www.jmscr.igmpublication.org
Impact Factor 5.84
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v5i3.10

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Article

Comparative Study on Sensitivity of Serum and Urinary Amylase in the Diagnosis of Acute Pancreatitis

Authors
Dr Jagdish Gupta[1], Dr Archit Gupta[2], Dr Karan Pao[3], Dr Arun Gupta[4], Dr Bhavesh Devkaran[5], Dr Arun Chauhan[6], Dr Amritanshu Sharma[7]
[1,6]Assistant Professor, Dept of General Surgery, Indira Gandhi Medical College, Shimla, Himachal Pradesh
[2]Post graduate student, Dept of General Surgery, Indira Gandhi Medical College, Shimla, Himachal Pradesh
[3]Department of General Surgery, AIIMS, New Delhi
[4,5]Professor, Department of General Surgery, Indira Gandhi Medical College, Shimla, Himachal Pradesh
[7]Senior Resident, Dept of General Surgery, Indira Gandhi Medical College,Shimla, Himachal Pradesh
Corresponding Author
Dr. Archit Gupta
Post graduate student, Dept of General Surgery, Indira Gandhi Medical College, Shimla, Himachal Pradesh.
Email: *archit9th@gmail.com, Phone no: 9805189895*

Abstract
Diagnosis of acute pancreatitis remains a challenge even in 21st century.
Aims & Objectives: *We conducted this study to determine the levels of serum and urinary amylase in patients with acute pancreatitis and compare their sensitivity.*
Material and Methods: *The present study was conducted from 30th June 2013 to 31st May 2014, in the departments of General Surgery and Biochemistry of our college. A total of 51 patients were included in the study. Patients were divided into mild, moderate and severe pancreatitis according to their Contrast enhanced CT findings. Values of serum and urinary amylase were then compared according to severity of disease and day of presentation.*
Results: *The sensitivity of serum amylase was 35%, 50% and 75% in mild, moderate and severe acute pancreatitis respectively, while the sensitivity of urinary amylase was 52.94%, 77.27% and 75% in mild, moderate and severe acute pancreatitis respectively. For patients presenting on the first 3 days, the sensitivity of serum amylase was 54.28% and that of urinary amylase was 62.85%. For patients who had presented on 4th to 8th day after the onset of pain, the sensitivity of serum and urinary amylase were 45% and 81.81% respectively. For patients presenting after 9 days of onset of pain, the sensitivity of urinary amylase was high at 80% and that of serum amylase was 40%.*
Conclusion: *Urinary amylase is a convenient and a more sensitive test for diagnosis of acute pancreatitis than serum amylase.*

Introduction

Acute pancreatitis is an acute condition presenting with severe abdominal pain and is usually associated with raised pancreatic enzyme levels in the blood or urine or both, as a result of inflammatory disease of the pancreas. Sir Berkeley Moynihan described pancreatitis in 1925 as "the most terrible of all calamities that occur in

connection with the abdominal viscera".[1] Acute pancreatitis remains a clinical challenge in spite of the advances made in the modern medical field. It is associated with a wide range of clinical presentations. Serum Amylase has been traditionally used as an enzyme which "makes or breaks" the diagnosis of acute pancreatitis. Yet in 19% of acute pancreatitis patients, serum amylase was found to be normal. Serum amylase has a short half-life of around 10 to 12 hours and returns to normal levels in 3 to 5 days.[2] This makes it quite inconsistent in the diagnosis of acute pancreatitis, especially in patients with mild form of the disease and those who present late. Amylase is excreted in urine, up to several days after the serum amylase levels have normalised.[3] Thus it was proposed that urinary excretion of amylase might be a more reliable and sensitive indicator of acute pancreatitis. The present study was undertaken to compare the sensitivity of urinary amylase and serum amylase in the diagnosis of acute pancreatitis and to study the relationship of serum amylase with that of urinary amylase.

Aims and Objectives

We conducted this study to determine the levels of serum and urinary amylase in patients with acute pancreatitis and compare their sensitivity.

Material and Methods

The present study was conducted from 30th June 2013 to 31st May 2014, in the departments of General Surgery and Biochemistry of our college. A total of 51 patients were included in the study. All the patients and/or their attendants were informed about the on-going study and an informed consent was taken.

All patients presenting with at least two of the following four features were included in the study: acute onset pain abdomen and tenderness in the upper abdomen, elevated levels of serum amylase in the blood, (at least three times the upper reference limit), elevated levels of urinary amylase (at least three times the upper reference limit), findings suggestive of acute pancreatitis on ultrasonography or contrast enhanced CT abdomen or MRCP. Patients with deranged RFTs, either as a result of acute renal injury or chronic renal failure were excluded.

Patients were divided into mild, moderate and severe pancreatitis according to their Contrast enhanced CT findings.

For measurement of serum amylase 3ml of clotted venous sample was collected in a sterile vial and activity was measured using the Beckman Coulter AU 680 chemistry system. The substrate 2-chloro-4-nitrophenyl-α-C-maltotrioside (CNPG3) is acted upon by the α-amylase to release 2-chloro-4-nitrophenol (CNP) and the resulting increase in light absorbance per minute is measured spectrophotometrically at 410-480nm. This increase in absorbance per minute is directly related to the α-amylase activity in the serum sample. Normal value was taken to be 29-110 U/L

For urinary amylase10ml of randomly voided urine sample was collected in a sterile plastic container. The activity of urine amylase was measured using Beckman Coulter AU 680 chemistry system. The substrate 2-chloro-4-nitrophenyl-α-D-maltotrioside reacts directly with α-amylase to form 2-chloro-4-nitrophenyl and the resulting increase in absorbance per minute is directly related to the amylase activity in the urine sample. This resulting increases in absorbance is measured The normal value was taken to be 24-400 U/L.

Student's t test for independent data and ANOVA was used to compare the Sensitivity of serum amylase and urinary amylase in different severity group

Observations

The age of patients ranged between 21 to 82 years of age. The mean age was 50.45yrs. Maximum numbers of patients were seen in the age group of 40 – 60yrs. Mild pancreatitis was seen in 17 patients, 22 had moderate pancreatitis and 12 had severe pancreatitis. The mean ages in patients with mild, moderate and severe acute pancreatitis were 51.53yrs, 48.09yrs and 53.25yrs respectively.

Table 1: Distribution of patients according to age

AGE GROUP	ACUTE PANCREATITIS			TOTAL
	MILD	MODERATE	SEVERE	
20- 40YRS	3	4	4	11
40- 60 YRS	8	14	6	28
≥ 60YRS	6	4	2	12
TOTAL	17	22	12	51
MEAN ± 2SD	51.53yrs±25.88yrs	48.09yrs±23.02yrs	53.25yrs±29.47yrs	50.45yrs±24.76yrs

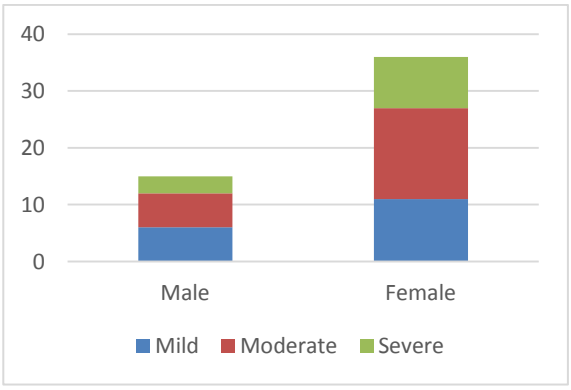

Figure 1: Severity of disease in males and females

Of the total 51 patients, 15 were males and 36 females. 6 males and 11 females had mild pancreatitis, while 6 males and 16 females had moderate pancreatitis and 3 males and 9 females had severe pancreatitis. The male to female ratio was 1:2.4. There was no significant difference in the incidence of acute pancreatitis in both the sexes (P= 0.505).

The serum amylase levels were seen in all 51 patients. Out of these, 10 patients had levels less than 110 u/dl, 15 patients had levels between 110u/dl and 330u/dl and 26 patients had values above 330u/dl. The mean was 938.96u/dl with standard deviation of 259.1u/dl. The p value was 0.019 and was significant.

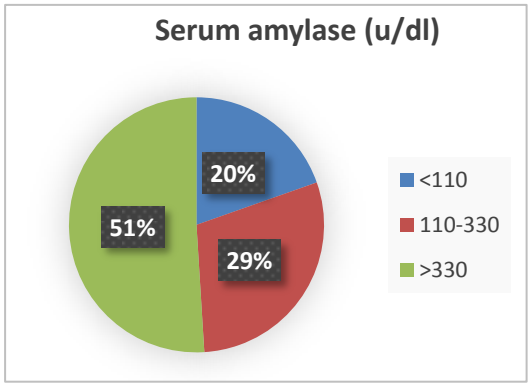

Figure 2: Levels of serum amylase as seen in our patients

In the mild pancreatitis group, serum amylase levels of less than 110u/dl was seen in 2 patients, while values of serum amylase between 110u/dl to 330u/dl were seen in 9 patients and 6 patients had levels above 330u/dl. The mean was 332.941u/dl with standard deviation of 71.85u/dl. In the moderate pancreatitis group, 7 patients had values less than 110u/dl. 4 patients had values between 110u/dl and 330u/dl and 11 patients had readings above 330u/dl. The mean was 828.32u/dl with standard deviation of 222.99u/dl. In the severe acute pancreatitis group, 1 patient had reading less than 110u/dl, 2 between 110u/dl and 330u/dl and 9 patients had values above 330u/dl. The mean was 1655.61u/dl with standard deviation of 576.955u/dl.The p value was 0.045 and significant.

Table 2: Levels of serum amylase compared with severity of disease

SERUM AMYLASE(u/dl)	MILD	MODERATE	SEVERE
0 – 110 u/dl	2	7	1
110-330 u/dl	9	4	2
>331 u/dl	6	11	9
TOTAL	17	22	12
MEAN± 2SD	332.941±143.7	828.32±446.00	1655.61±1153.91
P VALUE	0.045		

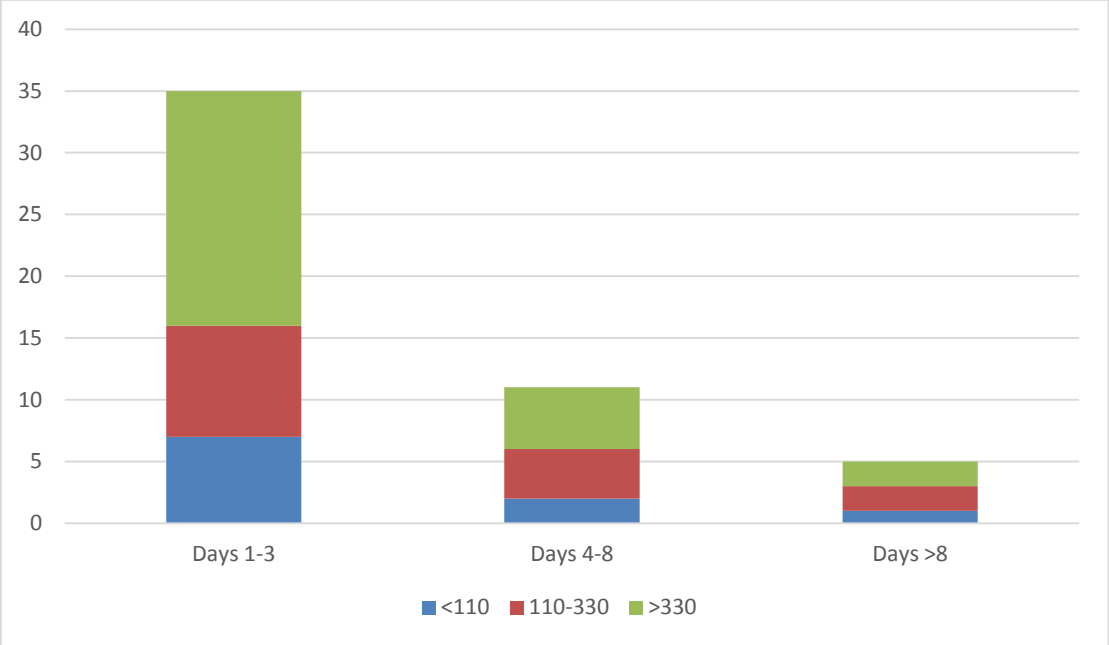

Figure 3: Distribution of serum amylase in relation to duration of disease at time of presentation p value was 0.265. High serum amylase values were less often seen with late presentation of patient as seen in figure 3.

The urinary amylase was measured in all the 51 patients. Distribution of urinary amylaseis depicted in Figure4. The mean was 3719.247u/dl with a standard deviation of 408.015u/dl. The p value was 0.002.

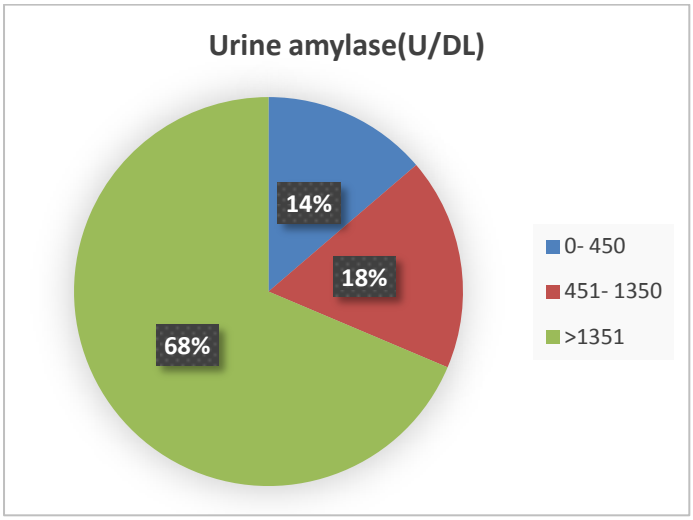

Figure 4 Levels of urinary amylase in our patients

In the mild pancreatitis group, 2 patients had values less than 450u/dl. 6 patients had values between 450u/dl and 1350u/dl and 9 patients had values above 1350u/dl. The mean for the mild pancreatitis group was 1398.76u/dl with a standard deviation of 209.25u/dl.

In the moderate pancreatitis group, 4 patients had values less than 450u/dl. 1 patient had values between 450u/dl and 1350u/dl and 17 patients had values above 1350u/dl. The mean was 2294.13u/dl with a standard deviation of 347.127u/dl.

In the severe pancreatitis group, 1 patient showed values less than 450u/dl, 2 patients had values between 450u/dl to 1350dl and 9 patients had values above 1350u/dl. The mean for severe acute pancreatitis group was 3697.50u/dl and the standard deviation was 667.668u/dl.

Table 3: Levels of urinary amylase compared with severity of disease

URINE AMYLASE(U/DL)	MILD	MODERATE	SEVERE
0-450U/DL	2	4	1
451-1350U/DL	6	1	2
>1351U/DL	9	17	9
TOTAL	17	22	12
MEAN± 2SD	1398.76±418.5	2294.13±694.254	3697.50±1335.33
P VALUE	0.052		

The difference in urinary amylase values was insignificant among all severity groups (p value was 0.052). The urine amylase was raised up to three times the upper reference value (450u/dl) in 9 out of 17 patients of mild acute pancreatitis, in 17 out of 22 patients of moderate acute pancreatitis and in 9 out of 12 patients of severe acute pancreatitis.

The values of urinary amylase were measured on the day of presentation to the hospital. There were 35 patients who had presented within the first 3 days of onset of pain. 6 had urinary amylase levels between 0 – 450u/dl. 7 patients had levels between 450u/dl and 1350u/dl. 22 subjects had levels above 1350u/dl.

11 patients had presented 4- 8 days after the onset of acute pancreatitis. Of this, 1 patient had levels of urinary amylase less than 450u/dl. 1 patient had levels between 450u/dl and 1350u/dl and 9 patients had levels above 1350u/dl. 5 patients had presented late, ie, on the 9th day or later, of whom only one patient had levels below 900u/dl and 4 had levels above 1350u/dl.

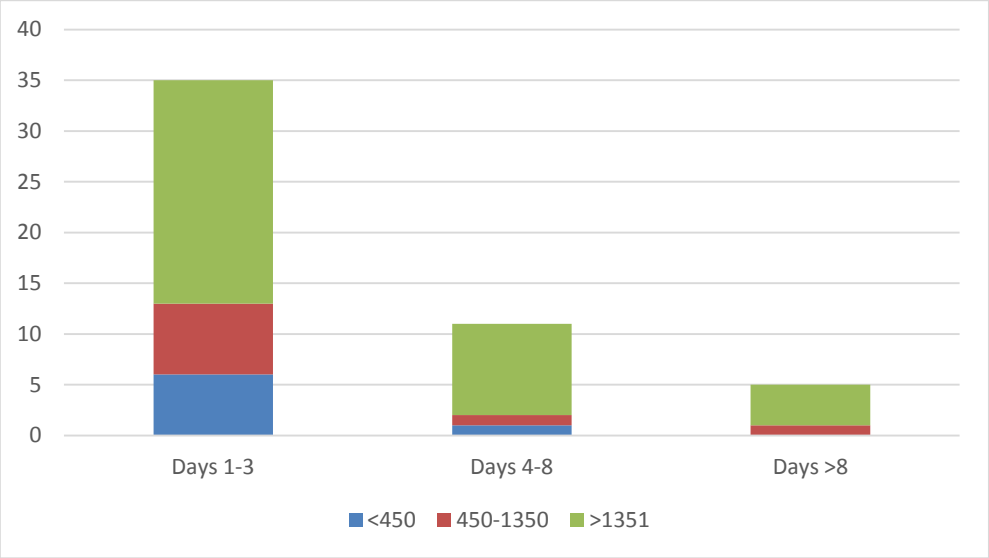

Figure 5: Distribution of urinary amylase in relation to duration of disease at time of presentation

The diagnostic reference point was taken as values greater than three times the upper reference value for both serum and urinary amylase. The diagnostic limit for serum amylase was values greater than 330u/dl and for urinary amylase were values greater than 1350u/dl. The sensitivity of serum amylase was 50.09% and that of urinary amylase was 68.62%.

The sensitivity of serum amylase was 35%, 50% and 75% in mild, moderate and severe acute pancreatitis respectively, while the sensitivity of urinary amylase was 52.94%, 77.27% and 75% in mild, moderate and severe acute pancreatitis respectively.

For patients presenting on the first 3 days, the sensitivity of serum amylase was 54.28% and that of urinary amylase was 62.85%. For patients who had presented on 4th to 8th day after the onset of pain, the sensitivity of serum and urinary amylase were 45% and 81.81% respectively. For patients presenting after 9 days of onset of pain, the sensitivity of urinary amylase was high at 80% and that of serum amylase was 40%.

Discussion

Acute pancreatitis is a common emergency, accounting for 3% of all patients admitted with acute pain abdomen.[4]The spectrum of the disease is wide ranging. The mild attacks often go undiagnosed predisposing to a severe second attack. Although the overall mortality of acute pancreatitis is static at 1 to 2%, in severe acute pancreatitis mortality is 10 to 30%.[5] Early diagnosis of acute pancreatitis is important to start

immediate and proper treatment. Yet the diagnosis of acute pancreatitis is still a major challenge. The clinical signs are non-specific and the presentations are atypical. The measurement of serum amylase has been the cornerstone in the diagnosis of acute pancreatitis since 1929.[6] There are over 200 different assays for the enzyme and no upper limit of normal values has been set. Although serum amylase is considered the most practical test in the diagnosis of acute pancreatitis, yet it poses various problems in the diagnosis of acute pancreatitis. Moreover, serum amylase remains elevated for a maximum of one week[7,8]after the onset of acute pancreatitis and also certain other conditions are associated with raised serum amylase levels like- intestinal infractions and perforation, appendicitis, hepatitis, peritonitis, cholecystitis etc.[9]

The average age of patients was 50.45yrs and there were 15 males (29%) and 36 females (71%). The male to female ratio was 1:2.4.Age was not found to be a significant factor in the occurrence of acute pancreatitis ($p>0.05$). Similarly, there was no significant difference in the incidence of acute pancreatitis in both the sexes ($P= 0.505$).

The normal upper limit for serum amylase was 110U/DL in the study. The mean value of serum amylase in patients with acute pancreatitis was 789.418 U/DL. Ten patients with acute pancreatitis had serum amylase values within the normal limits. Of these, 2 patients had mild acute pancreatitis, 7 patients were with moderate acute pancreatitis and 1 patient had severe acute pancreatitis. The sensitivity of serum amylase was 50.09%. Treacy et al had found a sensitivity of 45% for serum amylase using three times the upper limit of normal values for serum amylase as the cut off for diagnosis.[10] The findings of sensitivity in our study correlates closely to that by Treacy et al. However, Kempainnem[11] et al and Ventrucci[12] et al found a higher sensitivity of about 83% and 88% respectively. This might be because both the study used serum amylase for the diagnosis of acute pancreatitis, while Treacy et al like us used USG for the diagnosis of acute pancreatitis.

When serum amylase was compared in all the severity groups, the mean values increased with the grade of severity. This was statistically significant ($P=0.045$). The sensitivity of serum amylase was 35% for mild acute pancreatitis, 50% for moderate acute pancreatitis and 75% for severe acute pancreatitis. The sensitivity increased with increasing severity of acute pancreatitis.

The sensitivity of serum amylase was 45% for those presenting between 4 to 8 days of onset of pain. The sensitivity of serum amylase for those presenting after 9 days was 40%. 2 patients in the mild acute pancreatitis group had presented late on 13^{th} and 17^{th} day. Both had raised levels of serum amylase but the patient who had presented on the 17^{th} day had values of serum amylase below the cut off for diagnosis. Two patients with moderate acute pancreatitis had presented on the 9^{th} and other on 11^{th} day. One patient with severe acute pancreatitis had presented on the 11^{th} day. The sensitivity decreased as the time since the onset of pain increased. This observation was, however not statistically significant ($P=0.265$).

The normal upper reference limit for urinary amylase concentration in this study was 450u/dl in this study. The mean value of urinary amylase in our study was 3719.247 U/DL. Saxon[3] et al had found a mean of 1947U/DL, while Budd et al[13] found it to be 2926U/DL. 7 patients had a normal urinary amylase value. While Saxon et al in their study had found no patients with a normal urinary amylase level, Gambill et al[11] had observed normal urinary amylase levels in patients with acute pancreatitis. 2 patients in mild acute pancreatitis group, 4 patients in the moderate acute pancreatitis group and one patient in the severe acute pancreatitis group had insignificant values of urinary amylase. Thus 9.8% of the patients with acute pancreatitis had a normal value of urinary amylase when the serum amylase were abnormal, which correlates well with the finding of Gambill et al, who found that 7% of their patients had normal urinary amylase values associated with hyperamylasemia. The sensitivity for urinary amylase was 68.62% when three times the upper limit of normal was taken as a cut-off

for diagnosis. This sensitivity figures correlates with the findings of Treacy et al (62%) and Kempainnen et al (74%).The raise in amylase levels in the urine was significant in patients with acute pancreatitis, (P=0.002). The difference in the urinary amylase levels, amongst all severity groups was insignificant (P=0.052).

The sensitivity of urinary amylase was 52.94%, 77.27% and 75% in the mild, moderate and severe acute pancreatitis group respectively. The sensitivity was highest for moderate acute pancreatitis. This would be because of a greater amount of tissue inflammation when compared to mild acute pancreatitis. Severe acute pancreatitis may be associated with pancreatic exhaustion and necrosis, which might explain the early normalization of amylase levels in urine and blood. If three times the upper normal limit was taken as cut off, the sensitivity of urinary amylase was 62.85% in patients presenting within first 3 days. The sensitivity was 81.81% for those presenting between 4 to 8 days of onset of pain. The sensitivity of urinary amylase for those presenting after 9 days was 80%. 2 patients in the mild acute pancreatitis group had presented late on 13th and 17th day. Both had elevated urinary amylase levels. Two patients with moderate acute pancreatitis had presented on the 9th and other on 11th day. One patient with severe acute pancreatitis had presented on the 11th day. At the day of admission, she had urinary amylase below the diagnostic criteria. The sensitivity increased as the time since onset of pain increased. This observation however was not statistically significant (P=0.449).

When the sensitivity of serum amylase and urinary amylase was compared according to the severity of the disease, both showed increasing sensitivity with increasing severity. However, while serum amylase had a sensitivity of only 35% in mild acute pancreatitis, urinary amylase showed a sensitivity of about 52.94%. In moderate acute pancreatitis, urinary amylase was more sensitive than serum amylase (77.27% vs 50%). Saxon et al had proposed that urinary amylase might be a better diagnostic marker in mild pancreatitis. This observation correlates with the hypothesis proposed. However, serum amylase was equally sensitive as urinary amylase in severe acute pancreatitis (80%).

When the sensitivity of serum and urinary amylase were compared on the basis of day of presentation after the onset of pain, the sensitivity of serum amylase decreased as the days since onset of pain increased, while the sensitivity of urinary amylase increased as the days since onset of pain increased. Gambill et al had shown a similar result when they found that 15% of their patient had raised serum amylase when compared to 54% of patients with a raised urinary amylase days later when the acute process had by large subsided. [14]

The sensitivity of urinary amylase was higher than serum amylase in the study and also in mild and moderate Acute Pancreatitis patients and in those patients who had presented late to the hospital.

Table 4: Comparison of our study with other studies done previously

ARTICLE	TEST VARIABLES	SENSITIVITY	SPECIFICITY
VENTRUCCI 1989	LIPASE	100	94
	SERUM AMYLASE	88	89
	URINARY AMYLASE	----	----
KEMAINNEM 1997	LIPASE	---	----
	SERUM AMYLASE	83	95
	URINARY AMYLASE	74	95
TREACY 2001	LIPASE	67	97
	SERUM AMYLASE	45	97
	URINARY AMYLASE	62	97
OUR STUDY	LIPASE	---	----
	SERUM AMYLASE	50.09	----
	URINARY AMYLASE	68.62	----

Conclusion

Although serum amylase is considered the most practical biochemical marker for diagnosis of acute pancreatitis, yet it is not diagnostic in many cases like mild acute pancreatitis and in cases which present late after the onset of the disease. Urinary amylase is a convenient and a more sensitive test for diagnosis of acute pancreatitis.

Source of support: None

References

1. Russell R.C.G., Williams N.S., Bulstrode C.J.K., Bailey and love's short practise of surgery. 26th edition. London: crc press; 2013.
2. Clavien P-A, Robert J, Meyer P, Borst F, Hauser H. Acute pancreatitis and normoamylasemia. Not an uncommon combination. Arch Surg 1989;210:614-20.
3. Saxon EI, Hinkley WC, Vogel WC and Zieve L. Comparative value of serum and urinary amylase in the diagnosis of acute pancreatitis, Arch. Intern. Med., 1957;99:607-621.
4. Banerjee A, Kaul A, Bache E, Parberry A, Doran J, Nicholson M. Multicentre audit of death from Acute pancreatitis. Br J Surg 1994;81:1541
5. Corfield A, Cooper M, Williamson R. Acute pancreatitis: a lethal disease of increasing incidence. Gut 1985; 26:724-29
6. Elman R, Arnerson N, Graham EA. Value of blood amylase estimations in the diagnosis of pancreatic disease: a clinical study. Arch Surg 1929; 19: 943—67
7. Dragonetti GC, Licht H, Rubin W. Pancreatitis. Evaluation and treatment. *Prim Care*. 1996;23:525–34.
8. Tietz NW. Support of the diagnosis of pancreatitis by enzyme tests—old problems, new techniques. ClinChemActa. 1997;257:85–98
9. Ranson JH. Diagnostic standards for acute pancreatitis. *World J Surg*. 1997;21:136–42
10. Treacy J, Williams A, Bais R,Willson K, Worthley C, Reece J. Evaluation of amylase and lipase in the diagnosis of acute pancreatitis. ANZ J. Surgery 2001; 71: 577-82
11. Kempainnen EA, Hedström JI, Puolakainnen PA, Sainio VS, Haapiainen RK, Perhoniemi V, Osman S. Rapid measurement of urinary trypsinogen-2 as a screening test for acute pancreatitis. New England Journal of Medicine 1997; 336: 1788-93.
12. M. Ventrucci, R. Pezzilli, L.Gullo, L.Platé, G. Sprovieri and L. Barbara. Role of serum pancreatic enzyme assays in diagnosis of pancreatic disease. Digestive Diseases and Science 1997; 34: 39-45
13. Budd J J, Jr, Walter K E, Harris M L and Knight W A., Jr Urine diastase in the evaluation of pancreatic disease, Gastroenterology. 1959 mar;36(3):333-53
14. Gambill E E, Mason H L. One-hour value for urinary amylase in 96 patients with pancreatitis. .JAMA.1963 Oct 5;186:24-28.