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Ultrasound guided needle aspiration versus catheter drainage in management of liver abscess

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Abstract
Background: Image-guided percutaneous interventions are recent modalities practiced worldwide for the management of pyogenic liver abscess with different success rates.
Objective: To compare efficacy and safety of percutaneous needle aspiration (PNA) and pigtail catheter drainage (PCD) in the management of liver abscess.
Methodology: Thirty patients of liver abscess were randomized into two treatment groups: A- ultrasound guided PNA (n=20) and B- PCD (n=10) in conjunction with appropriate antimicrobial therapy. Demographic, clinical, haematological, radiologic findings were recorded and compared before and after treatment and analysed statistically.
Results: Most patients were of 41-50 years age with male predominance with alcoholism (60%) and diabetes mellitus (20%) as common comorbidities. Most common site of abscess was right lobe of liver and abdominal pain (70%) was common presenting symptom. Total white blood cell count, C-reactive protein, bilirubin, alkaline phosphatase, prothrombin time were significantly reduced in all patients in both the groups after treatment ($p<0.05$). Reduction in fever, abdominal tenderness, was observed at day 5-7 in both the groups ($p>0.05$). Abscess cavity of 5-7 cm size was reduced in 90% of patients of both groups while >7 cm size abscess cavity was reduced significantly more in group B ($p<0.05$).
Conclusion: PNA and PCD both are effective and safe in terms of success rate, abscess drainage, reduction in symptoms and abscess size and hospital stay without any significant difference. PNA being simpler, safer and more suitable choice for management of liver abscess with size <7 centimetres while for size >7 centimetres, PCD is better treatment option.
Key words: *liver abscess, percutaneous needle aspiration, percutaneous catheter drainage, pyogenic liver abscess*

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I. Introduction

Hepatic abscess is frequent complication and important health concern affecting all age groups particularly in tropical countries. Annual incidence of pyogenic liver abscess has been estimated at 2.3 cases per 100,000 populations and is associated with a significant mortality rate in both developing and developed countries (1). In Taiwan the incidence of pyogenic liver abscess (PLA) increased from 10.83 to 15.45 per 100,000 person in 2011 and its epidemiology continues to change based on data obtained from the Longitudinal Health Insurance Database 2000 (2). The incidence of pyogenic liver abscess based on hospital admissions ranges from 0.029 to 1.47% and 0.3 to 1.4% in autopsy studies. (3) There is a decline in the incidence of

pyogenic liver abscesses as well as a change in the relative frequency of pyogenic and amoebic abscesses but still it is matter of health concern in developing countries.

Early diagnosis and prompt treatment remains the key for reducing morbidity and mortality related to pyogenic abscess. Pyogenic liver abscess is having bacterial origin in most cases with occasional fungal infections. Most common organisms identified were Escherichia coli, Klebsiella, Proteus, Staphylococcus and Streptococcus etc. use of appropriate antimicrobials after culture and sensitivity testing can be very effective in reducing the morbidity. Ultrasonography, CT scan and MR technologies are used frequently for early and accurate diagnosis of the condition now-a-days. (3)

The basic principles lying behind the treatment of PLA was based on percutaneous catheter drainage of the abscess cavity, identification of the pathogen followed by appropriate antibiotic therapy. Continuous percutaneous catheter drainage has been most widely accepted and practiced therapy for treatment of pyogenic liver abscess with success rate ranging from 55.5% to 83%.(4) With the advent of latest imaging modalities like ultrasound CT scan and ultrasonography, image-guided percutaneous needle aspiration (PNA) is practiced in many cases of pyogenic liver abscess as PNA is less invasive and less expensive and do not require intensive catheter care. (4) Percutaneous aspiration and intravenous antibiotics are used for effective treatment of small abscesses during early detection. Liver abscess with a size larger than 5 cm require percutaneous catheter drainage (PCD) with antibiotic therapy. While abscess with smaller size can be effectively treated with PNA and proper antibiotic usage which have likely also contributed to further reductions in mortality. (5, 6)

A retrospective study by Gyorffy et al (7) has compared medical treatment, percutaneous and surgical drainage in total 26 pyogenic liver abscess and reported better results with surgical drainage. Various researchers has emphasized clearly that the treatment of pyogenic liver abscess should be individualized using all available treatment modalities. In a multivariate analysis by Chou et al age > 60 years, blood urea nitrogen > 20 mg per dL, serum creatinine > 2 mg per dL, total bilirubin > 2 mg per dL and albumin < 2.5 gm per dL were identified as independent significant factors predicting mortality in 352 pyogenic liver abscess patients (8).

Pyogenic liver abscess is a rare but fatal disease which was managed by surgical treatment historically but advances in technology has opened a new modalities in treatment like percutaneous drainage or USG guided needle aspiration or catheter drainage. Therefore, the aim of this study was to evaluate the comparative effectiveness and safety of continuous catheter drainage vs percutaneous needle aspiration in the management of liver abscesses patients.

II. Material and Method

This was a prospective study conducted in the general surgey department of a tertiary are teaching hospital on patients of pyogenic liver abscess. The study protocol was presented to the intuitional ethics committee and approval was obtained. All patients were explained clearly about the nature and purpose of the study and written informed consent was obtained from all patient before enrolment in the study. The Study was conducted during the period from July 2016 to October 2018 and patients presented with suspected liver abscess were screened. Patient with diagnosed case of pyogenic liver abscess of any age and gender having single and approachable abscess on basis of ultrasonography with abscess size >5cm and willing to undergo either percutaneous aspiration and pigtail catheter drainage were included in the study. Patients with abscess size less than 5 cm (which was managed conservatively) and abscesses that were treatable surgically only like rupture or concomitant surgical pathology requiring urgent surgical exploration were excluded from the study.

A detailed history of patient was recorded with demographic data, clinical presentation, past-surgical history, past history of liver abscess, history of alcoholism, diabetes, any immunodeficiency states, any history of biliary tract disorder history of amoebic dysentery & jaundice was taken. Patients were examined in detail. Blood and radiological investigations performed were recorded. Complete blood count (CBC), random blood sugar, liver function test, renal function test, prothrombin time and chest X-ray were done immediately on presentation. Preliminary Ultrasound of Abdomen and Pelvis was done on the same day of presentation. Follow-up USG done in all patients on day 3, 7, 21 & then as & when required afterwards. Complete blood count was repeated after 48 hours in all patients. LFT, PT were repeated after 48 hours in cases of abnormal preliminary reports. Patients were informed about any interventions required and consent taken and pus from the abscess was sent for culture and sensitivity testing.

The enrolled patients were randomized into two groups of treatment; Group A - pigtail catheter drainage (PNG) with antimicrobial drugs (n=10) and Group B - percutaneous needle aspiration (PNA) with anti-antimicrobial drugs (n=20).

Study procedure

All the patients with PNA were injected with atropine in a dose of 0.6mg I/M half an hour before procedure and diclofenac i.m injection was given as an analgesic. Intravenous line was maintained with a wide

bore cannula and oxygen was made constantly available. The site of aspiration was determined on the basis of few considerations that the cavity should be localised under ultrasound guidance and a shorter and a safer route for the presence of a pointing abscess or a localised bulge of the chest wall. The location of the point of tenderness was determined and in the absence of point tenderness the needle was introduced either in the ninth intercostal space in the mid axillary line or the seventh intercostal space in the mid clavicular line. The depth of needle penetration is determined by ultrasonography. Supine position with a 30 degree tilt to the left is used for anterior approach or a left lateral position for posterior approach. Percutaneous aspiration may be done with any large bore cannula (No. 16) or lumbar puncture needle. While the needle is being withdrawn or introduced, the patient is asked to take shallow breath throughout the procedure and hold his breath to minimise the liver trauma and haemorrhage. Once the needle enters the abscess cavity, the pus often gushed out if it under pressure. A 20 ml syringe is was attached to create a negative force which was regulated according to the resistance to the flow of pus. Aspiration was continued until no more pus can be evacuated. For catheter drainage the patient were positioned and a 4 mm stab incision was made through which an 18 G guide wire introducer needle was passed under sonographic guidance till it reached the center of the cavity. A guide wire was then introduced through the needle and positioned inside the cavity following which the needle was removed keeping the guide wire in situ. Serial dilators were then passed over the wire to dilate the tract. The tract was dilated to an adequate size depending upon the viscidity of the pus. A pigtail catheter of size smaller than the last dilator was passed over the wire and positioned in the center of the abscess cavity under sonographic guidance. The guide wire was then withdrawn and the pigtail catheter was connected to a closed drainage bag and fixed to the skin. Sterile dressing was applied and the pus was sent for aerobic culture. The pigtail catheter was removed when the patients shows clinical improvement, drainage become serous and minimal (<10 ml in 24 hrs) and USG shows collapsed cavity without any residual pus.

Outcome measures:

All patients were followed up thoroughly and follow-up USG done in all patients on day 3, 7, 21 & then as & when required afterwards. Complete blood count was repeated after 48 hours in all patients. Improvement in fever, reduction in size of abscess and overall recovery were recorded and analysed statistically.

Statistical analysis:

All the data is presented as actual frequencies, percentages, mean, standard deviation as appropriate. Data were recorded in Microsoft excel 2013 and analysed. Chi square test was for analysis of association and p value less than 0.05 was considered significant.

III. Results

Out of total 30 patients of liver abscess enrolled for the study, 20 underwent USG guided aspiration (Group A) while 10 patients were subjected to pigtail catheter drainage (Group B). Table 1 shows the demographic details of both the groups' patients. Majority of patients with liver abscess in both the groups were of 41-50 years age. In group A, 17 (85%) patients were male while 3 (15%) were female while in group B, 8 (80%) patients were male and 2 (20%) patients were female. It was also observed that 60% patients suffering from liver abscess in both the groups were alcoholic and 20% were having presence of diabetes mellitus.

Table 2 describes the presenting symptoms in patients with clinical investigation for liver abscess. The most frequent presentation was abdominal pain, 14 (70%) patients in group A and 6 (60%) Patients in group B followed by diarrhoea, 20% in both the groups. The loss of appetite and weight loss was in 10% and 20% patient belonging to group A and group B respectively. Tenderness was common clinical sign observed in all the patients while fever was observed in 80% of the patients. Haematological analysis revealed that leucocytosis was observed in 80% patient in group A and 70% in Group B; while elevated serum bilirubin level was observed in 80% in group A and 90% in group B. About 75% of group A and 60% in group B had normal Chest X-Ray. Major abnormality reported on x-ray was pleural effusion.

Table 3 shows comparative blood reports analysis of both the study groups before and after the intervention. Elevated levels of CRP (49.3) in group A and (56.7) in group B, Total bilirubin (31.4) in group A and (33.2) in group B, Alkaline phosphatase (170.9) in group A and (168.5) in group B, Prothrombin time (17.8) in group A and (16.9) in group B, Alanine aminotransferase (67.9) in group A and (72.5) in group B and Aspartate aminotransferase (89.4) in group A and (80.9) in group B were common blood investigation findings before treatment which was found to be significantly reduced after the treatment. ($p<0.05$)

As shown in table 4, the most common lobe affected in liver was right lobe in both the groups (75 % in group A and 70% in group B) compare to left lobe (25% in group A and 10 %) in group B. Solitary abscess cases were more common to multiple abscess. Volume of percutaneous drained pus was 22-1250 in Group a while 30-1550 in group B. The size of amoebic liver abscess was 100cc to 300 cc in group A while 110 cc to 265cc in group B.

On completion of surgery normalization of body temperature and reduction in abdominal pain tenderness was seen in all the patients for both the groups at 6, 5 and 7th postoperative day respectively as shown in Table 5. The abdominal pain was reduced in 19 (95%) patients in group A and 9 (90%) patients in group B.

By day 21, USG showed decreased size of abscess cavity in all patients. But residual cavity size was reduced more in group B; especially with original abscess cavity size of 8 cm. or more. Comparison between both groups for reduction in size of abscess on day 7 & day 21 is shown in table 6.

Table 1: Demographic parameters of the study patients

Age Group	**USG guided aspiration (Total no: 20)**	**Pigtail Catheter Drainage (Total no: 10)**
< 20 years	3 (15)	0 (0)
21- 30 years	3 (15)	1 (10)
31- 40 years	4 (20)	2 (20)
41-50 years	7 (35)	3 (30)
51-60 years	2 (10)	3 (30)
61-70 years	1 (5)	1 (10)
Total	20 (100)	10 (100)
Gender	**N (%)**	
Male	17 (85)	8 (80)
Female	3 (15)	2 (20)
Total	20 (100)	10 (100)
History		
Alcohol	12 (60)	6 (60)
Diabetes Mellitus	4 (20)	2 (20)
Total	20 (100)	10 (100)

Table 2: Clinical presentation and investigations of the study patients

Age Group	**USG guided aspiration (Total no: 20)**	**Pigtail Catheter Drainage (Total no: 10)**
Abdominal Pain	14 (70)	6 (60)
Diarrhoea	4 (20)	2 (20)
Loss of appetite and Weight Loss	2 (10)	2 (20)
Clinical Signs	**N (%)**	**N (%)**
Tenderness	20 (100)	10 (100)
Fever	16 (80)	8 (80)
Icterus	2 (10)	2 (20)
Pallor	4 (20)	2 (20)
Blood Investigation	**N (%)**	**N (%)**
Anemia (Hb < 10 gm/dl)	4 (20)	3 (30)
Leucocytocis	16 (80)	7 (70)
Serum Bilirubin (>1.5 mg/dl)	16 (80)	9 (90)
Elevated Alkaline Phosphatase	15(75)	8 (80)
Elevated Prothrombin time	18 (90)	8 (80)
Chest X-Ray Findings	**N (%)**	
Normal	15 (75)	8 (60)
Abnormal	5 (25)	2 (20)
• Right Pleural Effusion	2 (10)	1 (10)
• Bilateral Pleural Effusion	3 (15)	1 (10)

Table 3: Comparison of the blood investigation parameter before and after intervention in both study groups:

	USG guided aspiration (Total no: 20)		**Pigtail Catheter Drainage (Total no: 10)**	
Blood Investigation Parameter	**Before intervention**	**After intervention**	**Before intervention**	**After intervention**
WBC Count (*10^9 /L)	12.5±1.9	11.4±3.9	12.7±3.1	11.7±2.9
C-Reactive Protein	49.3±40.4	18.9±10.5	56.7±49.6	11.4±8.8
Total Bilirubin (mg/dL)	31.4±12.8	14.6±5.7	33.2±15.6	10.9±3.7
Alkaline Phosphotase	170.9±72.3	45.5±20.9	168.5±65.7	32.9±18.8
Prothrombin Time (s)	17.8±3.5	10.9±3.1	16.9±3.1	8.8±2.0
Alanine Aminotransferase (U/L)	67.9±12.4	32.6±10.9	72.5±13.7	28.7±8.9
Aspartate Aminotransferase (U/L)	89.4±43.2	46.7±15.8	80.9±56.7	44.9±18.9

(Reduction in all parameters after intervention was statistically significant: $p<0.05$)

Table 4: Site, size and drainage of the Liver abscess in both study groups:

Site of abscess	**USG guided aspiration (Total no: 20)**	**Pigtail Catheter Drainage (Total no: 10)**
Right Lobe	15 (75)	7 (70)
Left Lobe	5 (25)	3 (30)
Bilateral Lobe	0 (0)	1 (10)
Number of Abscesses		
Solitary	15 (75)	8 (80)
Multiple	5 (25)	2 (20)
Volume of percutaneously treated abscesses (mean±SD)	**22-1250 ml (365ml±300ml)**	**30-1550 ml (274±309 ml)**
Size of liver Abscess	**100 cc to 300 cc**	**110 cc to 265 cc**

Table 5: symptomatic improvement of the study patients of liver abscess undergoing either USG guided aspiration or pigtail catheter insertion

Symptoms	**USG guided aspiration (Total no: 20)**	**Days for reduction**	**Pigtail Catheter Drainage (Total no: 10)**	**Days**	**P-value**
Normalization of Body Temperature	20 (100)	5	10 (100)	6	0.06
Abdominal Pain	19 (95)	4	9 (90)	5	0.8
Liver Tenderness	20 (100)	7	10 (100)	7	0.4

Table 6: Comparison for reduction in size of liver abscess

	USG guided aspiration (Total no: 20)		**Pigtail Catheter Drainage (Total no: 10)**		**P value (for 5-7 cm size)**	**P value (for 7-10 cm size)**
	Reduction in abscess size in (%) (Original size 5 cm-7 cm)	**Reduction in abscess size in % (Original size 7 cm -10 cm)**	**Reduction in abscess size in (%) (Original size 5 cm-7 cm)**	**Reduction in abscess size in % (Original size 7 cm -10 cm)**		
USG ON DAY 7	6 (30%)	4 (20%)	5 (50%)	4 (40%)	0.62	0.01
USG ON DAY 21	18 (90%)	15 (75%)	9 (90%)	8 (80%)	0.48	0.05

IV. Discussion

Pyogenic liver abscess is common in developing countries and contributing to morbidity and mortality. Management of PLA with the help of non-surgical interventions using intravenous antibiotics alone is found to be inadequate in majority of cases where size of the abscess is >3 cm, hence image guided percutaneous interventions are indicated in complicated conditions with larger abscess filled with pus and multiple lesions which do not successfully respond to less invasive techniques. (9) Minimum invasiveness, complications and lower risk related to post-operative septicemia are key to manage PLA effectively. Intermittent needle aspiration and percutaneous catheter drainage are the most common image guided percutaneous treatment combined with parentral antibiotics are practiced worldwide. (9) However, selection of right technique still remains ambiguous. It was hence aimed to compare the safety and efficacy of Percutaneous fine-needle aspiration (PNA) with percutaneous catheter drainage (PCD) in management of liver abscess.

Earlier studies have reported age as a major prognostic factor. With rapid ageing population along with their comorbid conditions there has been a steady increase in incidence of PLA in old age patients however clinical and microbiological characteristics found to be similar in all age populations in this study. In current study men under age group of 51- 60 years of age were most likely to develop PLA due to comorbidities like diabetes mellitus, hypertension, coronary artery disease and cholelithiasis as compared to females and young age population which was consistent with previous observations. (10,11) Reasons for male predominance in development of pyogenic liver abscess can be contributed to presence of estrogen and other female sex hormones in females which plays a vital role in inflammatory response. There is a less chances of development of sepsis in females as estradiol reduces the proinflammatory cytokine burst. Also estrogen evidently reduces serum AST (aspartate aminotransferase) and ATL (alanine aminotransferase) levels simultaneously minimizing the number of infiltrating inflammatory cells leading to anti-inflammatory and antioxidant effects with an organ

protective role (12,13) Though clinical manifestations were almost similar in all age groups, it was observed that elderly patients with PLA were more prone to non-specific gastrointestinal complications like nausea and vomiting compared to younger patients which was consistent to previous studies. (14)

Patients with alcohol consumption has a positive predilection for development of liver abscess as liver ALA levels are higher due to high iron loads in chronic alcoholics. This increase in iron loads provides a suitable environment for growth of E. histolytica and some bacteria. It is also observed in previous studies that a gram-negative bacillus, Yersinia enterocolitica requires iron for its growth which causes severe multiple liver abscess in patients with heavy iron load. (15, 16) The observations in previous studies were in consistence to the observations of present study as majority of patients had history of alcohol followed by diabetes mellitus.

Abdominal pain and fever with tenderness are most prevalent clinical symptoms observed in majority of patients in both treatment groups followed by nausea and vomiting which is coinsding with the previous literature. (18) Laboratory investigation presented elevated levels of white cell count, anaemia, serum bilirubin, elevated transaminase, alkaline phosphatase and prothrombin time which were insignificant in diagnosis of liver abscess. (18-19) Elevated CRP levels was observed in more than 90% of patients with increased sedimentation rates which is in coherence with previous studies. (18-20)

Though laboratory studies were non-specific but they reveal gross liver abnormalities which may produce the need of targeted imaging studies. X-Ray, ultrasonography, CT scan and magnetic resonance imaging are the most commonly used imaging techniques for diagnosis of liver abscess with 85% sensitivity. Ultrasonography and CT scan are crucial means for guiding drainage and percutaneous aspiration with accurate and precise diagnosis ruling out various other entities with similar clinical manifestations (21) Chest X-ray were normal and non-significant in majority of patients apart from right pleural and bilateral pleural effusions in 5 cases. Unilateral effusion is a common symptom observed in patients with liver abscess arising due to sympathetic stimulation or rupture of abscess through the diaphragm which is also similar to other previous studies. (22)

Earlier patients with pyogenic liver abscess were treated using traditional surgical drainage process having significantly higher rates (10-40%) of morbidity and mortality. (23) Interventional radiology and minimum invasive percutaneous treatments has opened new avenues in management of pyogenic liver abscess over past few decades. Current gold standard for management of pyogenic liver abscess is amenable to treatment with combination of intravenous antibiotics and percutaneous needle aspiration (PNA) or percutaneous catheter drainage (PCD). (4-6)

Percutaneous drainage is practiced only after taking into consideration few clinical aspects like abscess size >5 cm, prolonged pyrexia after 48 to 72 hrs inspite of targeted antibiotic administration followed by imaging studies. Few recent literatures demonstrate the use of percutaneous drainage in cases with abscess size >5cm. (24) In this study most of the abscess (>70%) were found to be solitary and located in the right hepatic lobe probable cause is higher blood supply through superior mesenteric and portal veins. Similar findings were reported in previous studies as well (25). Very few cases (<25%) were diagnosed with abscess located in the left lobe followed by bilateral lobe. Also in 25% of patients multiple abscess was diagnosed due to co-morbid condition.

Many previous investigations have proved that PNA and PCD both are safe and effective however the success of the procedure depends on clinical condition of the abscess and experience. PNA is considered as a first-line approach for the treatment of PLA due to its simple process, better patient compliance and low cost. Previous studies have reported that PCD is a better treatment approach compared to PNA in case of larger liver abscess ≥10 cm in diameter as they are associated with larger quantity of pus which needs continuous drainage which is not suitable with PNA. (26, 27) Early trials reported a lower success rate (67-86%)as compare to our study with PNA approach as in many cases it demands higher number of aspirations attempts. Lack of response to a second attempt with percutaneous needle aspiration was considered as failure of treatment. Successive aspiration attempts with PNA in patients with larger abscess size results in poor success, ineffective treatment and more complications making PCD a superior approach. Earlier studies have also reported larger mean volume of abscess resulted in failure of PNA technique and can be successfully treated using PCD procedure which was in consistence to results of our study. Earlier studies have also concluded that PNA technique was successfully attempted in patients with lower abscess volume. (28,29) Clinical outcome in both the group of patients was found to be similar with no significant difference. All patients in both the groups were relieved from clinical symptoms within 7 days of the treatment. USG scans indicated that reduction in abscess size initiated within 7 days of and was significantly reduced in 21 days. PCD technique was found to be superior to PNA in reduction of abscess size in patients diagnosed with 7-10 cm abscess which is similar to observations of the earlier study. (30, 31)

Overall, this study has highlighted the management of pyogenic liver abscess in western India with comparison of PNA and PCD methods. Few limitations of the study included single centre and lack of long term follow up. Larger multicentre studies focusing on management of liver abscess and its outcome with long term follow up can be very helpful in throwing more light in the management of this rare but serious disease.

V. Conclusion:

Pyogenic liver abscess is a still a prevailing problem in developing country like India. Early diagnosis and treatment is essential for proper management of the patient. Image based percutaneous treatment (aspiration or catheter drainage) being safe and minimum invasive can be considered as first line therapy for effective management of pyogenic liver abscess. Percutaneous needle aspiration is safe and easy method but sometimes require multiple attempts for aspiration while percutaneous catheter drainage is found to be more effective in management of abscess more than 7 cm size. Both the techniques demonstrated similar outcomes with respect to success rate, reduction in symptoms and abscess size, hospital stay, morbidity and mortality rates indicating no significant difference in terms of safety and effectiveness. Significantly earlier clinical improvement and less time for 50% reduction in abscess cavity and reduced hospital stay in the percutaneous catheter drainage group, if abscess size is >7 cm. It can be concluded that intermittent needle aspiration is better in patient compliance and less expensive and can be practiced in patients with abscess size upto 5-7 cm, while in patients with abscess size larger than 7 cm, PCD still remains a first choice of treatment regimen.

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Conflict of interest: The authors have no competing interests to declare.

Ethics Approval: The study protocol was reviewed and approved by the Institutional Ethics Committee. The study was carried out following the standards of clinical study as laid down in Schedule Y and new drugs and clinical trial act, 2020.

Guarantor: The corresponding author is taking the full responsibility for the manuscript including accuracy and appropriateness of reference list.

Consent to Participate: All the participants were explained clearly about the nature and purpose of the study in the language they understood and written informed consent was obtained from them. All the participants were ensured that their identity will not be revealed at any stage of the study.

Author's Contribution: Dr. Abhijit Yadav has designed the concept of the study, literature review and data analysis. Dr. Prajesh Patel has contribution in data collection and Data analysis. Dr. Khan MD Shehzad Furkan Ahmed has contribution in Data collection and Data analysis. Dr. Rima Shah has contribution in study concept design, data analysis and manuscript writing.

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