

# Urinary Trypsinogen versus Serum Amylase in Early Diagnosis of Acute Pancreatitis

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## Introduction

Acute pancreatitis is a common cause of abdominal pain in the emergency department. 20% of acute pancreatitis attacks are severe, with about 10-25% of mortality rate in severe acute pancreatitis<sup>1,2,3</sup>. Early diagnosis of acute pancreatitis is required for adequate treatment and better prognosis<sup>1,3,4</sup>. Atypical presentation is so frequent in pancreatitis causing difficulty in diagnosis and distinguishing from other causes of abdominal pain<sup>4</sup>.

Pathophysiology in acute pancreatitis include activation of pancreatic proenzymes<sup>1</sup>. Premature activation of trypsinogen is considered as a common feature in all cases of acute pancreatitis irrespective of the cause. All the proenzymes are excreted in urine causing high levels of urinary amylase and trypsinogen<sup>1</sup>.

Serum amylase and lipase are routinely used for diagnosing pancreatitis<sup>3</sup>. An array of other diagnostic tests are used for diagnosing such as urine amylase, amylase creatinine clearance rate, serum elastase but none of the tests had shown any documented advantage over serum amylase and lipase.

Serum amylase levels begin to raise in 2-21 hours and remain elevated for 3-5 days. In 19% of cases serum amylase levels are elevated in other causes of abdominal pain causing decreased sensitivity<sup>1</sup>. Lipase is produced from acinar cells<sup>2</sup> of pancreas which helps in catalyzing triglycerides in diglycerides and fatty acids<sup>4</sup>. serum lipase levels raise in 48 hours and remain elevated up till 8-14 days. Sensitivity and specificity of lipase is varying due to different assay methods used in different studies. When compared to amylase and lipase trypsinogen is produced early and is long lasting.

Trypsinogen is a 25 KD pancreatic proteinase that helps in breaking down proteins into smaller peptides<sup>4,5</sup>. Pancreas secretes two forms of trypsinogen that are trypsinogen 1 & trypsinogen 26. In case of acute pancreatitis trypsinogen 2 levels in both serum and urine are raised, characteristic feature of elevation is that it is strong, rapid, and long lasting<sup>7</sup>. Urinary trypsinogen dipstick test is based on immune-chromatographic measurement of trypsinogen 2 level<sup>8</sup>. Detection limit for Actim dipstick is 50grams/liter<sup>4,5</sup>, in other causes of abdominal pain urinary trypsinogen level would be 1/3rd of detection value making it a more reliable diagnostic marker.

## Aims and objectives

- To assess role of urinary trypsinogen as an early diagnostic marker
- To assess role of urinary trypsinogen as a screening protocol
- To compare the sensitivity and specificity of urinary trypsinogen to serum amylase and lipase

## Materials and Methods

A total of 100 patients who were presented with complaints of abdominal pain to the emergency department of mamata academy of medical sciences during the period of January 2018 to January 2020 were included in this study. All those patients who have been priorly diagnosed of pancreatitis or referred with a diagnosis of pancreatitis and patients with low output due to chronic kidney disease have been excluded. Consent was obtained from the dean of the institution and institutional ethical committee

Out of 75 patients 40 patients had alcohol has etiological factor, 32 patients had gall stones etiological factor, 3 patients had anatomical abnormality in pancreas. On arrival thorough history was taken and examination is done and all patients were stabilized and resuscitated in the emergency department.

A clinical suspicion of pancreatitis is made if the patients had a history of abdominal pain radiating to the back, vomiting, nausea or with severe epigastric tenderness, guarding or rigidity on examination. Urine samples were collected from the patients in a container, and dipstick test was done immediately using Actim urinary trypsinogen dipstick. Patients were then followed by blood investigations, all those patients with pancreatitis are confirmed by contrast enhanced computed tomography (CECT).

## Results

In this cohort study conducted in mamata medical college during the period of January 2018 to January 2020 a total of 100 patients participated out of which 75 patients were diagnosed of pancreatitis on CECT abdomen.

In this study majority of patients were middle age group between 30-50 years (62%). This may be due to the increased incidence of etiological factors (alcohol, gall stones) in this age group. There is also a male preponderance of 91% in the study, may be due increased male patients presenting to the

emergency department in this region. Abdominal pain is the most common presentation in all the patients, followed by distention in 61 (81.3%), vomiting in 58 (77.3%) and fever in 18 patients (24%) in the 75 patients who were diagnosed of pancreatitis. 32 patients with pancreatitis and 8 patients without pancreatitis were also diagnosed of diabetes mellitus, increased incidence of diabetes in patients with pancreatic disorder is due to hinderance in insulin production from pancreas. Other co-morbid conditions noted in the study are hypertension in 15 patients and chronic kidney disease in 9 patients.

Out of the 75 patients who were diagnosed of pancreatitis actim dipstick test was positive in 72 patients giving it a sensitivity of 96%. 3 patients who were false negative may be having a relatively low levels of urinary trypsinogen in cases of mild attack of pancreatitis. There were no false positives in the study giving the test a specificity of 100%. Positive predictive value and negative predictive value for the dipstick were 100% and 89.3% respectively, hence the diagnosis of pancreatitis can be excluded if the test is negative and might need other enzyme values or radiological tests to confirm the disease. The concentration of urinary trypsinogen is higher in severe case (median 6980 gm/L) in comparison with mild disease (median 572 gm/L), whereas there is no much difference in the concentration of serum lipase in severe cases (median 714 IU/L) vs mild cases (668 IU/L). Chi- square test also suggests a significant co-relation between dipstick test and Pancreatitis (p< 0.001).

Pancreatitis	No. of Cases	Percentage
Yes	75	75%
No	25	25%
Total	100	100%

Table 1: No of cases of Pancreatitis.

75% of cases had Pancreatitis.

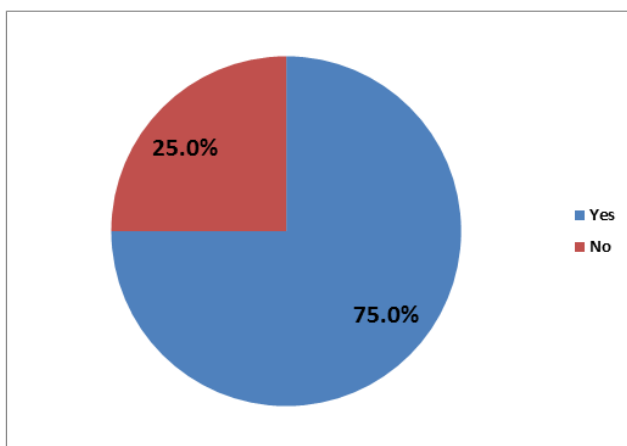


Figure 1: No of cases of Pancreatitis.

	Pancreatitis		Total
	Positive	Negative	

Age in years	Less than 30 years	Count	15	6	21
		% within Age in years	71.4%	28.6%	100.0%
30-50 years	30-50 years	Count	47	15	62
		% within Age in years	75.8%	24.2%	100.0%
Greater than 50 years	Greater than 50 years	Count	13	4	17
		% within Age in years	76.5%	23.5%	100.0%
Total		Count	75	25	100
		% within Age in years	75.0%	25.0%	100.0%

Table 2: Age in years and Pancreatitis.

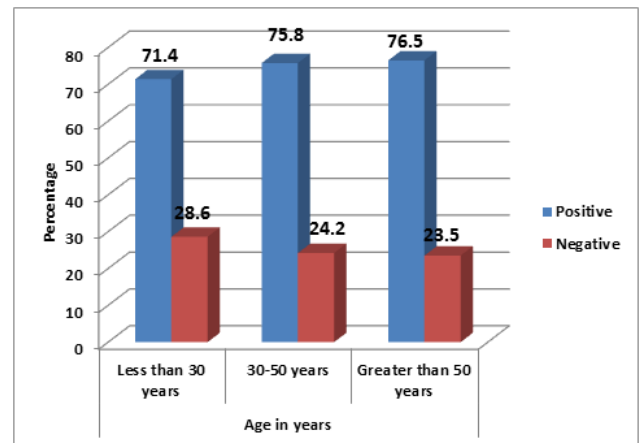


Figure 2: Age in years and Pancreatitis.

			Pancreatitis		Total
			Positive	Negative	
Sex	Male	Count	69	22	91
		% within Sex	75.8%	24.2%	100.0%
	Female	Count	6	3	9
		% within Sex	66.7%	33.3%	100.0%
Total		Count	75	25	100
		% within Sex	75.0%	25.0%	100.0%

Table 3: Sex and Pancreatitis.

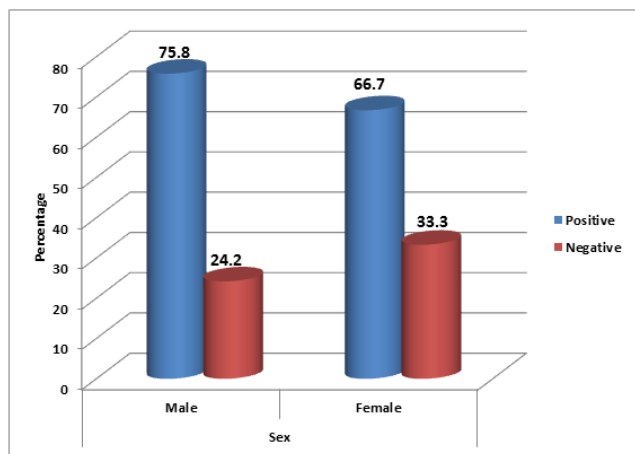


Figure 3: Sex and Pancreatitis.

Symptoms		Pancreatitis (75 patients)	
		With symptoms	Without symptoms
Abdominal pain	Count	75	0
	% with abdominal pain	100%	0
Vomiting	Count	58	17
	% with vomiting	77.3%	22.7%
Fever	Count	18	57
	% with fever	24%	76%
Distention	Count	61	14
	% with distention	81.3%	18.7%

Table 4: Symptoms.

Comorbid condition		With pancreatitis	Without pancreatitis
Diabetes mellitus (40)	Count	32	8
	Percentage	80%	20%
Hypertension (15)	Count	11	4
	Percentage	73.3%	26.4%
Chronic Kidney Disease (9)	Count	9	0
	Percentage	100%	0

Table 5: Co – morbidities.

	Amylase	Lipase	Dipstick	Cect
True positive	68	71	72	72
True negative	19	24	25	15
False positive	6	1	0	0
False negative	7	4	3	3

Accuracy	87%	95%	97%	96.67%
Sensitivity	90.7%	94.7%	96%	96%
Specificity	76%	96%	100%	100%
Positive predictive value	91.9%	98.6%	100%	100%
Negative predictive value	73.1%	85.7%	89.3%	83.4%

Table 6: statistical analysis.

Dipstick			Pancreatitis		Total
			Positive	Negative	
Dipstick	Positive	Count	72	0	72
		% within Dipstick	100.0%	0.0%	100.0%
	Negative	Count	3	25	28
		% within Dipstick	10.7%	89.3%	100.0%
Total	Count	75	25	100	
	% within Dipstick	75.0%	25.0%	100.0%	

Table 7: Correlation between Dipstick and Pancreatitis.

- Chi-Square Value = 85.714
- P value = < 0.001 Significant

The chi-square test shows that there is a significant correlation between dipstick test and Pancreatitis (p< 0.001).

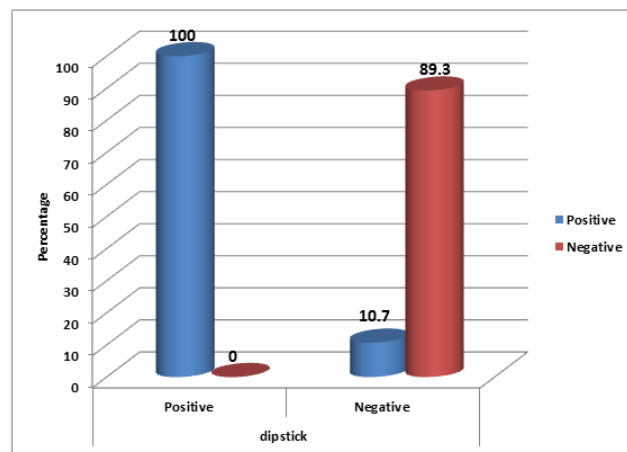


Figure 4: Correlation between Dipstick and Pancreatitis.

## Discussion

Acute pancreatitis is a common condition mostly in the middle-aged population<sup>1</sup>, in this study also we had a similar finding with 47 (62.7%) patients in 30-50 years age group. Studies show that there is a male preponderance in this disease we also had a similar finding in this study with 69 (92%) patients out of 75 were male patients<sup>1</sup>.

Alcohol and gall stones are the most common etiological factors for acute pancreatitis 9, even in the study we had similar results with 96% patients having these two as etiological factors. Main pathophysiology for acute pancreatitis is due to release of pancreatic pro-enzymes<sup>10</sup>. Pancreatitis is of two types acute and chronic, in acute pancreatitis there will be reversible changes whereas in chronic pancreatitis the changes are irreversible. Abdominal pain and epigastric tenderness are the common clinical features in almost all the patients with pancreatitis<sup>5</sup>, other features include vomiting, abdominal distention, fever, epigastric mass, grey-turners sign, cullens sign and fox sign<sup>2</sup>. Early detection of patients with pancreatitis is useful in providing adequate treatment, when there is a delay in diagnosis and treatment patients may go into hypovolemic shock<sup>3</sup> due to various inflammatory reactions causing intra vascular fluid to move out. Thus, early detection is paramount in cases of acute pancreatitis for a better prognosis<sup>2, 6</sup>.

Various biochemical and radiological tests are used for diagnosis of pancreatitis such as serum amylase, serum lipase, amylase creatinine clearance ratio, urinary amylase, ultrasound abdomen and CECT abdomen<sup>9</sup>. Actim urinary trypsinogen dipstick has higher sensitivity (96%) and specificity (100%) when compared to the quantitative tests as serum amylase and serum lipase<sup>11</sup>. Median concentration of urinary trypsinogen is 700 fold in pancreatic causes in comparison to the non-pancreatic causes<sup>4</sup>, and resulting in a high sensitivity and negative predictive value (89.3%). Thus, acute pancreatitis can be excluded in cases of negative test<sup>12</sup>. Urinary trypsinogen dipstick test can also be used for screening measures due to high sensitivity when compared to serum lipase.

Due to the false positive with serum amylase (6) and lipase (1) there is a low positive predictive value with them hence, to confirm the diagnosis of acute pancreatitis they should be combined with other enzymatic or radiological tests. CECT abdomen provides most accurate diagnosis in cases of pancreatitis, but it is costly and not feasible to be performed in all cases of pancreatitis hence urinary trypsinogen dipstick test can be used in diagnosing<sup>3,4</sup>. Unlike serum amylase and lipase levels which has no co-relation to severity of the disease, there are studies which show a strong co-relation between the concentration of trypsinogen 2 and severity of the disease<sup>12</sup>.

## Conclusion

Acute pancreatitis is common entity that comes across in the emergency department. Early diagnosis of acute pancreatitis would help in providing adequate treatment and for a better prognosis. Urinary trypsinogen dipstick can be used as a diagnostic marker for acute pancreatitis with faster and better

positive and negative predictive value compared the commonly used serum amylase and lipase.

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