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Comparative Study of Liver Function Test Pattern in Obstructive Jaundice Due to Stones and Malignancy

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Abstract

Background: Surgical jaundice is caused by complete or partial obstruction of biliary flow. The etiology can be benign or malignant, of which the malignancies carry a grave prognosis. In rural setup of our country patients undergo conservative management for long due to shortage of advanced radiological, clinical and laboratory setup, leading to delayed referral at tertiary care centres and worsening the scenario. Diseases causing jaundice reflect as a change in liver function which can be easily assessed by simple laboratory tests. *Aims & objectives:* To assess the difference of liver function derangement in obstructive jaundice due to stones and malignant causes and to analyse if there is any specific pattern of liver function derangement with respect to etiology. *Material and methods:* A prospective descriptive study was done with 50 patients of obstructive jaundice, with group 1 (stones, n=22) and group 2 (malignancy, n= 28). Patients presenting with obstructive jaundice were subjected to clinical, laboratory and radiological evaluation and those fulfilling our criteria were assigned either group. The data was recorded and evaluation was done, using MedCalc Statistical Software. *Results:* The mean and highest values of total and direct bilirubin, Alkaline phosphatase, GGT, was much higher in group 2. S. albumin was significantly lower in group 2 compared to group 1. *Conclusion:* These parameters appear to follow a pattern as per etiology. Considering the cut off patterns, a scoring/predictive system can be developed for early diagnosis.

Keywords: Hepatic; Biliary; Pancreatic.

Introduction

Jaundice [1] is yellowish discolouration of tissue resulting from deposition of bilirubin.

Surgical jaundice [2] as defined is caused by complete or partial obstruction of biliary flow, which can be either intrahepatic or extrahepatic. The various etiologies can be either benign or malignant, the most common benign cause being stones in biliary tract, while most commonly encountered malignancies causing obstructive jaundice are cancer of the gall bladder, bile duct malignancies, cancers of periampullary region and metastases.

Jaundice and its underlying pathology reflect as a change in liver function which can be quantitatively assessed by a battery of tests known as Liver Function Tests. These are further divided as tests reflecting detoxification and excretory function and tests that measure biosynthetic function of liver.

Parameters evaluated that we have considered in our study are as follows [3,4] -

- *Bilirubin* - It is derived as a breakdown product of haem, which initially produces unconjugated bilirubin, which is then taken to liver for conjugation by albumin, from

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where it is then released in bile. Anything causing obstruction in outflow of bile causes a rise of total, unconjugated and conjugated bilirubin in blood, clinically evident as jaundice.

- *ALT* and *AST* - Alanine aminotransferase is found in cytoplasm and Aspartate transaminase is both cytoplasmic and mitochondrial. They are most frequently utilized to test for hepatocellular necrosis and are specific indicators.
- *ALP* – Alkaline phosphatase are a family of zinc metalloenzymes that are found in the microvilli of bile canaliculi and on the sinusoidal surface of hepatocytes.
- *GGT* - Gamma Glutamyl transpeptidase can help differentiate between hepatic and non hepatic source of rise of ALP. Marked increase in both is typical of cholestasis.
- *Albumin* – It is synthesized in liver and reflects the biosynthetic function of liver.
- *P.T* - Abnormal P.T. prolongation may be a sign of serious liver dysfunction.

Increasing number of obstructive jaundice cases are being admitted in RIMS, Ranchi, Department of surgery of various etiologies and managed accordingly. Many patients give history of conservative management in primary or community health centres in rural and semiurban areas. Often due to shortage of clinical, laboratory and radiological advancements in those settings, there is delay in diagnosis of the underlying malignancy, causing delayed referral and hence present at specialized tertiary care centres at a very advanced stage, adding to the morbidity and mortality.

It was being noticed that the extent of liver function derangement varied markedly between the cases with benign etiology and malignant etiology leading to obstructive jaundice, however we did not have any definitive evidence to reach any conclusion.

A study was undertaken to evaluate and compare the above mentioned parameters quantitatively, for stones and malignancies causing obstructive jaundice. Our aim and objective was to assess if these parameters followed any particular pattern of derangement, suggesting either benign or malignant cause, which could be used further to develop a predictive/ scoring system based on simple laboratory tests, for early diagnosis and referral even at PHC level.

Materials & methods

This study was conducted at Rajendra Institute of Medical Sciences, Ranchi, India between November 2015 and October 2017, after approval from institutional ethical committee. Study eligibility included patients with obstructive jaundice due to either CBD calculi or malignancy, with no prior surgical intervention in this regard, who gave consent to participate in the study and admitted in our unit in Department of Surgery. Patients with any other associated liver diseases or etiology apart from mentioned above were excluded.

This was a prospective descriptive study.

All cases were subjected to detailed history, clinical examination, laboratory evaluation and radiological evaluation.

History - Patient particulars, chief complaints with duration, history of present illness, past illness history, personal history, family history, menstrual and obstetric history (female cases), treatment histoy pertaining to present complaints.

Examination - General survey, systemic examination

Laboratory investigation - routine blood and urine examination, specific liver function tests as already mentioned, namely total bilirubin, direct bilirubin, indirect bilirubin, total protein, serum albumin, serum globulin, GGT, ALP, AST, ALT, P.T, I.N.R.

Radiological evaluation - USG done as first line investigation. As per reports further CECT or MRCP done.

On the basis of data obtained a total of 50 patients were included in our study, and divided into group 1 (stones, n= 22) and group 2 (malignancy, n = 28).

Statistical analysis: The data obtained was compiled using an excel sheet. All parameters were noted and statistical analysis was done comparing both the groups. T tests were applied wherever needed and p value <0.05 was considered significant. Application used for statistical calculations - MedCalc Statistical Software Version 14.8.1 (2014) MedCalc Software Bvba, Ostend. http://www.medcalc.org

Results

The study comprised of total 50 cases, of which 22 were found to have calculus and assigned group 1, and 28 were found to have malignant etiology and assigned group 2. Of those in group 2, 13

were found to have cholangiocarcinoma, 8 were found to have periampullary carcinoma, 6 were found to have carcinoma of gall bladder and 1 had metastases. Mean age of patients in group 1 was 48 yrs and group 2 was 54 years.

Total bilirubin - The mean and highest values of total bilirubin between group 1 and group 2 was compared. The mean and highest values were markedly higher in malignancy group. [Tables 1&2 and Fig. 1].

Direct bilirubin - While no case in group 1 had direct bilirubin > 10 mg/dl, around 53.57% cases of group 2 had direct bilirubin > 10 mg/dl. [Table 3]

Alkaline phosphatase - Majority (81.82%) cases in group 1 had Alkaline Phosphatase within 500 U/L, while majority patients in group 2 had Alkaline Phosphatase >500 U/L [Table 4, Fig. 2]

The average values were 470 U/L and 751 U/L for stone and malignancy respectively.

Total bilirubin

Table 1: Showing comparison of total bilirubin between stone and malignancy in mg/dl

T. Bilirubin	Stones	Malignancy
Mean	8.4	17.6
Highest	17.7	32.4

Total Bilirubin

Table 2: showing % of cases in group 1 and 2 in a given range of bilirubin in mg/dl

Total bilirubin (in mg/dl)	% of cases, group 1	% of cases, group 2
0-10	59.09	17.86
10-20	40.91	35.71
20-30	0	39.29
30-40	0	7.14

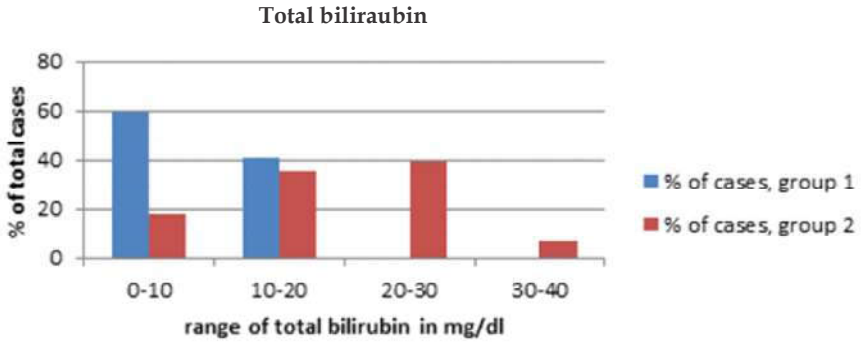

Fig. 1: Showing % of cases in group 1 and 2 in a given range of bilirubin in mg/dl

Direct bilirubin

Table 3 showing % of cases in group 1 and 2 in different ranges of direct bilirubin in mg/dl

Direct bilirubin (mg/dl)	% of cases, group 1	% of cases, group 2
0-5	59.09	17.86
5-10	40.90	28.57
10-15	0	25
>15	0	28.57

Alkaline Phosphatase

Table 4: Showing % of cases in group 1 and 2 in different range of Alkaline Phosphatase

Alkaline Phosphatase In U/L	% of cases, group 1	% of cases, group 2
0-500	81.82	32.14
500-1000	13.64	32.14
1000-1500	4.54	28.57
>1500	0	7.14

Gamma glutamyl transpeptidase - Majority cases in group 1 had GGT below 300 U/L, whereas majority cases in group 2 had GGT above 300 U/L [Fig. 3].

Serum albumin - Only 31.82% cases of group 1 had serum albumin less than 3 gm/dl, while in group 2, 64.28% cases in group 2 had serum albumin less than 3 gm/dl. [Fig. 4]

The difference of mean for *AST, ALT, I.N.R* was found to be insignificant [Table 5].

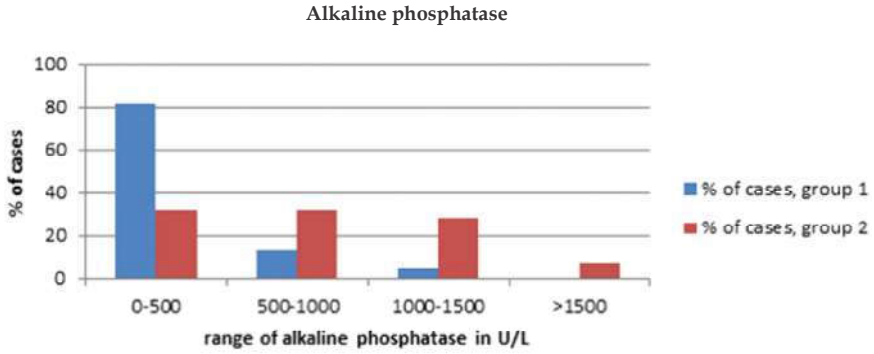

Fig. 2: Showing % of cases in group 1 and group 2 in different ranges of alkaline phosphatase

Table 5: Showing comparison of values of mean for group 1 and group 2 and the p values

Variable	Group 1 (Mean)	Group 2 (Mean)	p Value	Remarks
T. Bilirubin (mg/dl)	8.4	17.6	0.0001	Significant
D. Bilirubin (mg/dl)	4.59	10	0.0001	Significant
ALP (U/L)	470	751	0.03	Significant
GGT (U/L)	278.63	511.39	0.02	Significant
AST (U/L)	101	139	0.08	Insignificant
ALT (U/L)	90	113.71	0.39	Insignificant
I.N.R	1.25	1.55	0.053	Insignificant
S.Albumin (g/dl)	3.5	2.72	0.01	Significant

p values were calculated using independent t tests for each variable. Results were as shown in the table above 5.

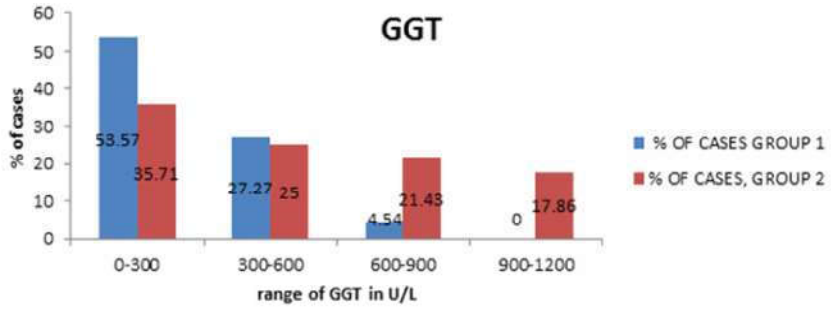

Fig. 3: Showing % of cases in group 1 and 2 in different range of GGT

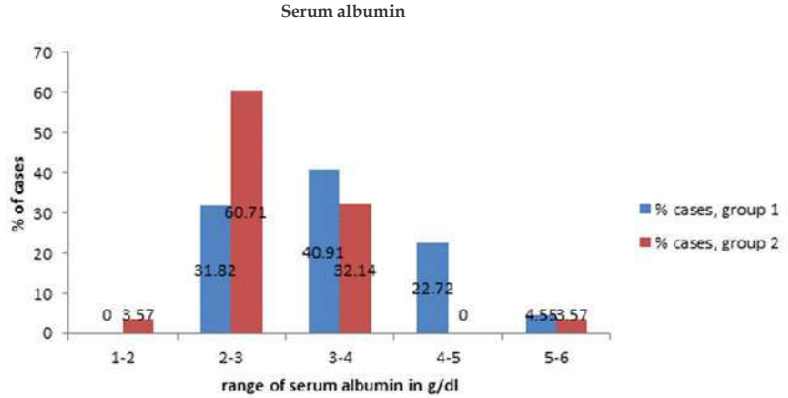

Fig. 4: % of cases in group 1 and 2 in different ranges of serum albumin

Discussion

In our study only 9.09% cases with stones as a cause of obstructive jaundice had total bilirubin above 15 mg/dl, while none had total bilirubin >20 mg/dl, whereas for malignant group 39.29% of cases had total bilirubin between 20-30 mg/dl and 7.14% had total bilirubin >30 mg/dl. K. Siddiqui et al., 2008 [5], described no significant difference of total bilirubin between stone and malignancy group unlike this study. A. Prabhakar et al., 2016 [6], described the mean total bilirubin for benign conditions causing obstructive jaundice to be 7.12 mg/dl, similar to this study and mean total bilirubin for malignancy to be 15.2 mg/dl which in this study we found to be 17.6 mg/dl. S. Ahmed et al., 2017 [7], described in their study the mean total bilirubin to be much higher in malignant obstructive jaundice than that of benign etiology.

In our study no case of stone had direct bilirubin >10 mg/dl, while 53.57% of group 2 cases had direct bilirubin >10 mg/dl. K. Siddiqui et al., 2008 [5], described no significant difference of direct bilirubin between stone and malignancy group unlike this study. A. Prabhakar et al., 2016 [6], described the mean direct bilirubin for benign conditions causing obstructive jaundice to be 4.65 mg/dl, similar to this study and mean direct bilirubin for malignancy to be 12.72 mg/dl . S. Ahmed et al., 2017 [7], described in their study the mean direct bilirubin to be much higher in malignant obstructive jaundice than that of benign etiology.

In this study 81.82% cases in group 1 had Alkaline Phosphatase <500 U/L, while majority cases with malignant etiology had Alkaline Phosphatase > 500 U/L. The mean values of alkaline phosphatase were 470 U/L and 751 U/L for group 1 and 2 respectively. K. Siddiqui et al., 2008 [5], described no significant difference of Alkaline Phophatase between stone and malignancy group unlike this study. M. Padda et al., 2009 [8], described a mean Alkaline phosphatase of 273U/L in cases of CBD calculi.

A. Prabhakar et al., 2016 [6], described the mean Alkaline phosphatase for benign conditions causing obstructive jaundice to be 243 U/L, and mean Alkaline phosphatase for malignancy to be 470.8 U/L, slightly lower than this study. S. Ahmed et al., 2017 [7], described in their study the mean Alkaline phosphatase to be much higher in malignant obstructive jaundice than that of benign etiology.

Maority (53.57%) cases in group 1 had GGT below 300 U/L, whereas majority (64.29%) cases in group 2 had GGT above 300 U/L.

ALT and AST in majority of cases in both groups were within 200 U/L. No significant difference between the groups w.r.t these parameters seen. ($p > 0.05$)

Majority cases in both groups had I.N.R ranging 1-2, mean values being 1.25 and 1.55 for stone and malignancy groups respectively. M. Padda et al., 2009 [8], described a mean I.N.R of 1.1 in cases of CBD calculi.

Only 31.82% cases in group 1 had serum albumin less than 3 gm/dl, while in group 2, 64.28% cases had serum albumin less than 3 gm/dl. M. Padda et al., 2009 [8], described a mean S.albumin 4.3 gm/dl in cases of CBD calculi.

Conclusion

It was observed that the following parameters varied significantly between calculus biliary obstruction and malignant biliary obstruction :-

- T. bilirubin
- Direct bilirubin
- Alkaline Phosphatase
- GGT
- Serum albumin

These parameters have been seen to follow a pattern as per etiology. Considering the cut offs specified in our results and discussion, a scoring system/ predictive system can be developed for early diagnosis and management of obstructive jaundice, specially in areas where radiological evaluation or expertise is not readily available.

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