MEDICAL SCIENCE

Forecasting Severities and Etiology of Acute Pancreatitis by Using Pancreatic Enzymes and Lipase: Amylase Ratio

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ABSTRACT

Background: Acute pancreatitis is a common disease with raising incidence and is potentially a life-threatening condition. Many patients with alcohol related pancreatitis were misdiagnosed as gallstone related pancreatitis. Early identification of such aetiology of pancreatitis was essential for prevention of unnecessary interventional procedure (like ERCP), which was less useful in pancreatitis patients of alcoholic origin. So, this study was under taken with aim to find out cause of acute pancreatitis by using pancreatic enzymes and Lipase: Amylase ratio. Additionally, the study aimed to assess the predictive value of these markers in determining the severity of pancreatitis. *Material and methods:* Present observational study was done at Medical Gastroenterology Department at Acharya Vinoba Bhave Rural Hospital, Wardha, India over 1 year period. Total 84 acute pancreatitis patients, who satisfied inclusion and exclusion criteria were selected and assessed for serum Amylase & Lipase and Lipase: Amylase ratio. *Results:* In current study, average patients age was 41.1 ± 12.7 years, where majority of patients were males (82%) and all alcoholic pancreatitis patients were also male ($p<0.05$). Most common etiology for acute pancreatitis was alcohol i.e., 48.8% followed by idiopathic cause around 31%, gall stone disease (16.7%), and others. There were non-significantly lower levels of serum lipase, serum amylase and serum lipase/amylase ratio among alcoholic pancreatitis and severe pancreatitis patients compared to their counterpart ($p>0.05$). *Conclusion:* Pancreatitis enzymes and Lipase: Amylase ratio was not much effective in predicting etiology and severity in patients of acute pancreatitis.

Keywords: Amylase, Acute Pancreatitis, Lipase, Alcohol, Lipase/Amylase ratio

1. INTRODUCTION

Acute Pancreatitis is inflammatory disorder of pancreas with clinical presentation of pain in abdomen and raised levels of pancreatic enzyme in

blood and differs in severity from self-limited mild disease to rapidly progressive disease with multiple organ involvement (Taori et al., 2023). It is common clinical condition and disease of varying severity in which certain patients might suffer from mild, self-limited episodes while other manifests as severe, highly morbid, and many a times lethal attack of pancreatitis (Bhatia et al., 2005; Taori et al., 2023).

Numerous conditions can cause acute pancreatitis, amongst which gallstones and chronic alcoholism are responsible for around two-thirds of cases (Taori et al., 2023). Past studies observed that around 10% to 20% of acute pancreatitis patients might suffer from severe disease, which typically had unfavorable disease progression and was related with poor prognosis. Forecasting of severity of disease could guide acute pancreatitis treatment and hence, there is improvement in the final outcome of disease. Failures of organ and infected pancreatic necrosis were common reasons of death in cases of pancreatitis (Li et al., 2017).

Aetiopathogenesis of acute pancreatitis is complex and unclear, though two most commonly identified causes were gall-stones and ingestion of alcohol (Gurusamy et al., 2013; Samanta et al., 2019; Taori et al., 2023). Generalised mortality rate among pancreatitis patients was 3–10%, but patients suffering from severe disease had higher chances of death, with 36 – 50% mortality rate (Parniczky et al., 2016; Banks et al., 2013). Gallstones (comprising microlithiasis) was common cause of acute pancreatitis noted in 40–70% pancreatitis patients, though approximately only 3–7% gallstones patients might suffer from pancreatitis. Cholecystectomy and clearing stones from common bile duct inhibits recurrence, showing cause and effect relationship.

Serum Lipase and Amylase were usually performed among abdominal pain patients who were suspected for acute pancreatitis. Interpretation of both of these investigations remains doubtful as both were also known to increases in other non-pancreatic illness. Gumaste et al., (1991) had suggested lipase/amylase ratio for distinguishing acute pancreatitis of alcoholic from non-alcoholic etiology. Further studies also found that lower levels of serum amylase and lipase/amylase ratio among alcoholic pancreatitis compared to non-alcoholic though serum lipase remain equal in both (Gumaste et al., 1991; Tenner and Steinberg, 1992).

Early identification of aetiology of pancreatitis was of utmost important for prevention of unnecessary interventional procedure, which was less useful in pancreatitis patients of alcoholic origin. Hence, this study was under taken to find out etiology of acute pancreatitis by using pancreatic enzymes and Lipase: Amylase ratio which was readily available in every pancreatitis patient and also to assess their role in predicting severity of pancreatitis.

2. MATERIAL AND METHODOLOGY

Current observational study done in acute pancreatitis patients at Medical Gastroenterology, Acharya Vinoba Bhave Rural Hospital, Wardha, India over 1 year period from August 2022 to July-23 after obtaining institutional ethical approval from DIMMS university. Diagnosis of acute pancreatitis was established on the basis of presence of two or more of following criterion:

1) Characterized abdominal pain of acute pancreatitis,
2) Characteristic findings of acute pancreatitis on USG and/or CT scan imaging of abdomen and
3) Levels of S. lipase and/or amylase > three times upper normal limit.

In case of recurrent acute pancreatitis, only index episode of pancreatitis was included in the study.

Exclusion Criteria

Younger than eighteen years
Pregnant females
Hemo-proliferative disease diagnosis or taking chemotherapy
Patient taking steroid drugs
Patient who had history of recent blood transfusions
Patient suffering from infection of various other organ structures
Patient with chronic pancreatitis (diagnosis based on previous health record or those with findings of chronic pancreatitis on imaging study)

84 acute pancreatitis cases were enrolled in study after fulfilling above criteria. Written and informed consent was taken from all cases. Serum lipase and amylase and other laboratory parameters were assessed. Acute pancreatitis patients also underwent through history taking and physical examination.

Statistical analysis

Data was collected and entered into Microsoft excel spread-sheets and analyzed by using 20.0 version of IBM Statistical Package for Social Sciences (SPSS) for Windows package (SPSS Science, Chicago, IL, USA) software. Chi square test was done to find statistical

relation between two qualitative data. One-way ANOVA test was done to find statistical relation among three groups of pancreatitis. Cut-off levels of lipase, amylase and its ratio for predicting alcoholic pancreatitis was calculated by using AUROC. Along with AUROC, Positive and Negative Likelihood ratio, Sensitivity, Specificity, Cut-off values of lipase/amylase ratio, lipase and amylase were also calculated. P value less than 0.05 was considering as statistically significant.

3. RESULTS

In current study, 84 acute pancreatitis patients were included after satisfying inclusion and exclusion criteria. Common clinical feature in acute pancreatitis patients were pain in abdomen which was present in all cases, followed by vomiting which was present in approximately 82.1%, anorexia was present in 31%; other patients experienced abdominal distension approximately 25%, breathlessness in 21.4% and fever in 16.7% (Figure 1).

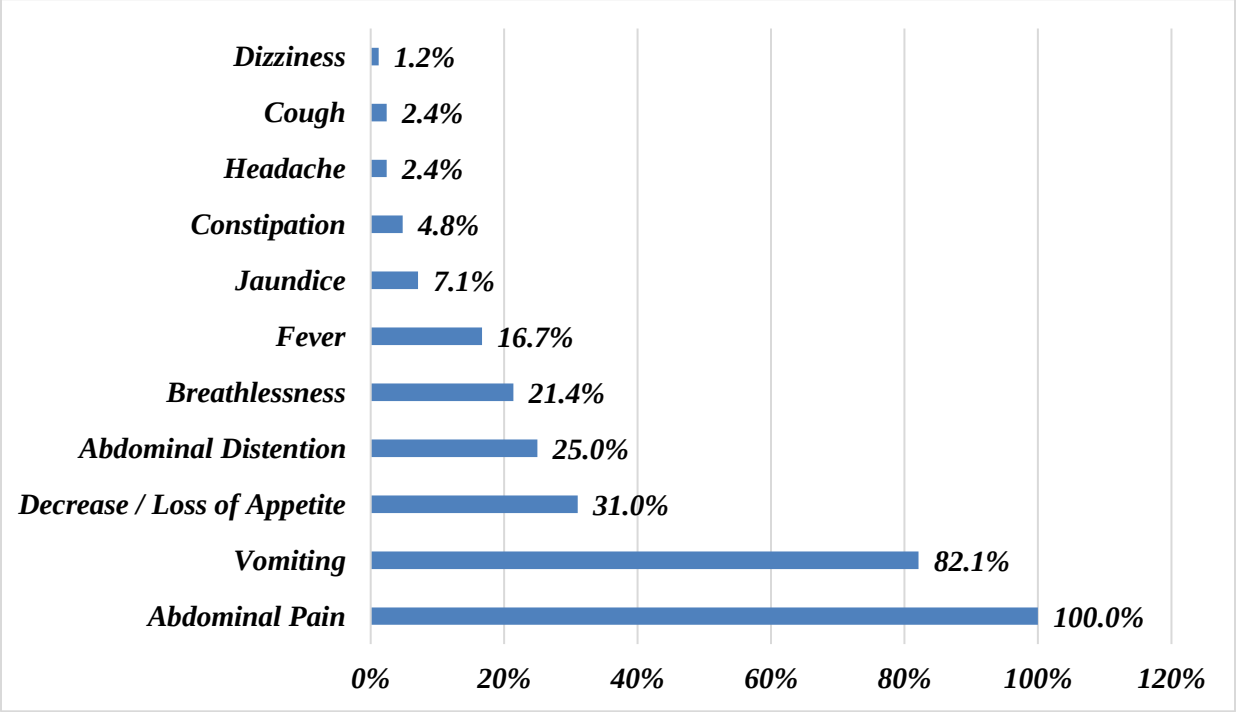

Figure 1 Distribution of acute pancreatitis patients based on Clinical features

Age of patients varied, ranging from 18-82 years, with mean age being 41.1 ± 12.7 years. Out of 84, 69 were male patients and rest 15 patients were female and relationship of gender with etiology of pancreatitis was statistically significant ($p<0.05$). Most common etiology for acute pancreatitis was alcohol i.e., 48.8% followed by idiopathic cause around 31%, gall stone disease (16.7%), and others. There were non-significantly lower values of serum amylase, serum lipase and serum lipase/amylase ratio among alcoholic pancreatitis patients compared to biliary and other cause induced pancreatitis ($p>0.05$) (Table 1).

Table 1 Comparison of variable with etiology of Pancreatitis

Variables		Etiology Pancreatitis			Total	P value
		Alcoholic	*Biliary*	*Other*		
No of patients		42	16	26	84	
Age (years)		39.02 ± 11.07	46.4 ± 13.7	41.2 ± 14.0	41.1 ± 12.7	0.143
Gender	*Male*	42 (100.0)	13 (81.2)	14 (53.8)	69 (82.1)	*<0.001*
	Female	0	3 (18.8)	12 (46.2)	15 (17.9)	
Serum Amylase (U/L)		336.8 ± 336.2	445 ± 423.9	468.7 ± 441.2	398.2 ± 388.4	0.348
Serum Lipase (U/L)		1876 ± 1969	3337 ± 6366	2761 ± 3690	2428 ± 3700	0.352
Lipase/Amylase ratio		6.55 ± 5.33	7.36 ± 6.18	6.74 ± 5.53	6.76 ± 5.50	0.886

*P<0.05 was statistically significant.

By using Revised Atlanta classification, mild pancreatitis was found in 42.9% patients (n=36), moderate pancreatitis was found in 15.5% patients (n=13) and severe pancreatitis found in 41.7% patients (n=35). Moreover, among severe pancreatitis patients, there was non-significantly lower values of serum amylase, serum lipase and serum lipase/amylase ratio compared to mild and moderate pancreatitis (p>0.05). Relationship of etiology with severity of pancreatitis was also statistically non-significant (Table 2).

Table 2 Comparison of variables with revised Atlanta classification

Variables		Severity of Pancreatitis			Total (n=84)	P value
		Mild (n=36)	*Moderate (n=13)*	*Severe (n=35)*		
Serum Amylase (U/L)		407.6 ± 378.2	518.2 ± 587.5	343.9 ± 301	398.2 ± 388.4	0.383
Serum Lipase (U/L)		3036 ± 5084	2081 ± 2091	1931 ± 2139	2428 ± 3700	0.429
Lipase / Amylase ratio		7.35 ± 5.55	6.87 ± 7.06	6.12 ± 4.86	6.76 ± 5.50	0.642
Etiology	*Alcoholic*	17 (47.2)	8 (61.5)	17 (48.6)	42 (50.0)	0.739
	Biliary	6 (16.7)	3 (23.1)	7 (20.0)	16 (19.0)	
	Others	13 (36.1)	2 (15.4)	11 (31.4)	26 (31.0)	

*P<0.05 was statistically significant.

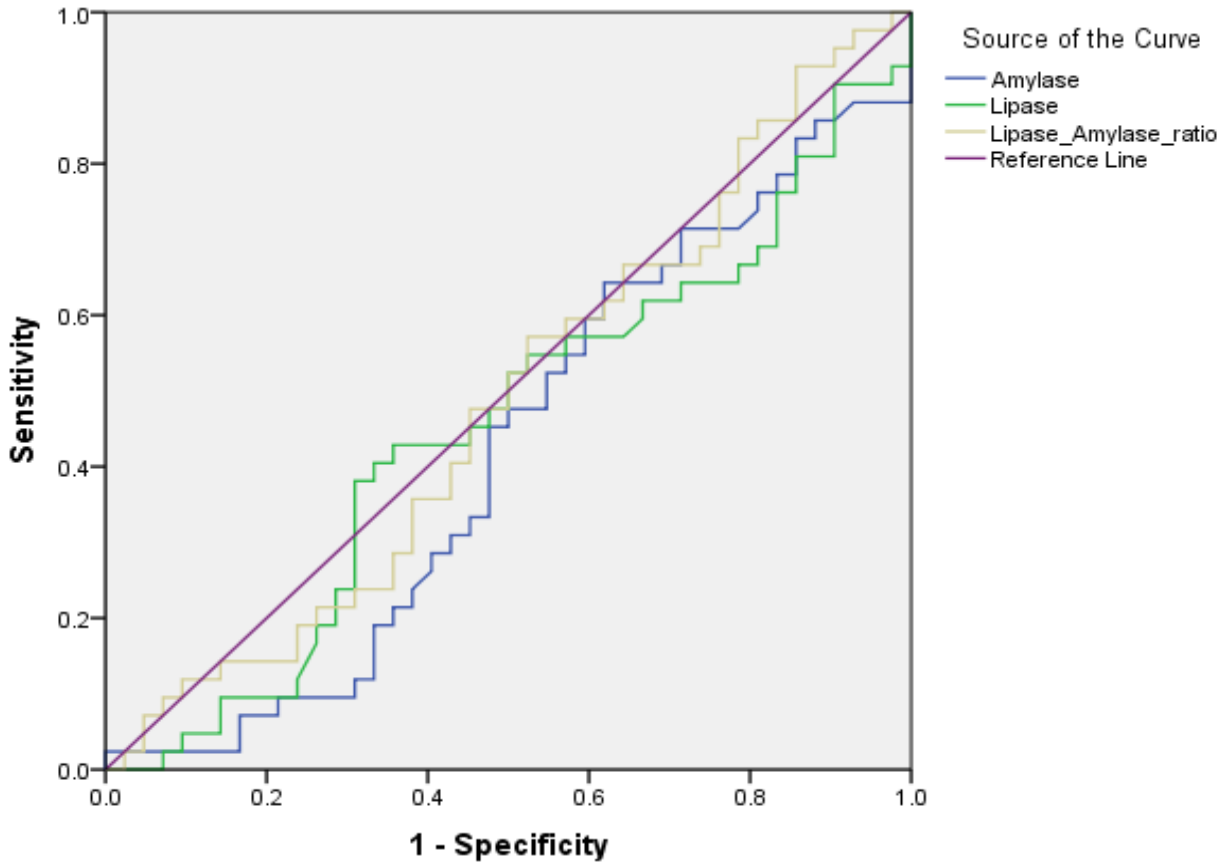

Figure 2 AUROC analysis of pancreatic enzymes with Alcoholic and Non-alcoholic Pancreatitis

AUROC (Area Under Receiver Operator Curve) value for predicting Alcoholic pancreatitis for Serum Amylase was 0.421 (Cut-off >160.5), for Serum Lipase was 0.452 (Cut-off >860) and Lipase/Amylase ratio was 0.485 (Cut-off >3.15) were non-significantly (p>0.05) (Table 3) (Figure 2).

Table 3 AUROC analysis of Amylase, Lipase and Lipase/Amylase ratio for predicting Alcoholic pancreatitis

Alcoholic vs Non-Alcoholic								
Indices	*Sn*	*Sp*	*LR+*	*LR–*	*Cut-off*	*AUROC*	*SE*	*P value*
Amylase	64.3%	38.2%	1.04	-0.03	>160.5	0.421	0.063	0.212
Lipase	61.9%	33.3%	0.93	0.05	>860	0.452	0.063	0.444
Lipase/Amylase Ratio	66.7%	35.7%	1.03	-0.02	>3.15	0.485	0.064	0.809

*P-value<0.05 was statistically significant. Sn=Sensitivity, Sp=Specificity, LR= Likelihood ratio.

4. DISCUSSION

Acute Pancreatitis is abrupt inflammation of pancreas, which can arise because of numerous causes; among them commonest are gallstones and chronic alcohol ingestion (Yadav and Lowenfels, 2013; Taori et al., 2023). Acute pancreatitis has variable clinical presentation, such as mild disease episode in majority of patients, while around 15-20% patients suffer from severe episode of pancreatitis (Forsmark and Baillie, 2007).

Common clinical features of pancreatitis in current study were nausea, vomiting and abdominal pain. Increase in Amylase and Lipase levels were not very specific for acute pancreatitis, as 11–13% patients with non-pancreatic abdominal pain had also raised amylase and lipase levels and around 24% diabetic ketoacidosis patients had non-specific rise in serum lipase level. Past studies found that many patients with gall stone related pancreatitis were misdiagnosed as alcohol related pancreatitis. Early identification of aetiology of pancreatitis was of utmost important for prevention of unnecessary interventional procedure like ERCP, which was less useful in pancreatitis patients of alcoholic origin (Devanath et al., 2009).

In present study, all the alcoholic pancreatitis patients were males, as Indian males were more prone to alcohol addiction compared to females. Similarly, other Indian studies had also documented that males were suffering more from alcoholic pancreatitis compared to females (Devanath et al., 2009; Singh et al., 2020). Current study observed, Lipase: Amylase ratio of more than 3 in most of patients of both alcoholic and non-alcoholic pancreatitis patients which was statically non-significant (Table 1, 3). AUROC analysis also found non-significant relation between alcoholic and non-alcoholic pancreatitis (Table 3) (Figure 2).

Current study findings had been supported by retrospective study of Kumar and Mridul, (2018) who also found non-significant relationship of Serum Lipase, Amylase and Lipase: Amylase ratio between alcoholic and non-alcoholic pancreatitis ($p>0.05$). Taiwan study by Chang et al., (2005) observed substantially higher levels of serum amylase and lipase among biliary as compared to alcoholic pancreatitis ($p<0.05$), but non-significant relationship of lipase: Amylase ratio between both groups ($p>0.05$). Prospective study by Azam et al., (2017) noted lipase: Amylase ratio was significantly higher among biliary pancreatitis (1.4±0.39) compared to acute alcoholic pancreatitis (2.89±0.79).

Study by Devanath et al., (2009) found contrasting results that in alcoholic pancreatitis patients had significantly lower levels of serum lipase and serum amylase and significant higher values of Lipase: Amylase ratio compared to biliary pancreatitis ($p<0.05$). Furthermore, they also found non-significantly lower level of serum amylase ($p>0.05$) and significantly lower levels of serum lipase and Lipase/Amylase ratio ($p<0.05$) among sever pancreatitis compared to moderate pancreatitis (Devanath et al., 2009).

This findings were also supported by Ekka et al., (2023), who had concluded that Lipase: Amylase ratio >3 had moderate accuracy for predicting alcoholic etiology of pancreatitis and could be used to predict alcoholism in the absence of better diagnostic methods. Prospective study by Singh et al., (2020) documented that lipase: Amylase ratio in acute alcoholic pancreatitis was ≥3, while in acute biliary pancreatitis ratio was <3 and this distinction were statistically significant ($p<0.05$).

Reason of increase in serum lipase/amylase ratio among biliary pancreatitis compared to alcoholic pancreatitis remains unknown and one of probable reason for that was different pathophysiology in both conditions. Lower proportion of increase in enzyme among alcoholic pancreatitis was mostly due to functional impairment of gland with pre-existing chronic diseases, which describe why both serum lipase and amylase were low among alcoholic compared to biliary pancreatitis, where attack arise in anatomically normal gland (Pezzilli et al., 1993).

Study by Pezzilli et al., (1993) on 66 acute pancreatitis patients observed that amylase, lipase and lipase: Amylase ratio were neither able to establish the etiology nor were able to forecast the severity of acute pancreatitis, as assessed by radiological studies. Study by Gumaste et al., (1991) found that lipase: Amylase ratio more than 2 had specificity of 78%. Tenner and Steinberg, (1992) found that specificities of lipase: Amylase ratio for value of more than two was 50% and for value of more than 3 was 78% (Tenner and Steinberg, 1992).

There are many studies, which favor use of lipase: Amylase ratio for identifying etiology and severity of acute pancreatitis, on other hand many other studies are against use of this ratio as a predictor of etiology and severity. However, there is no other well-

established marker to find out etiology of acute pancreatitis. Hence, this ratio could be used to predict alcoholic etiology of acute pancreatitis in the absence of better diagnostic methods but should not be used as a gold standard. Current study, however do not favor use of amylase, lipase and its ratio to identify etiology and severity of acute pancreatitis.

5. CONCLUSIONS

Use of serum lipase and amylase and their ratio had very limited role in predicting etiology and severity in patients of acute pancreatitis however, gender might play an important role for identifying alcoholic vs non-alcoholic pancreatitis, probably due to higher rates of alcohol addiction in Indian males.

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Author's Contribution

All authors have contributed substantially for the concept, assessment and evaluation, data acquisition and development of this work. All authors read and approved the final version of the manuscript.

Ethical approval

This study was approved by the Institutional ethical committee of DMIMS (DU) (Ethical approval number: DMIMS (DU)/IEC/2022/714).

Informed consent

Written & Oral informed consent was obtained from all individual participants included in the study.

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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