



SERUM AMYLASE AND SERUM LIPASE LEVELS IN DIABETIC KETOACIDOSIS

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ABSTRACT

Background- This study was planned to estimate serum amylase and serum lipase levels in patients presenting with diabetic ketoacidosis (DKA) and to correlate these enzyme levels with clinical presentation and serum triglycerides levels in patients with DKA.

Methodology- In this cross sectional study, serum amylase and serum lipase levels of patients presenting with DKA were assessed at admission (day 1) and on day 3. Serum triglycerides levels were assessed at admission (day 1).

Results- 80 patients with DKA were enrolled. Serum amylase level was raised in 16% at admission (day 1) and in 45% at day 3 with no evidence of acute pancreatitis. A positive correlation of serum amylase and lipase levels with pain in abdomen and serum triglycerides levels at both day 1 and day 3 was observed.

Conclusion- In patients with DKA, there is non-specific elevations in serum amylase as well as serum lipase levels irrespective of presenting symptoms (nausea, vomiting and pain in abdomen) with positive correlation with pain in abdomen and serum triglycerides levels.

KEYWORDS : Amylase, Lipase, Diabetes mellitus, Diabetic ketoacidosis.

INTRODUCTION-

Diabetic ketoacidosis (DKA) is a serious, life threatening complication in patients of diabetes mellitus (DM) and is mostly triggered by acute infection or missed insulin treatment or inadequate insulin therapy in patients with type 1 diabetes mellitus (T1DM) or type 2 diabetes mellitus (T2DM). Other possible triggers are emotional trauma, acute coronary or cardiovascular events and at times due to medications such as corticosteroids. Signs and symptoms of DKA often develop quickly, sometimes within 24 hours and predominantly includes nausea, vomiting and abdominal pain along with or without clinical signs of precipitating cause.^[1]

Though serum amylase and lipase enzymes are assumed to be markers for acute pancreatitis and are estimated as standard test to diagnose acute pancreatitis, it has been observed that significant non-specific elevations of these enzyme levels has been observed in patients of type 1 and type 2 DM presenting with DKA with no concomitant pancreatic involvement and levels of these enzymes decrease to normal levels after correction of hyperglycemia.^[2,3] Elevation of serum amylase and lipase less than or equal to three times of upper limit of normal is mostly considered as non-specific change, but elevation of more than three times of upper limit of normal is supposed to be diagnostic of acute pancreatitis. The electrolyte disturbances associated with DKA may be one of the causal factor for cellular damage with release of enzymes in many tissues of these patients.^[4]

There is paucity of data from central India about this observation. Hence this study was planned to estimate the levels of serum amylase and lipase levels in patients of DM presenting with DKA at Department Of Medicine, Gandhi Medical College, Bhopal and to correlate these enzyme levels with clinical presentation of diabetic ketoacidosis in studied participants.

METHODOLOGY-

This is a cross sectional study, done at Department of Medicine, Gandhi Medical College, Bhopal, Madhya

Pradesh, from year 2018 to 2019.

Inclusion criteria-

1. Patients of age 15 years and above.
2. Patients of T1DM presenting with DKA
3. Patients of T2DM presenting with DKA.

Exclusion criteria-

1. Patients of age less than 15 years.
2. T1DM or T2DM patients presenting with chronic pancreatitis.

After obtaining permission from Institute's ethical committee, all the patients with DKA were assessed and those who met inclusion criteria and gave written informed consent for the study were enrolled in the present study. A detailed history was obtained from all the patients and then they were subjected to clinical examination. Serum amylase and serum lipase levels were assessed at admission (day 1) and at day 3. Serum triglycerides level were assessed at admission (day 1).

Statistical analysis-

Data was compiled using Ms excel and analysed using SPSS software version 20. Frequency and percentage of grouped data was calculated. Chi square test was applied to assess the association between quantitative variables. Also correlation was calculated between various variables. P value less than 0.05 was considered significant.

RESULTS-

The study enrolled 80 patients after applying inclusion and exclusion criteria. About 30 (37.5%) patients were T1DM whereas 50 (62.5%) were suffering from T2DM. Duration of DM was less than 5 for majority of patients i.e. 48 (60%) followed by 5 to 10 years and more than 10 years in 30 (37.5%) and 2 (2.5%) patients respectively. Majority of patients with DKA were females i.e. 52 (65%) whereas only 28 (35%) patients were male. Maximum patients i.e. 26.2% belonged to 15 to 25 years of age group followed by 22.5% patients belonging to the age group of 36 to 45 years. The present study observed no

significant difference between the age group of males and females ($p > 0.05$).

Most common presenting symptom was nausea and vomiting in 100% patients followed by pain in abdomen (56.2%) and fever (26.2%). Least common symptom observed in present study was altered sensorium (7%). There was no significant difference in terms of presenting symptoms among genders ($p = 0.482$). Pain in abdomen was not radiating to back and it was not associated with abdominal tenderness in any of the patient.

Table 1- Serum amylase and serum lipase levels in study participants on admission (day1) and day 3-

Enzymes	Values (U/L)	Males n (%)		Females n (%)		χ^2	P value
		Day1	Day 3	Day 1	Day 3		
S. Amylase	≤140	26 (92.9)	22 (78.6)	46 (88.5)	40 (76.9)	4.59	0.03
	141-420	2 (7.1)	6 (21.4)	6 (11.5)	12 (23.1)		
	>420	0 (0)	0 (0)	0 (0)	0 (0)		
S. Lipase	≤140	26 (92.9)	23 (82.1)	49 (94.2)	45 (86.5)	3.22	0.07
	141-420	2 (7.1)	5 (17.9)	3 (5.8)	7 (13.5)		
	>420	0 (0)	0 (0)	0 (0)	0 (0)		

Serum amylase level was raised in 7.1% (2 males) and 11.5% (6 females) on day 1 whereas it was raised in 21.4% (6 males) and 23.1% (12 females) at day 3. Serum amylase level was significantly raised at day 3 as compared to day 1 value ($p < 0.05$). Similarly Serum lipase level was raised in 7.1% (2 males) and 5.8% (3 females) on day 1 which was higher at day 3 in 17.9% (5 males) and 13.5% (7 females) respectively and the observed difference was not statistically significant ($p > 0.05$). Serum amylase and lipase levels were not elevated to >420 U/L (>3 times of upper limit of normal) in any of the patients (Table 1).

Table 2- Correlation of serum amylase and serum lipase levels with pain in abdomen-

Day 1	R	R square	Adjusted R square	Std error	ANOVA	P value
S. Amylase	.032	.001	.012	54.786	.082	.776
S. Lipase	.081	.007	.006	43.088	.512	.476

The present study observed the insignificant positive correlation of serum amylase and lipase levels with pain in abdomen at both day 1 and day 3 (Table 2).

Table 3- Correlation of serum amylase and serum lipase levels with serum triglycerides levels-

Enzyme	Day	R	R square	Adjusted R square	Std error	ANOVA	P value
S. Amylase	1	.077	.006	.007	54.653	.463	.498
	3	.16	.03	.01	61.95	2.2	.15
S. Lipase	1	.016	.000	.013	43.224	.019	.891
	3	.06	.004	.009	53.38	.28	.59

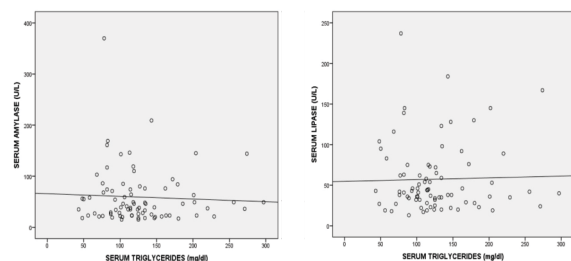


Figure 1A- Correlation of serum amylase and lipase levels with serum triglyceride levels at day 1-

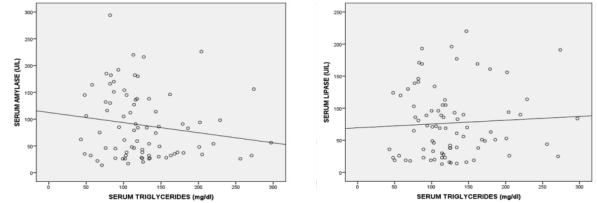


Figure 1B- Correlation of serum amylase and lipase levels with serum triglyceride levels at day 3-

Positive correlation of serum amylase and lipase levels was also observed with serum triglyceride levels at both day 1 and day 3 (Table 3, Figure 1).

USG abdomen was normal in 86.3% cases whereas it was suggestive of fatty liver in 8.8% cases followed by cystitis in 2.5% cases. USG abdomen findings suggestive of acute pancreatitis (i.e. peripancreatic fat stranding, peripancreatic fluid collection, bulky pancreas and necrosis of pancreas) were not present in any of the patient. Hence CECT abdomen was not done.

DISCUSSION-

The present study aimed to assess serum amylase and serum lipase levels in patients presenting with DKA and to correlate serum amylase and serum lipase levels with clinical presentation (nausea, vomiting, pain in abdomen) and serum triglycerides levels in these patients. Although DKA is more commonly associated with T1DM, it can also occur in patients with T2DM. Majority of patients in present study registered were with T2DM (62.5%) (60.7% males and 63.5% females). Kiyoun et al concluded that DKA most often occurs in type 1 DM. It also occurs in type 2 DM under conditions of extreme stress.^[5] In the present study duration of diabetes of less than 5 years was observed in majority of patients (60%) followed by 5 to 10 years and more than 10 years in 37.5% and 2.5% patients respectively. Feyfman et al have documented that adolescence, high level of HbA1c and long duration of diabetes as risk factors for DKA.^[6] The occurrence of DKA depends upon type and duration of DM as well as glucose control.^[7]

It is important to consider the differential diagnosis of acute pancreatitis in patients presenting with severe abdominal pain, particularly in association with DKA. Patients of DKA can have symptoms that may mask acute pancreatitis, such as abdominal pain, nausea and vomiting.^[8] In present study, most common presenting symptom was nausea and vomiting in 100% patients followed by pain in abdomen (56.2%) and fever (26.2%). Typical abdominal pain associated with acute pancreatitis i.e. pain in epigastrium that may radiate to back was observed in none of the cases in present study. Srividhya et al in their study on DKA suggested that as the clinical presentation i.e. nausea, vomiting and abdominal pain can present in both DKA and acute pancreatitis, the patients may need ultrasonogram and CECT scan of abdomen to diagnose acute pancreatitis in addition to serum amylase and lipase levels.^[9]

Serum amylase and lipase levels were analysed on admission (day 1) and on day 3 in all the patients of DKA in present study. Serum amylase was significantly raised in higher number of patients with diabetic ketoacidosis on day 3 as compared to day 1 ($p < 0.05$). But there was no significant difference in serum lipase level between day 1 and day 3 ($p > 0.05$). These enzymes were not raised to more than three times of upper limit of normal in any of the patients. It has been observed in the studies that serum amylase and lipase levels peak at 48 to 72 hours. However in present study serum amylase level returned to normal in 1 (1.25%) out of 8 (10%)

patients with high serum amylase on day 1 whereas in 2 (2.5%) patients out of 5 (6.25%) patients serum lipase levels returned to normal at day 3. Serum amylase peaked at day 3 in 18 (22.5%) patients whereas serum lipase was raised in 12 (15%) patients at day 3. Only in 6 (7.5%) patients and 3 (3.75%) patients respectively, serum amylase and lipase levels were raised at both the days i.e. at day 1 and day 3. Non-specific elevations of serum amylase and lipase levels occurs in 16–25% cases of DKA.^[2] Rizvi et al also reported non-specific elevations of serum amylase in patients with DKA and suggested that elevated lipase levels are specific for pancreatitis, that may accompany DKA and does not necessarily denote concomitant pancreatic inflammation.^[4]

Quiros et al also observed that lipase was elevated in 31% and amylase in 24% of the children with DKA and reported that pancreatic enzyme values peaked 12-24 hours after admission.^[10] Various pathology has been suggested for elevated enzyme levels in DKA. There could be coexistent acute pancreatitis, subtle injury to the pancreatic acinar cells may liberate them into the circulation, an extra-pancreatic origin triggered by the dysmetabolic state, like release of salivary gland amylase, or its accumulation secondary to suboptimal excretion in urine. Increase in lipase may be due to release of non-pancreatic lipolytic enzymes into the blood stream from sources such as stomach, liver, small bowel, tongue, esophagus, etc.^[11,12] Madole et al in their study observed low serum amylase and lipase levels in diabetes which could be due to insufficiency of pancreatic exocrine acinar cells. They observed pancreatic fibrosis, atrophy, fatty infiltration and loss of the exocrine acinar cells in patients of diabetes.^[13]

The present study observed a positive but insignificant correlation of serum amylase and lipase levels with pain in abdomen ($p > 0.05$). These findings were similar to study by Quiros et al in which the authors documented no significant correlation between pancreatic enzyme elevation and abdominal pain.^[10] Also the present study observed a positive but insignificant correlation of serum amylase and lipase levels with triglyceride levels ($p > 0.05$). Yadav et al in their study observed negative but insignificant correlation between serum amylase levels and triglycerides ($p > 0.05$).^[2] The positive correlation could be explained by activation of hormone sensitive lipase breakdown of triglycerides into free fatty acids. When body is shifted into a catabolic state with breakdown of glycogen stores, hydrolysis of triglycerides from adipose tissues and mobilization of amino acids from peripheral tissues leading to production of glucose and ketone bodies by liver.^[14,15]

CONCLUSION-

The present study documents that in patients with DKA, there is non-specific elevations in serum amylase and serum lipase levels irrespective of presenting symptoms (nausea, vomiting and pain in abdomen) with positive correlation with pain in abdomen and serum triglycerides level although statistically insignificant may be due to small sample size. None of the patients in present study showed pancreatic involvement in DKA. The study had certain limitations. Firstly, the sample size of study was small. Secondly, the serum amylase and lipase levels were observed only at admission (day 1) and at day 3. Long term effect of DKA on serum amylase and lipase levels could not be assessed. Thirdly, blood ketone levels and ABG could not be performed due to resource constraints.

Future prospective studies should be planned in large sample size to tease out the causality of raised levels of serum amylase and lipase enzymes in patients presenting with DKA with no features suggestive of acute pancreatitis.

Declarations of interest: None.

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