Obstructive Jaundice- Aetiological Spectrum, Clinical, Biochemical And Radiological Evaluation At A Tertiary Care Teaching Hospital.

S Verma, S Sahai, P Gupta, A Munshi, S Verma, P Goyal

Citation

Abstract
Objective–This study was done to assess the aetiological spectrum of obstructive jaundice as well as common clinical findings and relevance of laboratory and radiological imaging investigations.Methods: A prospective study of 110 patients with obstructive jaundice confirmed by thorough history and physical examination, biochemical tests and radiological investigations was done with final confirmation of diagnosis on histopathology. The data was analyzed using SOFA analytical software version 0.9.24.Results: Out of 110 patients 62 (56%) were male and 48 (44%) were female. The mean age of the study population was 50.4 years (range 3–85 years). Malignant obstructive was more common than benign (62.73% Vs 47.27%). Abdominal pain and clay coloured stools were more frequent in patients with malignant disease. Carcinoma (Ca) of the head of pancreas was commonest aetiology 37/110 (33.63%) followed by Choledocholithiasis 32/110 (29%), Ca gall bladder 20/110 (18.18%), periampullary carcinoma 6/110 (5.45%), cholangiocarcinoma 4/110 (3.64%), CBD stricture 3/110 (2.73%), acute pancreatitis 3/110 (2.73%) and HCC(1.8%). Regarding etiology of the obstruction, the accuracy of ultrasound, CT scan, MRCP and ERCP was 87.3%, 92.7%, 90% and 100%, respectively. The sensitivities of USG, CT, MRCP and ERCP in the diagnosis of benign disease were 85.3%, 84.6%, 92.3% and 100%, respectively, whereas specificities were 88.4%, 94.2%, 86% and 100%, respectively. Sensitivities for diagnosis of malignant disease were 88.4 %, 94.2 %, 86 % and 100% for USG, CT, MRCP and ERCP respectively whereas specificities were 85.3%, 85%, 92% and 100% respectively.Conclusion: Malignant obstructive jaundice is predominant in males compared to females. Benign obstruction is seen at a comparatively younger age group compared to malignant (Mean age 38.6yrsVs 58.7yrs). Carcinoma of head of pancreas and choledocholithiasis were the commonest malignant and benign etiology respectively. Ultrasound and CT have high diagnostic accuracy, sensitivities and specificities and along with MRCP have largely confined the role of invasive cholangiography (ERCP/PTC) to therapeutic/palliative procedures in biliary obstruction.

INTRODUCTION
The word “jaundice” comes from the French word jaune, which means yellow. Jaundice is a yellowish staining of the skin, sclera, and mucous membranes by bilirubin, a yellow-orange bile pigment. Bilirubin is formed by a breakdown product of hemoglobin rings, usually from metabolized red blood cells. The discoloration typically is detected clinically once the serum bilirubin level rises above 3 mg per dL (51.3 μper L). Jaundice is a common problem in both medical and surgical practice. Its cause can often be correctly anticipated clinically but usually biochemical and radiological imaging investigations are required for confirmation. It could be because of a variety of causes and is broadly divided into obstructive (surgical) and non obstructive (medikal) categories. Obstructive jaundice (jaundice due to intra or extrahepatic organic obstruction to biliary outflow), can present problems with the diagnosis and management. The surgical jaundice can be caused by the obstruction of the bile duct as with gall stones, strictures, malignancy, such as cholangiocarcinoma, carcinoma gall bladder and carcinoma head of pancreas & periampullary carcinoma. Various rare causes like Choledochal cyst; Caroli’s syndrome and primary and metastatic liver tumors have also been reported. The symptoms of obstructive jaundice include jaundice with
or without pain, dark urine, pruritis, pale stools, weight loss and anorexia.²

**BIOCHEMISTRY/HEMATOLOGY**

Elevated serum bilirubin level with a preponderance of the conjugated fraction is usually seen. In general, patients with benign disease have less hyperbilirubinemia than those with malignant obstruction. The transaminases (AST & ALT) may abruptly rise many fold above normal and decrease rapidly once the obstruction is relieved. Alkaline phosphatase and γ-glutamyltransferase are markers for cholestasis. As bile obstruction progresses, the levels of these two markers rise several times above normal.⁴

**RADIOLOGICAL IMAGING**

The need for radiological imaging in obstructive jaundice are:⁵

1. To confirm the presence of biliary system obstruction (i.e., to discriminate surgical versus medical jaundice),
2. To determine the level of the obstruction,
3. To identify the specific cause of the obstruction,
4. To provide complementary information relating to the underlying diagnosis (e.g., staging information in cases of malignancy).

The radiological investigations available for the diagnosis of obstructive Jaundice can be categorized into noninvasive ultrasonography, CT scan & MRCP and invasive ERCP and PTC.⁵

Routine abdominal ultrasonography shows the size of the bile ducts, may define the level of the obstruction, may identify the cause and gives other information related to the disease (e.g., hepatic metastases, gallstones, hepatic parenchymal change).

It identifies bile duct obstruction accurately though results are largely operator dependent. It readily demonstrates both benign and malignant causes of obstruction as well as any associated conditions or complications. Being relatively cheap, readily available and non invasive it is usually the preferred initial investigation.⁵⁶¹⁷²⁰

Endoscopic ultrasonography has various applications, with regard to the biliary system, EUS is useful for the detection and staging of ampullary tumors, detection of microlithiasis, cholelithiasis and evaluation of benign and malignant bile-duct strictures.⁷ It can further evaluate relationships to vascular structures. It may help define benign lesions mimicking cancer (e.g. sclerosing pancreatitis) if there is diagnostic doubt. Endoscopic ultrasound enables the aspiration of cysts and biopsy of solid lesions, but is operator-dependent and not readily available in most centers.

Computed tomography (CT) of the abdomen provides excellent visualization of the liver, gallbladder, pancreas, kidneys, and retroperitonium. It can differentiate between intra- and extra-hepatic obstruction with high accuracy.⁶ However, CT may not define incomplete obstruction caused by small gallstones, tumors, or strictures.⁵

Contrast-enhanced multi-slice CT is very useful for assessment of biliary malignancies.

Contrast agents given orally or intravenously are used and imaging done in unenhanced, arterial and venous phases.⁵

Magnetic resonance cholangiopancreatography (MRCP) is a relatively newer, noninvasive technique for visualization of the biliary and pancreatic ductal system. It is especially useful in patients who have contraindications for endoscopic retrograde cholangiopancreatography (ERCP). Excellent visualization of biliary anatomy is possible without the invasiveness of ERCP.⁵⁶²²²¹ But unlike ERCP, it is purely diagnostic with higher cost to patient being its limitations.

ERCP and PTC (Percutaneous transhepatic cholangiography) provide direct visualization of the level of obstruction. Endoscopic Retrograde Cholangiopancreatography (ERCP) is gold standard in evaluation of obstructive jaundice.⁵⁸⁹ ERCP can pick up choledocholithiasis, strictures of CBD, any obstruction of the CBD as well as helps in taking the brushing cytology.²⁴²⁵ PTC combined with biliary drainage is done as a diagnostic and palliative/ presurgical procedure to improve patient condition/ outcome.⁵²⁴ However ERCP and PTC being invasive, they are associated with complications like cholangitis, biliary leakage, pancreatitis and bleeding.⁵ Also these investigations require specific expertise and equipment and are of again limited availability.

This study was done to assess the aetiological spectrum of obstructive jaundice as well as common clinical findings and relevance of laboratory and radiological imaging investigations at a tertiary care teaching hospital and to compare the findings with similar studies done at various other centers internationally.

**PATIENTS AND METHODS**

This hospital based descriptive study was conducted in
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Department of Radiodiagnosis and Imaging and interventional Radiology, Subharti Medical College and affiliated CSS Hospital, Meerut from December 2008 till January 2011. Non-probability convenient sampling was done and 110 patients, who presented with obstructive jaundice because of any reason, were selected for the study. All patients of any age, sex and profession who had symptoms of obstructive jaundice confirmed with raised biochemical investigations (Serum bilirubin and alkaline phosphatase) and radiological investigations were included in the study. All patients with medical jaundice and cirrhosis of liver were excluded.

A thorough clinical history including age, sex and relevant features like presence of clay coloured stools, anorexia, weight loss, pruritis were taken and correlated with the examination findings of presence of jaundice, scratch marks, abdominal mass and hepatomegaly. A working diagnosis was then made and further workup was planned which included the Liver Function tests to see the bilirubin level and the levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and serum alkaline phosphatase.

Abdominal Ultrasound (Toshiba Apleo & Nemio models) was done as initial radiological investigation to look for the abnormality of Intra and Extrahepatic biliary channels, the common bile duct, level and possible cause of obstruction. Further radiological workup including CT (model GE CT/e), MRCP (model GE Signa HD e 1.5T) and ERCP or PTC was done as per the protocol as indicated mentioned in flow chart below.

![Flow chart showing the radiological investigation protocol for suspected obstructive jaundice](image)

The final diagnosis was then made on the basis of results of the radiological investigations and histopathology/surgical findings; the results were then compiled. The data was analyzed by the Statistics Open For All software version 0.9.24.

RESULTS

Out of 110 patients who were evaluated 62 (56%) were male and 48 (44%) were female. The mean age of the study population was 50.4 years (range 3–85 years). Majority of benign causes were seen in 31–60 years of age, while the malignant cases were more common between 41–80 year old. The difference in age distribution of the benign and malignant disease was statistically significant (p<0.05).

Malignant obstructive jaundice was seen in 69 (62.73%) patients while 41 (37.27%) had benign aetiology. Carcinoma head of pancreas was the most common aetiology and was seen in 37 (33.63%) cases. Choledocholithiasis was the next commonest aetiology seen in 32 (29.1%) cases followed by gallbladder malignancy in 20 (18.2%) cases, Incidence of other causes were as described in the table. (Table-1).

Table 1 – Incidence of various causes of obstructive jaundice

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>Total cases</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant</td>
<td>69 (62.73%)</td>
<td>46 (74.2%)</td>
<td>23 (48%)</td>
</tr>
<tr>
<td>Ca Head pancreas</td>
<td>37 (33.63%)</td>
<td>31</td>
<td>6</td>
</tr>
<tr>
<td>Ca Gallbladder</td>
<td>20 (18.2%)</td>
<td>6</td>
<td>14</td>
</tr>
<tr>
<td>Periampullary Ca</td>
<td>6 (5.45%)</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Cholangiocarcinoma</td>
<td>4 (3.64%)</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>HCC</td>
<td>2 (1.8%)</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Beningu</td>
<td>41 (37.27%)</td>
<td>16 (25.8%)</td>
<td>25 (52%)</td>
</tr>
<tr>
<td>Choledocholithiasis</td>
<td>32 (29.1%)</td>
<td>10</td>
<td>22</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>3 (2.73%)</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Benign CBD sticture</td>
<td>3 (2.73%)</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Choleodochal cyst</td>
<td>3 (2.73%)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Total cases</td>
<td>110</td>
<td>62</td>
<td>48</td>
</tr>
</tbody>
</table>

In male patients malignant causes of obstructive jaundice predominated (74.2%), whereas in females benign causes were predominant (52%). Carcinoma of head of pancreas was the most common cause of obstructive jaundice as a whole, as well as most common aetiology of malignant obstruction in male patients. In females Choledocholithiasis was the most common cause of biliary obstruction as well as
the most common benign aetiology. Gallbladder carcinoma was the most common cause for malignant obstruction in females.

Regarding the symptoms, clinical jaundice was most common, seen in 97 (88%) patients followed by right upper quadrant pain in 75 (66.2%) patients, dark urine in 64 (55.2%), pruritus in 60 (54.5%), clay colored stools in 54 (49.1%), weight loss in 48 (43.6%), and abdominal lump in 36 (32.7%) patients. The examination findings revealed that 24 (21.8%) patients had hepatomegaly, 20 (18.2%) had palpable gallbladder.

Total bilirubin concentration was less than 5 mg/dl only in 11 (10%) of the patients and the level increased to above 15 mg/dl in 34 (31%) of them. Increased serum ALT and AST levels (more than 35 IU/L) were found in 72% and 60% of the patients respectively. Also, a high level of ALP (more than 105 IU/L) was found elevated in 70% (78/110) cases.

The abdominal ultrasound was able to diagnose dilatation of biliary system (intra or extrahepatic) in 106/110 (96.4%) cases, level of obstruction was correctly identified in 38/41 (92.6%) benign cases while cause of obstruction was delineated in 35/41 (85.3%) cases. Level of obstruction was correctly identified in 63/69 (91.3%) and cause of obstruction in 61/69 (88.4%) of malignant cases.

CT scan was performed, in all cases of malignant obstructive jaundice and was able to delineate level of obstruction and cause of obstruction in 67/69 (97%) and 65/69 (87%) cases respectively, while in benign obstructive jaundice level of obstruction was delineated in all 13 cases in which CT was done while cause was revealed in 11/13 (85%) cases.

MRCP was performed in total of 20 cases and correctly identified level and cause of obstruction in 18 (90%) cases including choledocholithiasis, choledochal cysts, periampullary & hilar mass and CBD stricture.

ERCP was done in total of 15 cases and was able to delineate the level and cause of obstruction in all cases including malignant ductal and hilar cholangiocarcinoma, periampullary carcinoma and choledocholithiasis.

PTC combined with biliary drainage was done as combined diagnostic and predominantly palliative procedure in five cases of malignant obstructive jaundice with level of obstruction correctly identified in all cases with aetiological confirmation done in aid with other imaging modalities.
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DISCUSSION

This prospective study in a defined population revealed the aetiological spectrum, clinical features and utility of imaging in obstructive jaundice in our setting over a 26 months period, the jaundice being proved by clinical evaluation, laboratory and radiological investigations.

Majority of patients in this study had malignant obstructive jaundice, i.e., 62.73% (69/110) while the benign jaundice was seen in 37.27% (41/110).

Various other studies have been done for the evaluation of the etiological spectrum of obstructive jaundice and are compared with our study in the following table. (Table-2)

Table 2: Comparison of percentages of Malignant & Benign Jaundice

<table>
<thead>
<tr>
<th>Study</th>
<th>Malignant causes</th>
<th>Benign causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sharma MP et al, India</td>
<td>75.3%</td>
<td>24.7%</td>
</tr>
<tr>
<td>Siddique K et al, Pakistan</td>
<td>56.66%</td>
<td>43.33%</td>
</tr>
<tr>
<td>Moghimi M et al, Iran</td>
<td>60.15%</td>
<td>39.85%</td>
</tr>
<tr>
<td>Huis M et al, Croatia</td>
<td>25.83%</td>
<td>74.17%</td>
</tr>
<tr>
<td>Cheema K et al, Pakistan</td>
<td>65%</td>
<td>35%</td>
</tr>
<tr>
<td>Huang JQ et al, China</td>
<td>57.6%</td>
<td>42.4%</td>
</tr>
<tr>
<td>This study</td>
<td>62.73%</td>
<td>37.27%</td>
</tr>
</tbody>
</table>

As can be seen above our study is in agreement with most of the studies quoted except for the Croatian study which revealed higher incidence of benign causes (Choledocholithiasis) possibly related to regional dietary and social factors.
In this study, malignant obstructive jaundice was found more commonly amongst the males than females while females had more of benign obstructive jaundice which was statistically significant (p<0.05). The male to female ratio for benign jaundice was 1:1.8, while it was 2.9:1 for the malignant obstructive Jaundice. The incidence of malignancy of pancreas was statistically significantly (p<0.05) higher in males compared to females possibly related to alcohol abuse and higher incidence of smoking in males. Carcinoma of gallbladder was the commonest malignancy in females most likely related to higher incidence of chronic cholelithiasis and dietary factors.

The mean age of the patients with the benign and malignant aetiology of obstructive jaundice was 38.6 years and 56.7 years respectively. Most of the patients with the benign jaundice were between 31–60 years of age while malignant causes were more common in the older patients and were maximally seen between 41–80 years of age. The increased incidence of malignant obstructive jaundice with the increasing age has also been reported by studies.\textsuperscript{9,14}

Regarding the various malignant causes diagnosed carcinoma head of pancreas was the commonest (33.63\%) followed by the carcinoma gall bladder (18.18\%), periampullary carcinoma (5.45\%), cholangiocarcinoma (3.63\%) and HCC (1.8\%). Choledocholithiasis (29.1\%) was the most common among benign causes of obstructive jaundice with CBD stricture, pancreatitis and choledochal cyst accounting for rest of the cases (6.36\%)

Comparison of incidence of various etiologies of obstructive jaundice in various studies with our study is shown in the table below. Table-3.

**Figure 9**

Table -3 Comparison of Various Studies done for Aetiological Spectrum of Obstructive Jaundice

<table>
<thead>
<tr>
<th>Study</th>
<th>Ca pancreas</th>
<th>GB malignancy</th>
<th>CholangioCa</th>
<th>Periampullary Carcinoma</th>
<th>Choledocholithiasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Siddiqui K et al, Pakistan\textsuperscript{a}</td>
<td>30%</td>
<td>13.3%</td>
<td>11.66%</td>
<td>1.06%</td>
<td>33.5%</td>
</tr>
<tr>
<td>Sharma MP et al, India\textsuperscript{b}</td>
<td>36.5%</td>
<td>28.7%</td>
<td>10.8%</td>
<td>9.8%</td>
<td>12.4%</td>
</tr>
<tr>
<td>Huang JQ et al, China\textsuperscript{c}</td>
<td>21.5%</td>
<td>7.8%</td>
<td>10.4%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tjin M et al, Croatia\textsuperscript{d}</td>
<td>13.5%</td>
<td>3.3%</td>
<td>4.6%</td>
<td>74.17%</td>
<td></td>
</tr>
<tr>
<td>This study</td>
<td>32.63%</td>
<td>18.13%</td>
<td>3.63%</td>
<td>5.45%</td>
<td>29.1%</td>
</tr>
</tbody>
</table>

Among the symptoms, pain in the abdomen (the right hypochondrium) was noted more commonly in malignant causes (60/69, 87\%). Clay coloured stools was reported more commonly by patients with the malignant jaundice(45/69, 65.2\%). Pruritis was seen equally in both the benign and malignant cases. Anorexia and weight loss were more frequently seen amongst the patients of malignant jaundice. Hepatomegaly was appreciated in 21/69 of the patients with malignancy while palpable gallbladder was noted in cases of malignant obstruction thus supporting the ‘Courvoisier’s law’.\textsuperscript{16} The scratch marks were seen in equal percentage of patients amongst the benign and malignant conditions. These findings have also been confirmed by other studies.\textsuperscript{9,14,20}

The biochemical investigations done were liver function tests which showed high serum bilirubin and alkaline phosphatase level. The levels of serum bilirubin and alkaline phosphatase were statistically analyzed for the benign and malignant causes. No statistically significant difference in the values was noted whatever the cause of jaundice may be (p>0.05).

Amongst the radiological investigations the diagnostic accuracy of ultrasound in defining the level of obstruction was 91.8\% as compared to 97.5 \%, 90\% and 100\% for CT scan, MRCP and ERCP, respectively.

To measure the etiology of the obstruction, the accuracy of ultrasound, CT scan, MRCP and ERCP were 87.3\%, 92.7\%, 90\% and 100\%, respectively. The sensitivity of USG, CT, MRCP and ERCP in the diagnosis of benign disease was 85.3\%, 84.6\%, 92.3\% and 100\%, respectively, whereas specificity was 88.4\%, 94.2\%, 86\% and 100\%, respectively. Sensitivity for a diagnosis of malignant disease was 88.4 \%, 94.2 \%, 86 \% and 100\% for USG, CT, MRCP and ERCP respectively whereas specificity was 85.3 \%, 85\%, 92\% and 100\% respectively. These findings are broadly in agreement with studies done at various others centers for USG\textsuperscript{17,19,20,21}, CT\textsuperscript{18,21}, MRCP\textsuperscript{6,22,23} and ERCP\textsuperscript{9,22,24,25}. However the relatively lower sensitivities noted in older studies\textsuperscript{18,21} with regard to USG and CT could be due to resolution and technical factors which have vastly improved in last decade and hence this study sheds new light on diagnostic accuracies of the modern high tech equipment (including high resolution US and spiral CT) in context to biliary obstruction.

The final diagnosis was then made based upon the results of histopathology (post ERCP/biopsy/cytology/surgery) and then results were drawn and analysed.
CONCLUSION
Obstructive jaundice has different aetiological spectrum in males where malignant causes predominate compared to females who have more of benign disease. Benign causes are seen at a comparatively younger age group compared to malignant causes. Carcinoma of head of pancreas was the commonest malignant aetiology, while choledocholithiasis is the commonest benign cause. Ultrasound and Spiral CT have high diagnostic accuracy and specificity and along with MRCP have largely confined the role of invasive cholangiography (ERCP/PTC) to therapeutic/palliative procedures, rather than primary diagnostic tests in modern setup.

References
Author Information

Sameer R. Verma, MD,DNB
Subharti Medical College

Sharad B. Sahai, MD
Subharti Medical College

Pradeep K. Gupta, MD
Subharti Medical College

Avinash Munshi, MD
Subharti Medical College

Suresh Chandra Verma, MD
Subharti Medical College

Piyush Goyal, MD
Subharti Medical College