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A STUDY ON EVALUATION OF ROLE OF SERUM LIPASE TO SERUM AMLYASE RATIO IN DIFFERENTIATING ALCOHOLIC PANCREATITIS FROM NON-ALCOHOLIC PANCREATITIS

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ABSTRACT

Background: Acute pancreatitis is a prevalent surgical condition, frequently attributable to non-alcoholic etiologies. Determining the underlying cause is essential since management strategies vary accordingly. One such diagnostic parameter is the estimation of the serum lipase to serum amylase ratio. This study aims to evaluate the utility of this ratio in differentiating between alcoholic and non-alcoholic etiologies in patients presenting with clinical and radiological evidence of acute pancreatitis at our tertiary care center.

Materials and Methods: This prospective study included 60 patients exhibiting clinical, radiological, and biochemical markers indicative of acute pancreatitis. The research was conducted over a 12-month period in the Department of General Surgery at Rajarajeswari Medical College and Hospital.

Results: The majority of acute pancreatitis cases were attributed to alcoholic etiologies (60%). Alcoholic pancreatitis was significantly more prevalent in males, while non-alcoholic pancreatitis was more common in females. Cirrhosis and hepatomegaly were the predominant sonological findings in alcoholic pancreatitis. Conversely, patients with non-alcoholic pancreatitis frequently presented with biliary sludge, a statistically significant finding. Alcoholic pancreatitis was associated with markedly elevated levels of serum gamma-glutamyl transferase (GGT), indirect bilirubin, and serum lipase. Non-alcoholic pancreatitis demonstrated significantly higher levels of serum alkaline phosphatase (ALP) and direct bilirubin. Although serum amylase levels were higher in non-alcoholic pancreatitis, this difference was not statistically significant. A serum lipase to serum amylase ratio greater than 3 exhibited a sensitivity and specificity of 94.4% and 79.17%, respectively, while a ratio greater than 4 showed both sensitivity and specificity of 91.6%.

Conclusion: A serum lipase to serum amylase ratio exceeding 4 strongly suggests alcoholic pancreatitis, whereas values below 4 are indicative of non-alcoholic pancreatitis.

Keywords: pancreatitis, serum lipase, serum amylase, alcohol, non-alcohol, gallstones

INTRODUCTION:

Acute pancreatitis is one of the most prevalent causes of acute abdominal pain globally. The rising consumption of alcohol, coupled with unhealthy lifestyles leading to obesity and an increased propensity for gallstone formation, has resulted in a higher incidence of acute pancreatitis.[1]

This condition is characterized by inflammation of the glandular parenchyma, leading to injury and destruction of the acinar cells without accompanying fibrosis. The most common etiology of acute pancreatitis is gallstones, accounting for 40-70% of cases, followed by alcohol consumption. Other non-alcoholic causes include hypercalcemia, hypertriglyceridemia, medications (such as corticosteroids, diuretics, antibiotics, azathioprine, valproic acid, and estrogen), hereditary factors, Sphincter of Oddi dysfunction, pancreatic neoplasms, pancreas divisum, and other less common causes.[2-5]

The mechanisms underlying gallstone pancreatitis include the reflux of bile into the pancreatic duct due to obstruction by a gallstone at the Ampulla of Vater or the direct obstruction of the pancreatic duct by a gallstone. In contrast, alcohol-induced pancreatitis is attributed to ethanol-induced secretory over activity and an increase in ductal permeability, leading to premature enzyme activation and subsequent acinar cell destruction.[6, 7]

Serum amylase levels typically rise within 2-4 hours after the onset of acute pancreatitis, peak at around 48 hours, and return to baseline within 7-10 days. Serum lipase levels increase within 4-6 hours, peak at 48 hours, and normalize after approximately 10 days. An elevation in serum amylase and/or serum lipase to more than three times the upper limit of normal is diagnostic of acute pancreatitis.[8-9]

Differentiating between non-alcoholic and alcoholic pancreatitis is crucial due to the differing management strategies required for each etiology, with alcoholic pancreatitis often necessitating more extensive investigations. In 1991, Gumaste et al. proposed the calculation of the serum lipase to serum amylase ratio to differentiate between alcoholic and non-alcoholic acute pancreatitis.[10] Although numerous studies worldwide have validated this index, there is a notable paucity of literature from South India, prompting the undertaking of this study.

This study aims to address this gap and provide further insights into the diagnostic utility of the serum lipase to serum amylase ratio in distinguishing between the two primary etiologies of acute pancreatitis in a South Indian population.

MATERIALS AND METHODS:

This prospective observational study was conducted in the Department of General Surgery at Rajarajeswari Medical College and Hospital, Bengaluru, Karnataka, over a 12-month period from April 2023 to March 2024.

The study included all patients aged 18 years and above who presented with clinical, radiological, and biochemical evidence of acute pancreatitis. Exclusion criteria encompassed patients younger than 18 years, those who did not consent to participate, individuals presenting more than 72 hours after the onset of symptoms, and patients with a history of chronic pancreatitis.

Approval for the study was obtained from the institutional ethics committee. Written informed consent was obtained from all participants prior to their inclusion in the study, ensuring adherence to ethical research standards.

A comprehensive history was obtained from each patient, focusing on clinical symptoms, characteristics of pain, past medical history, and personal habits such as alcohol consumption. A thorough physical examination was conducted, including the assessment of vital signs and an abdominal examination.

All patients underwent a series of biochemical and radiological investigations. Biochemical tests included Complete Blood Count (CBC), Liver Function Tests (LFTs), and measurements of serum lipase and serum amylase levels. Radiological assessments primarily involved ultrasonography to evaluate the pancreatic and biliary anatomy.

Data analysis was performed using MS Excel (2010) and SPSS software (version 16). Statistical methods employed included descriptive statistics, Chi-square tests, Fisher's exact tests, and independent t-tests. Sensitivity, specificity, predictive values, false positive and negative rates, and the overall accuracy of the serum lipase to serum amylase ratio were calculated. A p-value of less than 0.05 was considered statistically significant.

RESULTS:

60 patients with presentation of acute pancreatitis were included in this study. The mean age of this study population is 38.47 ± 7.07years, ranging between 21 years to 55 years. Most of the patients were between 31-40 years (43.4%). Men were the predominant gender accounting to 63.3%. Females accounted for 36.7%. 60% of the patients had alcoholic pancreatitis while the rest 40% had non-alcoholic pancreatitis.

Fig 1: Alcoholic versus non-alcoholic pancreatitis

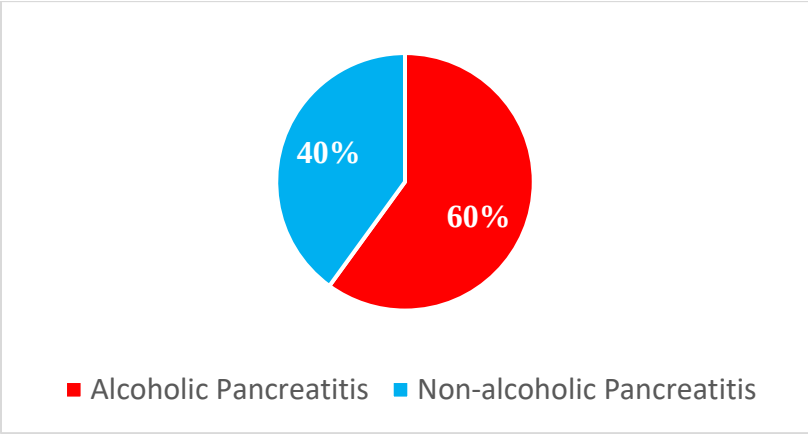

Table 1: comparison of different parameters in alcoholic versus non-alcoholic pancreatitis.

Parameter		**Alcoholic Pancreatitis**	**Non-Alcoholic Pancreatitis**	**P value**
Age (Mean ± Std. dev.)		37.86 ± 6.98years	39.38 ± 7.26years	0.214
Gender	**Male**	30 (83.3%)	8 (33.3%)	<0.001
	Female	6 (16.7%)	16 (66.7%)	

Symptomatology	**Pain abdomen**	29 (80.6%)	22 (91.7%)	0.293
	Nausea/Vomiting	22 (61.1%)	16 (66.7%)	0.662
	Distension	22 (61.1%)	18 (75%)	0.264
Ultrasonography findings	**CBD Stone**	2 (5.6%)	12 (50%)	<0.001
	Gall Stones	3 (8.3%)	19 (79.2%)	<0.001
	Biliary Sludge	5 (13.9%)	21 (87.5%)	<0.001
	Cirrhosis/ Hepatomegaly/Fatty Liver	32 (88.9%)	8 (33.3%)	<0.001
	Edema 0f Head/Body/ Tail Of Pancreas	28 (77.8%)	18 (75%)	0.803
	Peri Pancreatic Fat Stranding	22 (61.1%)	12 (50%)	0.395
Liver function tests	**Mean indirect bilirubin (mg/dl)**	2.09 ± 0.28	1.28 ± 1.66	0.005
	Mean direct bilirubin (mg/dl)	0.32 ± 0.13	1.85 ± 1.40	<0.001
	Mean GGT (U/L)	243.39 ± 65.17	140.25 ± 45.46	<0.001
	Mean ALP (U/L)	116.72 ± 30.46	228.67 ± 37.03	<0.001

Pancreatic enzymes	**Lipase (U/L)**	6154.11 ± 2953.78 **U/L**	3487.21 ± 1232.13 **U/L**	<0.001
	Amylase (U/L)	1237.03 ± 574.38 **U/L**	1270.21 ± 592.89 **U/L**	0.829
	Serum Lipase/ serum amylase ratio	5.02 ± 1.05	2.84 ± 0.61	<0.001

The mean age of patients with non-alcoholic pancreatitis was higher than that with alcoholic. However, the difference was not significant (p = 0.214).

Although males were the most predominant gender in the overall study, patients with non-alcoholic pancreatitis were mostly females. The difference was statistically significant (p = <0.001).

In present study, pain abdomen was the predominant compliant seen in both alcoholic (n = 29) and non-alcoholic pancreatitis, (n= 22) followed by abdominal distension (n = 40) and vomitings (n = 38). The difference in symptomatology was not statistically significant.

Edema of pancreas (n = 46) is the most common feature found in ultrasonography in entire study population, followed by hepatomegaly/ fatty liver/ cirrhosis of liver (n = 40). Amongst the patients with alcoholic pancreatitis, the common ultrasound findings were- hepatomegaly (88.9%), edema of pancreas (77.8%) and peripancreatic fat stranding (61%). Although these findings were more common in patients with alcoholic pancreatitis, presence of hepatomegaly (<0.005) was significantly more common than peripancreatic fat stranding (p = 0.395) and edema of pancreas (0.803) which were not significantly common.

Amongst the patients with non-alcoholic pancreatitis, the common ultrasound findings were - biliary sludge (87.5%); gall stones (79.2%); and CBD stones (50%). These findings were significantly higher (p value = <0.001) in patients with non-alcoholic pancreatitis than in alcoholic pancreatitis (biliary sludge – 13.9%; gall stones – 8.3%; CBD stones – 5.6%).

Patients with alcoholic pancreatitis had significantly higher indirect hyperbilirubinemia than those with non-alcoholic pancreatitis. The mean levels of serum gamma- glutamyl transferase (GGT) enzyme are also significantly higher in patients with alcoholic pancreatitis (p value = < 0.001).

In non-alcoholic pancreatitis, direct hyperbilirubinemia is significantly higher than alcoholic pancreatitis. The mean ALP levels are also significantly higher in non-alcoholic pancreatitis (p value = <0.001).

Serum lipase levels are significantly higher in patients with alcoholic pancreatitis (p value <0.001). Mean serum amylase levels are higher in patients with non-alcoholic pancreatitis, but it is not statistically significant (p value – 0.829). The mean ratio of serum lipase to serum amylase is significantly higher in alcoholic pancreatitis (p value <0.001).

Serum lipase to serum amylase ratio of <4 was predominantly seen in patients with non-alcoholic pancreatitis (91.7%), while ratio of >4 is predominantly seen in alcoholic pancreatitis (91.7%). This difference was found to be statistically significant (<0.001).

Table 2: Role of serum lipase/serum amylase ratio in acute pancreatitis.

serum lipase/serum amylase ratio	**Alcoholic Pancreatitis**	**Non-Alcoholic Pancreatitis**	**χ^2 Value**	**P Value**
<4	3 (8.3%)	22 (91.7%)	41.143	<0.001
>4	33 (91.7%)	2 (8.3%)		
Total	36 (100%)	24 (100%)		

Table 3: Sensitivity and specificity of Serum Lipase / Serum Amylase Ratio

Screening tools	**Serum Lipase/ Serum Amylase ratio**

	>3	**>4**
Sensitivity	94.44%	91.67%
Specificity	79.17%	91.67%
PPV	87.18%	94.29%
NPV	90.48%	88%
% of false positive	20.83%	8.33%
% of false negative	5.55%	8.33%
Accuracy	88.33%	91.67%

The Serum Lipase to serum amylase ratio of >3 in differentiating the type of acute pancreatitis was more sensitive, while ratio of >4 was more specific.

DISCUSSION:

Acute pancreatitis, a common surgical condition, presents with diverse clinical symptoms and causes, notably gallstones and alcohol. Various prediction modalities exist for assessing etiology and severity, though some are costly and less accessible. Early differentiation between alcoholic and non-alcoholic pancreatitis aids in effective diagnosis, treatment, and monitoring, yet an affordable, widely available diagnostic marker with high accuracy remains elusive. The study which was conducted on 60 acute pancreatitis patients in Rajarajeswari Medical College and Hospital, Bengaluru, Karnataka, aimed to evaluate the Serum Lipase/Serum Amylase ratio's role in distinguishing between alcoholic and non-alcoholic pancreatitis.

In our study, most common age group presenting with acute pancreatitis were between 31-50 years (81.7%). The mean age of entire study population was 38.47 ± 7.07years. However, the mean age difference between the ones with alcoholic pancreatitis and non-alcoholic

pancreatitis was not significant. This is accordance to studies done by Majharul et al[11] (44.35±16.90 years) and Harish Kumar et al [12] (39 years)

Men were the predominant in the entire study population, especially amongst patients with alcoholic pancreatitis. However, non-alcoholic pancreatitis was more common in females. This difference was found to be statistically significant. Majharul et al[11] assessed the role of serum Lipase to serum amylase ratio in determining the etiology and predicting outcomes in 71 patients with acute pancreatitis. Similar to present study, they also observed males being the predominant gender of the entire study population. Unlike present study where most of the patients with non-alcoholic pancreatitis were females, Arpita et al[13] observed that males were more commonly affected in both alcoholic and non-alcoholic pancreatitis.

In comparison with studies done by Arpita et al[13] (alcoholic pancreatitis – 46%; non-alcoholic pancreatitis – 54%), Harish et al [12] (alcoholic pancreatitis – 50%; non-alcoholic pancreatitis – 50%) and Monika et al [14] (alcoholic pancreatitis – 43.3%; non-alcoholic pancreatitis – 56.7%), where non-alcoholic pancreatitis was predominant, alcoholic pancreatitis (60%) was predominant in present study. this could be owing to the fact that the prevalence of alcohol abuse is higher in our region than others.

In present study, fatty changes of liver was the commonest sonological finding observed. in present study, patients with alcoholic pancreatitis had cirrhosis of liver (89%), edema of pancreas (78%) and peri-pancreatic fat stranding in 61%. In patients with non-alcoholic pancreatitis, biliary sludge was found in 87.5%; gallstones were found in 79.2% and CBD stone was found in 50% of the patients. Majharul et al[11] observed 32.4% had biliary pancreatitis and alcoholic etiology was observed in 10% of the patients. Arpita et al[13] observed that 55.1% of the patients had biliary pancreatitis.

Patients with alcoholic pancreatitis had significantly higher levels of serum GGT and indirect bilirubin, while those with non-alcoholic pancreatitis had significantly higher levels of serum ALP and direct bilirubin.

In present study the mean serum lipase levels in patients with alcoholic pancreatitis (6154.11 ± 2953.78) was significantly higher than in patients with non-alcoholic pancreatitis (3487.21 ± 1232.13). On the other hand, serum amylase levels were lower in patients with alcoholic pancreatitis (1237.03 ± 574.38) than in patients with non-alcoholic pancreatitis (1270.21 ± 592.89 U/L). However, in the study conducted by Arpita et al[13], alcoholic pancreatitis had significantly lower levels of serum amylase.

In present study, the serum Lipase to serum amylase ratio in Alcoholic Pancreatitis was 5.02 ± 1.05 and in patients with non-Alcoholic Pancreatitis was 2.84 ± 0.61. Studies done by Arpita et al[13] , Anita et al[15], Monika et al [14] and Chang et al [16] are in accordance with the present findings.

In present study, cut-off value of serum lipase to serum amylase ratio of >3 has 94.4% sensitivity, 79.17% specificity, 87.18% positive predictive value; 90.48% negative predictive value with an accuracy of 88.33%.

A cut-off value of >4 had sensitivity of 91.6%, specificity of 91.67%; positive predictive value of 94.2%, negative predictive value of 88% and an accuracy of 91.67%.

In 1990, Gumaste et al[10] observed that the serum lipase /amylase ratio of >2 had sensitivity and specificity of 91.0% and 78.0% respectively, in diagnosing acute alcoholic pancreatitis. Ratio of >5 has sensitivity of 21 - 31% for diagnosing alcoholic pancreatitis according to few studies.[13,17]

Kazmierczak et al[18] observed that L/A ratio >4.0 had a sensitivity of 92% but low specificity 60%. Considering the screening tool parameters Serum Lipase/ Serum Amylase ration >4 was more statistically significant and can be considered as a cut of value in distinguishing acute episodes of alcoholic from non-alcoholic pancreatitis.

CONCLUSION:

The study sought to establish a specific cut-off value for this ratio to aid in diagnosing and managing acute pancreatitis. The observations made in study indicated that Serum Lipase and Serum Amylase play crucial roles as biochemical markers in diagnosing and gauging the severity of acute pancreatitis, with varying distributions in different types of the condition. The ratio of

Serum Lipase/Serum Amylase showed significant variations between patients with alcoholic and non-alcoholic acute pancreatitis.

While not a definitive standard, the Serum Lipase/Serum Amylase ratio could serve as a valuable biochemical diagnostic tool alongside clinical and radiological assessments to differentiate between alcoholic and non-alcoholic pancreatitis. The study concluded that a ratio exceeding 4.0 (L/A>4) could effectively discern between these two types of acute pancreatitis, aiding in tailored management strategies for each subgroup.

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CONFLICTS OF INTEREST: No conflicts of interest declared.

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