TITLE: PERCENTAGE OF AMYLASE, LIPASE POSITIVITY WITH INCREASING SUGAR LEVELS IN DIABETES MELITUS PATIENTS

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Background: increased serum amylase and lipase influences the glucose homeostasis, and hence, control of hyperglycemia may be more difficult. increased serum amylase and lipase can also induce ketosis and hyperglycemia in a   patient having diabetes mellitus hence may be a primary event rather than   a sequel to Diabetes. That's why it was decided to take a cross sectional study on the elevation   of serum amylase and lipase in patients with Diabetes.

Methods 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 March 2018 to February 2019. Minimum 50 Diabetic attending outdoor & indoor clinic and patient admitted in wards of M.Y. Hospital, Indore, were Included. The study was approved by the Ethics Committee and informs consent was taken.

Result :
The association between elevated serum amylase, lipase levels and Sugar Level was found to be non-significant (P >0.05). 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. For Both Outcome, patients show 100% for Sugar Level 500 -550.

Conclusion : with increasing blood sugar levels, the chances of elevating serum amylase and serum lipase increases. How ever there was no clear association found.

Introduction: Type 2 diabetes mellitus is a chronic metabolic disorder due to resistance of insulin because of beta cells destruction in pancreas (1). The prevalence of diabetes mellitus estimated to be 347 million individuals globally in 2011, it may double itself till 2030, in India count may go as high as 73 million by 2030(2). Hyperglycemia leads micro and macro complications in T2DM patients involving multiple organ and systems. (3) In T2DM multiple pathophysiological alterations occur in pancreas leads to impaired insulin secretion and some changes amylase and lipase synthesis. (4) Pathological changes in pancreas leads to elevated serum amylase, lipase levels and are useful in diagnosing acute pancreatitis and other conditions particularly in diabetes mellitus.(5) The increased levels of serum lipase is early detective and sensitive biomarker for pancreatitis, pancreatic duct obstruction, and other pancreatic conditions particularly secondary T2DM.(6). This study was evaluated for positive correlation of serum amylase and lipase levels with blood sugar levels and useful for further progression of newly diagnosed T2DM. **SERUM AMYLASE (7)** It is a heterogeneous calcium dependent metallo enzyme of M54-62kDa. There are 2 iso enzymes exist: P type– Pancreatic, S-type-non Pancreatic. Highest activities of P-type enzyme is found in exocrine pancreas. S-type enzymes highest activities is being found in salivary glands. It has a very wide tissue distribution. Pancreatic acinar cells synthesize P-type amylase and secreted into the intestinal tract through the ductal system of

pancreas. The mild alkaline condition of duodenum favours the act on of P-type amylase. The S-type amylase is synthesized in salivary glands, and it starts the hydrolysis of starch when the food is swallowed and passing through the mouth and esophagus. The acid in the stomach terminates the act on of S type amylase. 22Extracts of testes, ovaries, fallopian tubes, mullerian ducts, striated muscles, lungs, adipose tissue, semen, colostrum, tears and milk are some of organs and secretions, where S-type amylase can be found. Kidneys excrete about 25% of plasma amylase, but the majority of excreted amylase is reabsorbed by the proximal tubule.

Hyperamylasemia causes: [7]

1. Pancreatitis, Pancreatic trauma, pancreatic tumors etc, are some of the pancreatic diseases showing elevated P-type amylase.

2. intra abdominal diseases: (eg) biliary treat diseases, obstruction, mesenteric infarction, liver disease, acute appendicitis – showing

elevated P-type amylase

3. Salivary gland infection, trauma, irradiation can cause raised S-type amylase.

4. Tumour of ovaries, prostate, testes, esophagus, thymus, thyroid, lung, ruptured ectopic pregnancy, and renal diseases including renal insufficiency can cause raised S-type amylase.

5. HIV, DKA, macroamylasemia and various drugs (opiates, diuretics, steroids) are miscellaneous conditions causing elevation of serum amylase.

SERUM LIPASE (7)

The triglycerides are hydrolysed by lipase. There are many forms of lipase available

1. Pancreatic lipase
2. Colipase
3. Lipoprotein lipase

CAUSES OF INCREASED LIPASE: (7)

Drugs: lipase values are Increased by corticosteroids.

Acute pancreatitis: When pancreatic acinar tissue is destroyed, the pancreatic enzymes are released in to the pancreas and peritoneal cavity.

Gastrointestinal disease: lipase values are 2-3 times increased by peritonitis, bowel obstruction, visceral obstruction (laparotomy). Neoplasia and hepatic diseases.

Decreased renal function: Decreased renal function can increase the lipase values upto 4 times the normal. When the lipase values are more than 3-4 times, diagnosis of pancreatitis should be considered, even if the patient is azotemic. (8) There are studies reporting non specific hyper lipasemia in patients with DKA. Only few possible explanations can be offered to this finding. The molecular weight of lipase is 46-52KD is filtered in the kidneys to get reabsorbed by the renal tubules. In renal tubules the lipase gets metabolized. In DKA patients even with normal renal function the handling of lipase by the kidneys is compromised due to hypovolemia. So it may cause the elevation of serum lipase. When pancreatic beta cells are destroyed by immune mediated attack in type 1 DM, spillover causes the pancreatic acinar to get damaged, thereby causing elevated serum lipase levels due to release in to the serum. Systemic derangement of carbohydrate metabolism in DKA can cause hyper amylasemia since salivary type amylase are widely distributed in glandular epithelium. The stomach and intestinal epithelium can release lipolytic enzymes in to the circulation in the presence DKA. When GFR is reduced due to the dehydration in DKA, it can lead to elevated serum lipase levels, without actual pancreatic involvement.

Hyper amylasemia has been reported very frequently in patients with DKA. During episodes of DKA, hyper amylasemia develops during hospitalization, not in the initial phase of DKA.

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.

Socio demographic details -

Table 1

Distribution on Basis of Age Groups

AGE GROUP	Frequency	Percentage
15-40 Year	31	62.0
40-60 Year	10	20.0
> 60 Year	9	18.0
Total	50	100.0

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

The highest percentage of respondents i.e. 62% belonged to 15-40 Years of age group followed by 20% in 40-60 years and least 18.0% in > 60 Years of age group.
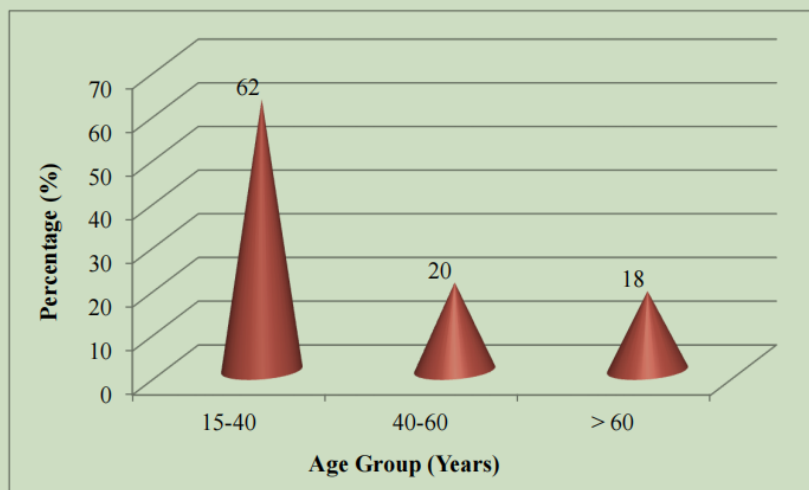
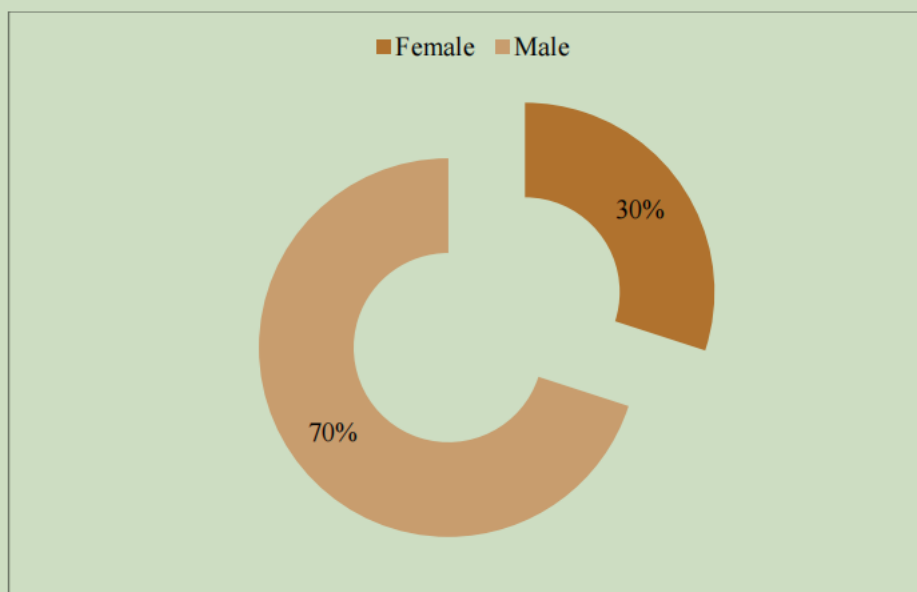**Graph 1: Distribution on Basis of Age Groups**

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.

**Graph 2: Distribution on Basis of Sex Groups**

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.
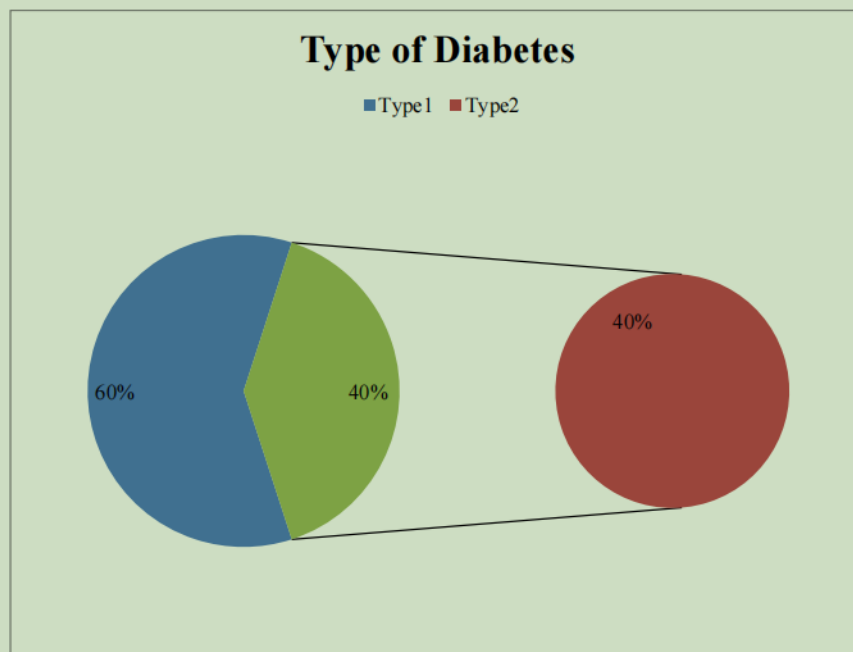
Graph 3: Association between Outcomes and Age Groups

Results-

Association between Outcomes and Sugar Level						
Sugar Level		**Outcome**				**Total**
		Amylase	**Both**	**Lipase**	**Normal**	
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%
450-500	Count	3	0	0	2	5
	%	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
	%	100.0%	100.0%	100.0%	100.0%	100.0%

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.

Discussion :

Hyper glycaemia is caused by improper secretion and insulin resistance due to dysfunction of beta cells of pancreas(9,10). Diabetes mellitus has multifactorial causation including dyslipidemia and changes of lifestyle, dietary habits. (11,12). It causes Micro and macro vascular complications like nephropathy, neuropathy, cardiovascular, cerebrovascular and peripheral vascular complications.   Present study focus on percentage of amylase lipase positivity with increased blood sugar levels. (13,14,15) Similarly previous studies also found that synthesis, excretion and degradation of serum amylase and lipase levels altered that given the limited pathological changes in T2DM and also they reported that several possible explanations for increased levels of serum amylase and lipase levels in newly diagnosed type 2 diabetes mellitus patients. (14,15) Some of the studies says that decreased levels of serum amylase and lipase levels are observed in T2DM patients, says that serum amylase and lipase levels are negatively correlated with the blood sugar, results found that the linkage of islets and acinar cells of pancreas (9,10).

In our study 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 the association between Outcomes and Sugar Level of the patient which was found to be non-significant (P >0.05). there is trend toward increase in amylase lipase level along with RBS although the p value is not significant .This is consistent with the studies of **Vantyghem MC et al[16] and Warshaw AL et al[17].**

Based on this conflict the present study supports that elevated serum amylase and lipase levels are useful for detection and progression T2DM patients at higher levels of blood sugars only.

Conclusion : with increasing blood sugar levels, the chances of elevating serum amylase and serum lipase increases. How ever there was no clear association found.

Limitation: This study didn't followed up and also less sample size, large sample size and follow up studies are required.

References

1. Henderson JR, Daniel PM, Fraser PA. The pancreas as a single organ: the influence of the endocrine upon the exocrine part of the gland. Gut. 1981;22:158-67.

2. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes estimates for the year 2000 and projections for 2030. Diabetes Care. 2004;27(3):1047-53.

3. Ewald N, Hardt PD. Diagnosis and treatment of diabetes mellitus in chronic pancreatitis. World J Gastroenterol. 2013;19(42):7276-81.

4. Yegneswaran B, Pitchumoni CS. When should serum amylase and lipase levels be repeated in a patient with acute pancreatitis?. Cleve Clin J Med. 2010;77:230-231.

5. Aughsteen AA, Abu-Umair MS, Mahmoud SA. Biochemical analysis of serum pancreatic amylase and lipase enzymes in patients with type 1 and type 2 diabetes mellitus. Saudi Med J. 2005;26:73-77.

6. Kaur A, N Verma. Proteomics: A hallmark tool for identification of biomarker (LIPASE) in type I & II diabetes mellitus patients. Adv Appl Sci Res. 2012;3(3):1842-847.

7.Sangeshwaran C. Dissertation on elevated serum amylase and lipase levels without actual pancreatic involvement in the presence of DKA – an observational study. Institute of Internal Medicine, Madras, Medical College, Chennai. April 2013.

8. Fishbein HA, Fishbein HA, Palumbo PJ: Acute metabolic complications in diabetes. In Diabetes in America. National Diabetes Data Group, National Institute of Health,1995, p.283–291 (NIH publ. no. 95-1468).

9.Gonzales-Perez A, Schlienger RG, Rodriguez LA. Acute pancreatitis in association with type 2 diabetes and antidiabetic drugs. Diabetes Care. 2010;33(12):580-2585.

10. Noel RA, Braun DK, Patterson RE. Increased risk of acute pancreatitis and biliary disease observed in patients with type 2 diabetes: a retrospective cohort study. Diabetes Care. 2009;32:834-38.

11. Chiolero A, Faeh D, Paccaud F, Cornuz J. Consequences of smoking for body weight, body fat distribution, and insulin resistance. Am J Clin Nutr. 2008;87:801-09.

12. The committee of Japan Diabetes Society on the diagnostic criteria of diabetes mellitus: Report of the Committee on the classification and diagnostic criteria of diabetes mellitus. J Jpn Diabetes Soc. 2010;53:450-67.

13.The committee of Japan Diabetes Society on the diagnostic criteria of diabetes mellitus: Report of the Committee on the classification and diagnostic criteria of diabetes mellitus. J Jpn Diabetes Soc. 2010;53:450-67.

14.Wang YM, Zhao LH, Su JB, Qiao HF, Wang XH, Xu F, et al. Glycemic variability in normal glucose tolerance women with the previous gestational diabetes mellitus. Diabetol Metab Syndr. 2015;7:82.

15. Nathan DM, Turgeon H, Regan S. Relationship between glycated haemoglobin levels and mean glucose levels over time. Diabetologia. 2007;50:2239-244.

16. Vantyghem MC, Haye S, Balduyck M, Hober C, Degand PM, Lefebvre J. Changes in serum amylase, lipase and leukocyte elastase

during diabetic ketoacidosis and poorly controlled diabetes. Acta
Diabetol. 1999 Jun;36(1-2):39-44.

17. Warshaw AL, Feller ER, Lee KH: On the cause of raised serum
amylase in diabetic ketoacidosis. Lancet 1: 929–931, 1977.