https://doi.org/10.48047/AFJBS.6.12.2024.4817-4828



African Journal of Biological Sciences Journalhomepage: http://www.afjbs.com

The Role of Urine Trypsinogen-2 Test in the Diagnosis of Acute Pancreatitis in Emergency Department at Suez Canal University Hospital

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Article History

Volume 6, Issue 12, 2024 Received: 12 May, 2024 Accepted: 27 May, 2024 Published: 27 July, 2024 doi: 10.48047/AFJBS.6.12.2024.4817-4828

ABSTRACT

Background: Acute pancreatitis (AP) is characterized by a prolonged clinical course, pancreatic necrosis, multi-organ failure, and increased morbidity and death in thirty percent of patients who first present with abdominal pain. The aim of the present study was to compare the results of the urine trypsinogen-2 test with those of conventional tests (serum amylase & lipase) in the diagnosis of acute pancreatitis in the Emergency Department. **Patients and methods:** This comparative study was conducted in the emergency room at Suez Canal University Hospital. The study involved 52 patients divided into study group included 26 patients with acute pancreatitis, andcontrol group included 26 patients without acute pancreatitis.

Results: In the present study 19 patients had mild AP (73%), 3 patients had moderate AP (11.6%) and 4 patients had severe AP (15.4%). Study group had significantly higher percentage of patients with bulky pancreas and GB stone. Serum amylase, lipase and Trypsinogen 2 were significantly higher among severe group than mild and moderate AP groups with statistical significant difference (p<0.05). Serum Trypsinogen 2 was significantly higher among study group than control group. Urine Trypsinogen 2 was significantly higher among study group than control group. The sensitivity of urinary trypsinogen 2 test in diagnosing AP was 100% and specificity was 92.3%. Positive predictive value was 92.9% and negative predictive value was 100%.

Conclusion: Urinary trypsinogen-2 test is a promising fast and easy test performed in the effort of diagnosis of acute pancreatitis.

Keywords: Acute Pancreatitis; Atlanta criteria; Urinary trypsinogen-2 test

Introduction

Acute Pancreatitis (AP) is a serious illness that has a 10% overall chance of mortality and a significant morbidity rate. AP is inflammatory conditionaffects a normal organ and is marked by abrupt pain in the abdomen, nausea, and vomiting.⁽¹⁾AP can appear with nonspecific clinical

manifestations, such as nausea, vomiting, and epigastric pain, which may not occur in 10% of cases.⁽²⁾

Pancreatitis is the most common gastrointestinal cause of hospital admissions in the United States, accounting for about 275,000 adult admissions to hospitals. ^(3,4)A patient is diagnosed with AP based on the Atlanta criteria if they have two out of three findings: typical imaging abnormalities, serum lipase and/or amylase levels that are at least three times higher than normal, and stomach pain that may indicate pancreatitis. Acute pancreatitis can range in severity from moderate (less than 1% death; usually goes away in a few days) to severe (up to 30% mortality).Patients with necrotizing pancreatitis, hemorrhagic pancreatitis, and multiorgan dysfunction or failure have the highest mortality rates.⁽⁵⁾

The most accurate noninvasive single technique for determining the severity of a disease at the moment is computed tomography (CT), yet its usefulness is constrained by its high cost, restricted availability, and possible negative impacts. Therefore, a fast and affordable marker that has strong predictive accuracy is needed, even in the early stages of the disease. $^{(6,7)}$

Since the salivary glands produce amylase, which may be normal in patients with recurrent alcoholic pancreatitis, detecting lipase levels is more sensitive and specific than measuring amylase levels.⁽⁸⁾ Levels of lipase or amylase that are more than three times normal are thought to be indicative of pancreatitis.⁽⁹⁾

It has been discovered that within hours of the onset of acute pancreatitis, significant levels of the pancreatic enzyme trypsinogen-2 are released into the urine. This suggests that this enzyme may be useful in the timely detection of acute pancreatitis.⁽¹⁰⁾

While AP can be diagnosed with a number of diagnostic methods, none of them have shown to be highly accurate, quick, or simple to use. It has been demonstrated that urinary trypsinogen-2 is a promising sign for the early detection of AP.⁽¹¹⁾

Pancreatic proteinase trypsinogen occurs in two subtypes: trypsinogen-1 and trypsinogen-2. Zymogens can activate pancreatitis in its early stages, and because of inadequate reabsorption, trypsinogen-2 can be found in greater concentrations in the urine.^(12,13)

Trypsinogen measurement is thought to be helpful in both diagnosing and evaluating AP. Trypsinogen-2 assessed by a fast urine dipstick is a sensitive and specific diagnostic test for acute pancreatitis with a cut-off of 50 ng/mL. The degree of the illness is correlated with the trypsinogen-2 concentration.^(14,15)

So, the aim of the study was to improve the outcome of patients with acute pancreatitis by comparing the results of the urine trypsinogen-2 test with those of conventional tests (serum amylase& lipase) in the diagnosis of acute pancreatitis in the Emergency Department.

Patients and Methods

This is comparative study was carried out at the emergency department of Suez Canal university hospital, Ismailia, Egypt during the period between January 2022 to October 2022. **Study population:**

- **Study group:** All patients with abdominal pain suspected to be acute pancreatitis attending the Emergency Department (ED) of Suez Canal University Hospital and fulfilling our inclusion criteria will be included in the study.
- **Control group:** all patients presented with abdominal pain not suspected to be acute pancreatitis attending the Emergency Department (ED) of Suez Canal University Hospital.

Inclusion criteria:

Patients with abdominal pain suspected to be acute pancreatitis using the Atlanta criteria. Adult (age > 18) and both genders were included.

Exclusion criteria:

Patients known to have chronic pancreatitis, previous pancreatic/gastrointestinal bypass surgery and post traumatic pancreatitis. Patients discharge on their demand, transferred to other hospitals.

Sample size:

The sample size were calculated using the following formula⁽¹⁶⁾:

 $n = \left[\frac{Z_{\alpha/2} + Z_{\beta}}{P_1 - P_2}\right]^2 (p_1 q_1 + p_2 q_2)$

Where: (**n** = sample size; $\mathbf{Z}_{\alpha/2} = 1.96$ (The critical value that divides the central 95% of the Z distribution from the 5% in the tail); $\mathbf{Z}_{\beta} = 0.84$ (The critical value that separates the lower 20% of the Z distribution from the upper 80%); \mathbf{P}_1 = Prevalence/proportion in the study group = proportion of urine trypsinogen positive subjects = 68.6% ⁽¹⁷⁾; \mathbf{P}_2 = Prevalence/proportion in the control group = proportion of urine trypsinogen negative subjects = 31.4% ⁽¹³⁵⁾; $\mathbf{q} = 1$ -p So, by calculation, the sample size is equal.

Ethical Consideration:

An approval of the study was obtained from Suez CanalUniversityAcademic and Ethical Committee. Written informed consent of all the participants was obtained. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Methodology

All patients with abdominal pain at Emergency Department were subjected to full history (from patient or relative) including patient's file number, patient personal data, time of admission and time of discharge to calculate the patient's length of stay, associated co-morbidity, and history of drug intake. Clinical evaluation of the patients were carried out on arrival to Emergency Department regarding:

- 1. Initial assessment of ABCDE (airway, breathing, circulation, dysfunction of the central nervous system, GCS and exposure) and O₂ saturation.
- 2. Assess the condition of the patients either stable or unstable which will determine the needed investigations and plane of management.
- 3. Taking the medical historyand doing physical examination for the patients.
- 4. Investigations include:
- Laboratory investigations as complete blood count, kidney function test, random blood sugar, liver function test, serum amylase, serum lipase and urinary and serum trypsinogen-2 on admission and after 48 hour.
- Radiographic investigations as abdominal Ultrasound or CT as needed.
- 5. Acute pancreatitis is diagnosed based on the Atlanta criteria if a patient has two out of three findings: serum lipase and/or amylase levels that are at least three times normal, characteristic imaging findings, and abdominal pain suggestive of pancreatitis (acute onset of a persistent, severe, epigastric pain that frequently radiates to the back).
- 6. Comparing the results of urinary trypsinogen-2 test with laboratory findings as serum amylase , lipase and radiographic investigations as US or CT.

Comparing the results between the two groups.

Treatment was concern with patients having acute pancreatitis either go under surgical exploration or be under observation.

Fate at Emergency Department whether admitted to intensive care unit (ICU), or admitted to inpatient under observation, or died at emergency room.

Urinary and serum trypsinogen-2

Using the Human Trypsinogen-2, Try-II ELISA Kit. A spectrophotometer is used to measure the colour intensity at 450 nm since the Stop Solution turns the blue colour into yellow. Using the calibration standards included in this Try-II ELISA Kit, one may determine the concentration of Try-II in the sample. A standard curve plotting optical density against Try-II concentration can be created by the operator by assaying the calibration standards concurrently with the samples. Proceeding to compare the O.D. of the samples to the standard curve yields the concentration of Try-II present in the samples.

The serum samples were centrifuged at about 3000×g for 10 minutes after being allowed to clot for 30 minutes. Assay and remove serum right away, or aliquot and keep samples at -20°C or -80°C. Do not freeze-thaw repeatedly. Samples of urine were collected in sterile tubes and centrifuged for 20 minutes at 2000–3000 rpm.

Appendix 1 contains the clinical data for the patient.

Statistical analysis:

Data analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis. According to the type of data qualitative represent as number and percentage, quantitative continues group represent by mean \pm SD. Differences between quantitative independent multiple by ANOVA. P value was set at <0.05 for significant results &<0.001 for high significant result.

Results

The current study showed a statistical insignificant differences in age, gender and comorbidities between two groups as p-value>0.05.It was found that the age of the studied patients ranged from 30-78 years old with majority 15 patients (57.7%) of them are males. The majority of them 16 patients (61.5%) didn't have comorbidities (**Table 1**).

There were statistical insignificant differences in ABCD evaluation, GCS and symptoms (abdominal pain, nausea and vomiting) between two groups as p-value>0.05.It was found that Abdominal pain is the most common presentation in all the patients followed by vomiting in 21(80.8%)and fever in 15 patients (57.7%)in the 26 patients who were diagnosed of pancreatitis(**Table 2**).

There were statistical insignificant differences in Hb, HCT, PLT, WBCs, TLC and RBS as p-value>0.05. Serum amylase was significantly higher among study group than control group (1755.5 \pm 1213.9 vs. 142.1 \pm 33.6, p<0.001). Serum lipase was significantly higher among study group than control group (2147.1 \pm 1475.9 vs. 81.1 \pm 12.3, p<0.001). Serum Trypsinogen 2 was significantly higher among study group than control group (1448.7 \pm 240.7 vs. 58.4 \pm 100.9, p<0.001)(**Table 3**).

Urine Trypsinogen 2 was significantly higher among study group than control group (1352.7 \pm 273.6 vs. 48.4 \pm 15.7 , p<0.001).All patients in study group had positive urinary trypsinogen 2, while only 2 patients had positive urinary trypsinogen 2 in control group with statistical significant difference (p<0.001) (**Table 3**).

There were statistical significant differences in US & CT findings among the study groups (as p<0.001). Study group had significantly higher percentage of patients with bulky pancreas and GB stone (**Table 4**).

According to Revised Atlanta classification; after 48 hour of admission, 19 patients had mild acute pancreatitis (73%), 4 patients had moderate acute pancreatitis (15.4%) and 3 patients had severe acute pancreatitis (11.6%)(**Figure 1**).

Three patients in study group needed ICU admission and 4 patients in control group discharged from ER, while the rest of both groups admitted inpatient recovered with statistical insignificant difference(**Table 5**).

Serum amylase, serum lipase and serum Trypsinogen 2 were significantly higher among severe group than mild and moderate acute pancreatitis groups with statistical significant difference (p<0.05)(**Table 6**).

Variable	Study group	Control group	P value
	(n= 26)	(n= 26)	
Age (years)			
mean± SD	52.5±13.5	54.4±13.2	0.699 ¹
Gender (n, %)			
Male	15(57.7%)	17(65.4%)	
Female	11(42.3%)	9(34.6%)	0.569^2
Comorbidities (n, %)			
No	16(61.5%)	14(53.8%)	
HTN	3(11.5%)	7(26.9%)	0.511³
DM	2(7.7%)	2(7.7%)	
Both HTN & DM	5(19.3%)	3(11.6%)	
СКД	0(0.0%)	0(0.0%)	
CLD	0(0.0%)	0(0.0%)	

Table (1):	Basic characteristics	of the study	grouns	(n=52).
\mathbf{I} and (\mathbf{I}) .	Dasic characteristics	o or the study	groups	(11-34).

1. Student t test; 2. Chi square test; 3. Fisher exact test. *p is significant at <0.05; HTN: hypertension, DM; diabetes mellitus CKD; chronic kidney disease, CLD; chronic liver disease.

Table (2): Clinical evaluation results of the study groups (n=52).

Variable	Study group (n= 26)	Control group (n= 26)	P value
Abdominal pain	26(100%)	26(100%)	1.00^{2}
Nausea and vomiting	21(80.8%)	19(73.1%)	0.108 ¹
Airway			
Patent	26(100%)	26(100%)	1.00^{2}
Obstructed	0(0%)	0(0%)	
Breathing			
Self-breathing	25(96.2%)	26(100%)	
Assisted breathing	1(3.8%)	0(0%)	1.00^{2}
Pulse			
<100 beat\minute	19(73.1%)	25(96.2%)	
>100 beat\minute	7(26.9%)	1(3.8%)	0.050^2
Temperature			
Normal	11(42.3%)	16(61.5%)	
>38 ⁰ C	15(57.7%)	10(38.5%)	0.231^2
Systolic Blood pressure			
>100 mmHg	19(73.1%)	25(96.2%)	0.050^2
<100 mmHg	7(26.9%)	1(3.8%)	
Respiratory rate			
<20\minute	26 (100%)	26(100%)	1.00^{2}
>20\minute	0(0%)	0(0%)	
GCS			
14-15	25(96.2%)	26(100%)	0.817^2
9-13	0(0%)	0(0%)	
_≤8	1(3.8%)	0(0%)	

1. Chi square test used; 2. Fisher exact test used. *p is significant at <0.05; GCS:Glascow coma scale.

Variable	Study group	Control group	P value
	(n = 26)	(n=26)	
Hb _(g\dl)	11.6±1.3	12.04±1.2	0.253 ¹
mean± SD			
HCT (%)	34.1±4.1	34±3.3	0.898 ¹
mean± SD			
$PLT (m m^{3})$			
mean± SD	203.1±23.1	196.7±22.7	0.316 ¹
TLC (m\mm ³)			
mean± SD	16.1±4.1	15.6±2.8	0.608 ¹
WBCs (m\mm ³)			
Normal	14(53.8%)	12(46.2%)	
<4000	0(0%)	0(0%)	0.723^2
>12000	12(46.2%)	14(53.8%)	
RBS			
Normal	23(88.5%)	22(84.7%)	
Low	0(0%)	1(3.8%)	0.899 ²
High	3(11.5%)	3(11.5%)	
Serum creatinine _(IU/I)			-
Normal	20(77%)	18(69.2%)	0.672^2
Elevated	6(23%)	8(30.8%)	
Serum amylase (IU/I)			
mean± SD	1755.5±1213.9	142.1±33.6	<0.001* ¹
Serum lipase (IU/I)			<0.001 ^{*1}
mean± SD	2147.1±1475.9	81.1±12.3	
Serum Trypsinogen 2 (µg/l)			<0.001 ^{*1}
mean± SD	1448.7±240.7	58.4±100.9	
Urinary Trypsinogen 2 _(µg/l)			-
mean± SD	1352.7±273.6	48.4±15.7	<0.001* ²
Positive	26(100%)	2(7.7%)	
Negative	0(0%)	24(92.3%)	

Table (3): Laboratory investigations results of the study groups on admission (n=52).

Student t test; 2. Fisher exact test. *p is significant at <0.05; Hb: hemoglobin, HCT: 1. hematocrit; PLT: platelet; TLC: total leucocytic count; WBCs: white blood cells, RBS; random blood sugar.

Variable	Study group (n= 26)	Control group (n= 26)	P value
Bulky pancreas	6(23.1%)	0(0%)	<0.001* ¹
Bulky pancreas & GB stone	12(46.2%)	0(0%)	
Not visible pancreas & GB stone	5(19.2%)	3(11.5%)	
Not visible pancreas & no GB stone	3(11.5%)	23(88.5%)	

1. Fisher exact test used. *p is significant at <0.05; GB: gall bladder.

There were statistical insignificant differences in US &CT findings among severity groups of acute pancreatitis (p=0.566)(Table 7).

The sensitivity of urinary trypsinogen 2 test in diagnosing acute pancreatitis was 100% and specificity was 92.3%. Positive predictive value was 92.9% and negative predictive value was 100%(Table 8;Figure 2).



Figure (1): Distribution of severity among study group according to Revised Atlanta classification (n=26). Table (5): Eate at the emergency department of the study groups (n-52)

Table (5). Fale at the emergency u	epartment of the s	tudy groups (n=3	<i>4</i>).
Variable	Study group	Control group	P value
	(n= 26)	(n= 26)	
ICU admission Inpatient admission Discharged from FP	3(11.5%) 23(88.5%) 0(0%)	0(0%) 22(84.61%) 4(15.3%)	1.00 ¹
Discharged from ER Died at ER	0(0%)	4(15.5%) 0(0%)	

1. Fisher exact test used. *p is significant at <0.05; ICU: intensive care unit; ER: emergency room.

Table (6): Distribution of study markers in differentiating severity of acute pancreatitis (n=26).

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Variable	Mild	Moderate group	Severe group	P value	
	group	(n=4)	(n= 3)		
	(n= 19)				
Serum amylase (IU/I)					
median(IQR)	1279(618)	2798(1008)	3090(2546)	0.017 * ¹	
Serum lipase _(IU/I)					
median(IQR)	1090(1213)	2832(1542)	3298(1045)	0.041 * ¹	
Serum Trypsinogen 2 (µg/l)				0.027* ¹	
median(IQR)	528(142)	1322(953)	2322(1152)		
Urinary Trypsinogen 2 (µg/l)				_	
median(IQR)	432 (102)	1132(897)	2143(1078)	1.00^{2}	
Positive	19(100%)	4(100%)	3(100%)		
Negative	0(0%)	0(0%)	0(0%)		
1. Kruskal Wallis test used; 2. Fisher exact test used. *p is significant at <0.05					

Kruskal Wallis test used; 2. Fisher exact test used. *p is significant at <0.05

Table (7): Abdominal US & C1 findings of the study groups (n=52).					
Variable	Mild	Moderate	Severe	P value	
	group	group(n=	group(n=		
	(n= 19)	4)	3)		
Bulky pancreas	4(21.1%)	0(0%)	1(33.3%)		
Bulky pancreas & GB stone	7(36.8%)	4(100%)	2(66.7%)	0.423^{1}	
Not visible pancreas & GB	5(26.3%)	0(0%)	0(0%)		
stone	3(15.8%)	0(0%)	0(0%)		
Not visible pancreas & no GB					
stone					

0 /1

1. *Fisher exact test used.* **p is significant at <0.05*; GB: gall bladder.

Table (8): correlation between urine trypsinogen 2 test and pancreatitis (n=52). * = chi square test is significant at the 95 % confidence level (2-tailed).

			Pancreatitis		Total	P-value
			positive	negative		
	positive	Count	26	2	28	
Urine trypsingen 2		%	92.9%	7.1 %	100%	0.001*
ti ypsinogen 2	negative	Count	0	24	24	
		%	0.0 %	100%	100%	
	Total		26	26	52	



Figure (2):ROC curve of urine trypsinogen 2 test in diagnosing acute pancreatitis.

Discussion:

Medical emergencies such as gall bladder stones, penetrating peptic ulcers, mumps infection, abdominal trauma, and post-endoscopic retrograde cholangiopancreatography (ERCP) can all lead to acute pancreatitis. This inflammatory disease is brought on by the activation of pancreatic proenzymes, particularly trypsinogen, inside the pancreas. Normally, this activation takes place in the duodenum and results in pancreatic autodigestion.⁽¹⁸⁾

Due to differing treatments, it is crucial to distinguish between other causes of acute abdomen that could be misinterpreted for acute pancreatitis. The American College of Gastroenterology Guidelines state that while increased serum lipase and amylase are the primary diagnostic factors for acute pancreatitis, distinctive abdominal imaging may be useful in certain situations.⁽¹⁹⁾

Finding a quick and simple laboratory test to diagnose acute pancreatitis is necessary because the conventional tests that use lipase and amylase take a long time and may not be very accurate.⁽²⁰⁾

In addition to the fact that acute pancreatitis is frequently the cause of acute abdomen, we have searched for a simple, quick, and affordable way to detect acute pancreatitis. In recent years, urinary trypsinogen-2 has emerged as a potentially useful test for the quick, simple, and affordable detection of acute pancreatitis. So, the aim of the study was comparing the results of the urine trypsinogen-2 test with those of conventional tests (serum amylase &lipase) in the diagnosis of acute pancreatitis in the Emergency Department.

This comparative study included 52 patients divided into two groups: study group included 26 patients with acute pancreatitis and control group included 26 patients without acute pancreatitis. This study showed that the age of the studied patients ranged from 30-78 years old with mean 52.5±13.5 years with majority 15 patients (57.7%) of them are males. These results agree with the results of a study conducted by **Yasuda et al.**⁽²¹⁾in which the mean age was 58.0 years (range: 25 to 92 years) with majority 50 patients (65.7%) of them are males. Similarly, **Mansab et al.**⁽²²⁾in which themean age of the patients was 38.14 ±7.42 years with majority 44 patients (60.3%) of them are males.

This study showed that majority 16 patients (61.5%) didn't have Comorbidities, while 7 patients (26.9%) had diabetes milletus. These results disagree with the results of a study conducted by **Balineni**⁽²³⁾ included 100 patients participated out of which 75 patients were diagnosed of pancreatitis inwhich 32 patients (42.6%) with pancreatitis had diabetes mellitus.

This study showed that abdominal pain is the most common presentation in all the patients followed by vomiting in 21(80.8%) and fever in 15 patients (57.7%) in the 26 patients who were diagnosed of pancreatitis. These findings agree with **Balineni**⁽²³⁾ who revealed thatabdominal 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.

In this study, there were statistical significant differences in US & CT findings among the study groups (as p<0.001). Study group had significantly higher percentage of patients with bulky pancreas and GB stone. In agreement with **Yasser et al.**⁽²⁴⁾ study included 35 (34 of them completed the study) cases of acute pancreatitis and 34 cases of acute abdomen other than pancreatitis. The study showed that the most common cause of acute pancreatitis was gall stone obstructive pancreatitis.Also,**Sethy et al.**⁽²⁵⁾who investigated 98 patients who were diagnosed with the feature of suggestive pancreatitis. Here, bulky head as well as peri-pancreatic fluid by ultrasound are consider as some of conditions that were associated with the acute pancreatitis.

According to Atlanta classification, in the present study 19 patients had mild acute pancreatitis (73%), 4 patients had moderate acute pancreatitis (15.4%) and 3 patients had severe acute pancreatitis (11.6%). According to BISAP score, in the present study 11 patients had mortality of 0.1%, 9 patients had mortality of 0.4%, two patients had mortality of 1.6%, three patients had mortality of 3.6% and one patient had mortality of 7.4%. The present study results found that, serum amylase, serum lipase and serum Trypsinogen 2 were significantly higher among severe group than mild and moderate acute pancreatitis groups with statistical significant difference (p<0.05).

These results disagree with the results of a study conducted by**Mishra Jet al.**⁽¹⁴⁾who reported that serum lipase concentration was not significantly higher in patients with severe AP (median: 689IU/L, range:256-1072IU/L)than in those with mild disease (median: 710IU/L, range: 30-2060IU/L).

In addition, **Yasuda et al.**⁽²¹⁾who revealed that the median levels of urinary trypsinogen-2 was lower (2.69 mg/dL) in patients with mild pancreatitis, than in those with severe pancreatitis(14.68 mg/dL), The median levels of serum amlyase and lipase were higher (9.28 \times

100 U/L and 8.10 × 100 U/L respectively) in patients with severe pancreatitis than in those with mild pancreatitis(6.28×100 U/L and 6.95×100 U/L respectively), according to CT Grade of the JMHLW criteria.

In the present study, serum Trypsinogen 2 was significantly higher among study group than control group (1448.7±240.7 vs. 58.4±100.9, p<0.001).Urine Trypsinogen 2 was significantly higher among study group than control group (1352.7±273.6 vs. 48.4±15.7, p<0.001). All patients in study group had positive urinary trypsinogen 2, while only 2 patients had positive urinary trypsinogen 2 in control group. This study found that, the sensitivity of urinary trypsinogen 2 test in diagnosing acute pancreatitis was 100% and specificity was 92.3%.Positive predictive value was 92.9% and negative predictive value was 100%. These results agree with **Yasser et al.**⁽²⁴⁾study in which the sensitivity and specificity of urinary trypsinogen-2 (100% for each) in diagnosing acute pancreatitis.

Similarly, **Abraham** ⁽²⁶⁾ study of 124 patients, 69 patients had final diagnosis of acute pancreatitis. The sensitivity and specificity of UT were, respectively, 73.9% (95% CI 61.9% to 83.8%) and 94.6% (95% CI 84.9% to 98.9%).⁽¹⁴⁷⁾

In the same line with **Kumar et al.**⁽¹¹⁾who conducted a prospective study compared 74 consecutive patients with acute abdominal pain. The urinary trypsinogen-2 test was sensitive in 96.1% cases and specific in 82.6% cases. The sensitivity is superior to that of serum lipase (sensitivity-90.2%) and serum amylase (sensitivity-84.3%). The high sensitivity of the urinary trypsinogen-2 test resulted in very high negative predictive value of 90.5%, hence a negative test almost rules out the diagnosis of acute pancreatitis. **Raja et al.**⁽²⁷⁾showed results near to ours regarding specificity of urinary trypsinogen2 in diagnosis of acute pancreatitis. The specificity in their study was 92.42 %.

Similarly, **Nittala et al.**⁽²⁸⁾, **Kamer et al.**⁽²⁹⁾, and **Chen, et al.**⁽¹⁵⁾ reported that sensitivity of urinary trypsinogen-2 dipstick test in diagnosis of acute pancreatitis was (100%, 91%, 89.6% respectively).

In addition,**Balineni**⁽²³⁾ reported that 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%.

Another recent **Simha et al.**⁽³⁰⁾ study included 187 patients, 90 were have acute pancreatitis and Urine trypsinogen dipstick test (UTDT) was positive in 61 (67.7%). In the 97 non pancreatitis cases, UTDT was positive in nine (9.3%). The sensitivity and specificity of UTDT for acute pancreatitis was 67.8% and 90.7%, respectively.

These results don't match the results of a study by **Yasuda et al.**⁽²¹⁾in which the sensitivity and specificity of urinary trypsinogen 2 was low (73.1% and 62.5% respectively).

There are various advantages of the proposed test. Important one being its non-invasive nature. We just ask for a urine sample from the patient. The test can be immediately performed in the casualty/emergency department/outpatients. Department and results will be obtained within 5 minutes. These results are objective, reproducible and hence reliable.

The study limitation was the limited number of patients in both groups which could have an impact on our findings.

CONCLUSION:

Urinary trypsinogen-2 test is a promising fast and easy test performed in the effort of diagnosis of acute pancreatitis.

At the secondary level of prevention which focuses on early diagnosis and prompt treatment, we have a quickness and reliability in the dipstick for urine trypsinogen-2 to identify the problem cases and go for an aggressive management.

Further studies on large number of patients are mandatory to confirm the findings in this study.

Conflict of interest: The authors declare no conflict of interest.

Sources of funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contribution: Authors contributed equally in the study.

References:

- 1- Jensen EH, Borja-Cacho D, Waddah B. Al-Refaie, Selwyn M. Vickers. Exocrine Pancreas. Sabist Textb Surg Biol Basis Mod Surg Pract 19th ed Philadelphia Elsevier Saunders. 2012;1519–22.
- **2-** Choudhury, Purujit. "Acute severe necrotising pancreatitis is really a surgical challenge: an overview." Journal of Evolution of Medical and Dental Sciences, vol. 4, no. 74, 14 Sept. 2015, pp. 12941.
- **3- Peery AF, Dellon ES, Lund J, et al.** Burden of Gastrointestinal Disease in the United States: 2012 Update. Gastroenterology. 2012; 143:1179–87.
- 4- Singla A, Csikesz NG, Simons JP, Li YF, Ng SC, Tseng JF, et al. National hospital volume in acute pancreatitis: analysis of the Nationwide Inpatient Sample 1998-2006. HPB (Oxford) . 2009 Aug;11(5):391–7.
- 5- Tenner S, Baillie J, DeWitt J, Vege SS. American College of Gastroenterology Guideline: Management of Acute Pancreatitis. Am J Gastroenterol. 2013;108(9):1400–15.
- 6- Bollen, Thomas L. Imaging Assessment of Etiology and Severity of Acute Pancreatitis.Pancreapedia: Exocrine Pancreas Knowledge Base.2016:31.
- 7- Bollen TL, Santvoort H C, Besselink M G, Leeuwen MS, Horvath K D, Freeny P. C. and Gooszen H. G. The Atlanta Classification of acute pancreatitis revisited. British Journal of Surgery 2008; 95: 6–21.
- 8- Walkowska, J.; Zielinska, N.; Tubbs, R.S.; Podgórski, M.; Dłubek-Ruxer, J.; Olewnik, L. Diagnosis and Treatment of Acute Pancreatitis. Diagnostics 2022, 12,1974.
- **9- Baillie J.** AGA Institute Medical Position Statement on Acute Pancreatitis. Gastroenterology [Internet]. 2007;132(5):2019–21.
- **10-** Pulkkinen J, Kastarinen H, Kiviniemi V, Jyrkkä J, Juvonen P, Räty S, et al. Statin Use in Patients With Acute Pancreatitis and Symptomatic Gallstone Disease. Pancreas [Internet]. 2014;43(4):638–41.
- 11- Kumar S, Aslam A, Nitish S, Prakash GS. A comparative analysis of urine trypsinogen-2 test strip with serum lipase and serum amylase in diagnosis of acute pancreatitis. Int Surg J. 2021;8(10):2921–6.
- 12- Alkan Kayaoğlu S, Uzun M.Comparison of Bedside Acute Pancreatitis Severity Index Score with Apache II Score in Predicting the Severity of Acute Pancreatitis. KSU Medical Journal 2021;16(2) : 143-148.
- 13- Sáez J, Martínez J, Trigo C, Sánchez-Payá J, Compañy L, Laveda R, et al. Clinical value of rapid urine trypsinogen-2 test strip, urinary trypsinogen activation peptide, and serum and urinary activation peptide of carboxypeptidase B in acute pancreatitis. World J Gastroenterol [Internet]. 2005 Dec 14;11(46):7261–5.
- 14- Mishra J, Mishra B, Firodous A.A comparative analysis of urine trypsinogen-2 test strip with serum lipase in diagnosis of acutepancreatitis in emergency set-up IntSurg J. 2019 Jan;6(1):252-256.
- **15-** Chen YT, Chen CC, Wang SS, Chang FY, Lee SD. Rapid Urinary Trypsinogen-2 Test Strip in the Diagnosis of Acute Pancreatitis. Pancreas [Internet]. 2005;30(3):243–7.
- **16-** Murie JA. Basic and clinical biostatistics. B. Dawson-Saunders and R. G. Trapp. 260 × 180 mm. Pp. 329 + ix. Illustrated. 1990. Norwalk, Connectieut: Appleton and Lange. Br J Surg

[Internet]. 1992;79(7):719.

- 17- Mayumi, T.; Inui, K.; Maetani, I.; Yokoe, M.; Sakamoto, T.; Yoshida, M.; Ko, S.; Hirata, K.; Takada, T. Validity of the urinary trypsinogen-2 test in the diagnosis of acute pancreatitis. Pancreas 2012, 41, 869–875.
- 18- Laharwal AR, Rashid A, Wani AA, Abbass M, Kakroo SM, Chalkoo MA. Akut pankreatit sonucunun tahmininde bilgisayarlı tomografi şiddet indeksinin rolü. Cukurova Med J [Internet]. 2016;41(1):17.
- **19- Hamada S, Masamune A, Kikuta K, Hirota M, Tsuji I, Shimosegawa T.** Nationwide Epidemiological Survey of Acute Pancreatitis in Japan. Pancreas [Internet]. 2014;43(8):1244–8.
- **20-** Hofmeyr S, Meyer C, Warren BL. Serum lipase should be the laboratory test of choice for suspected acute pancreatitis. South African J Surg [Internet]. 2014;52(3):72.
- 21- Yasuda, H.; Kataoka, K.; Takeyama, Y.; Takeda, K.; Ito, T.; Mayumi, T.; Isaji, S.; Mine, T.; Kitagawa, M.; Kiriyama, S.; et al. Usefulness of urinary trypsinogen-2 and trypsinogen activation peptide in acute pancreatitis: A multicenter study in Japan. World J. Gastroenterol. 2019, 25, 107–117.
- 22- Mansab A, Syed M, Adeel , Shahid R, Sughra P, Ahson M, Peer A and Hamid A. Frequency of Raised Urinary Trypsinogen-2 in Acute Pancreatitis.International Journal of Endorsing Health Science Research.March 2017. Volume 5 Issue 1.
- **23- BalineniP.**UrinaryTrypsinogen versus Serum Amylase in Early Diagnosis of Acute Pancreatitis. Int J Case Rep. 2021;Vol.05 No.05.
- 24- Yasser M, Mohamed M, El-Sorogy Md, Hesham A. Predictive Value of Urinary Trypsinogen-2 Dipstick for Early Diagnosis of Acute Pancreatitis in Emergency Medicine. Med J Cairo Univ. 2018;86(September):2427–33.
- 25- Sethy M., Tamang M., Soren D., Subedhi J., Krishna M. Evaluating the efficacy of urinary trypsinogen-2 Dipstick test in diagnosing acute pancreatitis / Panacea Journal of Medical Sciences 2022;12(2):284–288.
- **26-** Abraham P. Point-of-care urine trypsinogen-2 test for diagnosis of acute pancreatitis. J Assoc Physicians India. 2011;59:231–2.
- 27- Raja B, Srinath Kumar T. S., VijuWilbenV.Urinary trypsinogen-2 dipstick test for pointof-care screening of acute pancreatitis. Int J Res Med Sci. 2019 May;7(5):1822-182.
- 28- Nittala R, Basheer O, Sasi M. Acute pancreatitis: a study of urine trypsinogen-2 measurement as a screening test. Int J Res Med Sci [Internet]. 2014;2(3):897.
- **29- Kamer E.** Early diagnosis and prediction of severity in acute pancreatitis using the urine trypsinogen-2 dipstick test: A prospective study. World J Gastroenterol [Internet]. 2007;13(46):6208.
- **30-** Simha A, Saroch A, Pannu AK, Dhibar DP, Sharma N, Singh H, Sharma V. Utility of point-of-care urine trypsinogen dipstick test for diagnosing acute pancreatitis in an emergency unit. Biomark Med.2021;15(14):1271–6.