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Evaluating the efficacy of urinary trypsinogen-2 Dipstick test in diagnosing acute pancreatitis

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ABSTRACT

Background: Acute Pancreatitis (AP) is a very common cause of acute abdomen in emergency department. The disease may vary from mild self-limiting symptoms to multi organ failure and has high mortality rate. Although most of the cases are treated by mild symptomatic treatment but severe cases require intensive monitoring, so early diagnosis and goal directed treatment is very essential to reduce mortality and morbidity of disease.

Aims and Objective: The present study aims to know the efficacy of urinary trypsinogen-2 dipstick test in early diagnosis of acute pancreatitis.

Materials and Methods: The prospective study sample included 98 patients who were presented to emergency department of Maharaja Krishna Chandra Gajapati Medical College & Hospital (MKCGMCH), Berhampur between August 2018 and July 2020 with acute severe pain abdomen suggestive of acute pancreatitis. Urine sample were obtained and results were recorded. Blood sample of all the patients were sent for serum amylase, lipase. Urinary Trypsinogen (UT)-2 dipstick test, based on principle of immunochromatographic, was done at the time of admission and serum amylase and lipase were sent for all patients. Serum Lipase was done through Calorimetric Method and Serum Amylase was done through Coupled Enzymatic Assay Method. Ultrasonography (USG) and Contrast-Enhanced Computed tomography (CECT) abdomen were sent after 4-5 days of admission and final diagnosis was made on the basis of CECT report.

Results: Of 98 patients, 47 cases were final diagnosed to have acute pancreatitis. Sensitivity and specificity of Urinary Trypsinogen (UT)-2 was found to be 91.48% and 94.11% respectively and Positive Predictive Value (PPV) and Negative Predictive Value (NPV) was found to be 93.47% and 92.30% respectively. Sensitivity, specificity, PPV and NPV of Serum Amylase was found to be 76.5%, 74.5%, 74.5% and 74.5% respectively and similarly, sensitivity, specificity, PPV and NPV was found to be 80.85%, 72.5%, 73.1% and 80.4% respectively.

Conclusion: Urinary Trypsinogen (UT)-2 Dipstick test has high sensitivity, specificity, PPV and NPV and therefore can be used reliably in emergency setting for diagnosis and thereby start a goal directed treatment and thus, reduce the mortality and morbidity of the disease.

1. Introduction

Acute Pancreatitis (AP) is defined as the form of disorder that is related to pancreas and it is characterized by edema and when severe, necrosis. It is common and challenging

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disease that can develop local and systemic complication.[1] AP can be categorized as a mild form (interstitial edematous pancreatitis) and severe form (necrotizing pancreatitis). The mild form is categorized by interstitial edema of the gland and minimal organ dysfunction and majority of the patients will have milder form of disease and the mortality is around 1%. Severe form of pancreatitis is seen about 5-10% and is characterized by pancreatic necrosis, a severe systemic inflammatory response and multi-organ failure.[2]

Early diagnosis of pancreatitis is essential because goal directed treatment may improve the outcome of the disease.[3] AP clinical representation is very much alike like many other acute abdomen conditions, the diagnosis only on the basis of symptoms and signs is difficult. An Atlanta classification has revised the standard form of performing diagnosing of AP. Here, for the purpose to examine the acute condition of pancreatitis, assistance is taken from 2 or more criteria. The very first criteria is of analyzing serum as well as lipase >300 IU/L. A second criterion is for examining the abdominal pain. The third criteria is of characteristic finding in Computed tomography (CT) scan.[4] None of the above is very effective in diagnosis of the disease in early stage. Contrast enhanced CT-scan, although it is considered gold standard but it takes at least 72 to 96 hours to show characteristic finding for diagnosis.[5]

Trypsinogen, a precursor of trypsin is required for protein digestion. Premature trypsin activation leads to pancreatic self-digestion. Trypsinogen is a 25-kd pancreatic proteinase. In human pancreatic juice, there are three trypsinogen (TPS) isoenzymes, namely, cationic (TPS-1) and anionic TPS (TPS-2), and a minor isoenzyme (TPS-3).[6] Trypsinogen-2 is secreted in low concentration in normal individual. In the initial phase of the AP disease, it is strongly raised. Further, it remains increased for the different other weeks and days.[7] However, for the purpose to examine the initial phase acute pancreatitis urinary trypsinogen-2 dipstick test is taken into consideration. It is effective as well as simple method of performing testing. Moreover, dipstick test is used for the purpose to assess the concentration in urine trypsinogen-2. The given test can test up to 50 ng/mL.[8] This test is simple and can be taken through strip. If two lines occur in strip then the given thing will indicate positive result. One line will indicate negative result. In this urine can be dropped on strip and it can be read after 5 minutes.[9] After doing this study, we can analyse the efficacy of urinary trypsinogen-2 dipstick test for the purpose to examine the initial phase of AP.

2. Materials and Methods

This prospective study encompasses 98 patients who were admitted to the emergency section with sudden onset of acute severe epigastric radiating to back and other symptoms suggesting of acute pancreatitis was admitted to General Surgery Department, Maharaja Krishna Chandra Gajapati Medical College & Hospital (MKCGMCH) Berhampur for evaluation of Acute Pancreatitis. It is a prospective study conducted between August 2018 and July 2020. Study was approved by the Institutional Ethical Committee of M.K.C.G, Medical College & Hospital on human subject research.Urinary Trypsinogen (UT)-2 dipstick test, based on principle of immunochromatographic, was done at the time of admission and serum amylase and lipase were sent for all patients. Serum Lipase was done through Calorimetric Method and Serum Amylase was done through Coupled Enzymatic Assay Method. Ultrasonography (USG) and Contrast-Enhanced Computed tomography (CECT) was done for all patients at day 4-5 of admission, final diagnosis was made on the basis of CECT report.

2.1. Inclusion criteria

1. The patients who has the features of the acute pancreatitis.
2. An adults who is willing to give their consent.

2.2. Exclusion criteria

1. This includes those individual who do not want to participate in research.
2. All the people who do not want to give their informed consent.
3. The cases that are associated with the pancreatic cancer as well as critical condition of pancreatitis.

2.3. Patient data collection and evaluation

All the selected patients were resuscitated with intravenous fluids and analgesics. In this stage the medical details of the patients is carried out along with the physical analysis and it is recorded in standard proforma. In this dipstick test is used for the purpose to analyse the urine of patients. Serum amylase and serum lipase level estimation tests with other routine test were also simultaneously sent to laboratory for these patients. Data was collected according the predesigned standard Case proforma and compiled and tabulated in Microsoft® Excel and statistical analysis was done using IBM Statistical Packages for Social Science (SPSS) Version- 22.0 and using appropriate formulas.

3. Results

3.1. Following is the result examined from the conducted analysis

There were around 98 patients who were diagnosed with the feature of suggestive pancreatitis. Thus, they were taken in the study. Around (16.32%) were in age group of 21-30 years, 33 patients (33.62%) in 31-40 years, 40 patients (40.82%) in 41-50 years, 8 patients (8.16%) in 51-60 years and 1 patient (1.02%) >60 years. The very first figure entails

about the age distribution of cases. Here, it is assessed that majority of the individual belongs to age category of 31-40 years. The standard deviation for the same is 8.34.

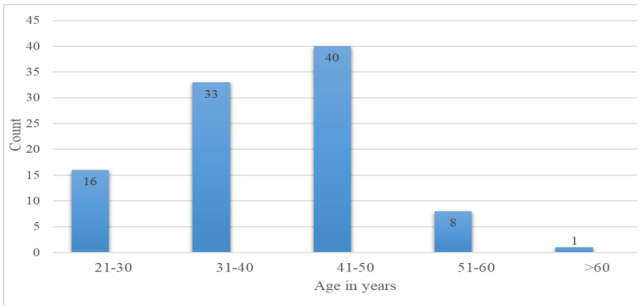

Fig. 1: Age distribution.

Out of 98 patients there were around 11 females as well as 87 were males. However, their ratio was 7.9:1. Figure 2 depicts gender distribution.

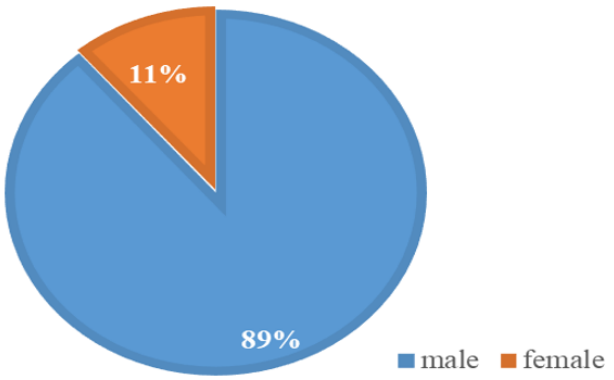

Fig. 2: Gender distribution

There were 47.9% patients who are identified with the condition like acute pancreatitis. But, rest of the individuals were diagnosed with the condition of abdominal pain and it is not because of the pancreatitis. This thing is presented in 3^{rd} figure.

The table that is given below entails regarding the reasons behind the acute pain.

Table 1: Other causes of acute pain abdomen:

Causes	Number	Percentage (%)
Acute gastritis	26	50
Acute calculus Cholecystitis	11	21.56
Acute acalculous Cholecystitis	2	3.9
Hollow viscus perforation	6	11.7
Abdominal malignancy	4	7.8
Liver Abscess	2	3.9
Total	51	100

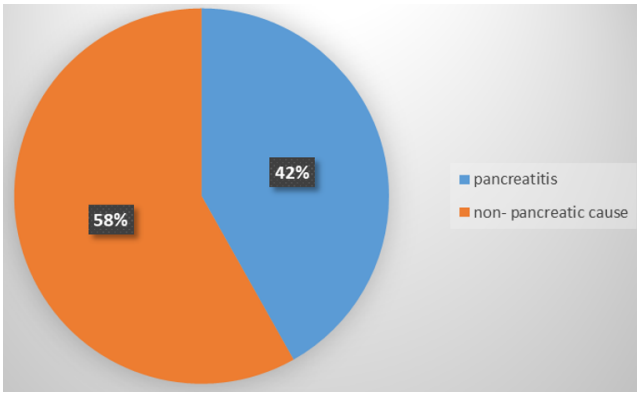

Fig. 3: Cause of acute pain abdomen

3.2. *Serum amylase and lipase*

There is a limit of around to 300IU/L of serum amylase and lipase and it is taken as the cut off for the purpose to consider the case of acute pancreatitis. There were 36 positive results that were true. However, 38 negative results that were consider as true. 11 negative report followed by 13 positive report that was consider as false with sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of 76.5%, 74.5%, 74.5% and 74.5% respectively. Serum lipase gave 38 true positive reports, 37 true negative, 14 false positive report and 9 false negative reports with sensitivity, specificity, PPV and NPV of 80.85%, 72.5%, 73.1% and 80.4% respectively.

Table 2: Analysis of serum amylase:

Serum Amylase (IU/L)	Acute Pancreatitis	Others
>300	36 (True positive)	13 (False positive)
≤300	11 (False negative)	38 (True negative)

Table 3: Analysis of serum lipase:

Serum Lipase (IU/L)	Acute pancreatitis	Others
>300	38 (True positive)	14 (False positive)
≤300	9 (False negative)	37 (Tue negative)

3.3. *Ultrasound of abdomen*

Here, ultrasound was conducted for the purpose to examine acute pain related with acute pancreatitis. Here, bulky head as well as peri-pancreatic fluid are consider as some of conditions that were associated with the acute pancreatitis.

Out of 98 cases, 39%of cases were diagnosed as a case of acute pancreatitis and rest 61% to have other disease or had normal reports as shown in figure 4. Sensitivity, specificity, PPV and NPV was found to be 63.08%, 88.23%, 84.21% and 75% respectively.

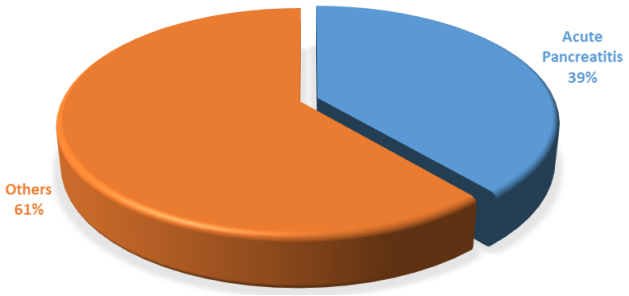

Fig. 4: USG diagnosis of acute pain abdomen

3.4. Urinary trypsinogen-2 dipstick test

Out of 47 cases of acute pancreatitis, UT-2 was positive in 43 cases (true positive), negative in 48 cases (true negative), falsely positive in 3 cases (false positive) and falsely negative in 4 cases (false negative). Hence in our study sensitivity, specificity, PPV and NPV of UT-2 was found to be 91.48%, 94.11%, 93.47% and 92.30% respectively.

Table 4: Analysis of urinary trypsinogen-2 dipstick test

Urinary Trypsinogen-2 Dipstick Test	Acute Pancreatitis	Others
Positive	43 (Tue positive)	3 (False positive)
Negative	4 (False negative)	48 (Tue negative)

4. Discussion

Acute pancreatitis continues to be a diagnostic and therapeutic challenge due to lack of a single pathognomonic laboratory test or a clinical sign. Early aggressive fluid resuscitation is recommended by the clinical practice guidelines and is a long-established corner stone in the initial management of acute pancreatitis.[9] However, for instituting early fluid therapy, the diagnosis of acute pancreatitis needs to be confirmed at the earliest.

In order to digest protein, trypsinogen will be required. Here, self-digestion of pancreatic occurs when premature trypsin will be activated. In this regard, it is examined that the trypsinogen will be around 25-kd pancreatic.[10] There are around three major types of trypsinogen (TPS) isoenzymes examined in the juice of human pancreatic. It consists of minor isoenzyme, cationic and anionic TPS. On the other hand, trypsinogen that is not active will be stored in the cytoplasmic zymogen granules. After this, it is secreted in the duct lumen and then it is sent to the small intestine. In the intestine, the aspect like enterokinase is activated. However, it can be said that the premature activation associated with the trypsinogen to the trypsin will be consider as the major pathophysiologic event. This finally leads to the acute pancreatitis. But, in the normal situation trypsinogen will be stowed in the fluid of pancreatic. Here, very small amount will be entered in the circulation. Here, because of no reason the trypsinogen-1 is higher than trypsinogen-2.[11]

Thus by performing UT-2 dipstick test on the spot at emergency setting we can diagnose a case of acute pancreatitis with very much accuracy.

For the purpose to examine the acute pancreatitis, the laboratory maker takes help from the aspect like serum amylase and lipase. But, it is identified that in the serum amylase the concentration will immediately increases to the peak within several hours of diagnosis. But, there are some that only rose for 3 to 5 days and after sometime it will came back to normal.[8] This, it can be said that both severity of pancreatitis as well as serum amylase are not correlated with each other. Serum lipase though its specific to pancreas but remains elevated for 8-14 days where as UT-2 remains elevated for up to 30 days. CECT though is the most accurate method of diagnosis and assessment of severity of disease but cannot always perform because of its cost, limited availability and contrast related side effects and often fails to demonstrate the pancreatic necrosis in first 72-96 hours of disease.[5]

In the present study with the population of 98 patients, a total of 47 patients were diagnosed to have acute pancreatitis and rest 51 were diagnosed to have other disease such as acute gastritis, acute calculus and acalculous cholecystitis, hollow viscus perforation, abdominal malignancy, liver abscess etc. The sensitivity, specificity, PPV and NPV of UT-2 was high compared to serum amylase and lipase. It was found to be 91.4%, 94.11%, 93.4% and 92.30% respectively which was comparable to Kemppainenen et al. (1997)[3] where sensitivity, specificity, PPV and NPV was found to be 94%, 95%, 68% and 99% respectively.

Study conducted by Abraham et al. (2011)[12] they found that the sensitivity, specificity, PPV and NPV of UT-2 was found to be 73.9%, 94.6%, 94.4% and 73.3% respectively. Similarly, in the study conducted by Anandh et al. (2016)[13] they found that the sensitivity, specificity, PPV and NPV was found to be 90%, 84.5%, 80% and 93.5% respectively. Jang et al. (2007)[8] found sensitivity and specificity of UT 100% and 96% respectively. Similarly, Nittala et al. (2017)[14] found sensitivity and specificity of UT as 100% and 85.71% respectively. In the study conducted by Niveditha et al. (2016)[15] they found that Sensitivity and Specificity of Urine Trypsinogen-2 were found to be 97.2% and 93.75% respectively.

5. Conclusion

It can be concluded that urinary trypsinogen-2 dipstick test is consider as simple. It is very cheap as well as can be conducted easily with the help of strip. By using this method, the problem can be detected at the initial phase and thus individual can get timely treatment. This will reduce the rate of mortality related with given disease.

Table 5: Comparison of diagnostic accuracy of different tests

Parameters	Sensitivity	Specificity	PPV	NPV
Serum Amylase	76.5%	74.5%	74.5%	74.5%
Serum Lipase	80.85%	72.5%	73.1%	80.4%
USG	63.08%	88.23%	84.21%	75%
Urinary Trypsinogen-2	91.48%	94.11%	93.47%	92.30%

Table 6:

Indices	Kemppainenen et al.[3]	Jang et al.[8]	Nittala et al.[14]	Niveditha et al.[15]	Abraham et al.[12]	Anandh et al.[13]	Present study
Sensitivity	94%	100%	100%	97.2%	73.9%	90%	91.4%
Specificity	95%	96%	85.71%	93.75%	94.6%	84%	94.11%
PPV	68%	-	-	-	94.4%	80%	93.4%
NPV	99%	-	-	-	73.3%	92.5%	92.30%

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7. Authors Contribution

All the authors put equal contribution in collecting and analysing data and writing the final paper.

8. Source of Funding

No financial support was received for the work within this manuscript.

9. Conflict of Interest

The authors declare they have no conflict of interest.

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