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AGT Score as a Predictor of Common Bile Duct Stone in Patients with Intermediate Probability Criteria According to ASGE Guidelines

Raja Taha Yaseen Khan, Adeel ur Rehman, Muhammad Manzoor ul Haque, Abbas Ali Tasneem, Farina M Hanif, Syed Mudassir Laeeq and Nasir Hassan Luck*

Department of Gastroenterology and Hepatology, Sindh Institute of Urology and Transplantation, Pakistan

Abstract

Background: Data is scarce regarding validation of intermediate probability of CBD stone. Previously, studies have validated laboratory investigations like GGT or ALP individually to be helpful in the diagnosis of CBD stone. However, no score has been predicted up to date which has collectively included all these parameters. The aim of our study was to identify the non-invasive risk factors for detection of CBD stone and also, to compute a score and then to evaluate the diagnostic accuracy of this score in prediction of Choledocholithiasis (CL).

Methods: It was a cross-sectional prospective study which was conducted over a period of one year (January 2018 to December 2018). All patients falling in intermediate probability criteria for CBD stone were included in the study and subsequently underwent Endoscopic Ultrasound (EUS) prior to ERCP. AGT score was formulated as a noninvasive predictor for CBD stone for each individual as (ALP+GGT)/(T.B). Finally, the sensitivity, specificity, PPV, NPV and diagnostic accuracy was calculated for the AGT score for the prediction of CBD stone.

Results: A total of seventy-one patients who were suspected for CBD stone as per intermediate probability criteria were enrolled in our study. The Mean age was 52.9+11.9 years and there were 42 (59.1%) males. Sixty-six (92.9%) patients presented with abdominal pain while five patients (7%) had gall stone pancreatitis. On Endoscopic Ultrasound (EUS), choledocholithiasis was observed in 49 (68.1%) patients while on ERCP, CBD stone was seen in 47 (66.2%) patients.

On comparative analysis, noninvasive laboratory investigations such as Total Leukocyte Count, Alkaline Phosphatase and Gamma Glutamyl Transferase were significantly higher in patients with CBD stone as compared to those without stone (8.16 *vs.* 6.96 and p=0.015) for TLC, (394 *vs.* 229, p ≤ 0.001 and 349 *vs.* 254, p=0.05) for Alkaline phosphatase and GGT respectively. There was a significant association of higher AGT score with presence of CBD stone with a p-value of ≤ 0.001. AUROC for AGT score was 0.837. At a cut-off value of ≥ 463 for AGT score in predicting choledocholithiasis, the sensitivity of the score was of 93.18%, specificity of 77.78%, NPV of 87.5%, PPV of 87.2% and diagnostic accuracy of 87.3%.

Conclusion: We have developed a scoring system (AGT score) based on three parameters (ALK P, GGT and Total Bilirubin) to predict the presence of CBD stone in patients falling in intermediate probability criteria according to ASGE guidelines with a diagnostic accuracy of 87.3%. However, in future more data and studies are required to validate this score.

Keywords: CBD stone; Intermediate probability criteria; Predictor of choledocholithiasis; AGT score

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Correspondence:
Raja Taha Yaseen Khan, Department of Gastroenterology and Hepatology, Sindh Institute of Urology and Transplantation, Pakistan; E-mail: raja_taha101488@hotmail.com

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Introduction

Cholelithiasis (CL) is a complication that is frequently encountered in patients with gall bladder stone undergoing cholecystectomy (5% to 10%) and/or patients presenting with symptoms or investigations suggestive of biliary pancreatitis (18% to 33%) [1-5]. The gold standard modality for detection and treatment of Choledocholithiasis (CL) is considered to be Endoscopic Retrograde Cholangiopancreatography (ERCP). However, certain short-term complications of ERCP are post-ERCP pancreatitis, post-endoscopic sphincterotomy bleeding, cholangitis and perforation that can prolong morbidity and can also result in significant financial burden for the patient [6]. However, ERCP has only proven to be cost effective when performed in patients with high likelihood of

Choledocholithiasis (CL) [7]. The ASGE guidelines published in 2010 for prediction of CL has predicted that the patients meeting high probability criteria were the one most aided from ERCP and secondly, it also predicted the probability of CBD stone in patients with suspected CL [8]. They patients were divided into three groups based on the presence of clinical, radiological and biochemical parameters. Patients who belonged to high likelihood of CBD stone (defined as >50% likelihood) were those with one of the following very strong predictors such as CBD stone on transabdominal Ultrasound (US), clinical ascending cholangitis or bilirubin >4 mg/dL, or those with both of the following strong predictors such as dilated CBD on US (>6 mm with gallbladder *in situ*) and bilirubin level between 1.8 mg/dL to 4.0 mg/dL; patients with intermediate likelihood of CBD stone (10% to 50% likelihood) were those with the presence of only one strong predictor or any moderate predictor (abnormal liver test, age older than 55 years or gallstone pancreatitis); and lastly, the patients with low likelihood of CBD stone (<10% likelihood) were those with no predictors of CL. The patients falling in intermediate probability criteria undergo Either Endoscopic Ultrasound (EUS) or MRC for detection of CBD stone. The sensitivity of MRCP in detecting CBD stones decreased with a decrease in the size of stone to less than 5 mm (67% *vs.* 100% if size ≥ 5 mm) as compared to EUS which has an excellent sensitivity in detecting stones less than 5 mm [9,10].

Although, previous studies have validated laboratory investigations like Alkaline Phosphatase (ALP) or Gamma Glutamyl Transferase (GGT) on individual basis to be helpful in the diagnosis of CBD stone. However, no score has been predicted up to date which has collectively included all these parameters [11,12].

The objective of our study was to identify the non-invasive risk factors for detection of CBD stone and secondly, to compute a score and then to evaluate the diagnostic accuracy of this score in prediction of choledocholithiasis.

Methods

The study was conducted over a period of one year (January 2018 to December 2018) at the Department of Hepatogastroenterology, Sindh Institute of Urology and Transplantation. It was a cross-sectional prospective study. All patients falling in intermediate probability criteria for CBD stone were included in the study and subsequently underwent Endoscopic Ultrasound (EUS) prior to ERCP. AGT score was formulated for each patient as (ALP+GGT)/(T.B) and was used as a non-invasive laboratory parameter to detect CBD stone. Finally, sensitivity, specificity, PPV, NPV along with diagnostic accuracy was calculated for the score in the prediction of Choledocholthiasis (CL).

Results

A total of seventy-one patients who were suspected for CBD stone as per intermediate probability criteria were enrolled in our study. The Mean age was 52.9+11.9 years and there were 42 (59.1%) males. Sixty-six (92.9%) patients presented with right hypochondrial pain while gall stone pancreatitis was seen in five (7%) patients. On Endoscopic Ultrasound (EUS), choledocholithiasis was observed in 49 (68.1%) patients while on ERCP, stone was seen in 47 (66.2%) patients. Among seven patients with gallstone pancreatitis, only 2 (28.6%) patients had choledocholithiasis on EUS which was confirmed on ERCP.

Whereas, on noninvasive investigations Total Leukocyte Count (TLC), ALP and GGT were significantly raised in stone positive

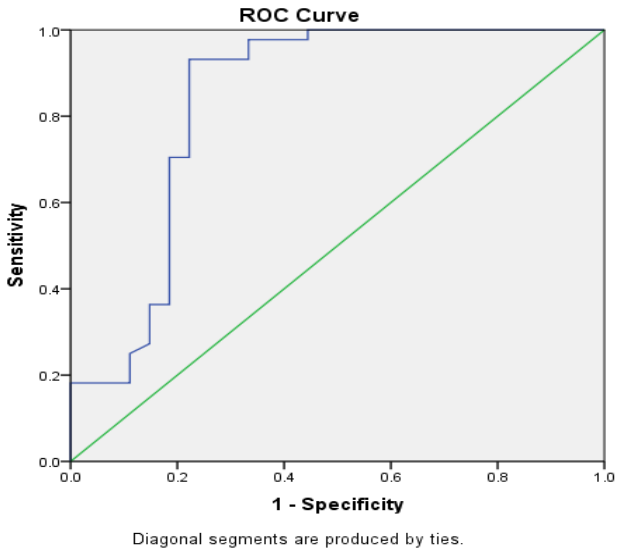

Figure 1: ROC curve for AGT score.

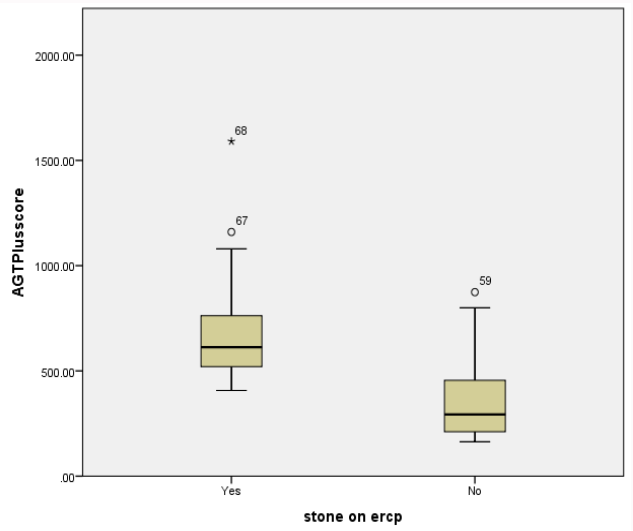

Figure 2: Box plot showing higher values of AGT score in patients with CBD stone.

group as compared to stone negative group while other laboratory parameters such as serum creatinine, hemoglobin, Total bilirubin, Alanine transaminase and Aspartate transaminase were non comparable between the two groups. (8.16 *vs.* 6.96 and p=0.015) for TLC, (394 *vs.* 229, p=0.000 and 349 *vs.* 254, p=0.05) for ALP and GGT respectively (Table 1). There was a significant association of higher AGT score with presence of CBD stone with a p-value of ≤ 0.001. Area under ROC (AUROC) for AGT score was 0.837. At a cut-off value of ≥ 463 for AGT score in predicting choledocholithiasis, the sensitivity of the score was of 93.18%, specificity of 77.78%, NPV of 87.5%, PPV of 87.2% and diagnostic accuracy of 87.3% (Table 2).

Discussion

ASGE guidelines for the prediction of suspected CL lacked accuracy. EUS examination comprises of endoscopic visualization with 2-dimensional US and is an excellent tool for biliary imaging. Radial array echoendoscopes are preferred by many endoscopists

Table 1: Showing the baseline characteristics of the population inducted in the study.

Characteristics	Stone on ERCP	Mean ± SD (n=71)	P value
Age of the patient	Yes	53.4 ± 11.7	0.278
	No	50 ± 13.5	
HB on admission	Yes	12.9 ± 1.9	0.474
	No	12.6 ± 1.6	
TLC on admission	Yes	8.2 ± 2.3	0.015
	No	6.96 ± 1.2	
Platelets on admission	Yes	342 ± 77.9	0.76
	No	336 ± 84	
Urea on admission	Yes	37.8 ± 24.9	0.083
	No	28.9 ± 11.1	
Creatinine on admission	Yes	0.85 ± 0.48	0.832
	No	0.9 ± 0.22	
Total bilirubin on admission	Yes	1.7 ± 0.9	0.043
	No	1.1 ± 0.4	
Alkaline phosphatase on admission	Yes	394 ± 103	≤ 0.001
	No	229.6 ± 135	
AST on admission	Yes	37.9 ± 29.9	0.797
	No	36 ± 30.6	
ALT on admission	Yes	62 ± 64	0.213
	No	45.3 ± 32.5	
GGT on admission	Yes	349 ± 171	0.049
	No	254 ± 235	
S. amylase levels	Yes	137 ± 241	0.317
	No	235 ± 570	
AGT score	Yes	669 ± 222	≤ 0.001
	No	405 ± 210	

Table 2: Showing the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of AGT score.

Statistics	Value	95% CI
Sensitivity	93.18%	81.34% to 98.57%
Specificity	77.78%	57.74% to 91.38%
Positive Likelihood Ratio	4.19	2.06 to 8.53
Negative Likelihood Ratio	0.09	0.03 to 0.27
Disease prevalence (')	61.97%	49.67% to 73.24%
Positive Predictive Value (')	87.23%	77.06% to 93.29%
Negative Predictive Value (')	87.50%	69.74% to 95.51%
Accuracy (')	87.32%	77.30% to 94.04%

because it allows elongated views of the bile ducts [13,14]. The overall performance for the prediction of CL in our population with intermediate probability was effective in nearly 68% of the patients with a sensitivity of 93.1% and specificity of 96%. However, data in this regard is scarce and more studies on larger scale are required to validate the intermediate probability criteria. Studies have revealed that EUS remains highly sensitive for detection of CBD stones smaller than 5 mm, and decreasing the stone size does not have an impact on its effectivity [15] (Figure 3).

Previously studies have validated that Endoscopic

Figure 3: Showing EUS with stack sign showing stone in CBD causing acoustic shadow.

Ultrasonography (EUS) is a safe replacement for ERCP in patients with biliary pancreatitis. Firstly, because in comparison with ERCP, EUS has revealed a higher successful examination rates (100% *vs.* 86%) and secondly, a lower morbidity as compared to the former (7% *vs.* 14%) [16]. In addition, EUS is an investigation that has performed excellently for the detection of small size (median of 4 mm) CBD stones, which may be useful in the cases of biliary pancreatitis. Rodrigo et al. [11] showed the lower (36.2%) risk of CBD stone in biliary pancreatitis than in patients without pancreatitis (65.9%) (OR: 0.30; 95% CI 0.17 to 0.55, p<0.001). In our population, stone was present in 2 (40%) of the patients with biliary pancreatitis further validating the fact stated by previous studies. Hence, the association of ERCP with high cost and increased morbidity and complications has limited its use to those who are most likely to benefit from it and the EUS or MRCP should be the modality of investigation in patients with gallstone pancreatitis who are not in cholangitis to confirm Choledocholithiasis (CL).

Older studies have validated that noninvasive investigations such as cholestatic parameters like GGT or ALP were individually found to be helpful in the diagnosis of CBD Stone [11,12]. No score has been predicted up to date that has collectively included all these parameters. In our study, laboratory parameters such as Total bilirubin, Alanine Transaminase, Alkaline Phosphatase and GGT were considerably raised in patients with CL as compared to those with stone negative disease.

So, we formulated an AGT score which was found to be significantly associated with presence of CBD stone and at cut off ≥ 463, it has an excellent sensitivity, specificity, NPV and PPV in predicting choledocholithiasis with an excellent diagnostic accuracy of 87.3%.

Strength of the study: Noninvasive cost-effective score.

Weakness of the study: Small sample size.

Conclusion

We have developed a scoring system (AGT score) based on three parameters (ALK P, GGT and Total Bilirubin) to predict the presence of CBD stone in patients falling in intermediate probability criteria according to ASGE guidelines with a diagnostic accuracy of 87.3%. However, further studies comprising of large small size are needed to validate this score.

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