

Diagnosis of Proximal Biliary Strictures: Role of serum bilirubin, alkaline phosphatase and abdominal ultrasound

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Abstract

Objectives: To determine the role of serum bilirubin, alkaline phosphatase and abdominal ultrasound in the diagnosis of proximal biliary strictures.

Study Design: Cross sectional

Place and Duration: Surgical Unit IV, Civil Hospital Karachi, from Jan 2007 to August 2008.

Methodology: A total of 407 patients with obstruction of the biliary tree on ultrasound and raised serum levels of alkaline phosphatase had ERCP performed on them. Serum bilirubin and alkaline phosphatase levels were recorded prior to the procedure. A total of 75 patients with strictures on ERCP were included in the study.

Results: Jaundice and abdominal pain were present in 68 (90.6%) and 41 (54.6%) of the total 75 patients respectively. A statistically significant difference was present in the mean bilirubin levels of different stricture groups ($p=.024$). Receiver Operator Curve analysis of serum bilirubin level of 19.2gm/dl showed a sensitivity of 43% and specificity of 77% with area under curve= 0.6. Abdominal ultrasound was found to be 31.8% sensitive and 79.2% specific in predicting the presence of proximal biliary strictures.

Conclusions: Serum levels of total bilirubin and alkaline phosphatase and abdominal ultrasound have minor role in the diagnosis of proximal biliary strictures.

Key Words: Strictures, Bilirubin, Alkaline phosphatase, Morbidity

Introduction:

ERCP can be utilized for diagnostic and therapeutic benefits. If a stricture is diagnosed, a stent can be placed in the biliary tree¹. Other expensive procedures like MRCP, Intraductal ultrasound and CT have variable efficiency in these patients for diagnosis². Strictures have been identified as an independent risk factor for the development of hepatic fibrosis and secondary biliary cirrhosis leading to increased morbidity and mortality³. Biliary strictures are very diverse in their location in the biliary tree⁴. Raised serum bilirubin has been shown as a significantly good marker to predict the malignant nature of biliary strictures and development of post operative biliary strictures^{5,6}. Similarly raised serum alkaline phosphatase can predict presence of hepatic fibrosis in patients with biliary strictures⁽³⁾. Proximal biliary strictures can pose a special

problem during surgery since they can extend into the liver parenchyma and sometimes partial resection of the liver is also required along with the segment of the extra hepatic biliary duct for the relief of patients complains, thus adding to complications⁷.

Due to the high inflow of patients requiring ERCP in our setting and limitations of time, the authors wanted to observe how sensitive lab investigations of serum bilirubin and alkaline phosphates and abdominal ultrasound were in predicting presence of proximal biliary strictures which have a higher morbidity and need prioritizing for early ERCP.

Methods:

This was a cross sectional study in which data of all patients who underwent ERCP from January

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2007 to August 2008 were analyzed for the presence of strictures. Patients who had any of the following findings were considered for ERCP.

1. Obstruction of biliary tree on abdominal ultrasound.
2. Raised serum Alkaline Phosphatase level with or without increase in serum Bilirubin levels.

Of all the patients who underwent ERCP, 75 patients were found to have strictures in the biliary tree at different levels. Demographic details, presence or absence of clinical jaundice and right upper quadrant pain and its duration, position of strictures on ERCP and any history of previous surgery were analyzed.

Patients with strictures were divided into three groups based on the level of stricture. Group I (Upper Biliary strictures) were patients with strictures of common hepatic, right or left hepatic or intrahepatic ducts above the level of entry of cystic duct into common bile duct on ERCP. Group II (Mid Biliary strictures) had strictures at the level of entry of cystic duct into common bile duct with proximal or distal extension and Group III (lower CBD strictures) had strictures in bile duct below the level of entry of cystic duct into common bile duct. Presence of clinical jaundice and right quadrant pain was determined in all patients with strictures. Serum bilirubin and alkaline phosphatase levels and ultrasound exam were performed on all patients prior to ERCP. On ultrasound exam presence of intra hepatic and/or extra hepatic duct dilatation with normal CBD was considered positive for proximal biliary stricture. Data were entered and analyzed on SPSS 11.

One way ANOVA was used for the analysis of quantitative data in different stricture groups while Chi Square tests were used to determine statistical significance of different qualitative variables. A p-value of <0.05 was considered significant.

Results:

A total of 75 patients were found to have strictures in the biliary tree with 38 males and 37 females. The mean age at presentation for patients with strictures was 53.2 ± 14.5 . The mean age at presentation for males was significantly higher (55.8 ± 12.6 v 50.6 ± 12.2) than that of females ($p=0.015$).

Out of total 75 patients with strictures, 6 patients had a history of previous surgery. All of them had open cholecystectomy performed on them. A total of 2 patients with upper biliary strictures and 4 patients with mid biliary strictures had a history of previous surgery. No history of previous surgery was present in any of the patients with lower biliary strictures.

Jaundice was present in 68(90.6%) of the total 75 patients with strictures while abdominal pain was present in 41(54.6%) patients with strictures. Duration of jaundice and abdominal pain were not found to be significantly different in different stricture groups i.e. ($p=0.477$) and ($p=0.844$) respectively (Table 1).

The mean bilirubin level was 19.2 ± 10 in upper biliary strictures. A statistically significant difference ($p=0.024$) was present in the mean bilirubin levels of upper, middle and lower biliary strictures (Table 1). Receiver Operator Curve analysis of serum Bilirubin level of 19.2 gm/dl showed a sensitivity of 43% and specificity of 77% (AUC 0.6, SE 0.073, 95% CI=0.459-0.745) Figure 1.

The mean alkaline phosphatase level in upper biliary strictures was 759.2 ± 486.6 . No statistically significant difference was present in alkaline phosphatase levels in different groups of strictures. ($p=0.526$) (Table 1).

Abdominal ultrasound correctly identified 7 out

Table 1: Relationship between different variables and stricture groups

Variables	Upper CBD	Mid CBD	Lower CBD	P value
Mean age at presentation (years)	52.9 ± 13.5	53.4 ± 9.2	53.2 ± 15.4	0.99
Duration of jaundice (months)	2.8 ± 4.9	2.4 ± 3.4	1.6 ± 1.3	0.477
Duration of abdominal pain (months)	2.0 ± 5.3	1.4 ± 1.8	1.9 ± 4.7	0.844
Total Bilirubin levels (mg/dl)	19.2 ± 10.6	15.8 ± 9.9	10.8 ± 10.8	0.024
Alkaline phosphatase (IU)	759.2 ± 486.6	920.5 ± 575.8	910 ± 549.5	0.526

Table 2: Ultrasound Findings in Patients with Strictures at Different Levels of Biliary Tree

	Level of stricture on ERCP			Total
	Upper CBD	Mid CBD	Lower CBD	
Mass in the CBD	0	0	2	2
Dilated Common Bile Duct	3	7	10	20
Dilated Intra hepatic/extra Hepatic ducts	7	6	3	16
Mass in the Gall Bladder	4	5	0	9
No significant finding	6	9	5	20
Mass in the Pancreas	2	1	4	7
Peri ampullary mass	0	0	1	1
Total	22	28	25	75

Ultrasound findings

of 22 patients with proximal biliary strictures with a sensitivity of 31.8% and specificity of 79.2%. The different ultrasound findings in patients with strictures are shown in Table 2.

Discussion:

Obstructive jaundice is associated with high morbidity and mortality⁸. Kloek et al⁹ showed in their study that jaundice and abdominal pain were present in patients with proximal duct strictures at a frequency of 76.4% and 44% respectively. In another study abdominal pain was present in all patients who presented with obstructive jaundice due to various etiologies⁽⁸⁾. In this study, the authors found that majority of the patients i.e.68 out of 75 (90.6%) with strictures had clinical jaundice while abdominal pain was present in 41 (54.6%) of these patients.

The likelihood of sustaining a bile duct injury leading to a stricture is far more likely with laparoscopic than open cholecystectomy^{10,11}. In the present study, all 6 patients with previous history of surgery had open cholecystectomy performed on them. However, the number of patients with a history of previous surgery was very small to determine any true significance.

Saluja et al¹² suggested that patients with malignant biliary strictures were usually males and presented at a later stage. In the present study, the authors noticed a significant difference in mean age at presentation between males and females with males generally presenting at a later age i.e. 55.8±12.6 vs 50.6± 12.2 years. However, the etiology of strictures and the possible stage

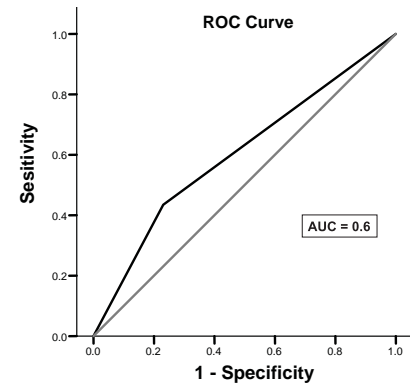


Figure 1: ROC Curve for serum Bilirubin level of 19.2 mg/dl

of the disease was not determined.

Raised serum bilirubin level has a profound effect on outcome in patients with obstructive jaundice in terms of morbidity and mortality¹³. In this study, there was a statistically significant difference (P.024) in serum bilirubin levels of patients within the three stricture groups. Studies have demonstrated higher serum levels of bilirubin in malignant vs non malignant strictures. However they did not compare the differences in bilirubin levels between proximal and distal malignancy of the biliary tree. Hayat et al¹⁴ observed comparatively higher levels of bilirubin in proximal biliary malignancy. In this study, the authors observed higher levels of serum bilirubin in proximal biliary strictures independent of their etiology (malignant or non malignant). However, ROC analysis showed that serum total bilirubin level of 19.2 mg/dl was only 43% sensitive in predicting the proximal location of biliary strictures.

Extrahepatic cholestasis leads to elevations of bilirubin and alkaline phosphatase levels^{15,16}. The authors observed no statistical difference in serum levels of alkaline phosphatase in different stricture groups despite of statistically different serum bilirubin levels.

It has been shown that abdominal ultrasound can show biliary dilation and correctly identify obstruction in almost all patients with pathology in the biliary tree¹². In this study the authors did not find abdominal ultrasound to be a very useful method in diagnosing proximal biliary strictures with a low sensitivity of 31.8% and specificity of 79.2% for proximal biliary strictures.

Several studies have shown the higher mortality rate sometimes exceeding 50% in patients with malignancy in the proximal biliary tree when they are followed for a few years post operatively with different surgical procedures¹⁷⁻²⁰. This emphasizes on early detection of proximal biliary strictures since they can have an underlying malignant etiology and thus higher morbidity and mortality.

Conclusion:

In this study, the authors observed that laboratory investigations of serum bilirubin and alkaline phosphatase does not show significant differences in strictures at different levels of biliary tree. Similarly abdominal ultrasound showed low sensitivity in predicting the presence of strictures in the proximal biliary duct. Therefore, these investigations have a trivial role in the diagnosis of proximal biliary strictures.

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