Section: General Medicine

Original Research Article

A STUDY SERUM AMYLASE AND SERUM LIPASE LEVELS IN DIABETIC KETOACIDOSIS

Srikanth Goud Gadiga[1], Jilla Naganna[2], Anthati Kirthi[3]

[1]*Associate Professor, Department of General Medicine, Government Medical College Nalgonda, Telangana, India.*
[2]*Associate Professor, Department of General Medicine, Government Medical College, Nalgonda, Telangana, India.*
[3]*Assistant Professor, Department of General Medicine, Government Medical College. Nalgonda, Telangana, India.*

Received *: 03/05/2025*
Received in revised form *: 17/06/2025*
Accepted *: 05/07/2025*

Corresponding Author:
Dr. Anthati Kirthi,
Assistant Professor, Department of General Medicine, Government Medical College. Nalgonda, Telangana, India.
Email: anthatikirthi119@gmail.com

DOI: 10.70034/ijmedph.2025.3.53

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2025; 15 (3); 297-301

ABSTRACT

Background: Diabetic ketoacidosis (DKA) is an acute complication of uncontrolled diabetes mellitus (DM). Abdominal symptoms and elevated pancreatic enzyme levels are common. The elevations of serum amylase and lipase levels in DKA can mimic acute pancreatitis, making diagnosis a challenge. This study aimed to compare serum amylase and lipase levels in DKA and non-DKA cases.

Materials and Methods: This cross-sectional observational study included 40 patients with diabetes, of whom 9 had DKA and 31 did not. They were evaluated clinically using biochemical variables (serum amylase and lipase), arterial blood gases, and abdominal imaging (ultrasound and CT as needed). The enzyme levels of the groups were compared, and correlations with indicators of DKA severity were analyzed.

Results: Patients with DKA showed a significant increase in blood glucose and anion gap levels and a decrease in pH and bicarbonate levels ($p<0.001$). Serum amylase and lipase levels were also significantly higher in the DKA group (248.6 ± 102.7 U/L and 162.4 ± 78.5 U/L, respectively; $p<0.001$). The higher the acidosis, the higher the enzyme levels. However, no pancreatic inflammation was detected by imaging studies in any of the cases, even in those with enzyme concentrations >3X above the upper limit of normal. Cases of abdominal pain were strikingly more common in DKA, which was not unique to pancreatitis.

Conclusion: Elevated serum amylase and lipase levels are common in DKA and correlate with the severity of metabolic derangement rather than true pancreatitis. Clinicians should interpret these enzyme elevations cautiously and rely on clinical and imaging findings to avoid misdiagnosis and unnecessary interventions.

Keywords: Diabetic Ketoacidosis (DKA), Serum Amylase, Serum Lipase, Acute Pancreatitis.

INTRODUCTION

Diabetic ketoacidosis (DKA) is a potentially life-threatening acute complication of uncontrolled diabetes mellitus. This occurs more commonly in type I diabetes mellitus although it may be in type 2 diabetes under certain conditions. DKA is characterized by hyperglycemia, metabolic acidosis, and ketonemia due to relative or absolute insulin deficiency. It is associated with increased counter-regulatory hormones i.e. glucagon, catecholamines, cortisol, and growth hormone.[1] These metabolic imbalances may cause numerous systemic complications, among them are gastrointestinal complaints, dehydration, electrolyte imbalances, and a change in the pancreatic enzyme levels. Among the biochemical abnormalities observed in DKA, higher serum amylase and lipase levels are frequently present. These enzymes which are primarily associated with pancreatic function are used for the diagnosis of acute pancreatitis. However, few studies have shown that their elevation in DKA does not necessarily correlate with actual pancreatic inflammation or necrosis [2,3] This poses a diagnostic dilemma since the differentiation of actual acute

pancreatitis versus pseudo-elevation of pancreatic enzymes in DKA is important to prevent any unnecessary intervention and to ensure appropriate clinical management. Hyperamylasemia and hyperlipidemia in DKA are most of the time associated with extrapancreatic causes, which include salivary gland hyperactivity, reduced renal clearance, or metabolic stress.[4] Moreover, nonspecific activation of digestive enzymes or microvascular pancreatic ischemia due to dehydration or acidosis can contribute to enzyme leakage into the bloodstream.[5] Lipase which is more specific as compared to pancreatic amylase can be found to be elevated in DKA even in the absence of clinical or radiological evidence of pancreatitis.[6] This has brought about the questioning of the threshold values and interpretation of pancreatic enzymes in cases of DKA. Studies in this field have shown that 25 – 50% of DKA patients can exhibit elevated serum lipase and amylase levels without the clinical or radiological evidence of acute pancreatitis.[7,8] Also since abdominal pain is a very common presentation in DKA and pancreatitis can further complicate the diagnostic process. Hence relying solely on enzyme levels can be misleading and therefore, requires a comprehensive evaluation including clinical presentation, serum enzyme trends, and radiological evidence including ultrasonography or contrast-enhanced computed tomography.[9] The incidence of True acute pancreatitis in DKA patients is low however, it is clinically significant, because DKA itself predisposes patients to pancreatic injury through the mechanism of free fatty acid toxicity or oxidative stress.[10] Therefore, it is important to identify cases with concomitant pancreatitis which can lead to longer hospital stays predisposing to systemic complications and poor prognosis. Because it is a common finding that there are elevated pancreatic enzymes in DKA with no evidence of pancreatitis. The proposed study aimed to determine the pattern and clinical relevance of serum amylase and lipase values in patients who were admitted with DKA. Such analysis in a contest of clinical and radiological findings aims to clarify the diagnostic utility and limitations of these enzymes in differentiating DKA-related enzyme elevation from true acute pancreatitis.

MATERIALS AND METHODS

This cross-sectional observational study was conducted in the Department of General Medicine, Government Medical College and Hospital, Nalgonda, Telangana. Institutional ethical approval was obtained for the study after duly following the protocol for human research.

Inclusion Criteria

1. Patients diagnosed with Diabetes mellitus based on Fasting Plasma Glucose (FPG) ≥126 mg/dL, 2-hour Plasma Glucose (2-h PG) during an Oral Glucose Tolerance Test (OGTT) ≥200 mg/dL and Glycated Hemoglobin (HbA1c): ≥6.5%.
2. Patients diagnosed with diabetic ketoacidosis (DKA) as per the American Diabetes Association (ADA) criteria, which include blood glucose >250 mg/dL, arterial pH <7.3, serum bicarbonate <18 mEq/L, positive serum or urine ketones, and increased anion gap metabolic acidosis.[11]
3. Males and females
4. Willing to participate in the study voluntarily

Exclusion Criteria

1. Patients with a known history or clinical/radiological evidence of acute or chronic pancreatitis.
2. Patients with gallstone disease or known biliary tract disorders.
3. Patients with a history of alcohol abuse or recent alcohol consumption.
4. Patients taking medications known to affect pancreatic enzyme levels (e.g., thiazide diuretics, corticosteroids, azathioprine).
5. Patients with renal failure (eGFR <30 mL/min/1.73 m²)
6. Patients with salivary gland disorders (parotitis) that may elevate amylase.
7. Pregnant or lactating women.
8. Patients with other causes of metabolic acidosis (lactic acidosis, uremia, toxic ingestions).
9. Patients are unwilling or unable to provide informed consent.

A total of n=40 patients were included based on inclusion and exclusion criteria. Among these, n=9 patients were diagnosed with diabetic ketoacidosis (DKA) as per the American Diabetes Association (ADA) criteria.[11] The rest 31 patients acted as a comparative group (non-DKA) and consisted of diabetic patients without ketoacidosis, admitted to a hospital not due to this condition. Clinical history was taken in detail after informed consent was obtained that included various symptoms like abdominal pain, vomiting, and the duration of diabetes. Hemodynamic assessment and detecting the abdominal status were determined by physical examination. Blood samples were collected on admission for the estimation of serum amylase and serum lipase levels using standard enzymatic colorimetric methods in the hospital biochemistry laboratory. Other investigations including random blood sugar, arterial blood gases (ABG), serum electrolytes, renal function tests, and urine ketones were also performed. Ultrasonography of the abdomen was done in all patients to assess for pancreatic abnormalities and to rule out acute pancreatitis. In selected cases with suggestive findings or elevated enzyme levels, a contrast-enhanced computed tomography (CECT) of the abdomen was performed.

Patients were categorized into two groups:
Group A (n=9): Patients with DKA
Group B (n=31): Non-DKA diabetic patients
Serum amylase and lipase values were compared between the two groups.
Statistical analysis was done using SPSS 25 software. Continuous variables were expressed as mean ± standard deviation (SD) and compared using the independent t-test. Categorical variables were expressed as percentages and compared using the chi-square test. A p-value <0.05 was considered statistically significant.

RESULTS

Table 1 depicts the baseline clinical and biochemical characteristics of the DKA group and the non-DKA group. Age, gender, and duration of diabetes were statistically similar across groups given non-significant p values. However, Group A showed significantly higher blood glucose levels (p<0.001), lower arterial pH and bicarbonate levels, and a markedly elevated anion gap (p<0.001), confirming metabolic acidosis. Abdominal pain was significantly more frequent in DKA patients (77.8% vs. 16.1%; p<0.001), highlighting its common but nonspecific presence in DKA, which may mimic or obscure symptoms of acute abdominal pathology.

Table 1: Baseline Characteristics of Study Groups

Characteristic	*Group A (DKA) (n=9)*	*Group B (Non-DKA) (n=31)*	*p-value*
Age (years)	48.3 ± 14.2	52.6 ± 11.7	0.32
Gender (M: F)	5:04	18:13	0.82
Diabetes Duration (yrs)	8.2 ± 5.1	10.4 ± 6.3	0.28
Blood Glucose (mg/dL)	478.4 ± 126.3	218.7 ± 74.9	<0.001*
Arterial pH	7.08 ± 0.15	7.38 ± 0.05	<0.001*
$HC0_3$- (mEq/L)	9.8 ± 3.2	22.1 ± 2.8	<0.001*
Anion Gap (mEq/L)	25.7 ± 4.9	12.5 ± 3.1	<0.001*
Abdominal Pain, n (%)	7 (77.8%)	5 (16.1%)	<0.001*

Significant

A critical analysis of Table 2 shows that pancreatic enzyme levels were significantly higher in DKA patients. Mean serum amylase and lipase were 248.6 U/L and 162.4 U/L, respectively, in Group A, compared to 85.3 U/L and 42.8 U/L in Group B (p<0.001). Elevated amylase and lipase were observed in 77.8% and 66.7% of DKA cases, respectively, while both enzymes were raised in 55.6%. In contrast, only one non-DKA patient (3.2%) showed dual elevation. These findings suggest that enzyme elevation is common in DKA, though not necessarily indicative of acute pancreatitis.

Table 2: Pancreatic Enzyme Levels in the cases of the study

Parameter	**Group A (DKA)**	**Group B (Non-DKA)**	**p-value**	**Elevated n (%)**
Serum Amylase (U/L)	248.6 ± 102.7	85.3 ± 32.4	<0.001*	7 (77.8%)
Serum Lipase (U/L)	162.4 ± 78.5	42.8 ± 19.6	<0.001*	6 (66.7%)
Both Elevated, n(%)	5 (55.6%)	1 (3.2%)	<0.001*	-
*Elevation defined as: Amylase > 125 U/L, Lipase >60 U/L (institutional norms)				

Significant

Table 3 shows the correlations between enzyme levels and biochemical severity markers in the DKA group. Serum amylase and lipase levels showed a significant inverse correlation with arterial pH and bicarbonate levels (p<0.05), and a positive correlation with anion gap (p<0.05), indicating that enzyme elevation increases with worsening acidosis. Correlations with blood glucose were positive but not statistically significant. These results suggest that pancreatic enzyme elevation in DKA may be associated with the severity of metabolic disturbance rather than actual pancreatic inflammation.

Table 3: Correlation of Enzymes with DKA Severity (Group A)

Parameter	Amylase (r)	Amylase (p)	Lipase (r)	Lipase (p)
Blood Glucose	0.38	0.31	0.42	0.25
Arterial pH	-0.72	0.03*	-0.68	0.04*
HC03-	-0.69	0.04*	-0.64	0.05*
Anion Gap	0.75	0.02*	0.71	0.03*
(r= Spearman correlation coefficient)				

Significant

Table 4 shows the ultrasound imaging showed normal findings in 77.8% of DKA patients and 96.8% of non-DKA patients. Mild fatty liver changes were noted in 22.2% of DKA cases and 3.2% of controls. No pancreatic edema or inflammation was observed in either group. CECT abdomen, performed in patients with enzyme levels >3× ULN, was normal in all cases. These imaging findings confirm that despite elevated enzyme levels in DKA patients, there was no radiological evidence of acute pancreatitis, supporting the concept of enzyme elevation without structural pancreatic injury.

Table 4: Abdominal Imaging Findings

Finding	*Group A (DKA) (n=9)*	*Group B (Non-DKA) (n=31)*
Ultrasound (USG)		
Normal	7 (77.8%)	30 (96.8%)
Fatty Liver	2 (22.2%)	1 (3.2%)
Pancreatic Edema	0	0
CECT Abdomen*	4 (44.4%)	1 (3.2%)
Normal	4 (100%)	1 (100%)
Pancreatic Inflammation	0	0
*Performed in patients with enzyme elevation >3x ULN		

Table 5 shows the clinical outcomes in cases of the cases of the study. DKA patients had significantly longer hospital stays (6.8 vs. 4.2 days; p=0.002) and higher insulin requirements (0.82 vs. 0.58 IU/kg/day; p=0.001) compared to non-DKA patients. Symptom resolution in the DKA group occurred within 24.6 ± 8.3 hours. Importantly, no patients in either group were diagnosed with acute pancreatitis during hospitalization. These findings indicate that while enzyme elevations in DKA are common and correlate with disease severity, they are not indicative of pancreatitis and should be interpreted in a clinical context to avoid unnecessary diagnostic procedures.

Table 5: Clinical Outcomes in cases of the study

Outcome	Group A (DKA)	Group B (Non-DKA)	p-value
Hospital Stay (days)	6.8 ± 2.1	4.2 ± 1.5	0.002*
Insulin Requirement (IU/kg/day)	0.82 ± 0.18	0.58 ± 0.15	0.001*
Resolution of Symptoms (hrs)	24.6 ± 8.3	-	-
Acute Pancreatitis Diagnosis	0	0	

Significant

DISCUSSION

Diabetic ketoacidosis (DKA) is a complication of diabetes mellitus characterized by hyperglycemia, ketonemia, and metabolic acidosis. Gastrointestinal symptoms such as abdominal pain, nausea, and vomiting are common in this condition such symptoms are also found to be commonly present in cases of acute pancreatitis. Interestingly pancreatic enzymes such as amylase and lipase are also often found to be elevated in DKA. Therefore, a pertinent question to be raised is whether these elevations are indications of true pancreatitis or a non-specific response to metabolic dysfunctions. The current study included 40 cases of diabetes out of which 9 were diagnosed with DKA and 31 were non-DKA cases. The results of this study showed that higher blood glucose levels, lower arterial pH and bicarbonate, and elevated anion gaps are all features of DKA. Abdominal pain was significantly more frequent in the DKA group (77.8% vs. 16.1%, p<0.001). The results of our study align with previous study in this field where they reported that 80% of DKA patients may report abdominal discomfort, which could occur despite no abdominal pathology.[2,13] We found that serum lipase and amylase levels were markedly elevated in the DKA group with mean values being significantly higher in DKA group. Elevated amylase and lipase levels were observed in 77.8% and 66.7% of the DKA group respectively. However, both enzymes were found to be elevated in 55.6% of cases of the DKA group. Interestingly none of the patients could meet the diagnostic criteria for acute pancreatitis both clinically and radiologically. We found that there was no evidence of pancreatic inflammation in any of the enzyme-elevated cases when subjected to ultrasonography or CECT. Other studies done in this field have also reported similar findings and they suggested that enzyme elevation in DKA is often non-specific and may result from factors such as decreased renal clearance, metabolic stress, or subclinical pancreatic ischemia.[3-5]

Hence it supports the growing body of evidence that in the absence of radiological findings, only enzyme elevations must not be interpreted as diagnostic for acute pancreatic cases in DKA cases.[13,14] Studies have revealed that pancreatic enzyme elevations in DKA have been attributed to salivary amylase elevations or metabolic acidosis rather than true inflammation.[15] Moreover, correlation analysis of the DKA group in this study demonstrated that both serum amylase and lipase levels were significantly associated with markers of DKA severity which includes arterial pH, serum bicarbonate, and anion gap. These correlations show that pancreatic enzyme elevations may reflect metabolic severity of DKA rather than actual pancreatic pathology. [6,16] The results of this study also show that the mean duration of hospital stay and insulin requirements were significantly higher in the DKA group which shows the intensity of medical management and slower recovery in these cases. In the end, this study confirms that elevated serum amylase and lipase levels were common in DKA and correlated with the severity of acidosis. Clinical and imaging studies are essential to differentiate true pancreatic involvement from enzyme elevation secondary to metabolic derangements in DKA.

CONCLUSION

This study highlights that serum amylase and lipase levels are typically elevated in patients with diabetic

ketoacidosis (DKA), but they may not always be associated with acute pancreatitis. Increased enzyme levels were strongly associated with the severity of metabolic acidosis, indicating a general inflammatory reaction to the metabolic disorder. No pancreatic inflammation was observed in any imaging study, which also proves the importance of a thorough clinical and radiological examination before the diagnosis of pancreatitis. Thus, caution must be exercised when using pancreatic enzyme levels in DKA, and unwarranted interventions must be avoided when there is no supporting clinical or imaging evidence.

REFERENCES

1. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. Diabetes Care. 2009;32(7):1335–43.
2. Nair S, Yadav D, Pitchumoni CS. Association of diabetic ketoacidosis and acute pancreatitis: observations in 100 consecutive episodes of DKA. Am J Gastroenterol. 2000;95(10):2795–800.
3. Wang YJ, Feng CC, Chou YH, et al. Elevated serum pancreatic enzymes in diabetic ketoacidosis do not always indicate pancreatitis. J Formos Med Assoc. 2013;112(7):412–18.
4. Umpierrez GE, Watts NB, Phillips LS. Clinical utility of amylase and lipase in the diagnosis of acute pancreatitis in diabetic ketoacidosis. Endocr Pract. 2003;9(5):405–09.
5. Yadav D, Agarwal N, Pitchumoni CS. A critical evaluation of laboratory tests in acute pancreatitis. Am J Gastroenterol. 2002;97(6):1309–18.
6. Lankisch PG, Apte M, Banks PA. Acute pancreatitis. Lancet. 2015;386(9988):85–96.
7. Steinberg WM, Goldstein SS, Davis ND, Shamma'a J, Anderson K. Diagnostic assays in acute pancreatitis. A study of sensitivity and specificity. Ann Intern Med. 1985;102(5):576–80.
8. Nair S, Pitchumoni CS. Diabetic ketoacidosis, hyperlipidemia, and acute pancreatitis: the enigmatic triangle. Am J Gastroenterol. 1997;92(9):1560–61.
9. Tenner S, Baillie J, DeWitt J, Vege SS. American College of Gastroenterology guideline: management of acute pancreatitis. Am J Gastroenterol. 2013;108(9):1400–15.
10. Wang GJ, Gao CF, Wei D, Wang C, Ding SQ. Acute pancreatitis: etiology and common pathogenesis. World J Gastroenterol. 2009;15(12):1427–30.
11. Gosmanov AR, Gosmanova EO, Dillard-Cannon E. Management of adult diabetic ketoacidosis. Diabetes Metab Syndr Obes. 2014 Jun 30; 7:255-64.
12. Umpierrez G, Freire AX. Abdominal pain in patients with hyperglycemic crises. J Crit Care. 2002 Mar;17(1):63-67.
13. Hameed AM, Lam VW, Pleass HC. Significant elevations of serum lipase not caused by pancreatitis: a systematic review. HPB (Oxford). 2015 Feb;17(2):99-12.
14. Andrew L Arshaw, Edward R Feller, Kang-Hyun Lee. On the cause of Raised Serum-Amylase in Diabetic Ketoacidosis. The Lancet 1977; 309: 929-31.
15. Quiros, J Antonio, Marcin, James P, Kuppermann, Nathan Nasrollahzadeh, Farid et al. Elevated serum amylase and lipase in pediatric diabetic ketoacidosis. Pediatric Critical Care Medicine 2008; 9(4):418-22.
16. Jain P, Rai S, Misra S. Serum amylase and lipase in diabetic ketoacidosis. J Assoc Physicians India. 2015;63(7):28–30.