JAZ INDIA

Journal of Advanced Zoology

ISSN: 0253-7214

*Volume **44** Issue **S-1 Year 2023** Page **968:973***

Urine Trypsinogen 2 as a Diagnostic Marker for Acute Pancreatitis: A Prospective Study

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Article History

Received: 06 June 2023
Revised: 05 Sept 2023
Accepted: 13 Oct 2023

Abstract

Background: Acute pancreatitis presents diagnostic challenges due to its diverse clinical presentation and limitations of traditional serum biomarkers. This study explores the diagnostic potential of urine trypsinogen 2 in acute pancreatitis, an area relatively unexplored in our institution. Methods: A prospective study involving 96 patients admitted between December 2020 and June 2022 with symptoms suggestive of pancreatitis was conducted. Urine trypsinogen 2 levels were quantitatively assessed alongside serum amylase and lipase. Radiological investigations were employed when necessary. The final diagnosis integrated clinical, biochemical, and radiological findings. Results: Urine trypsinogen 2 exhibited a sensitivity of 88.4% and a specificity of 91.7%, outperforming serum amylase and approaching serum lipase. Comparative analysis revealed significant advantages of urine trypsinogen 2 in sensitivity, specificity, and predictive values. Conclusion: Urine trypsinogen 2 emerges as a non-invasive, accurate, and early diagnostic marker for acute pancreatitis, with the potential to enhance diagnostic precision and improve patient outcomes. Further validation in diverse clinical settings is warranted.

Keywords: *Urine trypsinogen 2, acute pancreatitis, diagnostic marker, sensitivity, specificity, clinical diagnosis*

1. Introduction

Acute pancreatitis, a distressing medical condition characterized by excruciating abdominal pain, vomiting, and abdominal distension, poses a formidable diagnostic challenge to healthcare providers. Over the years, the evaluation of pancreatitis has predominantly relied on serum biomarkers, primarily serum amylase and lipase levels. However, despite their conventional usage, these markers have shown limitations in terms of sensitivity and specificity, leading to potential delays in diagnosis and suboptimal patient care. This prospective study is conducted with the primary objective of assessing the diagnostic utility of urine trypsinogen 2, a biomarker that has remained relatively underexplored within the confines of our institution [1-5].

Acute pancreatitis, often associated with gallstone disease and excessive alcohol consumption, is recognized as a multifaceted inflammatory process within the pancreas. While the clinical manifestations can be dramatic and painful, varying from mild to severe forms, the underlying pathophysiology involves auto-digestion of the pancreatic tissue by prematurely activated digestive enzymes, predominantly trypsin. This cascade of events can lead to extensive tissue damage, necrosis,

and systemic complications, making early and accurate diagnosis a crucial element of patient management [1-5].

Traditionally, serum amylase and lipase have been the frontline biomarkers for diagnosing acute pancreatitis. These enzymes are secreted by the acinar cells of the pancreas and released into the bloodstream when pancreatic tissue is injured. Although they have been valuable tools in the initial assessment of pancreatitis, their diagnostic accuracy has faced scrutiny. False elevations can occur in non-pancreatic conditions, and their sensitivity and specificity for pancreatitis have been reported to be suboptimal. Additionally, their elevation might be delayed, causing diagnostic delays that can negatively impact patient outcomes.

Against this backdrop, urine trypsinogen 2 emerges as a potential diagnostic alternative. Trypsinogen, the inactive precursor of trypsin, is one of the key enzymes involved in the pathogenesis of pancreatitis. Trypsinogen is prematurely activated to trypsin within the pancreatic ducts in the early stages of pancreatitis. While traditionally considered a serum biomarker, recent research has revealed that trypsinogen 2, a specific isoform of trypsinogen, can be detected in urine samples, offering a non-invasive and potentially more sensitive approach to diagnosing acute pancreatitis [6-9].

This study endeavors to fill a crucial gap in our institution's understanding of the role of urine trypsinogen 2 in diagnosing acute pancreatitis. By prospectively evaluating its diagnostic accuracy and comparing it to serum amylase and lipase, we aim to elucidate whether urine trypsinogen 2 can serve as a reliable and early diagnostic marker. The study timeline, spanning from December 2020 to June 2022, encompassed a diverse cohort of patients presenting with symptoms indicative of pancreatitis, including abdominal pain, vomiting, and abdominal distension.

Furthermore, given the complexity of acute pancreatitis diagnosis, which often necessitates radiological investigations, we incorporated ultrasonography and contrast-enhanced computed tomography (CECT) into our diagnostic protocol. These additional diagnostic modalities were applied when the clinical presentation and initial biomarker results warranted further investigation.

The ultimate diagnosis of acute pancreatitis in this study was arrived at by synthesizing information from three main sources: clinical findings, biochemical markers (including serum amylase, lipase, and urine trypsinogen 2), and radiological assessments. This comprehensive approach aimed to provide a holistic and accurate diagnosis, enabling us to assess the true potential of urine trypsinogen 2 as a diagnostic tool in comparison to the established serum markers.

In the subsequent sections of this research paper, we will present the materials and methods employed, the detailed results of our investigation, and an in-depth discussion of our findings in the context of existing literature. This study holds the promise of shedding light on a novel avenue in acute pancreatitis diagnosis and may potentially influence clinical practice, leading to earlier and more accurate diagnoses and improved patient care..

2. Materials And Methods

Study Design: This prospective study aimed to assess the diagnostic utility of urine trypsinogen 2 in acute pancreatitis. The research was conducted at our hospital, encompassing a cohort of 96 patients admitted between December 2020 and June 2022. Patients presenting with symptoms such as abdominal pain, vomiting, and abdominal distension were included in the study.

Patient Selection: Inclusion criteria encompassed patients exhibiting the aforementioned symptoms upon admission. Exclusion criteria included patients with a known history of chronic pancreatitis, those undergoing treatment for pancreatitis, and individuals with incomplete medical records.

Data Collection: After obtaining informed consent, urine samples were collected from each patient within 24 hours of admission. Simultaneously, blood samples were drawn to measure serum amylase and lipase levels. Urine trypsinogen 2 was quantitatively assessed using commercially available dipsticks specifically designed for this purpose.

Radiological Investigations: Radiological assessments, such as ultrasonography and contrast-enhanced computed tomography (CECT), were conducted when deemed necessary based on clinical

presentation and initial biomarker results. These investigations were performed by experienced radiologists following standard protocols.

Diagnostic Criteria: The final diagnosis of acute pancreatitis was established through a multi-faceted approach, considering clinical findings, biochemical markers, and radiological evidence. The clinical criteria included the characteristic symptoms of acute pancreatitis, while biochemical markers encompassed elevated serum amylase, lipase, and positive urine trypsinogen 2 results. Radiological findings consistent with pancreatitis, such as pancreatic edema, necrosis, or peripancreatic fluid collections, further substantiated the diagnosis.

Statistical Analysis: The data collected from this study were subjected to rigorous statistical analysis. Sensitivity and specificity of urine trypsinogen 2, serum amylase, and serum lipase were calculated, with reference to the final clinical diagnosis of acute pancreatitis. Positive predictive values (PPV) and negative predictive values (NPV) were also determined to assess the clinical utility of each parameter. All statistical analyses were performed using appropriate software packages.

Ethical Considerations: This study adhered to ethical guidelines, and all procedures involving human participants were approved by the institutional ethics committee. Informed consent was obtained from each patient before inclusion in the study. Patient confidentiality and privacy were strictly maintained throughout the research process.

Data Presentation: The findings of this study are presented in the subsequent "Results" section, which includes tables and figures to convey the diagnostic accuracy of urine trypsinogen 2 compared to serum amylase and lipase. The tables include data on sensitivity, specificity, PPV, and NPV.

3. Results and Discussion

In Table 1, we present an overview of the diagnostic accuracy of three key parameters—urine trypsinogen 2, serum amylase, and serum lipase—in the context of diagnosing acute pancreatitis. We assessed these parameters using key metrics: sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

Urine Trypsinogen 2 displayed a noteworthy sensitivity of 88.4%, indicating its proficiency in accurately identifying 88.4% of patients with acute pancreatitis. Furthermore, it demonstrated an impressive specificity of 91.7%, signifying its ability to correctly exclude acute pancreatitis in 91.7% of patients without the condition. The positive predictive value (PPV) of urine trypsinogen 2 stood at 91.0%, highlighting that a positive result from this test corresponds to a 91.0% likelihood of the patient having acute pancreatitis. The negative predictive value (NPV) was 88.9%, indicating that a negative result aligns with an 88.9% probability of the patient not having acute pancreatitis.

Conversely, serum amylase exhibited a sensitivity of 70.8%, indicating its capability to correctly identify 70.8% of patients with acute pancreatitis. However, it showed a lower specificity of 62.5%, implying a higher incidence of false-positive results. The PPV for serum amylase was 65.2%, suggesting that a positive serum amylase result corresponds to a 65.2% likelihood of the patient having acute pancreatitis. The NPV was 68.3%, indicating that a negative result aligns with a 68.3% probability of the patient not having acute pancreatitis.

Similarly, serum lipase demonstrated a sensitivity of 75.0%, indicating its proficiency in correctly identifying 75.0% of patients with acute pancreatitis. Its specificity was 72.9%, suggesting a lower occurrence of false-positive results compared to serum amylase. The PPV for serum lipase was 71.7%, signifying that a positive serum lipase result corresponds to a 71.7% likelihood of the patient having acute pancreatitis. The NPV was 75.4%, implying that a negative result aligns with a 75.4% probability of the patient not having acute pancreatitis.

In Table 2, we delve into the comparative analysis between urine trypsinogen 2 and serum amylase, highlighting the distinctions in their diagnostic performance. Urine trypsinogen 2 exhibited a higher sensitivity (+17.6%) compared to serum amylase, indicating its superior ability to accurately identify patients with acute pancreatitis. Furthermore, it displayed a significantly higher specificity (+29.2%) than serum amylase, implying that it generates fewer false-positive results. The positive predictive value (PPV) of urine trypsinogen 2 was +25.8% higher than that of serum amylase, suggesting its

greater reliability when the test yields a positive result. Additionally, urine trypsinogen 2 had a negative predictive value (NPV) +20.6% higher than serum amylase, signifying its stronger indication of the absence of acute pancreatitis with a negative result.

Table 3 provides a comparative analysis between urine trypsinogen 2 and serum lipase. Urine trypsinogen 2 exhibited a higher sensitivity (+13.4%) compared to serum lipase, underscoring its efficacy in correctly identifying patients with acute pancreatitis. It also demonstrated a higher specificity (+18.8%) than serum lipase, suggesting its lower tendency to yield false-positive results. The positive predictive value (PPV) of urine trypsinogen 2 was +19.3% higher than that of serum lipase, indicating its increased reliability when the test indicates the presence of acute pancreatitis. Additionally, urine trypsinogen 2 had a negative predictive value (NPV) +13.5% higher than serum lipase, emphasizing its stronger indication of the absence of acute pancreatitis when the test is negative.

Table 4 provides a concise summary of the comparative diagnostic performance of the three parameters: urine trypsinogen 2, serum amylase, and serum lipase. Urine trypsinogen 2 exhibited higher sensitivity compared to both serum amylase and serum lipase, indicating its superior ability to accurately identify patients with acute pancreatitis. It had higher specificity compared to serum amylase and was comparable to serum lipase, suggesting its lower false-positive rate. The positive predictive value (PPV) of urine trypsinogen 2 was higher than both serum amylase and serum lipase, rendering it a more reliable indicator of the presence of acute pancreatitis when the test yields a positive result. Additionally, urine trypsinogen 2 had a negative predictive value (NPV) higher than serum amylase and was comparable to serum lipase, underscoring its superior ability to indicate the absence of acute pancreatitis when the test is negative.

Table 1: Diagnostic Accuracy of Urine Trypsinogen 2, Serum Amylase, and Serum Lipase

Parameter	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
Urine Trypsinogen 2	88.4	91.7	91.0	88.9
Serum Amylase	70.8	62.5	65.2	68.3
Serum Lipase	75.0	72.9	71.7	75.4

Table 3: Comparison of Diagnostic Accuracy Between Urine Trypsinogen 2 and Serum Lipase

Parameter	Sensitivity Difference (%)	Specificity Difference (%)	PPV Difference (%)	NPV Difference (%)
Urine Trypsinogen 2 vs. Serum Lipase	+13.4	+18.8	+19.3	+13.5

Table 4: Comparative Analysis of Diagnostic Accuracy

Parameter	Urine Trypsinogen 2	Serum Amylase	Serum Lipase
Sensitivity	Higher	Lower	Lower
Specificity	Higher	Lower	Higher
Positive Predictive Value	Higher	Lower	Lower
Negative Predictive Value	Higher	Higher	Higher

The results of this study illuminate the potential of urine trypsinogen 2 as a valuable diagnostic marker for acute pancreatitis. The comparative analysis between urine trypsinogen 2, serum amylase, and serum lipase reveals intriguing findings with significant implications for clinical practice. Urine trypsinogen 2 emerged as the standout performer in our study, boasting superior diagnostic accuracy in multiple aspects. Its higher sensitivity of 88.4% compared to serum amylase (70.8%) and serum lipase (75.0%) signifies its effectiveness in correctly identifying patients with acute pancreatitis. A

higher sensitivity is crucial in acute pancreatitis, where prompt diagnosis can influence patient outcomes significantly [7-10].

Furthermore, urine trypsinogen 2 exhibited an impressive specificity of 91.7%, surpassing serum amylase (62.5%) and approaching serum lipase (72.9%). This finding indicates that urine trypsinogen 2 is less prone to producing false-positive results, a crucial attribute in clinical decision-making. The positive predictive value (PPV) of urine trypsinogen 2 (91.0%) also outshone both serum amylase (65.2%) and serum lipase (71.7%), indicating that when the urine trypsinogen 2 test is positive, there is a higher probability that the patient truly has acute pancreatitis. Similarly, the negative predictive value (NPV) of urine trypsinogen 2 (88.9%) suggested that when the test is negative, there is a lower likelihood that the patient has acute pancreatitis.

Comparative analysis reinforced the advantages of urine trypsinogen 2 over traditional serum markers. When compared to serum amylase, urine trypsinogen 2 exhibited significantly higher sensitivity (+17.6%) and specificity (+29.2%). This suggests that urine trypsinogen 2 is not only better at correctly identifying patients with acute pancreatitis but also more reliable in ruling out the condition when it is absent. Likewise, in comparison to serum lipase, urine trypsinogen 2 demonstrated a sensitivity advantage of +13.4% and a specificity advantage of +18.8%. These differences underscore the superiority of urine trypsinogen 2 as a diagnostic tool for acute pancreatitis.

The collective evidence from our study and comparative analyses aligns with recent research in highlighting the potential of urine trypsinogen 2 as a non-invasive, accurate, and early diagnostic marker for acute pancreatitis. Its robust performance across sensitivity, specificity, PPV, and NPV positions it as a promising addition to the diagnostic armamentarium. In clinical practice, timely and accurate diagnosis of acute pancreatitis is paramount for initiating appropriate treatment strategies promptly. The limitations associated with traditional serum biomarkers, such as serum amylase and lipase, are well-documented. The potential of urine trypsinogen 2 to overcome these limitations and offer superior diagnostic accuracy is an exciting prospect [11-13].

Nevertheless, it is essential to acknowledge certain limitations of our study. Firstly, the single-center design may introduce bias, and the sample size, though representative, could benefit from validation in larger, multicenter studies. Additionally, variations in the timing of radiological investigations, operator expertise, and the etiology of acute pancreatitis could influence the results.

4. Conclusion

In conclusion, our study underscores the promise of urine trypsinogen 2 as a reliable diagnostic marker for acute pancreatitis. Its higher sensitivity, specificity, and PPV compared to traditional serum markers suggest that it may enhance early diagnosis and patient care. Further research and validation in diverse clinical settings are warranted to solidify its role in acute pancreatitis diagnosis and potentially influence clinical guidelines. The pursuit of innovative biomarkers like urine trypsinogen 2 holds the potential to improve patient outcomes in acute pancreatitis, a condition where timely intervention is paramount.

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