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Original Research Article

Effectiveness of the Urine Trypsinogen-2 Test as a Diagnostic Tool for Cases of Acute Pancreatitis

Srinivas Bheemanadam[1], Manasa Tejaswini[2]

[1]Associate Professor, Department of General Surgery, Neelima Institute of Medical Sciences, Pocharam, Hyderabad 500088, Telangana State.
[2]Assistant Professor, Dept of General Surgery, Prathima Institute of Medical Sciences, Nagunoor, Karimnagar 505417, Telangana State

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Corresponding Author: Dr. Bheemanadam Srinivas
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Abstract:

Background: The objective of the study was to examine the significance and function of the urine trypsinogen-2 dipstick test in the differential diagnosis of acute pancreatitis within the Department of General Surgery, and to compare the findings with those obtained through other traditional tests.

Methods: Patients with acute upper abdominal symptoms, including pain, vomiting, and distention, admitted to our hospital's emergency department with the diagnosis of acute pancreatitis as per the inclusion criteria were included in the study. They were subjected to radiological investigations and lab investigations for serum amylase levels. The urine trypsinogen-2 dipstick test results were compared with serum amylase, serum lipase, and imaging studies in patients with a final diagnosis of acute pancreatitis.

Results: A total of 50 cases of suspected acute pancreatitis were included in the study. Out of these 31 cases were with acute pancreatitis and 19 cases were of non-pancreatic causes. Trypsinogen and amylase demonstrate the highest sensitivity (77.41% and 77.12%, respectively) in identifying acute pancreatitis, surpassing lipase's lower sensitivity (64.51%). Ultrasound exhibits a balanced sensitivity (74.19%) and high specificity (100.0%), serving as a valuable initial diagnostic tool. Contrast-enhanced CT has lower sensitivity (22.58%) but high specificity (100.0%), confirming suspected cases effectively.

Conclusion: we have determined that the Urine Trypsinogen-2 dipstick test serves as a direct, swift, convenient, and non-intrusive diagnostic tool proficient in confirming or excluding the presence of acute pancreatitis in a majority of cases. In contrast to serum amylase and lipase, the evaluation of Urine Trypsinogen-2 doesn't require access to laboratory facilities, delivering almost instant results within 5 minutes, unlike the potential hour-long wait associated with serum tests.

Keywords: Acute Pancreatitis, Urine Trypsinogen-2, Serum Amylase, Serum Lipase

Introduction

Acute pancreatitis, a prevalent disorder, places a significant strain on healthcare systems. It spans from mild, self-limiting symptoms to severe cases with a 3-10% mortality rate, with 11-30% representing severe disease with pancreatic necrosis. [1] Since 1974, multiple scoring systems have clinically and radiologically assessed prognosis. Severity assessment guides practical decisions, distinguishing mild cases requiring supportive care from severe ones demanding intensive monitoring and facing a guarded prognosis. [2] Reducing mortality and morbidity hinges on early detection and appropriate management. Ideally, a diagnostic method should differentiate between mild and severe cases, be user-friendly, widely available, accurate, and exhibit low inter-observer variability. Detecting early disease allows proactive monitoring and treatment. Currently, serum amylase and lipase, used for diagnosis, are relatively insensitive and nonspecific, leading to false positives or negatives. [3] Various scoring systems predict severity, but no single comprehensive test aids early and accurate acute pancreatitis detection. The proposed urinary trypsinogen-2 dipstick test, utilizing the immune-chromatographic method, aims to be a rapid diagnostic tool for early acute pancreatitis detection. Trypsinogen activation peptide (TAP) is the amino-terminus peptide released upon trypsinogen activation. In experimental acute pancreatitis, inappropriate trypsinogen activation within the pancreas leads to the release of TAP into the blood, urine, and peritoneum. [4,5] The concentration of urinary TAP is believed to directly correlate with the severity of acute pancreatitis, reflecting the degree of trypsinogen activation in the pancreas. [6-8] Previous reports have identified the concentration of urinary trypsinogen-2 as a candidate prognostic marker for severe acute pancreatitis (6 of WJG).

With this background, we in the current study tried to evaluate the usefulness of urinary trypsinogen-2 as a marker of acute pancreatitis.

Material and Methods

This cross-sectional study was conducted in the Department of General Surgery, Prathima Institute of Medical Sciences, Naganoor, Karimnagar, Telangana State. Institutional Ethical approval was obtained for the study. Written permission was obtained from all the participants of the study after explaining the nature of the study in the vernacular language. Those voluntarily willing to participate in the study were included.

Inclusion Criteria

1. Patients with features suggestive of Acute Pancreatitis
2. Male and females
3. Aged 20 - 60 years shall be selected.
4. Adult subjects were willing to give informed consent.

Exclusion Criteria

1. Cases of chronic pancreatitis or pancreatic cancer
1. Hereditary pancreatitis, cystic fibrosis
2. Not as per the inclusion criteria
3. Those not willing to participate in the study

Patients with acute upper abdominal symptoms, including pain, vomiting, and distention, admitted to our hospital's emergency department with the diagnosis of acute pancreatitis as per the inclusion criteria were included in the study. A complete history was obtained from the patients. The patients were subjected to thorough clinical examination. They were subjected to radiological investigations and lab investigations for serum amylase levels. The diagnosis of acute pancreatitis was based on the threefold increase in serum amylase levels and ultrasonographic findings. The urine trypsinogen-2 dipstick test results were compared with serum amylase, serum lipase, and imaging studies in patients with a final diagnosis of acute pancreatitis.

Statistical Analysis: All the available data was sorted, refined, and uploaded to an MS Excel spreadsheet and analyzed by SPSS version 21 in Windows format. The continuous values were represented as mean, standard deviation, and percentages, and the categorical values were calculated by Fischer's exact test and chi-square test the p values of (<0.05) were considered as significant.

Results

A total of 50 cases were studied in the duration of the study. In this study 42(84%) cases were males, and 8(16%) cases were females. The majority of patients fall within the 31-50 age range (39% combined). A notable proportion of patients are young adults aged 21-30 (24%). The number of cases significantly decreases in older age groups, with only 6% and 2% in the 51-60 and >60 age ranges, respectively (Table 1). Acute pancreatitis can affect all age groups: While middle-aged adults are the most commonly affected, the presence of significant cases in young adults and even a single case in an older individual highlights the possibility of this condition occurring across a broad age spectrum.

Table 1: Age-wise distribution of cases included in the study

Age Range (years)	No. of patients	Percentage (%)
21- 30	12	24.00%
31 - 40	13	26.00%
41 - 50	18	36.00%
51- 60	6	12.00%
>60	1	2.00%
Total	50	100 %

In this study out of 50 cases, acute pancreatitis was diagnosed in 31(62%) cases which included 28(90.32%) males and 3(9.68%) females. Table 2 summarizes the distribution of symptoms experienced by patients with acute pancreatitis in the study. It lists each symptom observed and its corresponding frequency and percentage of occurrence within the group of 50 patients. Abdominal pain is the dominant symptom: Pain in the abdomen is the most frequent symptom, reported by 60% of patients. Fever and vomiting follow closely, occurring in 24% and 54% of patients, respectively. Jaundice and abdominal distension are less common, observed in 12% and 32% of patients, respectively.

Table 2: Distribution of symptoms in the cases included in the study

Symptoms	Frequency	Percentage (%)
Pain abdomen	30	60%
Fever	12	24%
Vomiting	27	54%
Jaundice	6	12%
Abdominal distension	16	32%

Table 3 displays the distribution of underlying causes (etiologies) of acute pancreatitis among the 50 cases included in the study. Each row lists a specific etiology, followed by the number of patients diagnosed with it and the corresponding percentage within the total group. Alcohol is the overwhelming main cause: Alcohol consumption is identified as the cause of acute pancreatitis in a vast majority of cases (87.09%). Other etiologies are significantly less frequent: Gallstone disease, post-ERCP (endoscopic retrograde cholangiopancreatography) procedure, and hypertriglyceridemia are present in a much smaller proportion of cases, ranging from 3.22% to 6.45% each.

Table 3: The etiology of acute pancreatitis in the cases of the study

Etiology	Frequency	Percentage (%)
Alcohol	27	87.09%
Gall stone disease	2	6.45%
Post ERCP	1	3.22%
Hypertriglyceridemia	1	3.22%
Total	31	100%

Table 4 compares the frequency of various diagnostic parameters used in identifying acute pancreatitis among two groups: Acute Pancreatitis (31 cases) and patients diagnosed with confirmed acute pancreatitis. Others (19 cases): Patients whose symptoms were initially suspected to be acute pancreatitis but ultimately diagnosed with other conditions. Amylase and lipase: Elevated levels of both enzymes are observed in 23 and 18 cases of confirmed acute pancreatitis, respectively. However, a few cases in the "Others" group also show elevated levels, potentially due to other conditions mimicking pancreatitis. Trypsinogen: This parameter seems to have better-differentiating power, with positive results in 24 out of 31 acute pancreatitis cases and only 3 cases in the "Others" group. Imaging: USG (Ultrasound): Ultrasound was positive for characteristic findings in all 23 confirmed acute pancreatitis cases and none in the "Others" group, suggesting high sensitivity for this particular imaging modality. CECT (Contrast-enhanced Computed Tomography): CECT was less frequently used but showed positive findings in 7 cases of confirmed acute pancreatitis and none in the "Others" group.

Table 4: Comparison of different parameters used in the Diagnosis of Acute Pancreatitis

Parameters	Acute Pancreatitis (31)	Others (19)	Total (50)
Amylase	23	2	25
Lipase	18	2	20
USG	23	0	23
CECT	7	0	7
Trypsinogen	24	3	27

Table 5 shows that all listed parameters (amylase, lipase, trypsinogen, USG, and CECT) have a specificity above 88%, meaning they are very good at correctly identifying patients who do not have acute pancreatitis. Trypsinogen and amylase show the highest sensitivity: These two parameters have the highest sensitivity, meaning they correctly identify a high proportion of patients who have acute pancreatitis (77.41% and 77.12%, respectively). Lipase has lower sensitivity: Compared to trypsinogen and amylase, lipase has a lower sensitivity (64.51%). This means that a higher percentage of patients with acute pancreatitis could potentially be missed when using lipase alone. USG offers good sensitivity and specificity: Ultrasound offers a balance between sensitivity (74.19%) and specificity (100.0%), making it a valuable tool for the initial diagnosis of acute pancreatitis. CECT has low sensitivity but high specificity: CECT has the lowest sensitivity (22.58%), meaning it might miss a substantial portion of cases. However, it has the highest specificity (100.0%), making it useful for confirming a diagnosis in suspected cases.

Table 5: Comparison of sensitivity and specificity of different parameters

Parameters	Sensitivity	Specificity
Amylase	77.12	88.41
Lipase	64.51	89.74
Trypsinogen	77.41	91.02
USG	74.19	100.00
CECT	22.58	100.00

Urine trypsinogen was calculated for sensitivity and specificity. The Sensitivity = 77.41% and Specificity = 89.47%. Table 6 shows that out of 31 confirmed cases of acute pancreatitis, 24 (77.41%) had a positive urine trypsinogen test. This shows good sensitivity of the test, meaning it correctly identifies a high proportion of individuals with acute pancreatitis. only 2 out of 19 patients with non-pancreatic causes (10.53%) had a positive test. This indicates high specificity, meaning the test correctly identifies individuals without acute pancreatitis with good accuracy. Kappa statistic of 0.65: This further suggests moderate agreement between the urine trypsinogen test results and the actual presence of acute pancreatitis. Urine trypsinogen appears to be a promising test for diagnosing acute pancreatitis: Based on its good sensitivity and specificity, it can help differentiate acute pancreatitis from other conditions causing similar symptoms.

Table 6: Estimation of urine trypsinogen and its significance

Urine trypsinogen	Acute Pancreatitis	Non-pancreatic causes	Total
Positive	24	2	26
Negative	7	17	24
Total	31	19	50

Discussion

The diagnosis of acute pancreatitis relies on evaluating the clinical presentation along with amylase and lipase values. [10] While epigastric pain, nausea, and vomiting are common clinical signs, they lack specificity. Additionally, about 10% of patients with acute pancreatitis do not exhibit the typical clinical scenario. Amylase and lipase, though commonly used, are not pancreatitis-specific and have reduced sensitivity in late admissions, hypertriglyceridemia, and chronic alcohol intake. [11] Trypsinogen, a precursor to trypsin necessary for protein digestion, must undergo activation in a controlled manner. Premature activation can result in self-digestion of the pancreas. Human pancreatic juice contains three trypsinogen isoenzymes: cationic (TPS-1), anionic (TPS-2), and a minor isoenzyme (TPS-3). The inactive form of trypsinogen is stored in cytoplasmic zymogen granules of pancreatic acinar cells. [12] These are secreted into the adjacent duct lumen and delivered to the small intestine, where enterokinase activates them. Premature trypsinogen activation within the pancreas is a key event in the development of acute pancreatitis. The urine trypsinogen-2 test stands out due to its accessibility, user-friendly nature, and short result time of 5 minutes. Studies report the sensitivity of the urine trypsinogen-2 test for pancreatitis as ranging from 86% to 100%, [11,13,14] although Pezzilli et al. [15] found it to be 53%. In the current study, the sensitivity was determined as 64%, increasing to 83% when considering patients examined within the first 24 hours of symptom onset, aligning with literature findings. The specificity of the trypsinogen-2 test for pancreatitis ranges between 72% and 95%. In the present study, this figure was calculated as 85%, consistent with the literature. When restricting analysis to admissions within the first 24 hours, specificity remained at 87%. The test's sensitivity and specificity decline in admissions occurring after 24 hours.

In this study we found amylase and lipase had sensitivities of 77.12% and 64.51%, respectively, trypsinogen showed a higher sensitivity of 77.41%. The specificity for amylase and lipase was 88.41%, while trypsinogen exhibited a specificity of 91.02%. Contrast-enhanced computed abdominal tomography is highly accurate and useful for assessing pancreatitis severity. We found the specificity for CECT and USG as 100%. However, it's ionizing radiation and high-cost limit its routine use in Emergency Departments. Consequently, there has been a focus on developing reliable, cost-effective tests with rapid results. In this study false positive results occurred in three of 19 non-pancreatitis cases, involving two cases of gallstones and one case of renal failure. In renal failure, a defect in trypsinogen excretion led to a positive result. Further studies with larger sample sizes are needed to understand the etiology of the test's positivity in gallstone cases. Despite its lower sensitivity and specificity compared to amylase and lipase, the trypsinogen-2 dipstick test holds value in Emergency Departments due to its rapid result turnaround (in 5 minutes). [15] The negative predictive value of the trypsinogen-2 test, when considering all admissions, was 81%, increasing to 92% when focusing on admissions within the first 24 hours. These results fall within the range of negative predictive values reported for amylase and lipase (91% and 100%, respectively). Lempinen et al. [16] reported similar findings, further supporting the utility of the trypsinogen-2 test. A heightened negative predictive value holds significant importance in ruling out the diagnosis of pancreatitis, particularly when the test is employed alongside other clinical indicators. In our study, the positive predictive value of the urine trypsinogen-2 test was determined to be 72%. When restricting analysis to admissions within the initial 24 hours, this ratio increased to 75%. Chen et al. [11] reported a positive predictive value of 81.1%, while Kamer et al. [16] reported a higher value of 96.6%. However,

our study found a comparatively lower positive predictive value for this test in comparison to amylase and lipase (90% and 94%, respectively). Given that trypsinogen-2 levels may elevate in various conditions, including hepatobiliary, pancreatic, and colonic malignancies, a lower positive predictive value can be anticipated. Consequently, we recommend that this test be complemented by other diagnostic methods for a comprehensive evaluation in the diagnosis of acute pancreatitis.

Conclusion

Within the confines of the present study's limitations, we have determined that the Urine Trypsinogen-2 dipstick test serves as a direct, swift, convenient, and non-intrusive diagnostic tool proficient in confirming or excluding the presence of acute pancreatitis in a majority of cases. In contrast to serum amylase and lipase, the evaluation of Urine Trypsinogen-2 doesn't require access to laboratory facilities, delivering almost instant results within 5 minutes, unlike the potential hour-long wait associated with serum tests. The urinary trypsinogen-2 test shows promise as an efficient screening tool for identifying cases of acute pancreatitis. Fine-tuning the cutoff point in this assay improves its specificity to a level suitable for diagnostic purposes. The user-friendly nature of the qualitative rapid Urine Trypsinogen-2 test strip establishes it as a dependable and practical screening method for acute pancreatitis in routine medical settings, especially in healthcare units with limited access to laboratory facilities.

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