International Surgery Journal
*Satish KR et al. Int Surg J. 2021 Oct;8(10):2921-2926*
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: https://dx.doi.org/ 10.18203/2349-2902.isj20213969

**Original Research Article**

# A comparative analysis of urine trypsinogen-2 test strip with serum lipase and serum amylase in diagnosis of acute pancreatitis

**Satish Kumar R., Ashik Aslam*, Nitish S., Gagan S. Prakash**

Department of General Surgery, KIMS, Bengaluru, Karnataka, India

**Received:** 21 June 2021
**Revised:** 29 August 2021
**Accepted:** 01 September 2021

***Correspondence:**
Dr. Ashik Aslam,
E-mail: ashikaslam999@gmail.com



## ABSTRACT

**Background:** Acute pancreatitis possess difficulty in diagnosis in its emergency presentation. Hence segregation of this disease from other specific or non-specific causes of acute abdomen is important. In majority of the suspected cases, the urinary trypsinogen-2 test strip can be used to detect this disease, especially in emergency set-up. The aim and objective of the study was to evaluate the sensitivity and specificity of urinary trypsinogen-2 and to compare it with that of the standard biochemical markers of acute pancreatitis serum amylase and serum lipase.
**Methods:** All patients who presented to the surgical emergency with symptoms and signs suspicious of acute pancreatitis were included in the study, rapid urinary trypsinogen-2 test was done immediately at the bed side, serum amylase and lipase was send for all cases along with routine investigations.
**Results:** 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.
**Conclusions:** In patients with acute abdominal pain with suspicion of acute pancreatitis seen in emergency department, a negative dipstick for urinary trypsinogen-2 rules out acute pancreatitis with high degree of probability and therefore appears to be more suitable for screening of acute pancreatitis.

**Keywords:** Acute pancreatitis, Acute abdomen, Serum amylase, Serum lipase, Urine trypsinogen-2

## INTRODUCTION

Acute pancreatitis is a common cause of acute abdomen presenting to the emergency. It can mimic most cases of acute abdomen clinically like cholecystitis, perforated duodenal ulcer etc. Acute pancreatitis accounts for 5% of patients presenting with abdominal pain to surgical emergency.

Although most patients with pancreatitis have a mild disease that resolves spontaneously, 5-10% percent present with severe disease, which is characterized by a protracted clinical course, pancreatic necrosis and MODS, and is associated with increased morbidity and mortality. Early diagnosis of pancreatitis is essential, because therapy may improve outcome. Serum amylase and serum lipase have been the standard serum markers used for the diagnosis of acute pancreatitis. In AP, serum amylase levels increase within 2-12 hours and return to normal in 3-5 days and serum lipase rises within 48hours and remains elevated longer than serum amylase (8-14 days).[1] Measurement of amylase or lipase is the principal laboratory method for diagnosing acute pancreatitis, but the sensitivity and specificity of the assays for these enzymes are considered unsatisfactory.[2] Both the serum markers have their own advantages and disadvantages based on different clinical setting as elaborated later. Trypsinogen is 25 kD pancreatic proteinase with the two main isoenzymes, trypsinogen-1 (cationic) and trypsingen-2 (anionic).[3,4] Acute pancreatitis is most commonly

triggered because of extra pancreatic origin but irrespective of the etiology, premature activation of trypsin within the pancreas is considered a common feature at the acinar cell level.[5,6] In acute pancreatitis trypsinogen-2 levels increase rapidly both in serum and urine.[4,7,8] Thus, trypsinogen-2 and also the trypsin-2-a1-antitrypsin complex are accurate diagnostic markers of AP and show a marked correlation with the disease severity.[9] Contrast enhanced computed tomography (CECT) is the most accurate method for diagnosing and assessing the severity of acute pancreatitis. Because of its cost and limited availability CT scan cannot be done in all cases. CT scan is done only in specific indications in acute pancreatitis especially when there is a diagnostic dilemma or when local complications are expected. CECT is not usually required for diagnosis in the emergency room or on admission to the hospital.[10]

## METHODS

Prospective cohort study of a convenience sample of patients with symptoms consistent with acute pancreatitis presenting to surgical emergency.

Sample size calculated using the formula,

$$N = \frac{Z^2 PQ}{d^2}$$

N= desired sample, Z= standard deviation, P= prevalence, Q= 1-P, d= degree of accuracy.

### *Inclusion criteria*

Patients who were 18 years and above and all patients with clinical features consistent with the diagnosis of acute pancreatitis reporting to emergency department were included in the study.

### *Exclusion criteria*

Patients with anuric patients and with history of trauma were excluded.

Institutional ethical committee clearance was obtained for the study in accordance with the ICMR guidelines for clinical research.

74 patients with symptoms consistent with acute pancreatitis presenting to surgical emergency at KIMS Hospital and Research centre between December 2017 and April 2018 were investigated prospectively. In patients who presented to the emergency with symptoms characteristic of acute, i.e.; pain in upper abdomen which is sudden in onset, severe in nature and radiates to back, urine sample was obtained at the bed side and urine trypsinogen dip stick test was done, routine blood investigations were sent and patients were admitted. Patients who had hypotension, respiratory distress, oliguria, tachycardia were admitted in SICU/ICU for close monitoring and fluid management. Serum amylase and serum lipase was sent for all cases. Ultrasound abdomen was done in all cases as routine work up of acute abdomen. CT scan was only done when indicated in specific cases like- (a) if there is diagnostic uncertainty. In patients with severe acute pancreatitis, to distinguish interstitial from necrotising pancreatitis. In the first 72 hours, CT may underestimate the extent of necrosis. The severity of pancreatitis detected on CT may be staged according to the Balthazar criteria; (b) in patients with organ failure, signs of sepsis or progressive clinical deterioration; and (c) then a localised complication is suspected, such as fluid collection, pseudocyst or a pseudoaneurysm. A diagnosis of acute pancreatitis was arrived at if two of the three criteria under Revised Atlanta classification, definition of acute pancreatitis was present. The diagnosis of acute pancreatitis requires two of the following three features: (a) abdominal pain consistent with acute pancreatitis (acute onset of a persistent, severe, epigastric pain often radiating to the back); (b) serum lipase activity (or amylase activity) at least three times greater than the upper limit of normal; and (c) characteristic findings of acute pancreatitis on contrast-enhanced computed tomography (CECT) and less commonly magnetic resonance imaging (MRI) or transabdominal ultrasonography.

The serum amylase and lipase are considered to be positive only if it is elevated more than three times the reference range for the particular assay as- (a) serum amylase=05-100 IU/dl; and (b) serum lipase <38 IU/dl. Cases which did not meet the criteria for acute pancreatitis other diagnoses was considered and relevant investigations were done including upper GI endoscopy on the following day to diagnose acid peptic disease. Therefore, a need for a simple rapid and reliable test for acute pancreatits is required which can be used in the various different severities and etiologies of acute pancreatitis encountered commonly in the emergency. Diagnosing acute pancreatitis may help rule out other causes of acute abdomen that may require emergency operative procedure like sealed off perforation. It will also help in transferring the patient to an ICU set up for adequate monitoring and management, or referral to a specialist centre.

### *Statistical analysis*

In the qualitative evaluation of urinary trypsinogen-2 dipstick test for the diagnosis of acute pancreatitis, the sensitivity and specificity with 95% confidence interval were calculated. In the quantitative measurement of urinary trypsinogen-2 was plotted in Receiver operating characteristic (ROC) curve and Area under the curve (AUC) calculated by logistic regression analysis. Significance was defined by a p value of <0.05.

## RESULTS

Using the Table 1, the sensitivity, specificity, positive predictive value, negative predictive value and positive likelihood ratios were calculated and have been

summarized in the Table 2. On evaluating the three tests serum amylase, lipase and urinary trypsinogen-2 to detect acute pancreatitis, for sensitivity (84.3%, 90.2% and 96.1%), specificity (78.3%, 95.7% and 82.6%), PPV (89.6%, 97.9% and 92.5%), NPV (69.2%, 81.5% and 90.5%) and positive likelihood ratio (3.9, 20.8 and 5.5) respectively. Urinary trypsinogen-2 test is highly sensitive test and serum lipase is the highly specific test to detect acute pancreatitis among the three.

**Table 1: Contingency table used to calculate diagnostic accuracy of the three tests to detect acute pancreatitis.**

| Tests | Acute pancreatitis | | |
|---|---|---|---|
| | Present (n=51) | Absent (n=23) | Total |
| **Serum amylase test** | | | |
| Positive | 43 | 05 | **48** |
| Negative | 08 | 18 | **26** |
| **Serum lipase test** | | | |
| Positive | 46 | 01 | **47** |
| Negative | 05 | 22 | **27** |
| **Urinary trypsinogen- 2 test** | | | |
| Positive | 49 | 04 | **53** |
| Negative | 02 | 19 | **21** |

**Table 2: Comparison of diagnostic accuracy of urinary trypsinogen-2 test and those of serum amylase and serum lipase to detect acute pancreatitis.**

| Tests | Sensitivity | | Specificity | | PPV | | NPV | | Positive likelihood ratio (+ve LR) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | % | 95% CI | % | 95% CI | % | 95% CI | % | 95% CI | % | 95% CI |
| **Urinary trypsinogen-2 test** | 96.1 | 86.5-99.5 | 82.6 | 61.2-95.1 | 92.5 | 83.4-96.8 | 90.5 | 70.7-97.4 | 5.5 | 2.3-13.5 |
| **Serum amylase¥** | 84.3 | 71.4-92.9 | 78.3 | 56.3-92.5 | 89.6 | 79.7-94.9 | 69.2 | 53.5-81.5 | 3.9 | 1.8-8.5 |
| **Serum lipase¥** | 90.2 | 78.6-96.7 | 95.7 | 78.1-99.9 | 97.9 | 87.1-99.7 | 81.5 | 65.6-91.0 | 20.8 | 3.0-141.4 |

Note: ¥-cut off >3 times the upper limit was considered positive (serum amylase- 5-100 U/l and serum lipase 38 U/l.

Figure 1 shows the discriminatory ability of serum amylase and lipase in detecting acute pancreatitis. The areas under the curves for serum amylase and serum lipase of 0.87 (95% CI: 0.77-0.97; p<0.05) and 0.95 (95% CI: 0.89-1.00; p<0.05) respectively which were significant indicate that serum lipase has an excellent discriminatory ability and serum amylase has good discriminatory ability. Thus, on comparing, the areas, serum lipase with cut off more than three times the upper limit is a better predictor of acute pancreatitis compared to the serum amylase with cut off more than three times the upper limit. On plotting ROC curve for serum amylase and serum lipase values (Figure 2) in predicting positive urinary trypsinogen 2 test, AUCs for serum lipase and serum amylase were 0.92 (95% CI: 0.86-0.98, p<0.001) and 0.90 (95% CI: 0.81-0.99, p<0.001) respectively. The values of AUCs imply that both serum lipase and amylase has significant excellent accuracy in predicting positive urinary trypsinogen-2 test. Comparatively, serum lipase is the better one.

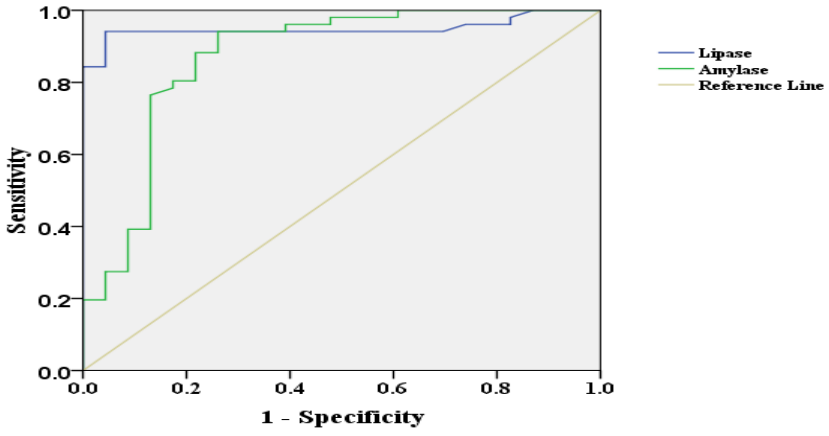


**Figure 1: ROC curve for serum amylase and lipase to detect acute pancreatitis.**

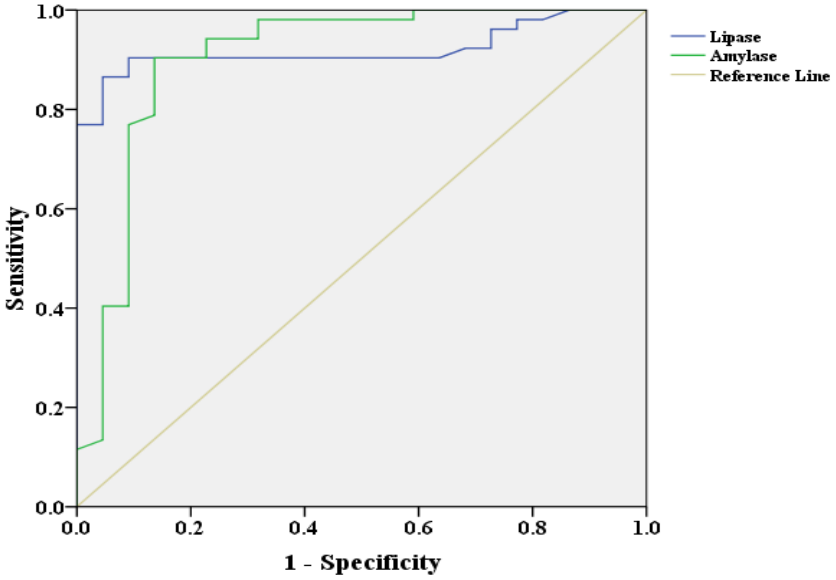


**Figure 2: ROC curve for serum lipase and amylase in predicting positive urinary trypsinogen 2 test.**

## DISCUSSION

Acute pancreatitis can mimic most causes of the acute abdomen and should seldom be discounted in differential diagnosis of acute abdomen, as part of the study we used the urinary trypsinogen dip stick in the emergency at the bed side and compared the results obtained with that of the standard serum biochemical markers amylase and lipase and compared the results.[10]

Majority of the patients in the study were male- 10 vs 65 (Figure 3). Most the patients in the study group were between the ages of 27 to 45 years of age (Figure 4).

Out of the 75 cases in the study group who 51 were confirmed to have acute pancreatitis as per Revised Atlanta classification. The other diagnoses included acid peptic disease, Calculous cholecystitis, hollow viscus perforation and subacute intestinal obstruction (Figure 5). The major etiology of acute pancreatits among the men was alcoholic pancreatitis where as in females the most common cause was biliary pancreatitis one case each of drug induced pancreatitis and hypertriglyceridemia was seen (Figure 6).

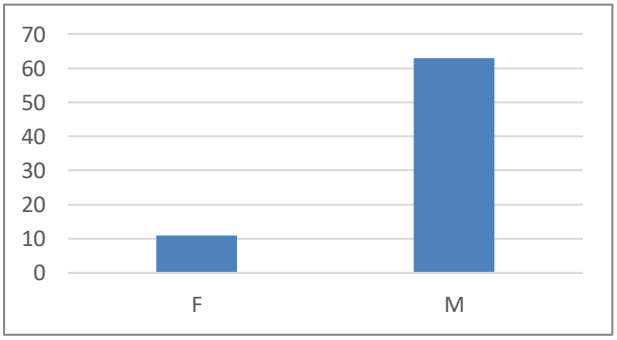


**Figure 3: Sex distribution.**

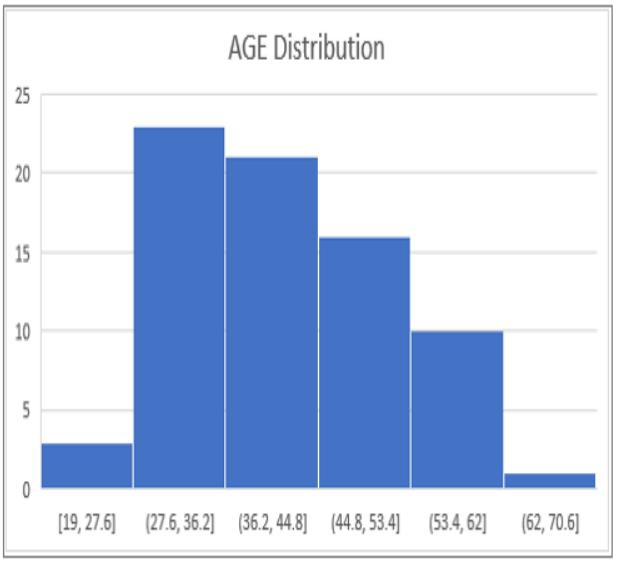


**Figure 4: Age distribution.**

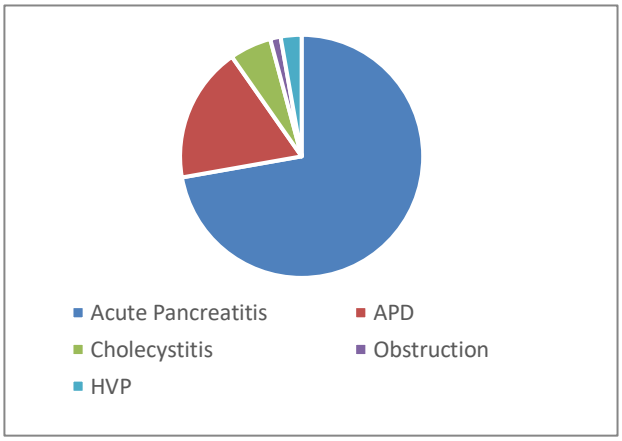


**Figure 5: Diagnosis.**

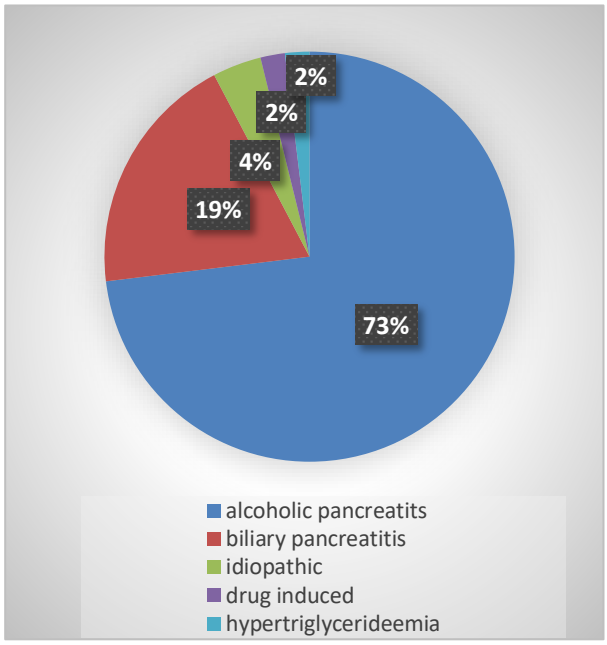


**Figure 6: Etiology.**

**Table 3: Acute pancreatitis sensitivity test.**

| Tests | Sensitivity | |
|---|---|---|
| | % | 95% CI |
| **Urinary trypsinogen-2 test** | 96.1 | 86.5-99.5 |
| **Serum amylase¥** | 84.3 | 71.4-92.9 |
| **Serum lipase¥** | 90.2 | 78.6-96.7 |

Note: ¥-cut off >3 times the upper limit was considered positive (serum amylase- 5-100 U/l and serum lipase 38 U/l.

Out of 51 patients diagnosed with acute pancreatits, 49 patients had a positive urine trypsinogen test. It was negative in 2 cases giving a sensitivity of 96.1% (86.5-99.5). The sensitivity of serum lipase which is the standard biochemical test for acute pancreatitis 90.2 (78.6-96.7). The sensitivity is the ability of a test to correctly identify those with the disease hence the sensitivity of urine trypsinogen is marginally better than that of lipase for diagnosis of acute pancreatitis.

Two false positive cases were seen in the study, one was a case of duodenal perforation in which the test was positive. In one case of calculous cholecystitis the test was positive, trypsinogen is also known to be expressed in the biliary tree and in the peribiliary tissue, this could explain the false positive results. Acute calculous cholecystitis is an important differential in cases of suspected acute pancreatitis.

Serum amylase is known to be normal in patients who present late i.e.; after a few days of onset of pain abdomen and it is also more commonly negative in cases of alcoholic pancreatitis with the probability of a negative test increasing with each recurrent attack. The same was seen in the study, serum amylase was negative in cases of recurrent alcoholic pancreatitis, which was confirmed by CT scan. This drawback was not found with urine trypsinogen test.

In two cases of acute on chronic pancreatitis, both serum amylase and serum lipase were found to be negative, but due to high clinical suspicion of pancreatitis CT scan was done and acute on chronic pancreatitis was confirmed. Both these patients were middle aged males who had history of recurrent pancreatitis attacks of alcoholic etiolgy. Serum amylase and serum lipase was found to be elevated to much higher values in cases of biliary pancreatitis as compared to alcoholic pancreatitis. Five patients out of the 51 (10%) cases of acute pancreatitis were classified as severe acute pancreatitis due to presence of organ failure lasting greater than 48 hours. In all these cases the urine trypsinogen was positive, hence it was able to identify all cases of severe acute pancreatitis.

Urine trypsinogen-2 test offers to be inexpensive, faster, simpler and universally utilizable. Early initiation of fluid resuscitation based on UTT report has the potential to improve outcomes in acute pancreatitis patients. The limitations of the study were its single-centre design and small number of patients with acute pancreatitis. Being an observational study, the investigations being compared in the study were not controlled with respect to their timing and imaging studies were not conducted in all patients.

## CONCLUSION

The rapid urinary trypsinogen-2 test is a reliable biochemical test for diagnosis of acute pancreatitis. The sensitivity of the test is better than that of serum lipase and serum amylase, with added advantage of being a bed side test and results being obtained within 5 min.

The test also has a very high negative predictive value; hence a negative test almost rules out the diagnosis of acute pancreatitis. The test was also able to identify all cases of severe acute pancreatitis, which helps with early intensive care management of referral to a higher centre. Rapid urine trypsinogen test is more sensitive especially in cases of recurrent alcoholic pancreatitis and in patients who present late after the onset of pain abdomen, in which case serum amylase and lipase may be negative. A multi-centric study with a larger sample size is needed to confirm the results.

## ACKNOWLEDGEMENTS

Authors would like to thanks Dr. V. T. Venkatesha, Dean and Principal KIMS Hospital for giving us an opportunity for conducting the study for his valuable support during study. We would also like to thank staff and to all patients who participated in this study.

*Funding: No funding sources*
*Conflict of interest: None declared*
*Ethical approval: The study was approved by the Institutional Ethics Committee*

## REFERENCES


1. Tietz NW, Shuey DF. Lipase in serum--the elusive enzyme: an overview. Clin Chem. 1993;39(5):746-56.
2. Wong EC, Butch AW, Rosenblum JL. The clinical chemistry laboratory and acute pancreatitis. Clin Chem. 1993;39(2):234-43.
3. Robinson LA, Kim WJ, White TT, Hadorn B. Trypsin in human pancreatic juice--their distributions as found in 34 specimens. Two human pancreatic trypsinogens. Scand J Gastroenterol. 1972;7(1):43-5.
4. Hedstrom J, Sainio V, Kemppainen E, Puolakkainen P, Haapiainen R, Kivilaakso E, et al. Urine trypsinogen-2 as marker of acute pancreatitis. Clin Chem. 1996;42(5):685-90.
5. Steer ML. Frank Brooks memorial Lecture: The early intraacinar cell events which occur during acute pancreatitis. Pancreas. 1998;17(1):31-7.
6. Figarella C, Amouric M, Guy CO. Enzyme activation and liberation: intracellular/extracellular events. Acute pancreatitis. Berlin: Springer; 1987: 53-60.
7. Hedstrom J, Korvuo A, Kenkimaki P, Tikanoja S, Haapiainen R, Kivilaakso E, et al. Urinary trypsinogen-2 test strip for acute pancreatitis. Lancet. 1996;347(9003):729-30.
8. Kemppainen EA, Hedstrom JI, Puolakkainen PA, Sainio VS, Haapiainen RK, Perhoniemi V, et al. Rapid measurement of urinary trypsinogen-2 as a screening test for acute pancreatitis. N Engl J Med. 1997;336(25):1788-93.
9. Hedstrom J, Sainio V, Kemppainen E, Haapiainen R, Kivilaakso E, Schroder T, et al. Serum complex of trypsin 2 and alpha 1 antitrypsin as diagnostic and prognostic marker of acute pancreatitis: clinical study in consecutive patients. BMJ. 1996;313(7053):333-7.
10. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis--2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013;62(1):102-11.
11. Norman W, Connel P, McCaskie A. Bailey and Love's short practice of surgery. 27th ed. India: CRC Press; 2018: 1223.


**Cite this article as:** Kumar SR, 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;8:2921-6.