Original Article

Test Tube or Computed Tomography Gantry - The Better Diagnostic Indicator of Severe Pancreatitis: A Retrospective Cohort Study

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Abstract

Background: Various studies have been done to assess the use of serum amylase, serum lipase, and amylase/lipase (A/L) ratio to differentiate between the causes of pancreatitis. Scoring systems (Ranson's, Glasgow, and APACHE II) have been developed to assess the severity of pancreatitis. Computed tomography (CT), a gold standard for prognosticating pancreatitis, is expensive and affordability is a concern in developing country like ours.

Methodology: We did a retrospective study in a tertiary care hospital to assess the use of A/L ratio to predict the severity of acute pancreatitis and to correlate with the presence on necrosis in comparison to that given by CT.

Results: The median A/L ratio was higher among those with severe and necrotizing pancreatitis, 0.19 (interquartile range [IQR] 0.124–0.304) and 0.183 (IQR 0.117–0.300), respectively. Cutoff of 0.14 was taken, based on the receiver operating characteristic curves, which could predict severity with 75% sensitivity and 53% specificity and necrosis with 73% sensitivity and 55% specificity. Higher A/L ratio correlated with a decrease in hematocrit ($P = 0.08$), blood glucose ($P = 0.042$), and aminotransferase ($P = 0.03$), which are indicators of clinical severity. Increase in A/L ratio had an increased trend to a longer duration of stay and a higher chance of detecting multiorgan dysfunction syndrome.

Conclusions: A/L ratio of >0.14 can be used as a predictor of severity as it indicates the presence or absence of necrosis, which further aids in referral and the need for a CT scan in low-resource settings.

Key words: Acute pancreatitis, Amylase/lipase ratio, Computed tomography severity index, Necrosis

INTRODUCTION

Acute pancreatitis (AP) is a potentially life-threatening disease and the spectrum of severity ranges from mild self-limiting disease to a highly fatal severe necrotizing pancreatitis.[1] Majority, 60–80%, of all cases of AP in developed countries are attributable to either gallstone disease or alcohol abuse.[2] >80% of AP attacks are mild and self-limiting which resolve without complications. In 20% of cases, it can be complicated by major morbidity or mortality.[3]

BACKGROUND

First severity assessment of AP came in 1974, proposed by Ranson *et al.*, which had to be done at the time of admission and 48 h.[4] Subsequently, multifactorial scoring systems came up in the 1980s, such as APACHE II and Glasgow.[5,6] In 1990, Balthazar proposed a computed tomography severity index (CTSI) to prognosticate pancreatitis, which is now the gold standard.[7]

There has been a controversy on amylase/lipase (A/L) ratio as an index to differentiate the types of pancreatitis. Some claim that the serum A/L ratio is not useful in distinguishing acute episodes of alcoholic from non-alcoholic AP while in contrast, Pacheco *et al.* found that the A/L ratio >3 was more often seen in alcoholic AP/acute on chronic pancreatitis than biliary AP, and it may be useful in differentiating these two causes of pancreatitis.[8] Gumaste *e t al.* concluded that the A/L ratio could be a new index distinguishing acute episodes of alcoholic (A/L >2) from non-alcoholic pancreatitis

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(A/L <2), with the critical value being A/L = 2.[9] This was validated by Choi *et al*. and results showed that A/L was found to be a significant index for distinguishing mild acute biliary pancreatitis from alcoholic pancreatitis. However, the critical value of A/L seemed to depend on the diet pattern and cultural background.[10] A study done in India, in 2009, concluded that A/L ratio of 3 cannot be used to differentiate severe AP from mild AP.[11]

CT scan is expensive and not affordable by many in a developing country like ours and the severity scores are cumbersome to calculate. These factors prompted to find a single biochemical parameter, such as A/L ratio, which could accurately predict the severity of AP, in comparison to Balthazar severity index (CTSI).

Objectives
Primary
The primary objectives of this study were to assess the correlation between A/L ratio and severity of pancreatitis and the presence of necrosis.

Secondary
The secondary objectives of this study were as follows:
1. To predict need for imaging studies based on A/L ratio.
2. To check the use of A/L ratio as an indicator for referral to the tertiary care center.

METHODOLOGY

The Institutional Ethical Clearance (Ref. No - 220/2017) was obtained and the Research Registration Unique Identification Number - research registry 3666. For this purpose, we conducted a retrospective chart review, including all patients diagnosed with AP in 2016, according to the Revised Atlanta Criteria[12] - (1) abdominal pain consistent with AP, (2) serum lipase activity (or amylase activity) at least 3 times greater than the upper limit of normal, and (3) characteristic findings of AP on CECT. All patients with questionable diagnosis of other possible abdominal conditions, incomplete data collections, and those with chronic pancreatitis were excluded from the study. A total of 50 patients were taken. Demographic details such as age, gender, comorbidities, and etiology and all laboratory values done at admission, the CTSI, course in the hospital as shown by ICU stay, multiorgan dysfunction syndrome (MODs), and length of stay was collected. All statistical analyses were performed using the SPSS V 20. Descriptive statistics such as frequencies, percentages, median, and standard deviation were used. As Shapiro–Wilk test showed that the data were not normally distributed ($P < 0.05$), all comparisons were done using non-parametric tests such as Kruskal–Wallis test and Mann–Whitney U-test. Receiver operating characteristic (ROC) curve was done to find out

the best cutoff of A/L ratio. Spearman's Rho correlation and independent *t*-test were used for continuous and categorical variables, respectively, for severity correlations in AP. The normal values of amylase and lipase in our hospital were 33–115 mIU/L and 25–393 mIU/l. The normal A/L ratio was 0.08. The results of the study have been reported according to the STROCSS criteria.[13]

RESULTS

Patients age ranged from 18 to 75 years, with the median age being 37 (interquartile range [IQR] 30–46) years. 42 (84%) were male and 8 (16%) were female. 9 (18%) had diabetes mellitus, 8 (16%) had hypertension, 2 (4%) had ischemic heart disease, and 1 (2%) had bronchial asthma. The median day of presentation after the onset of symptoms was 3 (IQR 2–5) days. Alcohol was the most common etiological factor [Figure 1].

Based on the CTSI (Balthazar's Index), the patients were classified AP into three groups: Mild (CTSI 0–3) - 7 (14%), moderate (CTSI 4–6) - 27 (54%), and severe pancreatitis (CTSI 7–10) - 16 (32%). 19 (38%) had necrosis and 31 (62%) had no necrosis. As A/L ratio was not normally distributed according to Shapiro–Wilk test ($P < 0.05$), non-parametric tests were used subsequently for analysis. Kruskal–Wallis test was done to assess the association between A/L ratio and the severity. The median A/L ratio was higher among those with severe pancreatitis, 0.19 (IQR 0.124–0.304), but was not statistically significant [Table 1]. ROC curve done to find the best cutoff value
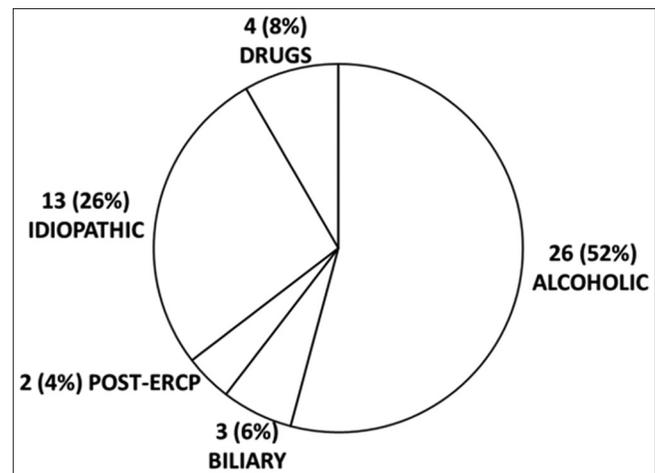

Figure 1: Etiologies of acute pancreatitis

Table 1: Association between A/L ratio and severity

Type of pancreatitis	A/L ratio		P value
	Median	IQR	
Mild	0.12	0.09–0.27	0.24
Moderate	0.13	0.098–0.217	
Severe	0.19	0.124–0.304	

of A/L ratio to predict severity showed a value of 0.14 could predict the severity with a sensitivity of 75% and specificity of 53%. The area under the curve was 0.647 [Figure 2]. On doing a Mann–Whitney U-test, the median A/L ratio was seen to be higher in those with necrotizing pancreatitis, 0.183 (IQR 0.117–0.300), which was not statistically significant [Table 2]. ROC curve done to find the best cutoff value of A/L ratio to predict the presence of necrosis showed a value of 0.14 could predict the severity with a sensitivity of 73% and specificity of 55%. The area under the curve was 0.66 [Figure 3]. Spearman Rho's correlation between A/L ratio and blood parameters showed that hematocrit, RBS, and aminotransferase (AST) had a significant negative correlation ($P < 0.05$), which was indicative of severe pancreatitis [Table 3]. The course in the hospital was described as stay in the ICU, MODs, and the length of stay. To assess the correlation between A/L ratio and the course in the hospital, independent t-test was performed. The mean A/L ratio was seen to have a higher value among those with admission to ICU

and those with a longer duration of stay [Table 4]. The median duration of stay was 7 (IQR 4–11) days.

DISCUSSION

In our study, majority were male, 42(84%) and the most common cause of AP was alcohol, which was similar to other studies.[8,11]

According to the CT, 16 (32%) had severe pancreatitis with a CTSI of 7–10. Among the 50, 19 (38%) patients showed the presence of necrosis on CT. Makoto *et al.* compared clinical/laboratory scoring systems with CECT to predict severity of AP. They found a mortality of 30.8% in patients who were categorized into severe pancreatitis by both CECT and clinical/laboratory scoring. However, 14.8% of case mortality was noted in patients assessed with clinical/laboratory scoring alone as severe AP. As there were no fatal outcomes in those labeled by CECT alone, they concluded that CECT is not required as a routine modality to assess severity and patients can be categorized as severe based on the clinical/laboratory parameters.[11]
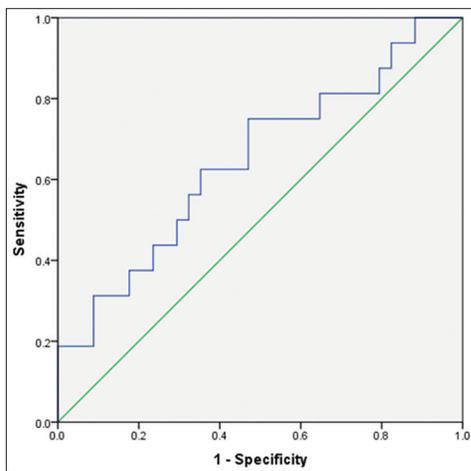

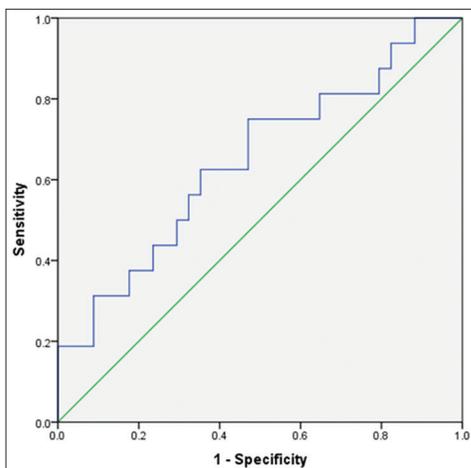**Figure 2:** Receiver operating characteristic curve - A/L ratio to predict severity

Figure 3: Receiver operating characteristic curve - A/L ratio to predict the presence of necrosis

Table 2: Association between A/L ratio and necrosis

Necrosis	A/L ratio		*P* value
	Median	**IQR**	
Absent	0.125	0.087–0.217	0.059
Present	0.183	0.117–0.300	

Table 3: Correlation between A/L ratio and blood parameters

Investigation	Mean A/L ratio	*P* value
TLC	0.139	0.36
Hematocrit	−0.528	0.008
RBS	−0.351	0.042
LDH	0.286	0.535
Albumin	−0.239	0.113
Serum creatinine	0.003	0.984
Serum calcium	0.084	0.686
Serum phosphate	0.238	0.570
AST	−0.325	0.03

TLC: Thin-layer chromatography, RBS: Red blood cells, LDH: Lactate dehydrogenase, AST: Aminotransferase

Table 4: Correlation between A/L ratio and course in the hospital

Course in hospital	Mean A/L ratio	*P* value
ICU		
No (36)	0.1941±0.11	0.805
Yes (14)	0.205±0.20	
MODs		
No (45)	0.197±0.14	0.977
Yes (5)	0.197±0.05	
Duration of stay		
≤7 (31)	0.174±0.13	0.141
>7 (19)	0.235±0.15	

Due to the potential of catastrophic deterioration, early assessment of severity is essential. A simpler, affordable, first-line investigation was then searched for to assess the severity on pancreatitis in places where CT is not available.

Based on the ROC curve, the best cutoff values of A/L ratio to predict severity, and hence, necrosis was 0.14. The median A/L ratio was higher among those with severe pancreatitis, 0.19 (IQR 0.124–0.304) and the sensitivity and specificity was 75% and 53%, respectively. Other studies validated the use of A/L ratio and a cutoff >3 had sensitivity and specificity of 68.9% and 52%, respectively, to predict severity, which was less in comparison to our study.[11,14]

Extent of pancreatic necrosis has been correlated with fatal outcome in the past few years. Necrotizing pancreatitis has a varied course and the morbidity is 34–95% and mortality ranges from 2% to 39%.[15] No studied has reported the relationship between serum pancreatic enzyme levels and the presence of necrosis as assessed by imaging procedure. Our results showed that median A/L ratio was seen to be higher in those with necrotizing pancreatitis, 0.183 (IQR 0.117–0.300). The sensitivity and specificity of A/L ratio of 0.167 to predict necrosis was 73% and 55%, which was much higher compared to the other studies. Chang *et al*. found that at the A/L ratio >2.0, the sensitivity and specificity in determining the AP in the severe group were 26.5% and 34.0%, respectively; positive and negative predictive values 41.5% and 20.8%.[16]

Higher A/L ratio was also associated with decrease in hematocrit ($P = 0.08$), blood glucose ($P = 0.042$), and AST ($P = 0.03$), which are predictors of severity used in the scoring systems and these correlated with other studies.[17] Other indicators for a severe pancreatitis, such as longer duration of stay and ICU admission, also showed an increased trend in the mean A/L ratio.

CONCLUSIONS

The presence and severity of pancreatic necrosis is often difficult to assess clinically. A/L ratio of >0.14 can predict severity of AP as shown by CT and, hence, can be used as a diagnostic indicator and an aid for referral to a higher center. Since higher A/L ratio can also predict the presence of necrosis, it can be used to determine the need for a CT scan, which is not affordable or not available in low socioeconomic and resource-limited settings. Multicentric prospective study is required to ascertain the use of A/L ratio as a prognostic marker in AP

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