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Original Research Article

Urinary amylase levels in the diagnosis of acute pancreatitis: a prospective case control study

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ABSTRACT

Background: Serum amylase has a short biological half-life and returns to normal levels within short time. Thus it's quite conflicting in the diagnosis of acute pancreatitis, particularly in patients with mild acute pancreatitis. Therefore, present study investigates the urinary amylase levels in the diagnosis of acute pancreatitis.
Methods: The present prospective study was conducted on 100 patients, 50 with acute pancreatitis and 50 normal subjects in the departments of General Surgery and our surgical hospital. All patients were examined by clinically, biochemical and radiological investigations and diagnosed acute pancreatitis. Serum amylase levels, serum lipase levels and urinary amylase levels were estimated in both groups: cases and controls. The sensitivity and specificity of serum amylase, serum lipase and urinary amylase levels were established after comparing their values in cases and controls.
Results: The preponderance of the patients was aged between 21 and 50 years. Increase the serum amylase, lipase and urinary amylase mean values of patients with acute pancreatitis were observed statistically significant ($p<0.001$). Serum amylase had the highest sensitivity (100%) and serum lipase had the highest specificity (96.53%). The sensitivity and specificity of urinary amylase was found to be 97.25% and 91.47% respectively. On ROC curve analysis, the area under the curve for serum amylase, serum lipase and urinary amylase was found to be 0.845, 0.945 and 0.934.
Conclusions: We conclude that urinary amylase is a convenient and a more sensitive test for diagnosis of acute pancreatitis.

Keywords: Acute pancreatitis, Serum amylase, Serum lipase, Urinary amylase

INTRODUCTION

Acute pancreatitis is an acute condition presenting with severe abdominal pain and is frequently connected with raised pancreatic enzyme levels in the blood or urine or both, as a result of inflammatory disease of the pancreas.[1] Acute pancreatitis is defined as an acute condition presenting with abdominal pain and is usually associated with raised pancreatic enzyme levels in the blood or urine as a result of pancreatic inflammation. It may be associated with both local and systemic complications. The hallmark of this disease is its association with little or no fibrosis.[2] The disease may range from a mild self-limiting inflammation of the pancreas to a more severe disease characterised by infected pancreatic necrosis, multiple organ failure and a high risk of mortality. Acute pancreatitis accounts for about 3% of all cases of abdominal pain among patients admitted to the hospital in the United Kingdom.[3] It is also the third most common gastrointestinal disease requiring acute hospitalization and the most common gastrointestinal discharge diagnosis in the United States of America.[4] The disease

may occur at any age with a peak in young men and older women. The causes of acute pancreatitis include gall stones, alcohol ingestion, post-ERCP status, hypertriglyceridemia, hypercalcemia, drugs, sphincter of Oddi dysfunction, abdominal trauma, pancreatic neoplasms, pancreatic divisum and others. In approximately 20% of the patients however, the cause is unknown.[5] The diagnosis of the disease is based on clinical examination, laboratory investigations and imaging techniques. Patients typically present with acute onset severe pain in the epigastric region that radiated to back. Serum levels of amylase and lipase more than three times the normal value usually indicate acute inflammation of the pancreas. Radiological investigations are used for diagnosis only when clinical and laboratory investigations do not meet the criteria to diagnose the disease despite there being a strong suspicion of acute pancreatitis. Serum Amylase has been usually 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.[6] 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 normalized.[7] Thus it was proposed that urinary excretion of amylase might be a more reliable and sensitive indicator of acute pancreatitis in many cases, urinary clearance of pancreatic enzymes from the circulation increases during pancreatitis; therefore, urinary levels may be more sensitive than serum levels. Also, urinary amylase levels usually remain elevated for several days after serum levels have returned to normal.[8] This is a study which intends to diagnose acute pancreatitis using urinary amylase levels which is a non-invasive method, is more sensitive and which remains elevated for a longer period than serum amylase. Therefore 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.

METHODS

The proposed prospective case control study was carried out in the department of General surgery, General Hospitals Palanpur associated with Banas Medical College and Research Institute and various surgical hospitals Palanpur, Gujarat, India for period of two years from November 2019 to October 2021. This study was carried out on total 100 study subject. Total 50 patients who have clinically, radiologically and investigation were performed for diagnosed of acute pancreatitis and they were included in study group and 50 subjects were included in control group. All patients with acute pancreatitis were admitted in General Surgery Department of General Hospital Palanpur. The written informed consent was obtained from each subject prior starts of study.

All patients were admitted in hospital after that all data was collected by standard operating procedure such as history taking, scrupulous physical examination and proper serological and radiological (USG) investigations, all patients admitted with acute pancreatitis, investigations were achieved in order to identify the cause for acute pancreatitis. Serum amylase levels, serum lipase levels and urinary amylase levels were estimated in all study subjects in both groups: study/cases and controls. The sensitivity and specificity of serum amylase, serum lipase and urinary amylase levels was established after comparing their values in patients with acute pancreatitis and controls subject. Another biochemical parameters random blood sugar, serum electrolytes, blood urea, serum creatinine, serum total protein, serum bilirubin, alkaline phosphate SGPT, lipid profile serum amylase and lipase, etc were determined by enzymatic method using commercial available diagnostic kit on fully automated biochemical analyzer The hematological parameters were estimated by five part hematological analyzer. USG was to be done on all study participants.

All patients fulfilled all the inclusion criteria were included in present study. Patients presenting to the General surgery department of Banas Medical College and Research Institute, Associated with General Hospital Palanpur with symptoms and signs suggestive of acute pancreatitis and patients expressed to the out-patient department for of Banas Medical College and Research Institute, associated with general hospital Palanpur for elective surgical procedures. Patients with uncontrolled blood sugar or diabetic, hypertensive and chronic kidney disease were excluded from present study and those patients not willing for study they were also excluded. The Study protocol was approved by Institutional ethics Committee human (IEC-H).

Statistical analysis

Data was analyzed using Statistical package for social sciences, version 20 (SPSS Inc., Chicago, IL). Results for continuous variables are presented as mean±standard deviation, and unpaired students't' test was used to compare mean data between study/cases and control groups. Chi-square test and Fischer's exact chi square test were used for the comparison of categorical variables and presented as percentage. The diagnostic accuracy of diagnostic markers in acute pancreatitis was assessed by receiver operat¬ing characteristic (ROC) curve analysis. The level $p<0.05$ was considered as significance.

RESULTS

In present study, age wise distributions of patients with acute pancreatitis and control subjects were shown in table 1. Majority of the patients were aged between 21

and 50 years. The mean value of age was statistically non-significant (p<0.05) between cases and control group. Similarly, there was no statistical significant (p>0.05) difference was observed with regard to the gender of the patient between cases and controls as per chi-square test.

Table 1: Age wise distribution of study subjects.

Age groups (years)	Study group/cases (n=50)	Control groups (n=50)
<20	2 (4%)	2 (4%)
21-30	10 (20%)	12 (24%)
31-40	22 (44%)	24 (48%)
41-50	8 (16%)	6 (3%)
>50	8 (16%)	6 (112%)
Total	50 (100%)	50 (100%)
(Mean±SD)	44.23±11.32	42.68±10.12

Table 2: Sex wise distribution of study subjects.

Sex	Study Group/ Cases	Control Group	Level of significance As per chi-square test
Male	42 (84%)	18 (36%)	p>0.05 (p=0.547) Not Significant
Female	08 (16%)	32 (64%)	
Total	50 (100%)	50 (100%)	

In our study, patients with acute pancreatitis expressed symptoms of pain abdomen and vomiting. All 50 (100%) patients showed pain abdomen while only 78 % of the patients expressed with vomiting. In study group, 80% of the patients were alcoholics and 20% of the patients were smokers among acute pancreatitis whereas 16% of the patients were alcoholics and 24% of the patients were smokers in control group. Among study group, 4% of the patients of acute pancreatitis were diabetic, 4% of the patients with acute pancreatitis were hypertensive, 2% of the patients had IHD and 10% of the patients were obese. Similarly, among controls group, 6% of the subjects were diabetic, 8% of the subjects were hypertensive, 2% subject with IHD and 6% of the subjects had obese. Ultrasound (USG) of the abdomen presented diffusely enlarged and hypo echoic pancreas in 52% of the patients with acute pancreatitis, diffusely enlarged and hypoechoic pancreas with cholelithiasis in 8% of the patients and pancreas obscured by bowel gas in 40% of the patients in study group.

This study, increase the serum amylase, lipase and urinary amylase mean values of patients with acute pancreatitis when compared with those without acute pancreatitis were observed statistically significant (p<0.001) (Table 4).

As per examination of the Receiver operating characteristic (ROC) curve of diagnostic markers in patients with acute pancreatitis showed in table 5. The serum amylase had a sensitivity of 100% and specificity of 98.82%. The area under curve when serum amylase was used for the diagnosis of acute pancreatitis was 0.845 and the p value was 0.01, which was statistically significant. The positive likelihood ratio (+LR) and negative likelihood ratio (-LR) was observed 16 and 0.0, respectively. Similarly, analysis of the ROC curves, serum lipase had a sensitivity of 98.82% and specificity of 96.53%. The area under curve when serum lipase was used for the diagnosis of acute pancreatitis was 0.945 and the p value was 0.005, which was statistically significant. The positive likelihood ratio and negative likelihood ratio was found to be 20.41 and 0.001, respectively. As per ROC curves, urinary amylase had a sensitivity of 97.25% and specificity of 91.47%. The area under curve when urinary amylase was used for the diagnosis of acute pancreatitis was 0.934 and the p value was 0.012, which was statistically significant. The positive likelihood ratio and negative likelihood ratio was observed 10.23 and 0.003, respectively.

Table 3: Baseline and USG Characteristics of cases and control subjects.

Baseline and USG Characteristics		Study group/ cases	Control group (n=50)
Symptoms	Pain abdomen	50 (100%)	00 (0%)
	Vomiting	39 (78%)	00 (0%)
Habits (n=50)	Alcohol	40 (80%)	8 (16%)
	Smoking	10 (20%)	12 (24%)
Co-morbidities (n=10)	DM	2 (4%)	3 (6%)
	HTN	2 (4%)	4 (8%)
	IHD	1 (2%)	1 (2%)
	Obesity	5 (10%)	3 (6%)
USG findings (n=50)	Diffusely enlarged and hypo echoic pancreas	26 (52%)	00 (0%)
	Diffusely enlarged and hypo echoic pancreas with cholelithiasis	4 (8%)	00 (0%)
	Pancreas obscured by bowel gas	20 (40%)	00 (0%)

DM; Diabetes Mellitus 2 Type, HTN; Hypertension, IHD; Ischemic heart Disease

Table 4: Diagnostic markers of acute pancreatitis in both groups.

Diagnostic markers	Study Group/Cases (n=50) (Mean ± SD)	Control Group (n=50) (Mean ± SD)	Level of Significance P value
Serum amylase (U/l)	689.45±289.67	42.86±68.59	p =0.001
Serum lipase (U/l)	761.56± 213.56	50.56±35.56	p =0.001
Urinary amylase (U/l)	1576.1.63±456.89	298.08±356.45	p =0.001

Table 5: Receiver operating characteristic (ROC) curve of diagnostic markers of acute pancreatitis.

Diagnostic Markers	Cut off	Sensitivity	Specificity	+ LR	−LR	AUC	P value
Serum amylase (U/l)	>68	100	94.56	16.00	0.0	0.845	0.001
Serum lipase (U/l)	>92	98.82	96.53	20.41	0.001	0.945	0.005
Urinary amylase (U/l)	>310	97.25	91.47	10.23	0.003	0.934	0.012

+LR: Positive likelihood ratio, −LR: Negative likelihood ratio, AUC: Area Under the ROC curve

DISCUSSION

Acute pancreatitis builds a chief hunk of our day to day admissions due to the gallstone disease being seen predominantly in our part of the world. The factors accomplished of impetuous acute pancreatitis are several and diverse. Nevertheless, biliary lithiasis and alcohol together account for about 80% of the disease.[9]

In our study, preponderance 40 (80%) belonged to age group of 21-50 years whereas as there were only 8 (16%) patients aged >50 years with 42 (84%) males and 8 (16%) females. Our results are similar with the results of the Chauhan et al, where in most affected age group was 50-59 years and mean age being 54 years.[10] As compared to female, male were more affected by acute pancreatitis in their study. In another study performed by Kandasami et al, in which the mean age of the patients was 43.5 years (SD±14.7 years) and with 77 males and 56 females.[11]

In our study, patients with acute pancreatitis expressed symptoms of pain abdomen and vomiting. All 50 (100%) patients showed pain abdomen while only 78% of the patients expressed with vomiting. Our findings are comparable with study done by Nehal Naik et al, in their study observed 100% of the patient's pain abdomen as the presenting symptoms, 66% of them presented with vomiting and 30% with abdominal distension.[12]

In our study we had 40 (80%) patients with alcoholic and 10 (20%) were smokers which is accordance with Kandasami et al studied alcohol as the predominant factor associated with acute pancreatitis in their study they noted 63 patients (47.7%) alcoholic.[11]

In our study, connected co-morbidities in the studied patients is concerned, diabetes mellitus were found in 2 (4%) patients, hypertension in 2 (4%) patients, IHD in 1 (2%) patients and obesity in 5 (10%) patients. A study done by Prakash et al in their study observed that 35% patients had one or more co-morbidities like type 2 diabetes mellitus, hypertension and ischemic heart disease.[10] Ultrasound (USG) of the abdomen presented diffusely enlarged and hypo echoic pancreas in 52 % of the patients with acute pancreatitis, diffusely enlarged and hypoechoic pancreas with cholelithiasis in 8% of the patients and pancreas obscured by bowel gas in 40% of the patients in study group, our outcomes comparable to several previous studies.[13-14]

In present study, increase the serum amylase, lipase and urinary amylase mean values of patients with acute pancreatitis when compared with those without acute pancreatitis were observed statistically significant ($p<0.001$). In a study done Naik et al most (92%) of the patient's serum amylase was 3 fold above normal value which is consistent with the findings of the present study.[12] Serum amylase level was again raised in 76.3% of patients studied by Terui et al.[15] Similar study done by MD Wani et al, found that comparing urinary amylase levels with serum amylase level at admission in the studied subjects, it was observed that 2 patients (18.2%) had <150 U/L, 0 (0%) 150-450 U/L and 1 (0.8%) >450 U/L serum amylase levels were having <400 U/L urinary amylase levels. 2 (18.2%), 9 (47.4%) patients and 23 (19.2%) with serum amylase levels of <150, 150-450 and >450 UL were observed to have 400-1000 U/L urinary amylase levels. The results are in accordance with the findings of the present study.[16]

In our study, sensitivity and specificity of serum amylase 100% and 94.56% in diagnosing of acute pancreatitis was observed, respectively. In the study conducted by Kemppainen et al, sensitivity and specificity of serum amylase in diagnosing acute pancreatitis was found to be 85% and 91% respectively.[17] In the study conducted by Gemaste et al and found that sensitivity and specificity of serum amylase in diagnosing acute pancreatitis was observed 72% and 99% respectively.[18] The results are in accordance with the findings of the present study. Similarly, sensitivity and specificity of serum lipase in diagnosing acute pancreatitis was reported 98.82% and 96.53% respectively in this study. In the study conducted by Gemaste et al and reported that sensitivity and specificity of serum lipase in diagnosing acute pancreatitis was observed 100% and 99% respectively. 18

In the study conducted by Kylanpaa-Back et al, sensitivity and specificity of serum lipase in diagnosing acute pancreatitis was reported 55% and 99% respectively which was similar to our outcomes.[19] In our study, sensitivity and specificity of urinary amylase in diagnosing acute pancreatitis was observed 97.25% and 91.47% respectively. In the study conducted by Kemppainen et al and found that sensitivity and specificity of urinary amylase in diagnosing acute pancreatitis was found 83% and 88% respectively.[17] In the study conducted by Treacy et al and reported that sensitivity and specificity of urinary amylase in diagnosing acute pancreatitis was found to be 62% and 97% respectively.[20] The results are in accordance with the findings of the present study.

Limitation of study

There are few limitations of the study, first is that this is a case control study, further retrospective longitudinal studies are needed to investigate the interactions between urinary amylase and acute pancreatitis. Second point of consideration is that we did not measure any systemic inflammatory marker which might be raise in acute pancreatitis. Third point is low sample size in our study and may be interference in statistical analysis.

CONCLUSION

We conclude that, though serum amylase is measured the mainly practical biochemical marker for diagnosis of acute pancreatitis, hitherto it is not diagnostic in several cases like mild and moderate acute pancreatitis and in cases which express late subsequent to the onset of the disease. Urinary amylase can be used in the diagnosis of acute pancreatitis as it was establish to have analogous sensitivity and specificity as that of serum amylase and serum lipase. On ROC curve analysis the areas under the curve for urinary amylase, serum amylase and serum lipase were found to be similar.

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