number	Percentage
Deep and infratentorial	45	86.5
Lobar	7	13.5
Total	52	100

Number of patients with deep and infratentorial microbleeds=45. Number of patients with strictly lobar microbleeds=7. Percentage of patients with deep and infratentorial microbleeds=86.5%. Percentage of patients with strictly lobar microbleeds=13.5%

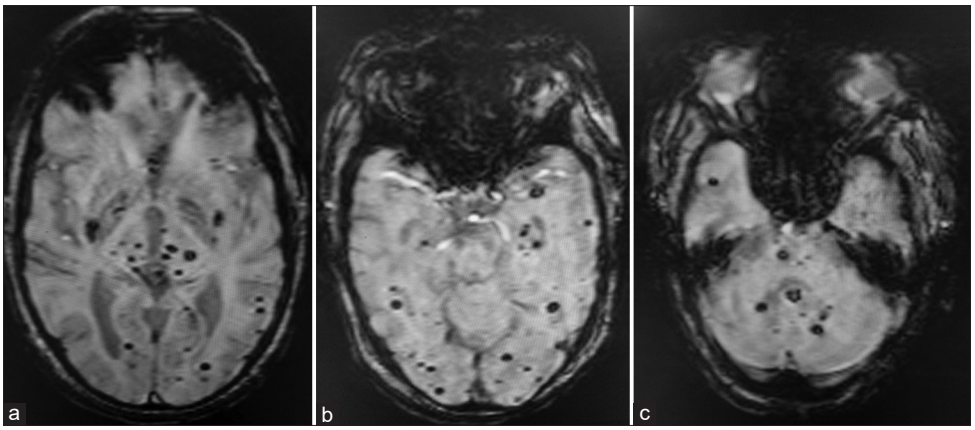

Figure 1: Multiple supratentorial and infratentorial microbleeds in a patient with chronic hypertension. (a) SWI showing multiple microbleeds in bilateral thalami and basal ganglia. (b) SWI showing microbleeds in bilateral occipital and temporal lobes. (c) SWI showing microbleeds in cerebellum

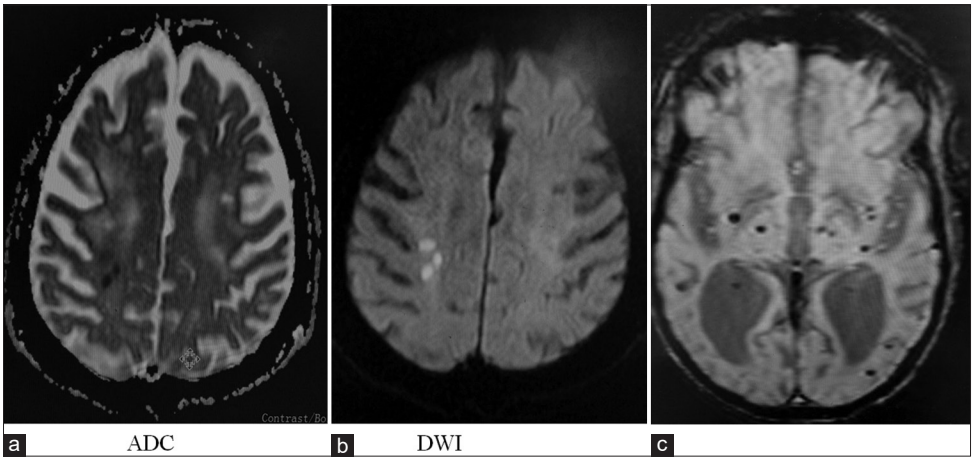

Figure 2: Microbleeds in a patient with acute lacunar infarct in right centrum semiovale. (a) Apparent diffusion coefficient – Area of diffusion restriction in right centrum semiovale. (b) Diffusion-weighted imaging - Area of diffusion restriction in right centrum semiovale. (c) SWI showing multiple microbleeds in bilateral basal ganglia and left occipital lobe

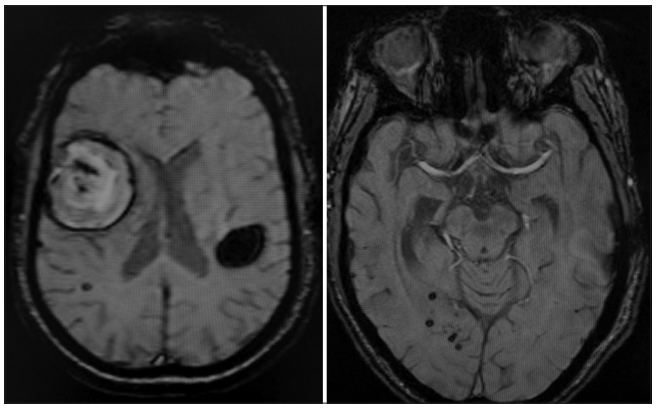

Figure 3: Lobar microbleeds in a patient with few lobar hemorrhages (probable CAA). Susceptibility weighted imaging showing blooming in lobar hemorrhages and microbleeds right parietal and occipital lobe

subjects was 63 years. Out of 200 study subjects, 111 were male, while as 89 were female. Out of 200 patients, 11 were detected with intracerebral hemorrhage, among which three patients had lobar hemorrhage and eight patients had hemorrhage in deep and infratentorial location (basal ganglia, thalami, brainstem, and cerebellum). One hundred and two patients had white matter hyperintensities. Out of 200 patients, 31 patients were detected with ischemic cerebrovascular disease (acute and chronic lacunar infarcts and large vessel infarcts). Out of 200 patients, microbleeds were detected in 52. Hence, the overall prevalence of CMBs in our study was found to be 26%. It has been found that frequency of CMBs varies enormously depending on the MRI study characteristics (such as field strength, sequence used for cerebral microbleed detection, and section thickness) and selection of study subjects. Several population based studies have reported on microbleed prevalence and according to Rotterdam scan study (performed using 1.5T MRI), the prevalence of CMBs in healthy older individuals can be as high as 23.5%.[11] The difference in the reported prevalence of CMBs can be attributed to higher field strength MRI (3T) used to perform the study apart from the differences in the study populations which may be present. This finding has also been seen by Stehling *et al*.[12]

who have reported that the detection rate and visibility of CMBs benefit from the higher field strength, resulting in a significantly improved depiction of iron-containing brain structures (CMBs) at 3.0T compared to that at 1.5T.

In our study, the prevalence of CMBs among males was found to be 26.1% and the prevalence among females was found to be 25.8%. No significant difference in cerebral microbleed prevalence between males and females was found. Similar findings were reported by Poels *et al*.[13] in the update of Rotterdam scan study.

In our study, the prevalence of CMBs in patients with ischemic cerebrovascular disease (acute and chronic lacunar infarcts and large vessel infarcts) was found to be 35.5%. Similar results were found by Naka *et al*.[14] and Tsushima *et al*.[15] The prevalence of microbleeds in patients having suffered from intracerebral hemorrhage (ICH) was found to be 72.7%. Similar finding was reported by Jeong *et al*.[16] They evaluated 102 patients with deep and lobar ICH and found that 70% had microhemorrhages and they were frequently multiple. A wide range in the prevalence of CMBs in different clinical conditions such as ischemic stroke and ICH has also been reported by Naka *et al*.,[14] Lee *et al*.[17] and Kato *et al*.[18]

Regarding the distribution of CMBs, deep and infratentorial microbleeds were found in 86.5% of the patients while as 13.5% of the subjects had microbleeds in strictly lobar distribution.

CONCLUSION

There is no significant gender-based difference in the prevalence of CMBs. The frequency of CMBs varies by population, its prevalence being lowest in healthy individuals, intermediate in patients with ischemic cerebrovascular disease, and highest in patients with intracerebral hemorrhage. CMBs can be considered as a sign of underlying small vessel pathology.

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Original Article

Association of Vitamin D Deficiency with Pre-eclampsia

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Abstract

Background: Vitamin D is emerging as a promising agent for pre-eclampsia (PE) prevention. Vitamin D deficiency is highly prevalent in women of reproductive age and in pregnant mothers. Vitamin D receptors on the heart and blood vessels of mother suggest that Vitamin D has a cardioprotective effect, and calcitriol can influence endothelial and vascular smooth muscle cell function as well as controlling inflammation and affecting the regulation of blood pressure through influences on the renin-angiotensin-aldosterone system.

Objective: The objective of the study was to study the prevalence, association, and impact of Vitamin D deficiency with PE and their outcome.

Methods: Before the onset of labor, blood samples were drawn from each participant and sent to laboratory for the estimation of Vitamin D levels. The results were reported deficient if it was <10 ng/ml, insufficient if 10–30 ng/ml, and normal when it was >30 ng/ml.

Results: Maternal complications observed were wound infection and eclampsia. Fetal and neonatal complications included intrauterine device (IUD), respiratory distress, early neonatal death, sepsis, prolonged neonatal intensive care unit (NICU) admission, and meconium aspiration syndrome. About 7.3% of patients with deficient Vitamin D had maternal complications. About 92.7% of live birth were seen in Vitamin D deficient women compared to 100% women with sufficient Vitamin D levels. IUD was seen in 7.3% of women with deficient Vitamin D compared to none in Vitamin D sufficient. Apgar score <7 was observed in 18.4% of women with Vitamin D deficiency compared to 5% women with sufficient Vitamin D. Prolonged NICU admission was observed in 5.3% of neonates of Vitamin D deficient mothers. Intrauterine growth restriction was seen in 13.2% of women with deficient Vitamin D compared to none in Vitamin D sufficient. Neonatal complications were seen in 26.3% of neonates delivered by mothers with deficient Vitamin D levels.

Conclusion: Vitamin D be added to all the antenatal patients as routine supplement to prevent the risk of PE and promote neonatal well-being.

Key words: Intrauterine device, Neonatal intensive care unit, Pre-eclampsia, Vitamin D

INTRODUCTION

Hypertensive disorders of pregnancy are a major cause of maternal and fetal morbidity, disability, and mortality.[1] Globally, 10% of pregnant women suffer from hypertensive disorders[2] including 3–5% of pregnancies that suffer from pre-eclampsia (PE). In recent years, the discovery of Vitamin D-specific receptors and metabolites in the placenta and decidua[3] has highlighted the role of Vitamin D in pregnancy-related disorders. Vitamin D is emerging as a promising agent for PE prevention.[4] Vitamin D deficiency is highly prevalent in women of reproductive age and in pregnant mothers.[5] If proven effective, the population level benefits of Vitamin D supplementation would be substantial and likely to impact the long-term health of offspring.[6]

PE is thought to originate in early pregnancy when the maternal immune system limits placental invasion in mothers vulnerable to cardiovascular disease. Calcitriol can be considered a pregnancy-supporting factor[7] that could work through several mechanisms to reduce PE risk,

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including a direct influence of calcitriol on implantation, placental invasion, and angiogenesis.[8,9] It is also believed to be important in directing immune responses by dendritic cells and macrophages at the fetal-placental interface as well as immunological adaptation by the mother to reduce the risk of infection and inflammation.[4,9] Compared to normal pregnancies, Vitamin D metabolism is markedly altered in PE. This may be due to reduced placental 1α-hydroxylase activity[10] resulting in lower circulating calcitriol concentrations compared to normotensive or chronically hypertensive pregnant women.[11,12] Vitamin D status is reportedly lower in pre-eclamptic mothers at the time of diagnosis,[11,13] but also before disease onset in some studies.[14,15]

Vitamin D receptors on immune cells express key enzymes involved in the hormonal activation (CYP27B1) and catabolism (CYP24A1) of Vitamin D metabolites, suggesting that the availability and effectiveness of calcitriol can be directly regulated by the cells of the immune system.[16] The net result of calcitriol on adaptive immune responses leads to a skewing towards a more tolerogenic status, which is a maternal immune adaptation required for the maintenance of a healthy pregnancy.[17]

In vitro studies have demonstrated that calcitriol administration leads to an upregulation of regulatory T-cell responses while pro-inflammatory responses are typically downregulated,[16] constituting an adaptation to maternal tolerance that would reduce the risk of PE. Vitamin D receptors on the heart and blood vessels of mother suggest that Vitamin D has a cardioprotective effect, and calcitriol can influence endothelial and vascular smooth muscle cell function as well as controlling inflammation and affecting the regulation of blood pressure through influences on the renin-angiotensin-aldosterone system.[18]

Objectives

- To study the association of Vitamin D deficiency with PE
- To study the prevalence of Vitamin D deficiency in the women who suffer from PE
- Impact of different levels of serum Vitamin D on final outcome.

MATERIALS AND METHODS

The present case–control study was conducted in the Postgraduate Department of Obstetrics and Gynaecology, SKIMS Medical College and Hospital, Bemina, Srinagar, over a period of 2 years. The patients fulfilling the selection criteria were recruited for the study.

Inclusion Criteria

Pregnant women with blood pressure more or equal to 140/90 mmHg on two occasions at least 6 h apart within 7 days with proteinuria were included in the study. It was ensured that the participants are not taking any Vitamin D supplementation during the pregnancy.

Exclusion Criteria

(i) Women with other associated comorbidities including gestational diabetes and hypothyroidism and (ii) women with a history of any drug intake except the routine supplements and antihypertensives.

This study was carried out on pregnant women already diagnosed with PE, selected from routine admissions in SKIMS MCH and equal number of healthy pregnant women who were randomly selected as control group.

Written informed consent was taken from all women recruited into the study.

Before the onset of labor, blood samples were drawn from each participant and sent to laboratory for the estimation of Vitamin D levels. The results were reported deficient if it was <10 ng/ml, insufficient if 10–30 ng/ml, and normal when it was >30 ng/ml.

The recorded data were compiled and entered into a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean ± SD and categorical variables were summarized as frequencies and percentages. Graphically, the data were presented by bar and pie diagrams. Student's independent t-test or Mann–Whitney U-test, whichever feasible, was employed for comparing continuous variables. Chi-square test or Fisher's exact test, whichever appropriate, was applied for comparing categorical variables. $P < 0.05$ was considered statistically significant. All *P*-values were two tailed.

RESULTS

The mean age of cases was 29.3 ± 42.0 years with a range of 20–37 years, and in controls, the mean age was 29.5 ± 3.49 years with a range of 21–38. Education and socioeconomic level were low in majority of patients in our study showing that lower socioeconomic status and less education are significant risk factors for PE. Out of 61 patients, 35 patients were diagnosed of PIH in their 30–34 weeks of gestation, 20 (32.8%) patients were diagnosed at 25–30 weeks of gestation, and only 6 (9.8%) patients were diagnosed to have PIH at >35 weeks. The mean gestational age of diagnosis of PIH was 30.9 ± 2.79 weeks. Symptomatic

features of PE and eclampsia included headache, edema, blurring of vision, and nausea. 2+ urinary protein was seen in majority of patients followed by 1+ and 3+.

Insufficient (10–30 ng/ml) Vitamin D levels were observed in 65.6% in cases group followed by normal Vitamin D levels (>30 ng/ml) in 32.8% of women while only 1.6% of women were Vitamin D deficient. Deficient (<30 ng/ml) Vitamin D levels were seen in 41 (67.2%) women with PE compared to 28 (45.9%) women without PE. Sufficient (>30 ng/ml) Vitamin D levels were observed with 20 (32.8%) pre-eclamptic women compared to 33 (54.1%) women without PE. Out of a total of 61 patients studied, the mode of delivery was cesarean section in 42 (68.9%) women while as vaginal delivery was observed in 19 (31.1%) patients. Maternal complications observed were wound infection and eclampsia. Fetal and neonatal complications like intrauterine device (IUD) were seen in 3 (4.9%) patients, respiratory distress in 5 (8.2%) patients, early neonatal death, sepsis, and prolonged neonatal intensive care unit (NICU) admission were observed in 2 (3.3%) patients each while as only one fetal/neonate was seen to have meconium aspiration syndrome. Impact of Vitamin D deficiency was in in 12 (29.3%) women who delivered vaginally compared to 7 (35.0%) patients with sufficient Vitamin D. Cesarean delivery was observed in 29 (70.7%) patients with Vitamin D deficient compared to 13 (65.0%) patients with Vitamin D sufficiency. Impact of Vitamin D deficiency on maternal outcome was observed in 41 patients with deficient Vitamin D levels compared to 20 patients with sufficient Vitamin D levels. Only 3 (7.3%) patients with deficient Vitamin D had maternal complications while none of the patient with sufficient Vitamin D levels had maternal complications.

Impact of Vitamin D deficiency on neonatal outcome was observed in this study. Thirty-eight (92.7%) live birth were seen in Vitamin D deficient women compared to 20 (100%) women with sufficient Vitamin D levels. IUD was seen in 3 (7.3%) women with deficient Vitamin D compared to none in Vitamin D sufficient. Apgar score <7 was observed in 7 (18.4%) women with Vitamin D deficiency compared to 1 (5%) women with sufficient Vitamin D. Prolonged NICU admission was observed in 2 (5.3%) neonates of Vitamin D deficient mothers. Intrauterine growth restriction (IUGR) was seen in 5 (13.2%) women with deficient Vitamin D compared to none in Vitamin D sufficient. Neonatal complications were seen in 10 (26.3%) neonates delivered by mothers with deficient Vitamin D levels.

DISCUSSION

The present case–control study was conducted in the Postgraduate Department of Obstetrics and Gynaecology, SKIMS Medical College and Hospital, Bemina, Srinagar, over a period of 2 years. In our study, there were 28 (45.9%) gravida 1 in cases and 21 (34.4%) in controls, 15 (24.6%) women were gravida 2 in cases and 13 (21.3%) in controls, and 14 (23.0%) gravida 3 were in cases and 17 (27.9%) in controls. There were only 4 (6.6%) women with >gravida 4 in cases and 10 (16.4%) in controls. The difference observed was statistically insignificant with $P = 0.261$. Dabbaghmanesh *et al*.[19] found that comparison of 25 (OH) Vitamin D levels between normal primigravida women and severe PE women groups showed no significant differences ($P > 0.05$). Our results are also in conformity with the findings of Bodnar *et al*.[14] wherein 72.7% of women were gravida 1, 16.4% women were gravida 2, and 10.9% were gravida 3. In another study by Jindal *et al*.,[20] gravida 1 was most common in all the study groups (PE without severe features 69.66%, PE with severe features 55.56%, and controls 54.4%) followed by gravida 2 and gravida 3.

Out of 61 patients, 35 patients were diagnosed of PIH in their 30–34 weeks of gestation, 20 (32.8%) patients were diagnosed at 25–30 weeks of gestation, and only 6 (9.8%) patients were diagnosed to have PIH at >35 weeks. The mean gestational age of diagnosis of PIH was 30.9 ± 2.79 weeks. Gong *et al*.[21] confirmed that pregnancy-induced hypertension-associated complications are more frequent in early-onset (<gestational week 32) compared to late-onset PE. In their study, 413 women with severe PE were divided into three groups according to the gestational age at the onset of PE as follows: Group A (<32 weeks, 73 cases), Group B (between 32 and 34 weeks, 71 cases), and Group C (>34 weeks, 269 cases). In the present study, there were 4 (6.6%) women who were having edema as signs and symptoms followed by headache with edema in 3 (4.9%) patients and headache in 2 (3.3%) patients. Headache with blurring of vision and headache with nausea were seen in 1 (1.6%) patient each. Symptomatic features of PE and severe PE include oliguria (<500 mL of urine in 24 h), cerebral or visual disturbances, and pulmonary edema or cyanosis.[22,23]

Majority of patients were found to have 2+ urinary protein followed by 20 (32.8%) patients who had 1+ protein in urine. 3+ urinary protein was observed in 4 (6.6%) patients and 4+ urinary protein in 2 (3.3%) patients. PE is hypertension and proteinuria (protein in urine >0.3 g/24 h (1+ dipstick) on two occasions >6 h apart) or edema (Roberts *et al*., 2003[24] and Zhang *et al*., 1997[25]). Insufficient (10–30 ng/ml) Vitamin D levels were observed in majority of patients, that is, 40 (65.6%) in cases group. Normal (>30 ng/ml) Vitamin D levels were seen in 20 (32.8%) patients while as deficient Vitamin D levels were found in 1 (1.6%) patient. Ullah *et al*.[26] did a study on the prevalence of Vitamin D deficiency. Among all the subjects, 78.19%

had serum 25 (OH) D levels <30 ng/ml. The mean (±standard deviation, SD) 25 (OH) D level was 24.53 (±0.71) ng/ml in our study population. It was lowest among women with eclampsia (21.56 ± 1.16 ng/ml), slightly higher in PE (23.96 ± 1.31 ng/ml) and highest among controls (24.86 ± 1.02 ng/ml). Normal (>30 ng/ml) Vitamin D levels were seen in 33 (54.1%) patients in control group while as insufficient (10–30 ng/ml) Vitamin D levels were observed in 28 (45.9%) in control group. Deficient (<30 ng/ml) Vitamin D levels were seen in 41 (67.2%) women with PE compared to 28 (45.9%) women without PE. Sufficient (>30 ng/ml) Vitamin D levels were observed with 20 (32.8%) pre-eclamptic women compared to 33 (54.1%) women without PE. The difference observed was statistically significant with $P = 0.018$.

The safety of Vitamin D supplementation during pregnancy has recently been evaluated by several randomized controlled trials. Intake of up to 4000 units of Vitamin D3 daily or 35,000 units weekly for 10 weeks has been reported to be safe during the 3rd trimester of pregnancy, without producing hypercalcemia or other adverse effects (Hollis *et al*., 2011[27] and Roth *et al*., 2011[28]). Jindal *et al*.[20] showed that 68% of controls and 77.53% of PE subjects without severe features were Vitamin D deficient. Vitamin D level of pre-eclamptic women with mild features when compared with controls was not found to be significant ($P = 0.30$). There were 68% of controls and 86.11% of PE subjects with severe features were Vitamin D deficiency. This result showed that more patients of pre-eclampsia with severe features were deficient in Vitamin D levels as compared to controls. This was statistically significant ($P = 0.046$).

The significant difference in the mean Vitamin D levels observed in a study by Jindal *et al*.[20] was observed as compared to the control group indicated a strong association between deficiency of Vitamin D and PE. These findings are also consistent with the studies done by Sharma *et al*.,[29] Nidhi *et al*.,[30] Sahu *et al*.,[31] Sangeeta *et al*.,[32] Kumari *et al*.,[33] and Goel *et al*.[34]

In our study, out of a total of 61 patients studied, the mode of delivery was cesarean section in 42 (68.9%) women while as vaginal delivery was observed in 19 (31.1%) patients. Impact of Vitamin D deficiency was in 12 (29.3%) women who delivered vaginally compared to 7 (35.0%) patients with sufficient Vitamin D. Cesarean delivery was observed in 29 (70.7%) patients with Vitamin D deficient compared to 13 (65.0%) patients with Vitamin D sufficiency. The mode of delivery was most likely affected by PE rather than Vitamin D deficiency. Ali *et al*.[35] established the association of Vitamin D deficiency to PE among women of reproductive age. In the control group with healthy pregnancies, 70.5% delivered vaginally and 29.5% delivered by cesarean delivery. In contrast, in the case group who developed PE, only 27% had vaginal deliveries and 73% had a cesarean delivery. It was also noticed that healthy pregnant group was more likely to be taking vitamin supplements than PE group ($P = 0.001$). The percentage of premature delivery (<36 weeks) was higher with eclampsia (56.09%) and PE (24.39%) than controls (19.51%) in a study done by Ullah *et al*.[26]

In our study, maternal complications were observed in three patients in which wound infection was seen in 2 (3.3%) patients while as eclampsia was seen in 1 (1.6%) women. Fetal and neonatal complications like IUD were seen in 3 (4.9%) patients, respiratory distress in 5 (8.2%) patients, early neonatal death, sepsis, and prolonged NICU admission were observed in 2 (3.3%) patients each while as only one fetal/neonate was seen to have meconium aspiration syndrome. Impact of Vitamin D deficiency on maternal outcome was observed in 41 patients with deficient Vitamin D levels compared to 20 patients with sufficient Vitamin D levels. Only 3 (7.3%) patients with deficient Vitamin D had maternal complications while none of the patient with sufficient Vitamin D levels had maternal complications. Impact of Vitamin D deficiency on neonatal outcome was observed in this study. Thirty-eight (92.7%) live birth were seen in Vitamin D deficient women compared to 20 (100%) women with sufficient Vitamin D levels. IUD was seen in 3 (7.3%) women with deficient Vitamin D compared to none in Vitamin D sufficient. Apgar score <7 was observed in 7 (18.4%) women with Vitamin D deficiency compared to 1 (5%) women with sufficient Vitamin D. Prolonged NICU admission was observed in 2 (5.3%) neonates of Vitamin D deficient mothers. IUGR was seen in 5 (13.2%) women with deficient Vitamin D compared to none in Vitamin D sufficient. Neonatal complications were seen in 10 (26.3%) neonates delivered by mothers with deficient Vitamin D levels. Ullah *et al*.[26] called a study and concluded that since PE and eclampsia can lead to serious complications for both mother and the offspring, Vitamin D may be supplemented during pregnancy in high-risk populations to decrease these adverse consequences. Maternal and neonatal complications are more common in cases of recurrent PE when compared to the initial episode (Dildy *et al*., 2007).[36] Sahu *et al*.[31] conducted a study in which most babies had preterm birth and almost 62 out of 100 required SNCU admission due to prematurity or other neonatal complications such as growth restriction, respiratory distress, meconium aspiration syndrome, or hypoxic ischemic encephalopathy. Babies of PE mothers were calcium deficient which may be because of the prematurity and low birth weight. About 36% of the PE and eclampsia group mothers had preterm babies and 18% in the control group were preterm. About 38%

were admitted to SNCU as compared to the control group with 15% admission.

CONCLUSION

Since PE and eclampsia can lead to serious complications for both mother and the offspring, Vitamin D be added to all the antenatal patients as routine supplement to prevent the risk of PE and promote neonatal well-being.

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