Title: Evaluation Of Serum Amylase, Lipase In Patients With Diabetes Mellitus, With Possible Correlation With Sodium And Potassium Levels.

shubham upadhyay^[1], Yogendra singh Gond [2] Pooja sounr^[3], Ashvin Chouhan^[4],

 Senior Resident Department of medicine MGM medical college and MY hospital Indore, Madhya Pradesh, India.

[2] Senior Resident Department of medicine MGM medical college and MY hospital Indore, Madhya Pradesh, India.

[3] Senior Resident Department of medicine, Sri Aurobindo Institute of Medical Sciences Indore, Madhya Pradesh, India.

[4] Assistant professor Department of Psychiatry MGM medical college and MY Hospital, Indore, Madhya Pradesh India.

Corresponding author -

Pooja Sounr [3] email id - poojasounr13@gmail.com Ph- 9179075455

Background: Sodium potassium derangements and elevated serum amylase lipase levels are not rare findings among diabetic patients, they often occurs simultenously with increased blood sugar levels. We here by try to find out association between these blood parameters.

Aims and objectives: to find out association between raised serum amylase, lipase levels and deranged sodium, potassium levels in patients with diabetes mellitus.

Method and materials: The study was conducted in the Department of Medicine, M.G.M. Medical College and M. Y. Hospital, Indore (M.P.) during the period from 908

March 2018 to February 2019. 50 Diabetic patients attending outdoor clinic and patients admitted in wards were Included. The study was approved by the Ethics Committee and informs consent was taken.

Results:For amylase outcome, 38.1 % for sugar levels 550-600 and 1 % for 400-450. for lipase outcome 33.3% % for sugar levels 550-600 and 22.2% for 500-550. Amylase outcome show higher percentage 52.4% for Sodium Level < 135 while, show lower percentage 9.5% for > 145 Lipase Outcome, patients show 100% for Sodium Level < 135. Amylase outcome show higher percentage 71.4% for Potassium Level 3.5-5.3 while, show none for < 3.5. For Lipase Outcome, patients show 100% for Potassium Level >5.0.

Discussion: the levels of amylase and lipase had shown increasing trends with increasing blood glucose levels, how ever the correlation was found to be non significant. The outcome of amylase and lipase had shown increasing trends with hyponatremia, and lipase levels had shown increasing trend with hyperkalemia How ever the results were found to be non significant

Limitation: sample size was lower and follow up studies are lacking

Conflict of interest: none

Electrolyte dysbalances are common in clinical practice, occuring in a broad spectrum of patients from asymptomatic to critically ill and associated with increased mortality and morbidity [<u>1-3</u>]. they are usually multifactorial in origin, has various pathophysiological factors, or acute illness, alone or in combination, play a key role.[2]

Diabetes mellitus (DM) is included among the common cause of electrolyte derangements as aforementioned factors (like hyperglycemia, impaired renal function, acid-base disorders, malabsorption syndromes and polydrug regimens) are often present in diabetics[4,5].

On the other hand, in type 2 DM nearly 25 % of patients has elevated lipase and amylase levels without symptoms of acute pancreatitis. *[6,7]*

In other study, 84 % of patients of acute pancreatitis had both amylase and lipase raised and 100 % of acute pancreatitis patients had lipase raised, irrespective of aetiology.[8,9]

This article provides an insight into possible association between electrolyte disturbances occurring in DM and elevated serum amylase and lipase in order to find their predictive value in acute pancreatitis

Causes of electrolyte disorders in diabetic patients [10]

Sodium disorders

Hyponatremia

Pseudohyponatremia (marked hyperlipidemia)

Hyperglycemia (hypertonicity)-induced movement of water out of the cells (dilutional hyponatremia)

Osmotic diuresis-induced hypovolemic hyponatremia

Drug-induced hyponatremia: hypoglycemic agents (chlorpropamide, tolbutamide,

insulin) or other medications (e.g., diuretics, amitriptyline)

Pseudonormonatremia (marked hyperlipidemia, severe hypoproteinemia)

Hypernatremia

Pseudohypernatremia (severe hypoproteinemia)

Loss of water in excess of sodium and potassium (osmotic dieresis), if this water loss

is replaced insufficiently

Potassium disorders

Hypokalemia

Shift hypokalemia: insulin administration

Gastrointestinal loss of K+: malabsorption syndromes (diabetic-induced motility

disorders, bacterial overgrowth, chronic diarrheal states)

Renal loss of K+: osmotic diuresis, hypomagnesemia, diuretics (thiazides,

thiazide-like agents, furosemide)

Hyperkalemia

Shift hyperkalemia: acidosis, insulin deficiency, hypertonicity, rhabdomyolysis, drugs (*e.g.*, beta blockers)

Reduced glomerular filtration of K+: acute and chronic kidney disease

Reduced tubular secretion of K+: hyporeninemic hypoaldosteronism, drugs

(angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, renin

inhibitors, beta blockers, potassium-sparing diuretics)

Magnesium disorders

Hypomagnesemia

Pseudohypomagnesemia: hypoalbuminemia

Shift hypomagnesemia: insulin administration

Poor dietary Mg2+ intake

Gastrointestinal Mg2+ losses: diarrhea as a result of diabetic autonomic neuropathy

Increased renal Mg2+ losses due to osmotic diuresis, glomerular hyperfiltration,

diuretic administration

Recurrent metabolic acidosis

Calcium disorders

Hypocalcemia

Pseudohypocalcemia: hypoalbuminemia2

Acute renal failure due to accompanying hyperphosphatemia

Advanced chronic renal insufficiency due to hyperphosphatemia and low levels of

vitamin D

Nephrotic syndrome: loss of 25-hydroxyvitamin D3 and its binding protein in the urine

Hypomagnesemia

Vitamin D deficiency

Drug-mediated: loop diuretics

Hypercalcemia

Concurrent hyperparathyroidism

Thiazide therapy

Phosphorus disorders

Hypophosphatemia

Osmotic diuresis

Drugs: thiazides, loop diuretics, insulin

Malabsorption syndromes

Primary hyperthyroidism

Vitamin D deficiency

Methods and materials: The present Cross Sectional study was conducted in the Department of Medicine, M.G.M. Medical College and M. Y. Hospital, Indore (M.P.) during the period from March 2018 to February 2019. Minimum 50 Diabetic patients presenting with abdominal pain attending medicine outdoor & indoor clinic and patient admitted in wards of M.Y. Hospital, Indore, were included in the study. The study was approved by the Ethics Committee of M.G.M. Medical College and M. Y. Hospital, Indore (M.P.). Each patient was included after receiving her informed consent.

INCLUSION CRITERIA

1. Diabetic patients (both diabetes mellitus type 1 and type 2) presenting with abdominal pain.

2. Male and Female sex both, >15 year old will be included

3. Consent given by both patient and care taker are included.

4. Patient and care taker both should be capable of responding to various testing method

EXCLUSION CRITERIA

1. Patients who refuse to participate in the study.

2. Patient who are severely ill and disabled so as to become incapable to participate in study

3. Patient having other causes of acidosis (respiratory and metabolic)

4. Pregnant females

Detailed clinical history was taken from all the patients who were included in the study. History of Symptoms of DKA and acute pancreatitis like polyuria, polydipsia, breathlessness, abdominal pain, abdominal distention, nausea, vomiting, loose stool, fever, dysuria, myalgia, chest pain, mental disturbance were elicited. The past history including whether the patient was having type 1 or type 2 diabetes mellitus, precipitation factors like omission of insulin elicited. Past history of hypertension, hyper lipidemia, jaundice, TB, epilepsy, CAD, CKD, CVA, thyroid abnormalities, were analyzed. Drug history, personal and family history all were elicited. After taking the detailed history, all the patients were examined clinically in detail. A detailed general examination was done including, nourishment, pallor, fever, mental status changes, icterus, clubbing, pedal edema, significant lymphadenopathy, cyanosis. Vital signs like pulse, blood pressure, temperature, respiratory rate were taken. All the systems were examined carefully including optic fundus.

The following investigations were performed

1) Compete blood count – to find the anemia, leukocytosis, infections.

2) Renal function tests- urea, creatinine, sodium, potassium, blood glucose.

3) Liver function test - total bilirubin, Direct bilirubin, Alkaline

phosphatase, transaminases, total protein, albumin, globulin.

- 4) Chest X-ray
- 5) Electro cardiogram
- 6) Urine routine- Albumin, sugar, deposits
- 7) Urine acetone
- 8) Serum calcium, phosphorous, chloride
- 9) Arterial pH
- 10) Pa Co2
- 11) Serum bicarbonate
- 12) Urine culture & Sensitivity
- 13) Serum osmolality calculation
- 14) Serum lipid profile Total cholesterol, Triglycerides etc.
- 15) Serum Amylase and lipase estimation
- The normal values are
- Serum amylase 20-85U/L
- Serum lipase 3-140 U/L

Statistical analysis : The normal distribution of data checked by using Kolmogorov Smirnov test. All the characters descriptively summarized. The mean and standard deviation about the arithmetic mean were used. Chi Square test was used as the test of significance.

The data was compiled in Microsoft excel spread sheets and analyzed using statistical package for social sciences (SPSS) for windows version 16.0.

Table 2

Distribution on Basis of Sex Groups					
Sex	Frequency	Percentage			
Female	15	30.0			
Male	35	70.0			
Total	50	100.0			

The above table shows the distribution of respondents based on their Sex Group.

The highest percentage of respondents i.e. 70% belonged to Male patients and 30% were female patients.



Table 3

Association between Outcomes and Age Groups

Type of Diabetes	Frequency	Percentage
Type 1	30	60.0
Type 2	20	40.0
Total	50	100.0

The above table shows the distribution of respondents based on Type of Diabetes.

The highest percentage of respondents i.e. 60% belonged to Type 1 diabetes group and remaining 40% were having Type 2 diabetes.



Graph 3: Association between Outcomes and Age Groups

Results:

Sugar Level		Outcome				Total
		Amylase	Both	Lipase	Normal	Total
250-300	Count	0	0	0	0	0
	%	0.0%	0.0%	0.0%	0.0%	0.0%
300-350	Count	0	0	0	0	0
	%	0.0%	0.0%	0.0%	0.0%	0.0%
350-400	Count	0	0	0	1	1
	%	0.0%	0.0%	0.0%	5.6%	2.0%
400-450	Count	1	0	0	0	1
	%	4.8%	0.0%	0.0%	0.0%	2.0%
150 500	Count	3	0	0	2	5
450-500	%	14.3%	0.0%	0.0%	11.1%	10.0%
500-550	Count	7	2	2	3	14
	%	33.3%	22.2%	100.0%	16.7%	28.0%
550-600	Count	8	3	0	10	21
	%	38.1%	33.3%	0.0%	55.6%	42.0%
>=600	Count	2	4	0	2	8
	%	9.5%	44.4%	0.0%	11.1%	16.0%
Total	Count	21	9	2	18	50
Total	%	100.0%	100.0%	100.0%	100.0%	100.0%

Association between Outcomes and Sugar Level

Chi Square = 17.071, df =15, P Value = 0.315 Non Significant

The above table shows the association between Outcomes and Sugar Level of the patient which was found to be non-significant (P >0.05). Patients having Amylase outcome show higher percentage 38.1% for Sugar Level 550-600 while, show lower percentage 1% for 400-450. For Lipase Outcome, patients show 44% for Sugar Level > 600 followed by 33.3% in 550-600 range and lowest 22.2% in 500-550 and For Both Outcome, patients show 100% for Sugar Level 500 -550. Similarly, for Normal Outcome, patients higher percentage 55.6% for Sugar Level 550-600 while, show lower percentage 1% for 350-400 range.

Sodium Level		Outcome				Total
		Amylase Lipase Both		Normal	Total	
< 135	Count	11	2	5	14	32
	%	52.4%	100.0%	55.6%	77.8%	64.0%
135-145	Count	8	0	3	3	14
	%	38.1%	0.0%	33.3%	16.7%	28.0%
> 145	Count	2	0	1	1	4
	%	9.5%	0.0%	11.1%	5.6%	8.0%
Total	Count	21	2	9	18	50
	%	100.0%	100.0%	100.0%	100.0%	100.0%

Chi Square = 4.188, df = 6, P Value = 0.651 Non Significant

The above table shows the association between Outcomes and Sodium Level of the patient which found to be non-significant (P >0.05). Patients having Amylase outcome show higher percentage 52.4% for Sodium Level < 135 while, show lower percentage 9.5% for > 145. For Lipase Outcome, patients show 100% for Sodium Level < 135. For Both Outcome, patients show higher percentage 77.8% for Sodium Level < 135 while, show lower percentage 11.1% for > 145. Similarly, for Normal Outcome, patients higher percentage 55.6% for Sodium Level < 135 while, show lower percentage 5.6% for > 145

Potassium Level		Outcome				Total
		Amylase	Lipase	Both	Normal	Total
< 3.5	Count	0	0	1	0	1
	%	0.0%	0.0%	11.1%	0.0%	2.0%
3.5-5.3	Count	15	0	4	14	33
	%	71.4%	0.0%	44.4%	77.8%	66.0%
> 5.3	Count	6	2	4	4	16
	%	28.6%	100.0%	44.4%	22.2%	32.0%
Total	Count	21	2	9	18	50
	%	100.0%	100.0%	100.0%	100.0%	100.0%

Association between Outcomes and Potassium Level

Chi Square = 10.922, df = 6, P Value = 0.091 Non Significant

The above table shows the association between Outcomes and Potassium

Level of the patient which found to be non-significant (P > 0.05).

Patients having Amylase outcome show higher percentage 71.4% for

Potassium Level 3.5-5.3 while, show none for < 3.5.

For Lipase Outcome, patients show 100% for Potassium Level >5.0.

For Both Outcome, patients show higher percentage 44.4 % for 3.5-5.3

and > 5.3 Potassium Levels while, show lower percentage 11.1% for <

3.5 level.

Similarly, for Normal Outcome, patients show higher percentage 77.8%

for Potassium Level 3.5-5.3 while, show none for < 3.5.

Discussion:

In our comparative study, the association between elevated amylase, lipase levels and sugar levels were found to be non significant.

However amylase and lipase outcome showed higher percentage at higher sugar levels.

On similar lines, association between amylase lipase outcomes and sodium levels were found to be non significant. However amylase outcome was seen higher for Sodium levels < 135 mg/dl in comparision with Sodium levels > 135 mg/dl. And lipase outcome was exclusively for Sodium levels < 135 mg/dl, which shows sodium < 135 mg/dl has higher chances for amylase lipase outcome compare to >145 mg/dl.

The association between amylase lipase outcomes and potassium levels were found to be non significant. Positive Amylase outcome was found in patients with normal potassium levels and none in hypokalemic patients. Positive lipase outcome was exclusively present in hyper kalemia which shows amylase lipase outcomes are either present in normal and hyperkalemia but not in hypokalemia.

In our study, although the associations between sodium potassium and amylase lipase outcome was found to be non significant, but that could be due to limitations as some degree of exclusiveness and relation could be seen in results. Limitation: lower sample size. No follow up data available. Conflict of interest: none

References:

1. Liamis G, Milionis HJ, Elisaf M. A review of drug-induced hypocalcemia. *J Bone Miner Metab.* 2009;27:635–642. [PubMed] [Google Scholar]

2. Liamis G, Kalogirou M, Saugos V, Elisaf M. Therapeutic approach in patients with dysnatraemias. *Nephrol Dial Transplant*. 2006;21:1564–1569. [PubMed] [Google Scholar]

 Liamis G, Rodenburg EM, Hofman A, Zietse R, Stricker BH, Hoorn EJ. Electrolyte disorders in community subjects: prevalence and risk factors. *Am J Med.* 2013;126:256–263. [PubMed] [Google Scholar] 4. Elisaf MS, Tsatsoulis AA, Katopodis KP, Siamopoulos KC. Acid-base and electrolyte disturbances in patients with diabetic ketoacidosis. *Diabetes Res Clin Pract.* 1996;34:23–27. [PubMed] [Google Scholar]

5. Steinberg WM, Nauck MA, Zinman B, Daniels GH, Bergenstal RM, Mann JF, Steen Ravn L, Moses AC, Stockner M, Baeres FM, Marso SP, Buse JB; LEADER Trial investigators. LEADER 3--lipase and amylase activity in subjects with type 2 diabetes: baseline data from over 9000 subjects in the LEADER Trial. Pancreas. 2014 Nov;43(8):1223-31. doi: 10.1097/MPA.00000000000229. PMID: 25275271; PMCID: PMC4206347.

 Ibarra G, Majmundar MM, Pacheco E, Zala H, Chaudhari S. Hypernatremia in Diabetic Ketoacidosis: Rare Presentation and a Cautionary Tale. Cureus. 2020 Dec 2;12(12):e11841. doi: 10.7759/cureus.11841. PMID: 33409080; PMCID: PMC7781561.

7. Batra HS, Kumar A, Saha TK, Misra P, Ambade V. Comparative study of serum amylase and lipase in acute pancreatitis patients. Indian J Clin Biochem. 2015 Apr;30(2):230-3. doi: 10.1007/s12291-013-0416-y. Epub 2014 Jan 24. PMID: 25883434; PMCID: PMC4393381.

8. https://www.wjpls.org/home/article_abstract/609

 Electrolyte Disturbances among Diabetic Patients Admitted in a Multi-specialty Hospital in Southern India.

DO - 10.7860/JCDR/2019/38487.12573

JO - JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH

10. Liamis G, Liberopoulos E, Barkas F, Elisaf M. Diabetes mellitus and electrolyte disorders. World J Clin Cases. 2014 Oct 16;2(10):488-96.

doi:10.12998/wjcc.v2.i10.488. PMID: 25325058; PMCID: PMC4198400.