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Evaluation of serum amylase and serum lipase as biochemical markers of pancreatic exocrine function in type II diabetes mellitus

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Abstract---Background: Diabetes mellitus is a metabolic ailment characterized by hyperglycemia in which there is a severe derangement of the endocrine functionality of the pancreas. Studies have demonstrated the association of pancreatic enzymes as biomarkers of exocrine function in DM-II. Material and methods: In this case-controlled study total 90 subjects were included, which were separated into two groups DM (n=45) and non-DM (n=45). The non-diabetic control group was age and sex-matched. After inclusion, written informed consent was acquired from all the individuals and they were investigated for serum amylase and lipase levels. Other routine investigations were also done. The data was then recorded and statistical analyses were done. Results: This study showed that mean amylase in DM group (44.69±15.57) was lesser than in non-DM group (60.69±21.67). Similarly, the mean lipase in DM group (35.44±11.30) was lesser than in non-DM group (48.47±12.73). With increase in Glycated haemoglobin, both enzyme levels decreased substantially when assessed with the non-DM groups. It was also showed that in patients with higher LDL (> 110) the serum amylase levels decreased further compared to the non-DM patients. Similar results were reported for serum lipase also. Conclusion: From this study it can be concluded that in type 2 DM, serum amylase and lipase activity is substantially decreased. This highlighted the importance of these two

enzymes as a biochemical marker for exocrine functionality of pancreases in these individuals.

Keywords---serum amylase, serum lipase, type II diabetes mellitus, endocrine-exocrine axis of pancreas.

Introduction

Diabetes mellitus mainly occurs due to two different biochemical causes that include lack or reduced insulin secretion and resistance of body organs to the action of insulin, hence the two types, type 1, and type 2, respectively. Resistance to insulin hormone is explained as the decrement in the sensitivity that is shown by the target organs against the effects of insulin [(1)].The beta cells of the pancreas are responsible for the secretion of insulin. Both type 1 and type 2 diabetes are distinguished by high glucose levels in the blood of individuals also known as hyperglycemia. The presence of persistent hyperglycemiais associated with multiple complications in diabetic individuals. It is interesting to note that the pancreas can behave as an exocrine as well as an endocrine gland [(2)]. The presence of islet cells is in the proximity of the acinar cells and hence any defect in the islet cells will have an impact on the acinar cells present in the neighbouring sites in the pancreas. The defects in the secretion of insulin and function cause hyperglycemia and may further lead to issues in the synthesis of enzymes and their release from the exocrine part of the pancreas. The enzymes protease, lipase, and amylase are secreted by the pancreas (3).

The pancreas under normal conditions releases these enzymes to aid in digestion for example the enzyme lipase aids in the breakdown of triglycerides into monoglycerides and fatty acids that can be further solubilized by the action of bile salts. The exocrine role of the pancreas can be disturbed in both type 1 and type 2 diabetic individuals [(4,5)]. Nearly one-third of individuals with diabetes have been suggested to have severe exocrine dysfunction of the pancreas that is reflected by the reduced concentration of the fecal elastase-1 in 30% of T2DM patients and 26-40% of T1DM individuals [(5)]. There is uncertainty in the cause for the insufficiency of exocrine function. Mostly these have been perceived as diabetes complications but recently discussions are underway for the hypothesis that these alterations may attribute to a disease of the entire pancreas and may be categorized into a new form of diabetes as type 3c diabetes [(5)]. This investigation highlighted low levels of lipase and amylase in the T1DM individuals whereas in T2DM individuals the levels of amylase were substantially low in comparison to control subjects. The fasting blood sugar levels were high in both T1DM individuals and in T2DM individuals in comparison to control subjects. Comparable observations were seen in another study, where 20.4 ± 8.8 u/l (amylase) and 19.8 ± 5.6 u/l (lipase) were observed in T1DM individuals, respectively. In the case of T2DM, the reduced levels for lipase and amylase were found to be 26.5 ± 7.8 u/l and 35.3 ± 17.8 u/l, respectively.

Methodology

This study was conducted at Department of General Medicine, SKBS M.I.R.C., Dhiraj Hospital, Sumandeep Vidyapeeth institute, Pipariya, Vadodara. The study was case control study. The study was started after getting approval from the institutional ethics committee. The study was conducted in a period of one and a half years between December 2019 and June 2021. A sample size of 90 (45 cases and 45 controls), were studied belonging to all age and sex groups who visited Dhiraj Hospital, SBKS MIRC, Suman deep Vidyapeeth institute, Pipariya. Patients attending OPD/IPD were recruited in our study abiding the inclusion and exclusion criteria and after getting informed consent from the patient in written format. Informed consent for the study were enclosed here. The format of the consent form was either in English, Hindi and Gujarati version. Privacy of all patient's data was maintained.

Inclusion Criteria

- Age > 18 years.
- Patients who are known case of type II diabetes mellitus or newly detected type II diabetes mellitus as per ADA (American Diabetic Association) criteria were enrolled as cases.
- ADA criteria for diagnosing diabetes mellitus.

Exclusion Criteria

- Any person who is not willing to participate in study.
- Age < 18 years.
- Patients with acute or chronic pancreatitis.
- Chronic alcoholic individuals.
- Patients having gall stones.
- Type I diabetic patients.

Age and sex matched non-diabetic individuals were be taken as controls after obtaining written informed consent.

All participants included in this study were subjected to complete history including demographic profile, detailed history about diabetes mellitus and other co- morbidities. Complete clinical examination including general, systemic and fundus examination was done. Serum Amylase and Serum Lipase were measured in EM200 machine. The levels were measured by Enzymatic Colorimetric estimation method in the central lab at Dhiraj Hospital. For estimation of levels, 2 ml blood was withdrawn from patient preferably in a fasting state. Blood was collected in a plain vacuette with the help of a sterile disposable plastic syringe. Reference value of S. Amylase – upto 96 U/L Reference value of S. Lipase – upto 60 U/L. Apart from this, participants were subjected to routine investigations like complete hemogram (CBC), urine routine micro, renal function tests, serum electrolytes, liver function tests, electrocardiography, USG abdomen-pelvis and FBS, PPS and HbA1cas a part of diabetic work up.

Results

Table 1
Gender wise distribution in DM & Non-DM group

			Group		Total
			DM Group	Non-DM Group	
Sex	Female	Count	18	15	33
		% within Sex	54.5%	45.5%	100.0%
		% within Group	40.0%	33.3%	36.7%
	Male	Count	27	30	57
		% within Sex	47.4%	52.6%	100.0%
		% within Group	60.0%	66.7%	63.3%
Total		Count	45	45	90
		% within Sex	50.0%	50.0%	100.0%
		% within Group	100.0%	100.0%	100.0%

P-value = 0.512 (Not Significant)

In DM group (n=45), male patients (60.0%) were higher than female patients (40.0%) and also in Non-DM group (n= 45), male patients (66.7%) were higher than female patients (33.3%). However, this association was not statistically significant (p =0.512).

Table 2
Mean age among groups

Group	Sex	N	Mean age	Std. Deviation	P-value
DM Group	Female	18	54.78	15.082	0.456
	Male	27	57.67	10.706	
	Total	45	56.51	12.556	
Non-DM Group	Female	15	44.93	17.023	0.533
	Male	30	41.40	18.099	
	Total	45	42.58	17.633	
Total	Female	33	50.30	16.505	0.746
	Male	57	49.11	17.029	
	Total	90	49.54	16.755	

In DM group (n=45), the mean age was 56.51±12.56 years. Out of this, the mean age in males (57.67±10.71 years) was higher than the mean age in females (54.78±15.08 years). However, this distribution was not statistically significant (P = 0.456). In Non-DM group (n=45), the mean age was 42.58±17.63 years. Out of this, the mean age in males was 41.40±18.09 years and the mean age in females was 44.93±17.02 years. There was no significant difference between the age group in males and females for Non-DM group (P = 0.533).

Table 3
Mean amylase and lipase in DM & Non-DM group

Variable	DM Group			Non-DM Group			
	n	Mean	SD	n	Mean	SD	P-value
Amylase	45	44.6889	15.5663	45	60.6889	21.6720	0.0001
Lipase	45	35.4444	11.3028	45	48.4667	12.7254	<0.0001

The mean amylase in DM group (44.69±15.57) was lesser than the mean amylase in Non-DM group (60.69±21.67) with a P value <0.0001. This difference is statistically significant. The mean lipase in DM group (35.44±11.30) was lesser than the mean lipase in Non- DM group (48.47±12.73) [P<0.0001]. This is statistically significant.

Table 4
co-relation of mean amylase and lipase with glycemic control (hbA1c)

	HbA1c Group	N	Mean	Std. Deviation	P-value
Amylase	< 7.5	15	52.80	18.440	0.006
	7.5-8.5	6	47.33	6.439	
	8.5-10	9	47.00	12.339	
	> 10	15	34.13	11.109	
	Total	45	44.69	15.566	
Lipase	< 7.5	15	40.07	12.127	0.020
	7.5-8.5	6	39.33	5.922	
	8.5-10	9	37.00	11.136	
	> 10	15	28.33	9.271	
	Total	45	35.44	11.303	

In DM group of patients, the mean amylase in patients with hba1c more than 10 was 34.13 and that in patients with hba1c less than 7.5 was 52.80. This difference was statistically significant (p = 0.006). Hence, it was seen that as the hba1c of the patient increases, amylase levels decrease. Similarly, this difference between lipase values was also found to be significantly reduced in patients with poor glycemic control. (p = 0.020)

Table 5
Variation in Mean amylase and lipase with Duration of DM

Duration of DM		N	Mean	Std. Deviation	P-value
Amylase	0-5 Years	24	49.00	18.685	0.052
	5-10 Years	14	43.00	7.200	
	>10 Years	7	33.29	9.673	
	Total	45	44.69	15.566	
Lipase	0-5 Years	24	38.58	11.647	0.035
	5-10 Years	14	34.64	10.233	
	>10 Years	7	26.29	7.158	
	Total	45	35.44	11.303	

In this table, the mean lipase levels in patients with duration of diabetes > 10 years was on lower side when compared to those with duration of less than 5 years, which was statistically significant. (26.29 vs 38.58, p =0.035). However, the relation between amylase levels and duration of diabetes was not statistically significant [P=0.035].

Discussion

Diabetes mellitus is a metabolic ailment characterized by hyperglycemia. In this disorder there is a severe derangement of the functionality of endocrine functionality of the pancreas. Studies have pointed out association of the exocrine and endocrine pancreatic functions. Lipase and amylase are two enzymes secreted from the exocrine part of the pancreas. Diabetes mellitus mainly occurs due to two different biochemical causes that include lack or reduced insulin secretion and resistance of body organs to the action of insulin. Resistance to insulin hormone is explained as the decrement in the sensitivity that is shown by the target organs against the effects of insulin [1]. The beta cells of the pancreas are responsible for the secretion of insulin. Both type 1 and type 2 diabetes are distinguished by high glucose levels in the blood of individuals also known as hyperglycemia. The presence of persistent hyperglycemia is associated with multiple complications in diabetic individuals. Diabetes mellitus is a metabolic disease which is rapidly increasing across the world and is projected to double by the year 2030 [11]. This defects in insulin secretion results in hyperglycemia and thus affects the enzyme synthesis and release of the enzyme. The exocrine part of the pancreas is associated with the release of enzymes such as lipase, amylase, andproteases [12].

Studies have also pointed out that patients with diabetes has a lower level of serum amylase compared to the healthy controls [13]. In diseases of pancreas including the pancreatic duct obstruction or in pancreatic cancer the level of serum lipase and amylase increases [14]. In the present study total 90 patients were included. Among them 45 patients were in the DM group and 45 patients were in the non-DM group. In both the groups no. of male patients were higher compared to the female patients. The mean age of DM patients were 58.5±12.5 years. Out of this, the mean age in males (57.6±10.7 years) was higher than the mean age in females (54.7±15.0 years). There was no significant difference between males and females for DM group (P = 0.456). In Non-DM group (n=45), the mean age was 42.5±17.6 years. Out of this, the mean age in males (41.4±18.0 years) was higher than the mean age in females (44.93±17.02 years). However, these age and gender distribution did not show any statistical significance.

In this study it was found that in the Diabetic patients the mean amylase level (44.69±15.57) is substantially lower as compared to their non diabetic counterparts, and this observation was statistically very significant, (44.6 + 15.5 Vs 60.7±21.6; P<0.0001). This study also found that even serum lipase levels were also on lower side in diabetic population (35.4±11.3 Vs 48.4±12.7, P<0.0001). Aughteen et al conducted a similar study where they concluded that serum amylase and lipase levels were on lower side in diabetic population when compared to the healthy controls.[15] Skrha J et al. [8] discovered that insulin-dependent diabetic individuals had decreased serum lipase and isoamylase levels

in a study conducted by them. This finding could be explained by reduced acinar cell function in the region of insulin-depleted islets. Nakajima in a review pointed out that in several metabolic disorders and also in obesity, the level of serum amylase decreases. In obese subjects however, the level of salivary amylase decreases. They have correlated this fact with the change in the copy number of these enzymes in individuals [16]. These findings were evaluated by several theories that can evaluate this change in the enzyme status. Reduced amylase secretion in diabetic pancreas may be attributed to reduced cytosolic free calcium concentration (Ca^{2+}) and gene expression for amylase, rather than gene expression of cholecystokinin (CCK) a receptor in pancreatic acinar cells, according to Patel R et al [9]. On the contrary, there were one or two studies which showed that the enzyme levels increased in diabetic patients [6]. Steinberg WM et al [17] in his study showed that amylase and lipase levels were raised above baseline in type 2 diabetic patients. In another study by Yadav et al lower level of amylase were reported in diabetic patients compared with the healthy controls similar to our study [18].

As far as glycemic control and mean decrease in amylase levels were concerned, our study found a statistically significant correlation with $p < 0.01$. With poor glycemic control, the mean amylase levels were on lower side, when compared to diabetics with good glycemic control. In those with HbA1C > 10 had a mean amylase level of 34.13±11.11, which was lower than those with HbA1c < 7.5, 52.8±18.4. Serum lipase level also showed the same pattern as amylase when correlated with glycemic control, (28.3±9.2 Vs 40.07, p- 0.02). Serum lipase levels were much lower when compared to amylase levels in patients with poor glycemic control (34.13±11.11 Vs 28.3±9.2). Because of diminished insulin action induced by insulin resistance and/or insufficient insulin synthesis, low serum amylase and lipase levels in diabetes were observed to be associated with higher blood glucose levels indicating a negative correlation. In both type 1 and type 2 diabetes, the insufficiency of pancreatic exocrine acinar cells resulted in a decrease in amylase, which was linked to a decrease in lipase indicating a positive correlation. The majority of diabetics have pancreatic fibrosis and other abnormalities such as fatty infiltration, atrophy, and loss of functionality of exocrine acinar cells. Hyperglycemia may be toxic to acinar amylase secretion, reducing exocrine reserves, suggesting a relationship between low circulating amylase levels and poor glycemic management [10]. These findings may not be in line with those of Blaak et al. In this study the authors reported found no significant link between Glycated haemoglobin and pancreatic amylase activity in an early study. [7] In a research article published in 2021 by Ananthi N et al at a medical college, they found a significant co-relation between HbA1c levels and amylase lipase levels in diabetic patients. They found out that the levels reduced with poor glycemic control. It shows that there is further damage to pancreas as the disease remains uncontrolled causing further exocrine insufficiency. In a previous study conducted by Ata et al it was reported that with improvement in the glycemic control, the serum amylase and lipase levels increased significantly in diabetic patients from before when there was no glycemic control. This study reported that basal HbA1c levels have a correlation with the serum lipase and amylase level and monitoring level of both the enzymes can significantly help in understanding the glycemic control among diabetic individuals [19].

Our study reported that higher duration of DM has no statistical significance with the serum amylase levels [P=0.052]. However, our study showed that duration of diabetes has a statistically significant co-relation with lipase levels [p=0.035]. As the duration of diabetes increases, the lipase levels decreases. In a study conducted by Akhter QS et al[20] in 2015, they studied the levels of amylase and lipase in diabetic patients and compared that with the duration of the disease where in they found out that the enzyme levels had negative co-relation with the duration of the disease meaning as the duration of diabetes in patients increased, the levels of both amylase and lipase decreased in patients. Moreover, in patients with long-standing diabetes the amylase levels also gets affected because of the change in the pancreatic functionality [21]. Another study by Aughsteen AA et al pointed out that in patients with long standing diseases the level of both the amylase and lipase decreases significantly. Also, reduction in levels of both enzymes was higher in long standing illness indicating duration of disease has a role in affecting the exocrine functioning of pancreas [22].

Conclusion

The present study reported that in type 2 diabetes, serum amylase and serum lipase levels were shown to be considerably lower. Also, the levels were lower with poor glycemic control of the patients. Lipase levels significantly reduce with the duration of diabetes. Both amylase and lipase levels reduced with the presence of diabetic complications. In the treatment and progression of DM, serum amylase and serum lipase should be investigated further as biochemical indications of pancreatic exocrine function. The current study shows an pancreatic exocrine destruction in type 2 DM. Serum pancreatic enzymes can be used as an extra explanatory parameter for the evaluation of progression of the disease and response to treatment.

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