ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Clinical profile, management, and outcome of obstructive jaundice patient at a tertiary care center: A prospective study

Gulab Dhar Yadav[1], Anju Yadav[2], Shraddha Verma[3], Mohammad Tahir Hussain[4]

[1]Professor and Head, [2]Specialist, Department of Paediatrics, ESIC Hospital Kanpur, [3]Assistant Professor, [4]Postgraduate Resident, Department of General Surgery, Vidyarthi in Ganesh Shankar Vidyarthi Memorial Medical College, Kanpur, Uttar Pradesh, India

Submission: 20-01-2022 Revision: 30-03-2022 Publication: 01-05-2022

ABSTRACT

Background: There are various causes of obstructive jaundice, choledocholithiasis is the commonest cause. Patients with obstructive jaundice need early diagnosis to established level and nature of obstruction in biliary system. The history and clinical examination in arriving at a correct pre-operative diagnosis in almost always possible today because of advances in imaging techniques over the decades. Presents study attempts to determine the various causes, age and sex pattern in Extra Hepatic obstructive jaundice. **Aims and Objectives:** The aim of the study was to study clinical profile, management, and outcome of obstructive jaundice, patient at a tertiary care center: A prospective study. **Materials and Methods:** The present hospital based prospective interventional study was conducted on patients with obstructive jaundice, those were admitted in the Department of General Surgery at GSVM Medical College Kanpur, patients of age more than 12 years both sex after obtaining the consent form the patient or their relatives were studied during the period of study from January 2020 to October 2021. **Results:** Of the 50 patients; 29 (58%) were female and 21 (42%) were male, their mean age being 51.10 years. Malignant obstructive jaundice was seen in 19 (38%) patients while 31 (62%) had benign etiology. Amongst the obstructive jaundice cases; pain in abdomen (100%) was commonest symptoms and icterus (100%) was the most common sign. The most common malignancy was Carcinoma (Ca) of the head of pancreas 09 (18%) followed by distal common bile duct (CBD) cholangiocarcinoma 04 (08%), and hilar cholangiocarcinoma 03 (06%). Choledocholithiasis 25 (50%) was the most common benign cause followed by benign stricture of common bile duct 03 (06%). **Conclusion:** Obstructive jaundice is one of the common causes of surgically amenable jaundice. Its etiology is varied and diagnosis usually depends on appropriate imaging. Proper diagnosis and treatment is necessary as delay in the diagnosis may cause irreversible pathological changes causing increased morbidity and mortality.

Key words: Choledocho-duodenostomy; Choledocholithiasis; Obstructive jaundice

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v13i5.42527

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Obstructive jaundice is a common surgical problem that occurs when there is an obstruction to the passage of conjugated bilirubin from liver cells to intestine.[1] It is among the most challenging conditions managed by general surgeons and contributes significantly to high morbidity and mortality.[2] There is a discrepancy between the recognized causes of obstructive jaundice at various centers and it is mandatory to determine preoperatively the existence, the nature of obstruction because an ill chosen procedure can lead to high morbidity and mortality.[3] The mortality and morbidity of biliary obstruction depend on the causes of the obstruction.[4] Better understanding of factors responsible for increased morbidity and mortality in these patients will better guide appropriate management. Late presentation of the cases associated with lack of modern diagnostic and therapeutic facilities is common scenario in developing countries.

Address for Correspondence:
Dr. Mohammad Tahir Hussain, Junior Resident, Department of General Surgery, GSVM Medical College, Kanpur - 208 002, Uttar Pradesh, India. **Mobile:** 7392043499. **E-mail:** donaayan@gmail.com

Aims and objectives

The objectives are as follows:

- To study the clinical profile of patients with obstructive jaundice at our center.
- To study etiopathogenesis, diagnosis, treatment (surgical/palliative), and outcome of obstructive jaundice patients at our center.

MATERIALS AND METHODS

The present hospital-based prospective interventional study was conducted on patients with obstructive jaundice patients those were admitted Department of General Surgery at GSVM Medical College, Kanpur of age more than 12 years both sex after obtaining the consent form the patient or their relatives were studied during the period of study from January 2020 to October 2021. The study was approved by the Institutional Ethics Committee for the final permission (ref No.: EC/BMHR/2021/51, Dated 28-06-2021).

This was prospective observational study on 50 patients presenting with sign and symptoms suggestive of obstructive jaundice. Inclusion criteria of this study including patient age above 12 years and the patients which clinically diagnosed as suffering from obstructive jaundice, and patients proved to have obstructive jaundice by any investigative modality. Exclusion criteria of this study were patients below 12 years of age; and patients with jaundice due to causes other than obstructive pathology such as hemolytic or hepatocellular jaundice, and patients who attended OPD but not admitted or missing/incomplete record and patients with other concomitant malignancy, comorbidities such as uncontrolled diabetes, hypertension, CVA, TB, CAD, and kidney diseases and the pregnancy which was excluded in our study.

RESULTS

A prospective clinical study consisting of 50 cases of obstructive jaundice was undertaken to investigate the pattern of clinical presentation and lab parameters to study the cause of obstructive jaundice and the different modes treatment adopt.

Out of total 50 patients included in the study, the mean age range is found to be 51-60yrs (32%) for patients suffering from obstructive jaundice. The mean age of presentation was 51.10 years. The minimum age was 12 years and maximum age was 80 years.

Out of 50 patients, the most common presenting complaint was pain in abdomen present in 50 patients (100%), and yellowish discoloration of sclera (jaundice) in 50 patients (100%), followed by clay colored stool (58%), followed by fever (54%), and followed by anorexia (42%) and itching (40%). The analysis of signs in the studied cases showed that the most common sign was icterus which was present in all the cases (100%) followed by abdominal tenderness (66%%), itching marks (34%), palpable gall bladder (20%), and hepatomegaly (14%).

The level of bilirubin ranges from 3.2 to 27.6 mg%. Maximum patients (42%) in our study had bilirubin level 11–20 mg%. The mean value of total bilirubin was 11.58 mg% with while median value was 10.7. The bilirubin value ranges from 3.2 to 27.6 mg%.

In this study, out of 50 patients of obstructive jaundice, maximum percentage of cases (62%) are of benign etiology followed by (38%) cases are of malignant etiology. Out of 31 patients of benign etiology, maximum number of patients with benign etiology was of Choledocholithiasis 25 patients (80.64%), followed by common bile duct (CBD) stricture 03 (9.67%) and choledochal cyst in three patients (9.67%). Out of 19 patients of malignant etiology maximum number of patients with malignant etiology was of carcinoma head of pancreas 09 patients (47.36%) followed by distal CBD cholangiocarcinoma four patients (21.05%), followed by three patients (15.78%) of hilar cholangiocarcinoma and carcinoma gall bladder each.

Out of the 31 patients with benign etiologies, 25 patients of gall bladder with CBD calculi (80.64%), 10 of them underwent cholecystectomy with CBD exploration with choledochoduodenostomy (40%), 07 of them underwent cholecystectomy with CBD exploration with T-tube insertion (28%), and 07 of them patients with CBD calculi underwent endoscopic interventions (28%). One patient underwent cholecystectomy with CBD exploration with hepaticojejunostomy (4%). Three patients of biliary stricture (9.67%), 02 of them underwent CBD exploration with hepaticojejunostomy (66.67%), and 01 of them underwent CBD exploration with choledochoduodenostomy (33.33%). Three patients of choledochal cyst (9.67%) underwent hepaticojejunostomy (100%). Out of the 19 patients with jaundice of malignant causes (38%), procedures were carried out with therapeutic and palliative intent. Whipple's procedure was performed in 08 patients (42.10%). In 11 patients, surgical palliation was done (57.89%), out of them five patients underwent Triple bypass procedure (45.45%), out of them three patients underwent percutaneous transhepatic biliary drainage (27.27%), out of them two patients underwent palliative stenting (18.18%) and one patient underwent hepaticojejunostomy (09.09%).

The most common post-operative complication in studied cases was found to be wound infection (20%), followed by cholangitis (6%) and septicemia (4%). The other less common complications included anastomotic leak (4%) and dyselectrolytemia (2%). Stent occlusion or dislodgement and ERCP induced pancreatitis (2%) each.

DISCUSSION

(Table 1) In our study, maximum number of cases of obstructive jaundice was in 6th decade of life (32%). The mean age was 51.10 years. This study was in correlation with study of Padhy et al.,[5] the mean age was found to be 55.5 years and study of Saadoon,[6] the mean age of obstructive jaundice was 52 years. The study found that females (58%) were affected more than males (42%). The male: female ratio is 0.7:1. In this study, the benign cause of obstructive jaundice was more common in younger age group (<40 years) with female preponderance as compared to malignant cause of obstructive jaundice which is more common in older age group (>40 years) and male predilection. This study was in correlation with study of Chalya et al., in 2011,[7] both the benign and malignant obstructive jaundice were found to be more commonly among the females than males. Zollinger et al.,[8] stated that sex incidence is equal in both sex. This discrepancy can be explained by different rate of admission among male and female.

(Table 2) In our study, the most common presenting complaint was pain in abdomen and jaundice in all cases (100%), followed by clay colored stool present in (58%) and fever in (54%) cases. Saddique and Iqbal[1] concluded in his study that the pain in abdomen was the most common presenting complaints in the patient of obstructive jaundice. Goyani et al.,[10] concluded that jaundice was the most common symptom seen in 96% of the patients followed by abdominal pain seen in 86% of the patients. Gupta et al.,[11] concluded in his study that the most common symptoms of obstructive jaundice were jaundice (91.67%), loss of appetite (77.78%) and pain in abdomen (75%). In our study, most common sign was icterus which was present in all the cases (100%). The other common signs were abdominal tenderness (66%), itching marks (34%), and palpable gall bladder (20%). Chalya et al.,[7] appreciated palpable gallbladder in 50.9% patients with malignancy. Miller[12] observed palpable gallbladder in 30% of patients in his series.

(Table 3) In our study, the analysis of bilirubin level ranges from 3.2 mg% to 27.6 mg%. Maximum patients (42%) in our study had bilirubin level 11–20 mg%. The mean value of total bilirubin was 11.58 mg%. In this study, the raised bilirubin levels are much higher (>10 mg%) in malignant cause of obstruction as compared to benign cause (<10 mg%). Garcea et al.,[13] study concluded that raised bilirubin levels are predictor of malignancy which is correlating with this study. Chaudhry et al.,[14] study concluded that serum bilirubin level (100 μmol/L) was found to be extremely sensitive but less specific marker of malignancy in patients of obstructive jaundice which make it a good screening tool for malignancy among such patients. Study conducted by Hayat et al[15] proved that the level of total bilirubin raised in cases of obstructive jaundice which is correlating with my study.

(Table 4) In our study, out of 50 patients of obstructive jaundice, maximum percentage of cases (62%) is of benign etiology followed by (38%) cases are of malignant etiology. Out of 31 patients of benign etiology, maximum number of patients with benign etiology was of choledocholithiasis 25 patients (80.64%), followed by CBD stricture and choledochal cyst in three patients (9.67%) each. Out of 19 patients of malignant, etiology maximum number of patients with malignant etiology was of carcinoma head of pancreas nine patients (47.36%), followed by

Table 1: The distribution of cases as per age

S. No.	Age groups (in years)	Number of patients	Percentage
1.	12–20	02	04
2.	21–30	03	06
3.	31–40	08	16
4.	41–50	12	24
5.	51–60	16	32
6.	61–70	08	16
7.	>71	01	02

Table 2: Symptomatic distribution of cases

S. No.	Symptoms	Number of patients	Percentage
1.	Jaundice	50	100
2.	Pain in abdomen	50	100
3.	Lump in abdomen	21	42
4.	Itching	20	40
5.	Loss of appetite	21	42
6.	Fever	27	54
7.	Clay colored stool	29	58
	Clinical signs		
8.	Icterus	50	100
9.	Itching marks	17	34
10.	Palpable gall bladder	20	40
11.	Hepatomegaly	14	28
12.	Tenderness	33	66

Table 3: The distribution of cases as per total bilirubin levels

S. No.	Bilirubin levels (mg%)	Number of patients	Percentage of pts.
1.	<5	04	08
2.	5–10	20	40
3.	11–20	21	42
4.	21–30	05	10

distal CBD cholangiocarcinoma 04 patients (21.05%), 03 patients (15.78%) of hilar cholangiocarcinoma and carcinoma gall bladder each. Padhy et al.,[5] study concluded out of 100 patients with obstructive jaundice 67 malignant causes, out of which carcinoma head of pancreas was commonest in 40 cases followed by cholangiocarcinoma and periampullary carcinoma 10 patients each. Wang and Yu[16] study concluded that, the causes of obstructive jaundice are varied, but it is most commonly due to choledocholithiasis; benign strictures of the biliary tract, pancreaticobiliary malignancies; and metastatic disease. Kurian and John[17] conducted a study on Assessment of Clinical Profile of Patients with Obstructive Jaundice on 46 patients found out be 78% of the lesions were benign and 22% were malignant lesions.

(Table 5) In our study, it has been found that, out of the 31 patients with benign etiologies, 25 patients of gall bladder with CBD calculi (80.64%), ten of them underwent cholecystectomy with CBD exploration with choledochoduodenostomy (40%), seven of them underwent cholecystectomy with CBD exploration with T-tube insertion (28%), and seven of them patients with CBD calculi underwent endoscopic interventions (28%). One patient underwent cholecystectomy with CBD exploration with hepaticojejunostomy (4%). Three patients of biliary stricture (9.67%), two of them underwent CBD exploration with hepaticojejunostomy (66.67%), and one of them underwent CBD exploration with choledochoduodenostomy (33.33%). Three patients of choledochal cyst (9.67%) underwent hepaticojejunostomy (100%). Out of the 19 patients with jaundice of malignant causes (38%), procedures were carried out with therapeutic and palliative intent. Whipple's procedure was performed in 08 patients (42.10%). In 11 patients, surgical palliation was done (57.89%), out of them five patients underwent Triple bypass procedure (45.45%), out of them 03 patients underwent percutaneous transhepatic biliary drainage (27.27%), out of them two patients underwent palliative stenting (%) and one patient underwent hepaticojejunostomy (9.09%). Fortner in his study on 52 patients with obstructive jaundice reported palliative procedures in 38 (73.1%) cases including endoprosthesis placement in 22 (42.31%) and bypass surgery in 16 (30.8%) cases. Chalya et al.,[7] major surgeries like pancreatoduodenectomy, hepatectomy, and Whipple's procedure were not performed as majority of patients requiring these procedures presented late with advanced disease and the only treatment option was palliative surgery. Mohamed and Syed[1] study, the majority of patients with malignant obstructive jaundice underwent palliative surgery mainly by bypass surgery, whereas the majority of patients with benign obstructive jaundice underwent curative surgery.

(Table 6) In our study, it has been found that, the most common post-operative complication in studied cases was found to be wound infection (20%) followed by cholangitis (6%) and septicemia (4%). ERCP induced pancreatitis found to be in 1 (2%) patient. Pancreatitis was treated conservatively. Anastomotic leak and electrolyte imbalance were seen in 3 patients who were died in due course. One patient who had stenting done was readmitted for stent dislodgement and underwent laparotomy for the same. Two (4%) patients developed septicemia and were started on higher antibiotics. In our study, complication rate was recorded in 40% of cases. Of this, surgical site infection was the most common postoperative complications. Our complication rate in this study was higher than that of 22.4% reported previously by Chalya et al.[7] High incidence

Table 4: Frequency of benign and malignant obstructive jaundice

S. No.	Etiology of obstructive jaundice	Number of cases	Percentage
A.	Benign disease:		
1.	Choledocholithiasis	25	80.64
2.	Biliary stricture (benign)	03	9.67
3.	Choledochal cyst	03	9.67
	TOTAL	31	100
B.	Malignant Disease		
1.	Carcinoma head of Pancreas	09	47.36
2.	Distal CBD cholangiocarcinoma	04	21.05
3.	Hilar cholangiocarcinoma	03	15.78
4.	Carcinoma of Gall Bladder	03	15.78
TOTAL		19	100

Table 5: Various intervention for obstructive jaundice patients

S. No.	Intervention	Number of patients	Percentage
1.	PTBD	03	6
2.	Palliative stenting	02	4
3.	Choledochoduodenostomy	10	20
4.	RNY hepaticojejunostomy	07	14
5.	Whipples procedure	08	16
6.	Triple bypass	05	10
7.	CBD exploration with T-tube	08	16
8.	ERCP stone extraction/stent	07	14

Table 6: Complications occurs after interventions

S. No.	Complications	Number of patients	Percentage
1.	Anastomotic leak	02	04
2.	Wound infections	10	20
3.	Pancreatitis	01	02
4.	Cholangitis	03	06
5.	Electrolyte imbalance	01	02
6.	Stent occlusion/ dislodgement	01	02
7.	Septicemia	02	04

of surgical site infection in our study may be due to contamination of the wound during the surgical procedure. In the present study, complication rate was significantly high in patients with malignant causes, Chalya et al.,[7] 32 complications were recorded in 26 patients giving a complication rate of 22.4%. Of these, postoperative wound sepsis was the most common complications. In our study, it has been found that, mortality occurred in three cases. Two patients with carcinoma head of pancreas underwent triple bypass and the patient expired postoperatively, out of them one having anastomotic leak and another having severely dyselectrolytemia. One patient underwent with metastatic carcinoma gall bladder with liver secondaries and porta hepatis nodes. Patient underwent palliative drainage (PTBD) and patient expired. The mortality rate is 6% of the cases. Sanie et al., quoted[18], there were nine mortalities in the 15 patients who had surgery of obstructive jaundice (60%). Dalwani and Shaikh[9] study has showed a high mortality rate in about 11.25% of cases.

Limitations of the study

Every hospital-based study has some limitations and the present study undertaken is no exception to this fact. The limitations in the present study are mentioned below,

1. The patients taken up for the study were predominantly from northern India, in and around Kanpur district. Therefore, the results of the present study may not be representative of the whole of the country or the world at large.
2. The number of patients included in the present study were less in comparison to other studies.
3. Because the trial was short, it was difficult to remark on complications and mortality.

CONCLUSION

(Table 1) In this study, population obstructive jaundice is prevalent more in females than males and more common in 5th to 6th decade, the mean age of presentation was 51.10 years. (Table 2) The most common symptomatology was pain in the abdomen and jaundice and the commonest clinical sign was icterus. (Table 3) The raised bilirubin levels are much higher (>10 mg%) in malignant cause of obstruction as compared to benign. (Table 4) Choledocholithiasis was the most common cause overall and in benign etiology and carcinoma head of pancreas in malignant obstructive jaundice. USG abdomen is the first line imaging modality, due to its easy availability, non-invasive nature, and cost effectiveness. MRCP is quick, accurate, and non-invasive imaging modality for the assessment of obstructive jaundice, sensitivity, and specificity for malignant cases is more than benign cases. (Table 5) ERCP has got the advantage of diagnostic as well as therapeutic modality. For choledocholithiasis, ERCP has preferred modality and others CBD exploration, for malignancy operative curative procedure was Whipple's surgery and palliative procedure was triple bypass, ERCP and PTBD. The proper diagnosis and appropriate treatment is must as delay in treatment may cause the malignant growth to become unresectable (in malignant diseases). Even in benign conditions delay in management may cause irreversible pathological changes (secondary biliary cirrhosis in cases of biliary strictures). (Table 6) The most common post-operative complication is wound infection, cholangitis, and septicemia.

TAKE HOME MESSAGES

Obstructive jaundice in adults patients (above 12 years) should be thoroughly investigate and properly manage because age of patients increases with severity of diseases increase. Younger patients, benign cause more and less morbidity and mortality and faster recovery found. Older age group, more neoplastic etiology and more morbidity and mortality occurs.

ACKNOWLEDGMENT

I wish to thank Department of Surgery, Ganesh Shankar Vidyarthi Memorial Medical College, Kanpur for granting me permission to carry out the project, and also thank to all the individuals included in this study.

REFERENCES

1. Saddique M and Iqbal SA. Management of obstructive jaundice: Experience in a tertiary care surgical unit. Pak J Surg. 2007;23(1):23-25.
   https://doi.org/1002-1-973-1-10-20151207
2. Gaffor A, Buladi GQ and Imran M. Role of imaging in obstructive jaundice. J Surg Pak Sep. 2004;9(3):24-26.
   http://doi/1002-1-973-1-10-20151207
3. Khuram M, Durani AA, Hassan Z, ul Ala Butt A and Ashfaq S. Endoscopic retrograde cholingopancreatography evaluation of patients with obstructive jaundice. J Coll Physicians Surg Pak. 2003;13(6):325-328.
4. Acalovschi M. Cholangiocarcinoma: Risk factors, diagnosis and management. Rom J Intern Med Rev Roum Med Interne. 2004;42(1):41-58.
5. Padhy B, Murmu D, Samal D and Jha S. Clinical study of surgical jaundice: An institutional experience. Int Surg J. 2017;5(1):138-142.
   http://dx.doi.org/10.18203/2349-2902.isj20175883
6. Saadoon SN. Review of the causes of obstructive jaundice and the role of endoscopic retrograde cholangiopancreaticography (ERCP) in the management. Iraqi J Med Sci. 2016;14(4):359-365.
   http://doi/10.22578/IJMS.14.4.9
7. Chalya PL, Kanumba ES and Mchembe M. Etiological spectrum

and treatment outcome of obstructive jaundice at a university teaching hospital in Northwestern Tanzania: A diagnostic and therapeutic challenges. BMC Res Notes. 2011;4(1):147.
http://doi/10.1186/1756-0500-4-147

8. Zollinger MD, Roger D, Williams MD, Dan W, Elliott MD, Robert M. Ama Arch Surg. 1960;80(6):992-997.
http://doi/10.1001/archsurg.1960.01290230110014
9. Dalwani AG and Shaikh AR. Devanand Evaluation of Various Causes and Treatment of Obstructive Jaundice at Liaquat University Hospital {Original Article (Medicine)} Corpus ID: 53077822
10. Goyani B, Ukani B, Patel M, Shah B and Vadel M. Ultrasonography and magnetic resonance cholangiopancreatography correlation in patients with obstructive jaundice. Int J Med Sci Public Health. 2015;4(7):1010-14.
http://doi/1010-6.10.5455/ijmsph.2015.26032015205
11. Gupta AK, Singh A, Goel S and Tank R. Profile and pattern of obstructive jaundice cases from a tertiary care teaching hospital of Uttar Pradesh. Int Surg J. 2017;4(2):743-746.
http://dx.doi.org/10.18203/2349-2902.isj20170225
12. Miller JR, Aggenstoss AH and Comfort AH. Malignant obstructive jaundice. Cancer. 1951;4:233.
http://doi/10.1001/archsurg.1952.01260020303012
13. Garcea G, Ngu W, Neal CP, Dennison AR and Berry DP. Bilirubin levels predict malignancy in patients with obstructive jaundice. HPB. 2011;13(6):426-30.
http://doi/10.1111/j.1477-2574.2011.00312.x
14. Chaudhry SM, Khan AZ, Chohan S, Ch WM and Ghufran S. Bilirubin level as a predictor of malignancy in patients with obstructive jaundice. J Fatima Jinnah Med Univ. 2017;11(2): 22-6.
http://doi/10.1.1.614.5863
15. Hayat JO, Loew CJ, Asrress KN, McIntyre AS and Gorard DA. Contrasting liver function test patterns in obstructive jaundice due to biliary structures and stones. QJM. 2005;98(1):35-40.
http://doi/10.1093/qjmed/hci004
16. Wang L and Yu WF. Obstructive jaundice and perioperative management. Acta Anaesthesiol Taiwanica. 2014;52(1):22-29.
http://doi/10.1016/j.aat.2014.03.002
17. Kurian JM and John PK. Assessment of clinical profile of patients with obstructive jaundice. Int J Contemp Med Res. 2015;4(1):4.
18. Sanie B. Surgical palliative drainage in un-resectable malignant biliary obstruction. J Vasc Med Surg. 2016;4(4):1-4.
http://doi/10.4172/2329-6925.1000281

Authors Contribution:
GDY - Concept and design of the study, prepared first draft of manuscript; **MTH** - Interpreted the results; reviewed the literature and manuscript preparation; **SV** - Concept, coordination, statistical analysis and interpretation, preparation of manuscript; **AY** - revision of the manuscript

Work attributed to:
Ganesh Shanker Memorial Medical College, Kanpur - 208 002, Uttar Pradesh, India

Orcid ID:
Dr. Gulab Dhar Yadav - https://orcid.org/0000-0002-5570-4748
Dr. Anju Yadav - https://orcid.org/0000-0001-5910-8655
Dr. Shraddha Verma- https://orcid.org/0000-0003-2296-7477
Dr. Mohammad Tahir Hussain - https://orcid.org/0000-0002-6357-8876

Source of Support: None, **Conflict of Interest:** None.