



## Prospective Study to Determine the Importance of Prognostic Markers for Patients with Obstructive Jaundice

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### ABSTRACT

**Background:** To determine the prognostic factors and their importance in the overall outcome of Obstructive Jaundice.

**Objective:** To study prognostic value of each individual factor in overall outcome of patients with obstructive jaundice.

**Material and Methods:** This is an observational prospective study of total of 25 cases of patients with Obstructive Jaundice. These included patients of all age groups and both genders. Patients were chosen at random from those who visited the out patient department with clinical symptoms, laboratory diagnosis, or radiological diagnosis of Obstructive Jaundice. Moribund patients and those who refused to give consent to be part of the study were not included in the study.

**Results:** A total of 25 patients were chosen for the study, of which 11 were males and 14 females. The mean age group was 48.08 years with a standard deviation of 17.72 years. All patients presented with clinical symptom of epigastric pain, and most (22) also had associated symptoms such as vomiting and anorexia. Majority of the patients belonging to morbidity present group had Hb less than 10 gm/dl, direct bilirubin value more than 10 gm/dl, SGPT more than 250 U, alkaline phosphatase more than 300 U, and proteins less than 6 gm/dl. ERCP was the most commonly done diagnostic and therapeutic procedure in our study.

**Conclusion:** Morbidity increases statistically significantly in patients having malignant condition, age above 65 years, hemoglobin less than 10%, total protein less than 7gm%, Direct bilirubin value more than 10gm/dl, PT value above 14 sec, SGPT value above 250IU, Alkaline Phosphatase value above 300 IU. ERCP was found to be the most statistically significant mode of diagnoses and therapeutics in our study.

### KEYWORDS

Obstructive Jaundice, Prognosis, Billirubin, ERCP

### INTRODUCTION

Jaundice, also known as icterus, is a yellowish pigmentation of the skin, the conjunctival membranes over the sclerae (whites of the eyes), and other mucous membranes caused by high blood bilirubin levels. This hyperbilirubinemia subsequently causes increased levels of bilirubin in the extracellular fluid. Concentration of bilirubin in blood plasma is normally below 1.2 mg/dL (<25µmol/L). A concentration higher than approx. 3 mg/dL (>50µmol/L) leads to jaundice. The term jaundice comes from the French word *jaune*, meaning yellow.

Jaundice is often seen in liver disease such as hepatitis or liver cancer. It may also indicate leptospirosis or obstruction of the biliary tract, for example by gallstones or pancreatic cancer, or less commonly be congenital in origin (e.g., biliary atresia).

Post-hepatic jaundice, also called obstructive jaundice, is caused by an interruption to the drainage of bile containing conjugated bilirubin in the biliary system. The most common causes are gallstones in the common bile duct, and pancreat-

ic cancer in the head of the pancreas. Also, a group of parasites known as "liver flukes" can live in the common bile duct, causing obstructive jaundice. Other causes include strictures of the common bile duct, biliary atresia, cholangiocarcinoma, pancreatitis, cholestasis of pregnancy, and pancreatic pseudocysts. A rare cause of obstructive jaundice is Mirizzi's syndrome.

In complete obstruction of the bile duct, no urobilinogen is found in the urine, since bilirubin has no access to the intestine and it is in the intestine that bilirubin gets converted to urobilinogen to be later released into the general circulation. In this case, presence of bilirubin (conjugated) in the urine without urine-urobilinogen suggests obstructive jaundice, either intra-hepatic or post-hepatic.

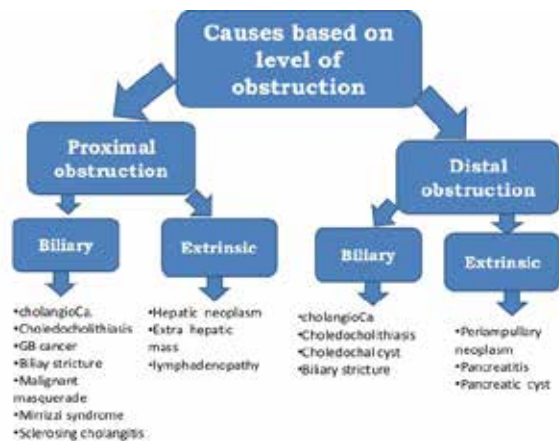
No single test can differentiate between various classifications of jaundice. A combination of liver function tests is essential to arrive at a diagnosis.

Differential Diagnosis of Jaundice

Pathology	serum bilirubin			urine bilirubin	urine urobilinogen	AST, ALT	alk.phos., γGT
	total (T)	direct (D)	D/T *				
Hemolysis	↑	=	< 0.2	=	↑↑	=	=
Liver Disease							
hepatocellular	↑↑	↑↑	0.5 : 0.1	↑↑	=	↑↑	↑
obstructive							
partial	↑ <sup>Δ</sup>	↑ <sup>Δ</sup>		↑ <sup>Δ</sup>	=	↑	↑↑
complete	↑↑↑	↑↑↑	0.7 : 0.1	↑↑↑	=	↑↑	↑↑
cirrhosis	↑	↑		↑	=	↑	↑
Neonatal Jaundice	↑↑↑	=	< 0.2	=	=	=	=

**Causes of Obstructive Jaundice**

Obstructive Jaundice is primarily caused by the obstruction of the intrahepatic or extrahepatic biliary tree. Impaired transport and excretion and biliary ductal obstruction result in hyperbilirubinemia that is primarily conjugated. Some patients have multiple defects in normal metabolism. For example, a patient with biliary obstruction from a tumor may develop secondary hepatocellular dysfunction. Therefore these classification systems may be simplifications of more complex disease processes. Diseases causing bile duct obstruction may be further divided into conditions causing 1) complete obstruction, 2)intermittent obstruction, 3) chronic incomplete obstruction, or4) segmental duct obstruction. Patients with complete biliary obstruction will have clinical jaundice, and those with intermittent obstruction may develop symptoms (pain, pruritus, fevers) and biochemical changes without necessarily developing clinical jaundice. Patients with chronic incomplete obstruction can eventually develop hepatic fibrosis and biliary cirrhosis.



**MATERIALS AND METHODS**

**Inclusion Criteria-**

- All age group
- Patients who wish to give informed consent.
- Both the gender
- Patients visiting surgical outpatient department
- Patient complaining of classical symptoms of obstructive jaundice
- Patients clinically diagnosed with obstructive jaundice
- Patients diagnosed with obstructive jaundice based on the laboratory parameters.
- Patients diagnosed with obstructive jaundice with ultrasonography, ERCP, CT scan and other diagnostic procedures.

**Exclusion criteria**

Moribund patients Patients not willing to give informed consent.

Total 25 were included in the study randomly, who visited surgical OPD department with the complaints suggestive of obstructive jaundice. Then they were subjected to following test

**Hemoglobin**

- Complete blood count
- Renal function test

**Liver function test**

- Prothrombin Time/INR
- Bilirubin- direct and Indirect
- Tumor markers
- USG abdomen
- CT scan/ MRI/ Endoscopic Ultrasound (Optional)
- Endoscopic retrograde cholangio-pancreatography
- Percutaneous transhepatic cholangiography (PTC)

Patient will be followed before and after the diagnostic procedure or any operative procedure and repeat blood investigations will be done.

**RESULTS AND DISCUSSION**

A prospective study was undertaken to determine prognostic markers for patients with obstructive jaundice. Surgery in patients with jaundice secondary to extrahepatic biliary obstruction carries a high rate of mortality,1-2 attributed mainly to deranged hepatic function. Several studies have been carried out to identify the factors which predict the outcome of surgery in these patients. The adverse prognostic factors identified in retrospective studies include physiological variables (age greater than 60 years, sex), clinical diagnosis (benign/malignant), duration of disease, associated conditions (diabetes, pancreatitis), presence of infection and hematological and biochemical criteria such as hematocrit, leucocyte count, renal function tests and liver function tests. There is thus no agreement on specific factors associated with postoperative mortality. A number of these factors are interrelated and nonspecific. In addition, none of them provides a quantitative measure of functional capacity of the liver, which is impaired due to cholestasis.<sup>13</sup>

In clinical practice, the greatest weight has been given to the serum bilirubin level, which is a static test. Decrease in the level of serum bilirubin is not necessarily associated with improved liver function.

**DEMOGRAPHIC RESULTS**

**TOTAL NUMBER OF PATIENTS**

We recruited a total of 25 patients in the study. And were followed till discharge, another study done by Nazareth HM et al studied twenty patients with extrahepatic obstructive jaundice (12 males, 8 females, aged 25-73 years, median 44).

The diagnosis was based on clinical features, ultrasonography and CT abdomen and MRCP.

**AGE**

Mean age group 48.08 years , with standard deviation 17.72 years.

Age group (Years)	No. of patients
11-20	1
21-30	5
31-40	3
41-50	4
51-60	3
61-70	4
71-80	2
81-90	1

**GENDER**

Male recruited in the study were 11 and females recruited in 14.

**HABITS**

- Smoking-was seen in 6 patients
- Non vegetarian diet was seen in 13 patients

**PAST HISTORY**

- Two patients received Blood transfusion
- One patient was diagnosed with Diabetes Mellitus.
- Six patients suffered from hypertension

**CLINICAL PRESENTATION**

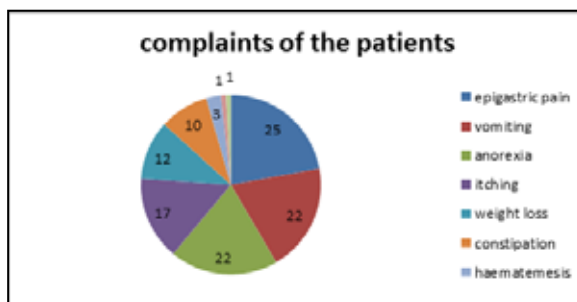
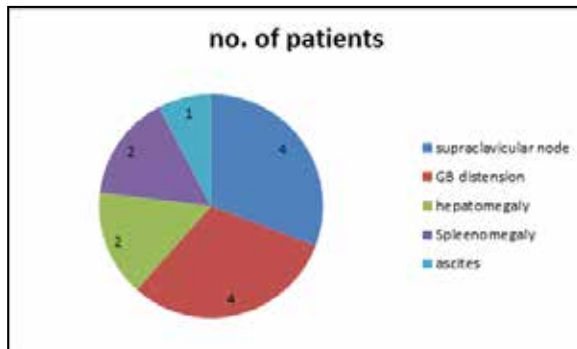
Two patients presented with Splenomegaly and hepatomegaly.

Four patients presented with GB distension

Four patients presented with abdominal lump.

One patient presented with ascites.

Four patients with enlarged supraclavicular node.



**LABORATORY PARAMETERS**

**HEMOGLOBIN**

Hemoglobin values (gm/dl)	Morbidity absent group (n=17)	Morbidity present group(n=8)
Less than 10	1	8
More than 10	16	0

While in patients in morbidity present group Hb was less than 10gm/dl. A study done by Guoma et al. also confirmed our finding that anemia in obstructive jaundice patient is associated with morbidity present group.<sup>14</sup>

**Total count**

Count values	Morbidity absent group (n=17)	Morbidity present group(n=8)
Below 5000	1	0
5001-8000	5	4
8001-11000	2	4
11001-20000	8	0
Above 20000	1	0

Majority of the patients belonging to morbidity absent group had total count more than 11,000 mcl. A study done by Mabula et. al suggested that patients having obstructive jaundice and WBC count > 10 X 10<sup>9</sup>/L have morbidity absent group and vice-versa. 15

**UREA**

Urea values mg/dl	Morbidity absent group (n=17)	Morbidity present group(n=8)
10-40	17	8
Above 40	0	0

No patient had altered urea level. This finding was different from John Fraser et.al who reported that later stages of obstructive jaundice was having elevated blood urea. A study by Dhara et. al reported the same finding. 16

**SERUM CREATININE**

Values	Morbidity absent group (n=17)	Morbidity present group(n=8)
Less than 0.8	8	3
0.8-1.3	9	5
Above 1.3	0	0

Majority of the patients belonging to good and bad prognosis group had Serum creatinine value less than 1.3 gm/dl. A study done by Sitprijia studied renal function with respect to water clearance and renal hemodynamics was studied in 15 patients with obstructive jaundice due to cholangiocarcinoma.

**17DIRECT BILIRUBIN**

Direct Bilirubin values	Morbidity absent group (n=17)	Morbidity present group(n=8)
Less than 10	16	1
Above 10	1	7

A study done by Sitprijia et. al studied the effect of bilirubin as prognostic marker in obstructive jaundice suggested that elevated direct bilirubin is associated with poor prognostic value.

A study done by Sitprijia et. al studied the effect of direct bilirubin as prognostic marker in obstructive jaundice suggested that elevated direct bilirubin is associated with poor prognostic value.

**TOTAL BILIRUBIN**

Total bilirubin values	Morbidity absent group (n=17)	Morbidity present group(n=8)
2-20	15	4
Above 20	2	4

Majority of the patients belonging to morbidity absent group had total bilirubin value less than 20 gm/dl. Majority of the patients belonging to morbidity present group had total bilirubin value more than 20 gm/dl. A study done by Sitprijia et. al studied the effect of total bilirubin as prognostic marker in obstructive jaundice suggested that elevated total bilirubin is associated with poor prognostic value. 17

A study done by Gundry et.al in his study also reported decreased in serum bilirubin after intervention in his study which was performed on twenty-five patients PBD was done for an average of nine days before operation; Serum bilirubin levels before PTHC were 16.5±7.6 mg/dL and 14.9±7.6 mg/dL in PBD and non-PBD groups, respectively. Serum bilirubin levels decreased to 6.5±6.2 mg/dL preoperatively in patients having PBD. One week after operation, bilirubin levels were 4.2 ±4.3 mg/dL and 9.0±5.2 mg/dL in the PBD and non-PBD groups, respectively.

**18SGPT**

Values	Morbidity absent group (n=17)	Morbidity present group(n=8)
Less than 250	12	0
Above 250	5	8

As many as 25% of the patients with AST levels greater than 10 times the upper reference limit may have acute extrahepatic biliary tract obstruction, which can be heralded by a peak in aminotransferase levels (> 50 times the upper reference value

in 1%–2% of patients) that rapidly subsides once the obstruction has been removed. Levels above 250 suggest poor prognostic sign.<sup>19</sup>

**ALKALINE PHOSPHATASE**

Values	Morbidity absent group (n=17)	Morbidity present group(n=8)
Below 300	15	1
Above 300	2	7

Majority of the patients belonging to morbidity absent group had Alkaline Phosphatase below than 300U .While in patients in morbidity present group had alkaline phosphatase more than 300 U. ALP alteration due to common bile duct obstruction may be heralded by a peak in aminotransferase levels, typical symptoms and conjugated hyperbilirubinemia, especially in the acute setting, or the ALP levels may have a fluctuating pattern (± GGT alteration) with normal serum bilirubin in "valve" choledocholithiasis as reported by study of Anciaux et.al.<sup>20</sup>

**PROTHROMBIN TIME**

Values	Morbidity absent group (n=17)	Morbidity present group(n=8)
10-14 sec	13	2
Above 14 sec	4	6

Majority of the patients belonging to morbidity absent group had prothrombin time less than 14 sec. While in patients in morbidity present group had prothrombin time was more than 14 sec. Prognostically, a rise of the precursor concentration indicates return of hepatic synthetic capacity even though the patient's prothrombin time remains abnormal. Parenteral administration of vitamin K 10 mg will correct the prothrombin time of the obstructed patient to normal within 24 hours, while that of the hepatocellular icteric patient will improve only partially or not at all. A prothrombin time at least 10 seconds over control in a jaundiced patient and the inability to correct it with vitamin K is a poor prognostic sign.<sup>21</sup>

**TOTAL PROTEINS**

Values	Morbidity absent group (n=17)	Morbidity present group(n=8)
Below 6 gm/dl	1	8
Above 6 gm/dl	17	0

Majority of the patients belonging to morbidity absent group had total proteins more than 6gm/dl. While in patients in morbidity present group total proteins was less than 6mg/dl..

**ERCP**

ERCP with or without stenting was performed in 18 patients out of this 17 had morbidity absent group, and one patient died. It is a most commonly done diagnostic and therapeutic

procedure with immense success was ERCP in our study. The findings were similar to the study done by Lauri A. et. al , killj et. al. 22

P value based on Fischer's exact test and unpaired t-test, value less than 0.05 was considered as significant.

Morbidity increases statistically significantly in patients having malignant condition, age above 65 years, hemoglobin less than 10%, total protein less than 7gm%, Direct bilirubin value more than 10gm/dl, PT value above 14 sec, SGPT value above 250IU, Alkaline Phosphatase value above 300 IU, in patients without ERCP with or without stenting increases morbidity.

In our study eight patient had malignant lesions as compared to study done by Nazareth HM et.al where out of 20 patients, sixteen patients had malignant lesions while four patients had benign pathology. The duration of illness ranged from 6 months to 2 years.<sup>13</sup>

In our study, 3 patients died, all in underlying malignant condition after whipple's surgery, our study finding was similar to an study done by Nazareth HM et.al where four patients died after basal investigations. Five patients underwent definitive surgery. The remaining 11 patients were subjected to percutaneous transhepatic biliary decompression. Four patients died during the drainage period, while surgery was carried out for seven patients within 1-3 weeks of drainage. Of 20 patients, only six patients survived. Basal liver function tests were comparable in survivors and non-survivors. Discriminant analysis of the basal data revealed that plasma bilirubin, proteins and antipyrine half-life taken together had a strong association with mortality.<sup>13</sup>

**CONCLUSION & RESULTS**

- Obstructive jaundice is a common surgical problem in our setting and poses diagnostic and therapeutic challenges.
- A prospective study was undertaken in 25 patients to determine prognostic markers for patients with obstructive jaundice till discharge..
- Most of the patients belonging to morbidity absent group had Hb more than 10 gm/dl.
- While in patients in morbidity present group Hb was less than 10gm/dl. .
- Majority of the patients belonging to morbidity absent group had total count more than 11,000 mcl. While in patients in morbidity present group total count was less than 11, 000 mcl.
- Most of the patients belonging to good and bad prognosis group had blood urea in normal range. No patient had altered **urea** level.
- Majority of the patients belonging to good and bad prognosis group had Serum creatinine value less than 1.3 gm/dl.
- A large number of the patients belonging to morbidity absent group had direct bilirubin value less than 10 gm/dl. Majority of the patients belonging to morbidity present group group had direct bilirubin value more than 10 gm/dl.
- Majority of the patients belonging to morbidity absent group had total bilirubin value less than 20 gm/dl. Majority of the patients belonging to morbidity present group had total bilirubin value more than 20 gm/dl.
- Most of the patients belonging to morbidity absent group had SGPT below than 250U.
- While in patients in morbidity present group group had SGPT more than 250 U.
- Most of the patients belonging to morbidity absent group had Alkaline Phosphatase below than 300U .While in patients in morbidity present group had alkaline phosphatase more than 300 U.
- Majority of the patients belonging to morbidity absent group group had prothrombin time less than 14 sec. While in patients in morbidity present group had prothrombin time was more than 14 sec.
- A large percentage of the patients belonging to morbidity absent group group had total proteins more than 6gm/dl. While in patients in morbidity present group total proteins was less than 6mg/dl.
- In our study, 3 patients died, all in underlying malignant condition after whipple's surgery.
- ERCP in our study was good prognostic marker.

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