ORIGINAL ARTICLE

Role of Alanine Aminotransferase in Determining the Biliary Etiology in Acute Pancreatitis

Bharti SV[1], Sharma A[1]

ABSTRACT

Introduction: Acute pancreatitis a disorder that has numerous causes and an obscure pathogenesis. It can be a serious abdominal emergency associated with significant morbidity and mortality. Cholelithiasis is most common cause of acute pancreatitis and excessive alcohol consumption is second most frequent cause which together account for approximately 80% of underlying etiology. The detection of biliary etiology is crucial to delivery of definitive therapy to prevent repeated attacks of acute pancreatitis. During an attack of acute pancreatitis, elevation of alanine aminotransferase to >150 IU/L is a predictive factor for biliary cause of acute pancreatitis. **Aims:** To investigate the predictive value of raised alanine aminotransferase in determining biliary etiology in patients presenting with acute pancreatitis. **Methods:** A prospective study was done among 70 patients who were admitted in surgery department over a period of one year with diagnosis of acute pancreatitis. Peak alanine aminotransferase within 48 hours of presentation was recorded. The diagnosis was based on typical clinical presentation of acute pancreatitis combined with an increase in serum amylase levels ≥ 3 times the upper limit of the laboratory reference value. All biliary cases were confirmed by abdominal ultrasonography. **Results:** The mean age of the patients was 47.9 ±15.7 years (19-88 years). Acute pancreatitis was common in 31-40 years of age group. Among them, 40(57.1%) were male and 30(42.9%) were female. Forty two (60%) patients had biliary pancreatitis, 20(28.5%) had alcoholic pancreatitis, 2(2.8%) patients had drug induced pancreatitis and 6(8.5%) patients had idiopathic pancreatitis. Mean alanine aminotransferase for biliary pancreatitis was 205.9U/L, while cases with other etiologies (alcoholic 58.4U/L; drug induced 62.6 U/L; and idiopathic 48.3 U/L) showed significantly lower values (p=0.001). **Conclusion**: An elevated alanine aminotransferase strongly supports a diagnosis of gallstones in acute pancreatitis.

Keywords: Acute pancreatitis, Alanine aminotransferase, Biliary pancreatitis

Authors:

1. Dr. Shiv Vansh Bharti
2. Dr. Anup Sharma

[1] Department of Surgery, Nepalgunj Medical College and Teaching Hospital, Kohalpur, Banke.

Address for Correspondence:

Dr. Shiv Vansh Bharti
Assistant Professor
Department of Surgery
Nepalgunj Medical College & Teaching Hospital
Kohalpur, Banke
Email:shivbharti26984@gmail.com

INTRODUCTION

Acute pancreatitis (AP) is a common surgical disorder that has numerous causes and an obscure pathogenesis. Gallstones and excessive alcohol consumption are the most frequent causes of AP and together account for approximately 80% of underlying aetiology.[1] Up to 60% of all presentations of AP are secondary to gallstones.[2] Other aetiologies are diverse and include pancreatic divisum, malignancy, endoscopic retrograde cholangiopancreatography (ERCP), hypercalcaemia, drug use and infection.[3] Acute Pancreatitis (AP) is an acute inflammatory process of pancreas that frequently affects the peripancreatic tissue and less frequently the systemic organs. The clinical severity of AP ranges from mild to severe, with an overall mortality of about 10%.[4] Identification of biliary cause of pancreatitis is important to provide definite management in form of cholecystectomy to prevent further attacks.[5,6] Several biochemical investigations have been proposed to identify a biliary etiology, including bilirubin, alanine aminotransferase (ALT), alkaline phosphatase and aspartate transaminase. An elevated ALT is widely considered the most useful of these markers. During an attack of acute pancreatitis, the elevation of alanine aminotransferase to >150 IU/L is a predictive factor for biliary cause of acute pancreatitis. A previous meta-analysis has indicated that this threefold elevation in alanine aminotransferase has a positive predictive value of 95% in diagnosing acute gallstone pancreatitis.[7]

METHODS

A prospective study was done among 70 patients of acute pancreatitis, who were admitted in surgery department of

Nepalgunj Medical College, over a period of one year (July 2018 to June 2019). Peak ALT within 48 hours of presentation was recorded. The diagnosis was based on the typical clinical presentation of AP combined with an increase in serum amylase levels ≥ 3 times the upper limit of the laboratory reference value. Gallstone pancreatitis was confirmed by the presence of gallstones on ultrasonography. The Abdominal ultrasound (AUS) was performed in the emergency room and later, after ward admission. The diagnosis of AP as defined by revised Atlanta classification was taken into consideration.

All patients admitted with acute pancreatitis with elevated serum amylase level ≥3 times normal were included and conditions associated with increased alanine aminotransferase other than acute pancreatitis were excluded. The data were analyzed using Statistical Package for Social Sciences Programme v.21. Sensitivity, specificity and positive and negative predictive value of ALT was determined in relation to etiology of acute pancreatitis. When the variables were found to be approximately normally distributed, parametric testing was used to compare mean values between the causes of AP, using analysis of variance (ANOVA) test.

RESULTS

The mean age of the patients was 47.9 ±15.7 years (19-88 years). AP was common in 31-40 years of age group. Among them, 40(57.1%) were male and 30(42.9%) were female. Forty two (60%) patients had biliary pancreatitis and rest of the patients had other causes **(Table I)**. Among females, most (80%) had biliary etiology while among males 45% had biliary and 40% alcoholic etiology. Serum amylase and ALT levels were significantly greater in patients with biliary pancreatitis than in the other non-idiopathic subgroups. Mean ALT for biliary pancreatitis was 205.9U/L, while for alcoholic, drug induced and idiopathic, the values were 58.4U/L, 62.6U/L, and 48.3U/L, respectively. Comparing between the groups showed ALT raise to be significant in biliary pancreatitis (p = 0.001).

The mean ALT for male and female showed significant difference **(Table II)**. The mean ALT for patients older than 40 years was 146.2 U/L while it was 144.8 U/L in younger patients. It was highest in the age group 30-40 yrs.

The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of alanine aminotransferase with cut off of 100 U/L for biliary pancreatitis was 67%, 94%, 93% and 73.8% respectively. Correlation between alanine aminotransferase and etiology of AP was statistically significant.

Etiology	Mean ALT(U/L)	Std. Deviation	n (%)	p-value
Gallstones	205.9	100.2	42 (60%)	0.001
Alcohol	58.4	30.5	20 (28.5%)	
Drugs	62.6	10.6	2 (2.8%)	
Idiopathic	48.3	16.3	6 (8.5%)	

Table I: Comparing mean ALT in different etiology of pancreatitis.

Sex	Mean ALT(U/L)	Std. Deviation	n	P value
Female	176.8	112.3	30	0.033
Male	122.1	97	40	

Table II: Comparing mean ALT with Sex.

Age group (years)	Mean ALT(U/L)	Std.Deviation	n	P value
19-30	148.9	107.14	9	0.99
31-40	143.0	111.36	21	
41-50	156.1	88.43	12	
51-60	132.9	114.4	12	
61-70	148.9	131.7	9	
70-80	142.3	86.92	5	
80-90	163.8	203.36	2	
<40	144.8	108.2	30	0.95
>40	146.2	106.7	40	

Table III: Comparing mean ALT with different age groups.

SENSITIVITY	67%
SPECIFICITY	94%
PPV	93%
NPV	73.8%

Table IV: Comparison of Sensitivity, Specificity, PPV and NPV of ALT in our study for predicting Biliary Pancreatitis.

DISCUSSION

Worldwide gallstones and alcohol are the most common etiologies of pancreatitis. These account for almost 80% of the cases of acute pancreatitis. Baker, et.al, Baing, et.al, Nawaz, et.al showed that incidence of non-biliary pancreatitis is more common in their institute, whereas, Lakhey, et.al. and Joshi, et.al showed a higher incidence of biliary pancreatitis.[8,9,10,11]In our study, incidence of biliary pancreatitis is higher than that of non -biliary pancreatitis. The exact cause of this geographical variation is not well known, but growing evidence suggests that environmental and possibly genetic cofactors may also play a role in the development of AP. The current study demonstrates that a raised ALT within 48 hr of presentation to hospital is strongly predictive of a biliary origin in AP. This finding is supported by a number of previous studies which found that the predictive value of ALT is even greater than that demonstrated

by this study. In the present cohort of patients, an ALT of >100 units/L had a PPV for gallstones of 93%, compared with a 1994 meta-analysis which found a PPV of 95% for the ALT level of 150 U/L.[12]More recent studies have found that ALT levels that are three times the normal level or >150 units/L have PPVs for gallstones of 92–93%.[13,14]Another study found that an ALT of > 60 units/L had a PPV for gallstones in AP of 78.8%.[15] Although AUS carries no risk and is inexpensive and readily available, it risks the possibility that a negative result will be interpreted as a reason not to perform cholecystectomy, although 21–80% of these patients will have a biliary etiology depending on the level of ALT. This risk is further underlined by data indicating that untreated biliary AP (BAP) has been associated with recurrent attacks in 13% of patients within 1 month of hospital discharge and in 17% at a median of 18 weeks after the initial episode.[16,17] In addition, recurrent admissions for this tend to increase in length and are associated with greater morbidity.[17,18] Thus, omitting cholecystectomy in the presence of occult biliary disease can be associated with significant morbidity, whereas early intervention with laparoscopic cholecystectomy is safe and effectively reduces recurrence rates.[19]

It is probable that this current study significantly under-diagnoses the incidence of gallstones in AP. Firstly, routine access to endoscopic ultrasound (EUS) is not possible. Several studies have shown that EUS has a greater sensitivity and specificity for BAP than AUS and reduces the number of patients diagnosed with idiopathic disease. In the current study, 14% of patients were of unknown etiology, compared with 7–11% in studies using EUS. One of these studies found that EUS diagnosed cholecystolithiasis or choledocholithiasis in 15% of patients with a negative AUS and CT.[2,13,14,20] It was difficult to assess the predictive value of AUS in the current study as the investigation represents part of the reference standard such that the result of the AUS influences the final diagnosis and decision for further investigations. The second reason for an underestimation of the true prevalence of biliary pancreatitis is that a negative initial AUS may have falsely reassured the investigating clinician and the patient may not have been followed up with further investigations. Although magnetic resonance cholangiopancreatography (MRCP) has been shown to have similar accuracy to ERCP in diagnosing BAP.[21,22] This investigation is not employed routinely in patients with a negative AUS and resolving AP because of its limited availability. An underestimation of the true prevalence of BAP may explain why the PPV for ALT produced in this study is lower than that reported in other similar papers. If a number of the patients with a raised ALT were misdiagnosed as having non-biliary etiology, the sensitivity and PPV of the test would be underestimated.

In addition, ALT within the normal range reduces the likelihood of gallstones in AP to 25%. The results of a recent review article indicate that the likelihood ratio (LR) for BAP associated with a negative AUS is 0.14–0.35.[2] Using the combination of these two factors in the clinical setting would therefore reduce the need for unnecessary cholecystectomy, thus reducing surgical workloads and hospital waiting lists, as well as enabling a more rapid investigation into alternative causes for the presenting pancreatitis.

LIMITATIONS

There are few limitations to this study. The sample size is small. Abdominal ultrasound is highly specific, but has poor sensitivity for BAP and so is limited in its ability to completely exclude this diagnosis.

CONCLUSION

Alanine aminotransferase is a useful marker for predicting gallstones in acute pancreatitis. In addition, a combination of positive abdominal ultrasound and elevated alanine aminotransferase may be utilized to diagnose biliary pancreatitis with much accuracy.

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