

Diagnostic Accuracy of Ultrasound in Correlation to Alkaline Phosphatase Levels in Patients with Biliary Obstructions

Muhammad Tariq^{1*}, Syed Amir Gilani¹, Aslam Shahid¹ and Mazhar Ul Khaliq¹

¹University Institute of Radiological Sciences and Medical Imaging Technologies (UIRSMIT), Faculty of Allied Health Sciences, (FAHS), the University of Lahore, Lahore, Pakistan.

*tariq1615@gmail.com

Abstract:

Abdominal Ultrasonography (USG) is an appropriate initial screening method for detection of biliary tract disease the consultants sometimes encounter patients who only have findings of dilatation of the Common Bile Duct (CBD) on US without specific biliary symptoms or jaundice.

Objective:

To determine the diagnostic accuracy of ultrasound in correlation to alkaline phosphatase levels in patients with biliary obstructions.

Methods:

Total 100 patients were selected during 6 months. Data were tabulated and analyzed by SPSS version 24.0. The quantitative variables were presented in form of mean $\pm$ S.D and Chi square test was used to test the association between categorical variables. A semi-structured questionnaire was prepared and finalized after pre-testing.

Results:

59 (0.59%) females and 41 (0.41%) males. 63 (0.63%) patients presented with abdominal pain. 85(0.85%) have CBD, 64 (0.64%) has stones as common cause of obstruction. The mean scoring of Alkaline Phosphate Level (APL) was 439.9 $\pm$ 10.54. There was significant association between the age groups and cause of obstruction in patients, gender and complaints of patients (p-value < 0.05).

Conclusions:

A significant number of causative biliary tract lesions in asymptomatic adults with dilatation of the CBD on routine abdominal US; no laboratory or demographic parameters were useful for discrimination.

Key words:

Ultrasonography, Alkaline Phosphate Level, Common bile duct, Biliary obstruction

Introduction:

Ultrasound is a noninvasive, risk-free imaging technique that can be used to screen gallbladder and biliary tree obstruction. Ultrasound utilizes sound waves rather than x-rays or radiation to create medical images. The procedure is typically pain-free and requires no injections. Ultrasound is useful for evaluating a number of conditions and specific parts of the human body such as pregnancy and gynecologic issues, thyroid, abdomen, pelvis, scrotum, and vascular structures such as carotid arteries and the arteries of the lower extremities. The main goals of imaging procedure in clinically suspected cases of obstructive jaundice to confirm the presence of obstruction, its location, extent, probable cause and to provide a sufficiently accurate overview of the biliary tree that will help the surgeon to determine the approach to each individual case^{1,2}. Obstructive jaundice can be caused by a plethora of conditions. These include benign as well as malignant conditions. Obstructive jaundice can be caused by the obstruction of the intra-hepatic bile ducts and Chronic Heart Disease (CHD) with hepatic masses, common bile duct (CBD) stones, strictures, malignancy such as cholangiocarcinoma (in which the jaundice is persistent and progressive), periampullary carcinoma, carcinoma gall bladder and carcinoma head of pancreas, Castlemann disease, Caroli's syndrome and metastatic liver tumor³. Ultrasonography (USG) is fairly accurate to detect dilated and non-dilated bile ducts. USG allows dynamic and real time

evaluation of the biliary tree. Diagnostic procedures using ultrasound are painless, harmless, relatively inexpensive, easily available and free of ionizing radiation⁴. Gross intrahepatic dilatation is easy to detect sonographically and result in the “too many tubes” sign, created by the increased number of radiolucent channels in the liver, or the “parallel channel sign”, formed by dilated intrahepatic ducts running anterior and parallel to the portal vein tributaries,⁵ (double barrel sign). The normal diameter of CHD measures 4-5mm or less on sonograms. The CBD measures 4-6mm normally, with a 6-7mm diameter considered equivocal. A diameter of more than 8mm is indicative of ductal dilatation. The diameter of CBD increases normally by 1mm every decade. Other sonographic studies established 4mm as normal mean CBD diameter at age of 40 years, 5mm at 50 years and 8mm at 80 years⁶. The width of CBD ranged from 1-8.6 and it dilated 0.04mm/year⁷. USG is primary modality used in the initial evaluation of obstructive jaundice. As this modality is fairly easily available, and constitutes the prima facie radiological investigation for the condition, a study was designed by Yang MH *et al.*, to evaluate the diagnostic role and accuracy of Ultrasonography in clinically suspected cases of obstructive jaundice⁸. Physical exam findings include jaundice, scleral icterus, and right upper quadrant pain. Fever may be present or absent. Liver biochemistry tests can reveal that aminotransferases increase initially, but rarely exceed a level of 500 IU. This is followed by the elevation of total bilirubin (both fractions), alkaline phosphatase, and Gamma-Glutamyl Transferase (GGT obstructive pattern)⁹. Extra hepatic obstructions: ALP levels are elevated in nearly 100% of patients, except in some cases of incomplete or intermittent obstruction. Values are usually greater than 3 times the upper limit of the reference range, and in most typical cases, they exceed 5 times the upper limit. An elevation less than 3 times the upper limit is evidence

against complete extra hepatic obstruction. Intrahepatic obstruction: ALP levels are usually elevated, and they often are less than 3 times the upper limit of the normal reference range. However, 5-10% of patients have a greater degree of elevation¹⁰. When liver chemistries are normal, the likelihood of biliary obstruction is very low⁸. Trans abdominal ultrasound is the initial imaging test of choice due to its attractive cost and safety profile. Trans abdominal ultrasound can show cholelithiasis, common bile duct (CBD) or intrahepatic duct dilation, and choledocholithiasis. Historically, Trans abdominal ultrasound was reported to have a poor sensitivity (22% -55%) for detecting common bile duct stones but now it has a sensitivity of 82% and specificity of 88%(9) when done by experienced sonologist. CBD dilation is more reliably detected by TUS (sensitivity 77%-87%)¹⁰. A CBD diameter > 6-8 mm is considered to be dilated in patients with normal gallbladders. A normal bile duct diameter on TUS has a 95% to 96% negative predictive value for choledocholithiasis¹¹.

Björnsson E *et al.*, in 2008 stated that etiological spectrum of obstructive jaundice and diagnostic ability of ultrasonography clinician's perspective and find that Sonography correctly established the presence of obstructive jaundice in 380 of 429 patients. Of 429 patients (mean age 62.5 +/- 34.2 yrs, 229 males and 194 females) the sensitivity of ultrasound to correctly diagnose and establish the site of etiology of obstruction was 94% with a specificity of 96%. Malignant SOJ was much more common than benign causes (75.3% Vs. 24.7%). Carcinoma (CA) of the gallbladder (28.7%) was the commonest aetiology followed by Ca pancreas (26.5%), choledocholithiasis (12.4%), cholangio CA (10.8%) benign stricture (10.8%) and ampullary CA (9.8%). A total of 167 subjects (44%) had high block while 213 (56%) had low block. Block at the porta hepatis was due to gallbladder CA in 91% of patients. CA pancreas was the cause of lower end block in 76% of patients. SOJ, as seen in this large series of

patients was most often due to malignant cause and gallbladder CA was the commonest cause in North Indian patients. The clinician should utilize the ability of the ultrasound to diagnose the presence of obstructive jaundice and its location¹². Laig FC. (2016) stated the gallbladder and bile ducts and find that Air in the biliary tree may result from transient or prolonged communication with the gastrointestinal tract. Air from the duodenum is introduced into the bile duct as the sphincter of Oddi opens with passage of a stone or with ERCP. Sustained communication occurs following sphincterotomy, an endobiliary stent placement, or biliary enteric fistula. Gas can also arise in the biliary tree as a result of infection, from reflux, emphysematous cholecystitis, or biliary necrosis with secondary abscess formation. On US biliary air gives a typical appearance of smooth, linear, bright echoes that are located adjacent to the portal veins. There may or may not be associated biliary ductal dilatation. Biliary duct necrosis is a critical complication that may occur following liver transplantation, usually secondary to ischemia from hepatic artery stenosis or thrombosis. If biliary necrosis occurs, the ducts become enlarged and filled with pus or necrotic debris. On ultrasound they may appear echogenic, irregular, and enlarged without the usual anechoic bile. Echoes are frequently nodular in appearance. Shadowing may occur if gas is also present¹³. Yang MH *et al.*, (2014) stated the Biochemical predictors for absence of common bile duct stones in patients undergoing laparoscopic cholecystectomy. Eighty-eight (8.8%) patients with gallstone disease who underwent laparoscopic cholecystectomy had concurrent common bile duct stones. Among all diagnostic tests, endoscopic retrograde cholangio pancreatography had the highest sensitivity (96.0%), specificity (99.1%), probability ratio (107.3), accuracy (98.0%), and positive predictive value (98.8%) in detecting common bile duct stones. At least one abnormal elevation among the five biochemical

parameters had the highest sensitivity (87.5%). Total bilirubin had the highest specificity (87.5%), highest probability ratio (3.9), highest accuracy (84.1%), and highest positive predictive value (27.4%). All five biochemical predictors had high negative predictive values; gamma glutamyl transferase was highest (97.9%), while the lowest was total bilirubin (94.7%). Multivariate analysis showed only gamma glutamyl transferase, alkaline phosphatase, and total bilirubin to be independent predictors; gamma glutamyl transferase appeared to be the most powerful predictor (odds ratio 3.20). Biochemical tests, especially gamma glutamyl transferase with 97.9% negative predictive value, are ideal noninvasive predictors for the absence of common bile duct stones in patients undergoing laparoscopic cholecystectomy. They suggest that unnecessary, costly, or risky procedures such as endoscopic retrograde cholangio pancreatography can be omitted prior to laparoscopic cholecystectomy in patients without abnormal elevation of these biochemical values.¹⁴

Although abdominal ultrasonography (US) is a proper initial screening method for detection of biliary tract disease, the researcher sometimes encounter patients who only have findings of dilatation of the common bile duct (CBD) on US, without specific biliary symptoms or jaundice. This study aimed to evaluate the causes and clinical significance of dilatation of the CBD in patients without biliary symptoms, jaundice, or causative lesions at US.

Methods:

Descriptive cross-sectional study design was followed and Simple random sampling technique was used to collect data. The patients residents of South Punjab aged between 25-80 years were included in the study. Unwilling, non-residents of south Punjab were excluded from the study. Ultrasound scanning and measurements was conducted with the help of available equipment at Mazhar Ultrasound

Centre, Multan using US machine Aloka 3500 Japan having facilities of power color Doppler, tissue harmonic with convex & linear probe. Total 100 patients were selected in duration of 6 months. Data were tabulated and analyzed by SPSS version 24.0. A semi-structured questionnaire was prepared and finalized after pre-testing. The quantitative variables were presented in form of mean $\pm$ S.D and qualitative variables were presented in percentage chi square test was used to test the association between categorical variables and p value less than 0.05 was considered significant.

Results:

The descriptive statistics of patient's age and Alkaline Phosphate Level (ALP) were shown in Table 1. The minimum and maximum age of patients was 27 and 72 respectively. The mean age of participants was 51.09 ± 10.238 years. The minimum and maximum ALP Level was 32 and 1142 respectively. The mean scoring of ALP Level was 439.99 ± 10.54 . There were 59(0.59%) females and 41(0.41%).

Variable	Minimum	Maximum	Range	Mean $\pm$ SD
Age of patients	27	72	45	51.09 ± 10.238
ALP Level	32	1142	1110	439.99 ± 10.54

Table 1: Descriptive Statistics of Age and Alkaline Phosphate Level (ALP) level

Out of 100, 37 patients complained about Jaundice and 63 patients about abdominal pain. Majority of patients were having complained about abdominal pain. 85 were having CBD, 3 were having Pancreatic Head, 6 were having Distal Head and 6 were having proximal head. 64 were having stone, 19 were having mass, 3 were having portal Hepatic Mass and 14 were having stricture, Table 2.

Variable	Frequency (%)
Complaints of Patients	
Jaundice	37(0.37%)
Pain Abdominal	63(0.63%)
Level of Obstruction	

CBD	85
Pancreatic Head	03
Distal Head	06
Proximal Head	06
Causes of Obstruction	
Stone	64
Mass	19
Portal Hepatic Mass	3
Stricture	14
ALP Levels	
Normal	19
Above normal	81

Table 2: Patients History

In age group 25-35, out of 11, 7 patients were having stone, 0 with mass, 0 with portal hepatic mass and 4 were having stricture. In age group 36-45, out of 6, 6 patients were having stone, 0 with mass, 0 with portal hepatic mass and 0 were having stricture. In age group 46-55, out of 51, 28 patients were having stone, 16 with mass, 3 with portal hepatic mass and 4 with stricture. In age group 56-65, out of 26, 17 patients were having stone, 3 with mass, 0 with portal hepatic mass and 6 were having stricture. In age group 66-75, out of 6, 6 patients were having stone, 0 with mass, 0 with portal hepatic mass and 0 were having stricture. There was significant association between the age groups and cause of obstruction in patients (p-value < 0.05), Table 3.

Age Categories	Cause of Obstruction				Total	p-value
	Stone	Mass	Portal Hepatic Mass	Stricture		
25-35	7(63.6%)	0(0.0%)	0(0.0%)	4(36.4%)	11(100%)	0.002
36-45	6(100.0%)	0(0.0%)	0(0.0%)	0(0.0%)	6(100%)	
46-55	28(54.9%)	16(31.4%)	3(5.9%)	4(7.8%)	51(100%)	
56-65	17(65.4%)	3(11.5%)	0(0.0%)	6(23.1%)	26(100%)	
66-75	6(100.0%)	0(0.0%)	0(0.0%)	0(0.0%)	6(100%)	
Total	64(64.0%)	19(19.0%)	3(3.0%)	14(14.0%)	100(100%)	

Table 3: Association between age categories and Cause of Obstruction in Patients

Out of 59 females, 15(25.4%) were having jaundice, 44(74.6%) pain abdominal. Out of 41

males, 22(53.7%) were having Jaundice and 19(46.3%) were having pain abdominal. There was significant association between gender and complaints of patients (p -value < 0.05), Table 4.

Gender of patients	Complaints		Total	p -value
	Jaundice	Pain Abdominal		
Female	15(25.4%)	44(74.6%)	59(100%)	0.004
Male	22(53.7%)	19(46.3%)	41(100%)	
Total	37(37.0%)	63(63.0%)	100(100%)	

Table 4: Association between Gender and Complaints of Patients

Out of 59 females, 32(54.2%) were having stone, 16(27.1%) had mass, 3(5.1, 0(0.0%) portal hepatic mass and 8(13.6%) had stricture. Out of 41 males, 32(78.0%) were having stone, 3(7.3%) had mass, 0(0.0%) portal hepatic mass and 6 (14.6%) had stricture. There was significant association between gender and complaints of patients (p -value < 0.05), Table 5.

Gender of Patients	Cause of Obstruction				Total	p -value
	Stone	Mass	Portal Hepatic Mass	Stricture		
Female	32(54.2%)	16(27.1%)	3(5.1%)	8(13.6%)	59(100%)	0.026
Male	32(78.0%)	3(7.3%)	0(0.0%)	6(14.6%)	41(100%)	
Total	64(64.0%)	19(19.0%)	3(3.0%)	14(14.0%)	100(100%)	

Table 5: Association between Gender and Cause of Obstruction in Patients

Discussion:

In current study 59(0.59%) were females and 41(0.41%) males. The minimum and maximum age of patients 27 and 72 respectively. The mean ages of participants were 51.09+10.238. The minimum and maximum ALP Level were 32 and 1142 respectively. The mean scoring of ALP Level was 439.99+10.54. Out of 100, 64(0.64%) have stone, 19 (0.19%) have mass, 3(0.03%) have portal Hepatic Mass and 14 (0.14%) have stricture. The most common cause of obstruction was stone. A study conducted by Wiwanitkit V in 2001, 102 males and 96 females with mean age of 49.4+16.1 years. Patients have high level of ALP ranging from 1001 to 3067 IU/L. The study concluded that the high serum ALP levels were specifically found in patients with obstructive

biliary diseases, sepsis and infiltrative liver disease. The results revealed that there were such 41 patients in whom the evidence of the biliary obstruction or local abscess was not demonstrated by imaging techniques¹⁵. Another study conducted by Lesur G *et al.*, have reported that the increased level of serum alkaline phosphate was caused by bile duct but also may be due to alcoholic liver disease. All these findings were similar to the current study¹⁶. In current study out of 100 patients, 37(0.37%) patients complaint about Jaundice and 63(0.63%) patients complaint about pain abdominal. Majority of patients had complain about pain abdominal. A study conducted by Lapis JL *et al.*, showed that 47 patients with Cholestatic jaundice were evaluated for biliary obstruction by ultrasonography. They also reported that the patients who have larger bile ducts had higher bilirubin concentrations, longer duration of jaundice and were more reliably detected by sonography¹⁷. A study conducted by Bacher GN *et al.*, in 2013 reported the an age-dependent change in the diameter of the extrahepatic bile duct. Total 251 patients were enrolled in this study among which there are 126 men and 125 women aged from 20- 94 years. The mean age of participants were 52.5+17.63 which was in accordance to the current study. There was a significant correlation between common bile duct size and age was observed by the study conducted by Bacher GN which contradict the current study¹⁸. In current study 64 (0.64%) have stone, 19 (0.19%) have mass, 3(0.03%) have portal Hepatic Mass and 14 (0.14%) have stricture. The most common cause of obstruction was stone. A study conducted by Zeman R *et al.*, elaborated that eight patients with dilatation of the biliary tree, six of whom had no clinical or laboratory evidence of biliary tract disease except for elevated levels of serum alkaline phosphatase. In two patients, dilatation was caused by obstruction of only one hepatic duct; in three, it was caused by a pancreatic tumor; and in three, it was associated with gallstones which

exercised a ball-valve effect, producing intermittent obstruction. The elevation of the alkaline phosphatase level in six of these patients suggested that it is a more sensitive indicator of biliary tract obstruction than the serum bilirubin level.¹⁹ In current study out of 59 females, 15(25.4%) have jaundice, 44(74.6%) pain abdominal. Out of 41 males, 22(53.7%) have Jaundice and 63(63.0%) have pain abdominal. There was significant association between gender and complaints of patients (p-value < 0.05). A study conducted by Matsuda Y reported the factors the patency of biliary stents. Total 228 patients with malignant biliary obstructive disease were enrolled in this study. The results showed that the older age, male gender, no stent cleaning, and high level of bilirubin levels were significant unfavorable prognostic factors for patency. These results are in accordance to the current study.²⁰

Conclusions:

A significant number of causative biliary tract lesions in asymptomatic adults with dilatation of the CBD on routine abdominal US; no laboratory or demographic parameters were useful for discrimination.

References:

- 1- Nadkarni KM, Jahagirdar RR, Kagzi RS, Pinto AC, Bhalerao RA. Surgical obstructive jaundice. Journal of postgraduate medicine. 1981 Jan 1;27(1):33.
- 2- Baron RL, Stanley RJ, Lee JK, Koehler RE, Melson GL, Balfe DM, Weyman PJ; A prospective comparison of the evaluation of biliary obstruction using computed tomography and ultrasonography. Radiology, 2014; 145(1): 91-98.
- 3- Sharma MP, Ahuja V; Aetiological spectrum of obstructive jaundice and diagnostic ability of ultrasonography clinician's perspective. Trop Gastroenterol; 2016; 20:67-9.
- 4- Naffisaadedin; Comparison of ultrasonography and computed tomography

to evaluate causes of biliary obstruction; Euroasian journal of hepatogastroenterology, 2013; 2(2):98-103.

- 5- Reinus WR, Shady K, Lind M, Scott R; Ultrasound evaluation of the common duct in symptomatic and asymptomatic patients. AmJ Gastroenterol, 2013; 87 (4): 489-492.
- 6- Joshi BR. Sonographic variations in common bile duct dimensions. Journal of Institute of Medicine. 2009; 31(3): 27-9.
- 7- Bachar GN, Cohen M, Belenky A, Atar E, Gideon S. Effect of aging on the adult extrahepatic bile duct: a sonographic study. Journal of ultrasound in medicine. 2003 Sep; 22(9): 879-82.
- 8- Yang MH, Chen TH, Wang SE, Tsai YF, Su CH, Wu CW, Lui WY, Shyr YM. Biochemical predictors for absence of common bile duct stones in patients undergoing laparoscopic cholecystectomy. Surgical endoscopy. 2008 Jul 1; 22(7): 1620-4.
- 9- Einstein DM, Lapin SA, Ralls PW, Halls JM. The insensitivity of sonography in the detection of choledocholithiasis. AJR Am J Roentgenol 2016; 142: 725-8.
- 10- Bonheur, Jennifer Lynn, and P. Ellis. "Biliary Obstruction. Emedicine." (2001).
- 11- Jennifer Lynn Bonheur (2016). Biliary Obstruction Workup. [Last accessed on: November 27, 2008]. Retrieved from: <http://emedicine.medscape.com/article/187001-workup#c5>
- 12- Björnsson E, Gustafsson J, Borkman J, Kilander A. Fate of patients with obstructive jaundice. Journal of Hospital Medicine: An Official Publication of the Society of Hospital Medicine. 2008 Mar; 3(2): 117-23.
- 13- Laig FC; The gallbladder and bile ducts. In Rumack, Wilson SR, Charboneau JW (eds): Diagnostic ultrasound, 2nd ed. St. Louis, CV Mosby, 2016(2); 175-224.
- 14- Yang MH, Chen TH, Wang SE, et al.,

- Biochemical predictors for absence of common bile duct stones in patients undergoing laparoscopic cholecystectomy. *Surg Endosc* 2014;22:1620-4.
- 15-Wiwanitkit V. High serum alkaline phosphatase levels, a study in 181 Thai adult hospitalized patients. *BMC family practice*. 2001 Dec;2(1):2.
 - 16-Lesur G, Levy P, Flejou JF, Belghiti J, Fekete F, Bernades P. Factors predictive of liver histopathological appearance in chronic alcoholic pancreatitis with common bile duct stenosis and increased serum alkaline phosphatase. *Hepatology*. 1993 Nov 1;18(5):1078-81.
 - 17-Lapis JL, Orlando RC, Mittelstaedt CA, Staab EV. Ultrasonography in the diagnosis of obstructive jaundice. *Annals of internal medicine*. 1978 Jul 1;89(1):61-3.
 - 18-Bachar GN, Cohen M, Belenky A, Atar E, Gideon S. Effect of aging on the adult extrahepatic bile duct: a sonographic study. *Journal of ultrasound in medicine*. 2003 Sep;22(9):879-82.
 - 19-Zeman R, Taylor KJ, Burrell MI, Gold J. Ultrasound demonstration of anicteric dilatation of the biliary tree. *Radiology*. 1980 Mar;134(3):689-92.
 - 20-Matsuda Y, Shimakura K, Akamatsu T. Factors affecting the patency of stents in malignant biliary obstructive disease: univariate and multivariate analysis. *American Journal of Gastroenterology*. 1991 Jul 1;86(7):843-849.