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Assessment of Serum Amylase in Type-II Diabetes Mellitus Patients with a Putative Link to Pancreatic Function

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Abstract: ***Background**: The malfunctioning of the pancreas is intimately linked to diabetes mellitus. Because of their close anatomical and functional relationship, this study is aimed to look at the effects of hyperglycaemia on the exocrine and endocrine parts of the pancreas. **Aims and Objectives**: The purpose of this study was to evaluate serum amylase levels in type 2 diabetic patients and healthy persons, as well as to examine if there was a link between serum amylase levels, fasting blood glucose levels, and glycated haemoglobin (HbA1c) in type 2 diabetic patients and healthy people. **Materials and Methods**: The present hospital based case control study was conducted on 140 subjects, out of which 70 were cases diagnosed with type 2 diabetes mellitus and 70 were healthy controls with the age group of 40 to 65 years, irrespective of gender. Serum samples taken for fasting blood sugar, HbA1c and serum amylase level of all the subjects and run on Siemens Dimension RXL Max. Unpaired Student's 't' test and Pearson's correlation coefficient (r) test were used for statistical analysis. **Results**: Low blood amylase concentrations were seen in the cases as compared to the controls, and there was also a negative link between serum amylase levels and the duration of sickness. **Conclusion**: The diabetic participants in this study had a considerable drop in serum amylase levels, which could point to aetiology of reduced insulin action related to insulin resistance. This causes the exocrine-endocrine axis to become disrupted, resulting in decreased enzyme secretion.*

Keywords: Serum Amylase, Type 2 Diabetes Mellitus, Exocrine and Endocrine Pancreas

1. Introduction

Diabetes mellitus is a metabolic regulatory imbalance marked by a rise in blood glucose levels over the normal range (hyperglycaemia).[1] Polyuria, polydipsia, and polyphagia are the most common signs of diabetes mellitus. Impaired insulin secretion, aberrant action, or a combination of the two may be the root reasons for this.[2] Diabetic consequences include both microvascular and macrovascular problems.[3] Chronic diabetes mellitus is connected to long-term damage that leads to organ failure, with the kidneys, eyes, nerves, and heart being the most commonly affected organs.[4]

Fasting blood glucose (FBG) 126mg/dL or 2 hour after 75 gm glucose 200mg/dL or Random blood glucose (RBG) 200mg/dL or glycosylated haemoglobin (HbA1c) 6.5 percent are diagnostic criteria for diabetes mellitus.[5] Morbidity and mortality are higher in those who have this condition than in the general population. According to a recent study by the International Diabetes Federation, diabetes mellitus affected more than 382 million persons worldwide aged 20 to 79 years in 2013.[6] By 2040, it is estimated that the number of people who may contract this disease will climb to 642 million.[7]

Type-1 diabetes mellitus (owing to a complete lack of insulin secretion) and Type-2 diabetes mellitus (cause is a combination of insulin resistance and a lack of compensatory insulin secretion) are the most common types of diabetes.[8]

Anatomically, pancreas is a mixed gland [endocrine (2%) and exocrine (84%)]. The remaining 10% and 4% are taken up by extracellular matrix, ductal cells, and blood vessels, respectively. Acinar tissue can be found close to the islets. As a result, the pancreatic exocrine function appears to be influenced by the pancreatic endocrine function. Type 2 diabetes mellitus may alter enzyme synthesis and release from the exocrine pancreas because of numerous abnormalities in insulin secretion and communication.[9] Due to insuloacinar portal system, the pancreatic acinar cells are directly influenced by the hormones secreted from the islets of Langerhans. In physiological situations, the acinar cells are stimulated by insulin and increase the enzyme secretion whereas anti-insulin hormones work vice-versa. Thus, in patients of type 2 diabetes mellitus due to more activity of anti-insulin hormones, decrease in pancreatic enzyme secretions is expected. Since 1943, pancreatic enzyme deficiency in type 2 diabetic patients has been studied.[10]

The pancreatic exocrine acinar cells synthesize more than 10 enzymes which includes amylase(AMY), lipase(LPS), trypsin (TRY), chymotrypsin (CHY), elastase(E1) and many others. Among these, assay of serum amylase plays a vital role as it hydrolyses the complex carbohydrate molecules into smaller components within the lumen of the small intestine.[11]

Human amylase (α-amylase) has ability to cleave polysaccharides by acting on α (1-4) linkage to produce the end products that are dextrans, maltose and some glucose molecules[12]. Amylase is produced in large amounts by pancreatic acinar cells and salivary glands, whereas it is produced in lesser amounts by adipose tissue, the gonads, the fallopian tube, the digestive system and the skeletal muscles.[13] These are categorized into two types: 1. Endoamylase, hydrolyzes carbohydrates into linear and branching molecules of various lengths 2. Exo-amylase which reduces it into short molecules. [14] It is degraded and excreted by kupffer cells of the liver and kidney. [15]

For many years, it was assumed that low serum amylase levels indicated pancreatic damage owing to severe pancreatic illness, however recent research has shown that low serum amylase levels are linked to metabolic syndrome

and type 2 diabetes mellitus also.[16] Hyperamylasemia, on the other hand, can be caused by a variety of pancreatic disorders such as pancreatic malignancy, pancreatic blockage, or acute pancreatitis. Its level may also rise in severe malignant conditions like breast, ovary, colon and lung cancers. Elevated serum amylase levels are also seen in some non- pancreatic conditions such as pregnancy, use of drugs like opiates, diuretics, steroids etc., hepatitis, cirrhosis, acidosis, chronic alcoholism, head injury and many more complications.[17]

Flatulence, loose bowel movements, and abdominal discomfort are common gastrointestinal symptoms in diabetic patients with pancreatic exocrine insufficiency (PEI).[18] In type 2 diabetes mellitus; these less pancreatic secretions can also leads to deficiency of macronutrients, malnutrition andsteatorrhoea.[19]

Exocrine pancreatic function and its relationship to diabetes mellitus have received very little attention in our country's human diabetic research. The majority of investigations relied on metabolic disturbances caused by decreased insulin action and prolonged hyperglycemia. So, the current study was designed to look at serum amylase levels in people with type 2 diabetes mellitus in resource-constrained environments with lab facilities in order to see if there was a link between the functional entities of the pancreas.

2. Materials and Methods

After receiving ethical approval from the Sri Guru Ram Das Institute of Medical Sciences and Research in Sri Amritsar, the current investigation was carried out that included 140 people in the age range of 40 to 65 years old, regardless of gender (70 cases who were diagnosed with type 2 diabetes mellitus and 70 healthy controls). Patients were chosen from the Medicine OPD at Sri Guru Ram Das Institute of Medical Sciences and Research, Sri Amritsar, using a non-randomization approach after giving their informed consent. After taking a full history of the current or previous disease, the individuals were chosen for general physical examination, and a systemic examination, and then tested for fasting blood sugar, HbA1c, and serum amylase levels.

2.1 Sample Collection

5 mL of venous blood was drawn in a dry disposable syringe and needle (21 gauge) under all aseptic conditions from the antecubital vein in the grey top vacutainer for the assay of plasma blood glucose level (FBS), purple top vacutainer (EDTA) for the assay of HbA1c, and red top vacutainer for the assay of serum amylase after an overnight fast. After allowing the blood sample to sit for half an hour, it was centrifuged for 17 minutes at 3000 rpm. The supernatant (serum) was collected, and various biochemical tests were carried out on it.

2.2 Equipment

Siemens Dimension RXL Max

3. Method

1) The enzymatic technique was used to measure serum amylase using the Siemens Dimension RXL Max. [20]
2) Based on the principle of turbidimetric inhibition immunoassay, estimation of haemoglobin –A1c (HbA1c) utilizing Siemens Dimension RXL Max (TINIA).[21]
3) On the Siemens Dimension RXL Max, the hexokinase approach was used to estimate plasma blood glucose.[22]

3.1 Inclusion Criteria

- **Group 1**- It included 70 individuals in the age range of 40 to 65 years old, of either gender, who had already been diagnosed with Type 2 Diabetes Mellitus according to the American Diabetes Association (ADA) diabetes-2019 criteria.
- **Group 2**-It enlisted the participation of 70 healthy non-diabetic persons between the ages of 40 and 65, independent of gender.

3.2 Exclusion Criteria

The following patients were excluded from the study:

- Patients with Type 1 diabetes mellitus.
- Patients under the age of 40 and those over the age of 65.
- Patients on insulin therapy.
- Patients with acute or chronic pancreatitis
- Renal insufficiency patients (progressive kidney failure, renal replacement therapy, and hemodialysis on a regular basis)
- Patient with history of alcoholism.

1. Statistical Analysis

The data was presented as Mean Standard Deviation (Mean ± SD). Unpaired Student's 't' test and Pearson's correlation coefficient (r) test were used for statistical analysis.

2. Results

1) General characteristics are presented in Table I. It covers information such as age, the number of males and females, and blood pressure. In any of the variables, there were no significant differences between the patients and the controlsin any of the variables.
2) As shown in table 2, it showed the serum amylase activity in diabetic patients and controls. It showed the activity of serum amylase in diabetic patients and healthy people. Patients with type 2 diabetes had significantly decreased mean serum amylase levels. Mean serum amylase was considerably lower in patients with type 2 diabetes mellitus ($p<0.001$).
3) Figures 1 and 2 sequentially show the relationship between serum amylase levels with fasting blood glucose and HbA1c in diabetic patients.
4) As demonstrated in table 3 and figure 3, the average duration of diabetes was 6.55 ± 4.40 %. Hence, most of the cases suffering from type 2 diabetes mellitus were

with the duration of disease less than or equal to 10 years.

5) In terms of correlation, serum amylase revealed a negligible negative link with diabetes duration, with a Karl Pearson's Correlation Coefficient of -0.078, as shown in table-3.

Table 1: General characteristics of the subject in both groups (n-=140)

Variable	Controls (n=70)	Diabetics (n=70)
Age (years)	48.31 ± 6.46	53.06 ± 6.86
Male No. (%)	27 (38.6%)	22 (68.6%)
Female No. (%)	43 (61.4%)	48 (68.6%)
Systolic BP (mmHg)	126.41± 12.50	128.57± 11.64
Diastolic BP (mmHg)	82.71± 7.08	81.71± 6.86

Sex distribution has been shown in number and percentage. All other results are expressed as means ± SE. Unpaired students 't' test was performed for comparison between groups. n= number of subjects

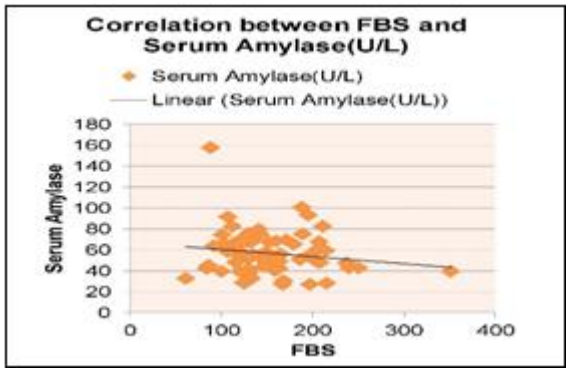

Figure 1: Correlation b/w FBS and serum amylase

Table 2: Serum Amylase activity in diabetic patients and control

Variable	Controls (Mean ± SD)	Cases (Mean ± SD)	T Value	p Value
Serum Amylase (U/L)	66.78 ± 21.91	56.81 ± 20.65	2.771	0.006

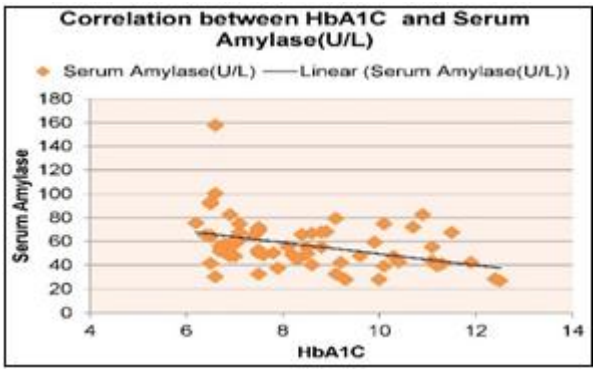

Figure 2: Correlation b/w HbA1C and serum Amylase

Table 3: Average, distribution database

Duration (yrs)	Cases		Total	r Value	p value
	N	%			
< =10	58	82.9	58	-0.078	0.519
> 10	12	17.1	12		
Total	70	100.0	140		
Mean ± SD	6.55 ± 4.40				

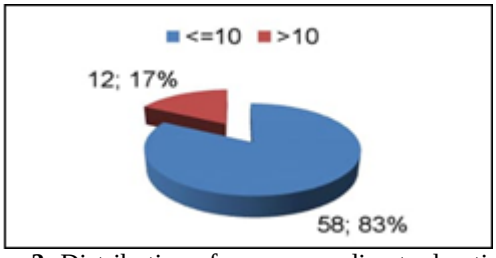

Figure 3: Distribution of cases according to duration of diabetes

1. Discussion

In the present study, subjects with type 2 diabetes mellitus had a mean (SD) age of 53.06 ± 6.86 years, whereas controls had a mean (SD) age of 48.31 ± 6.46 years, indicating a significant difference with p<0.001. Ladgotra et al. found a substantial association between cases and controls with the mean age of patients (52.32 ± 8.05) and controls (48.33 ± 7.30),[23] which is similar to our findings. Swati and her colleagues also discovered a similar trend in their study, with the mean age of type 2 diabetes patients being 54.12 ± 10.4 years. The findings were also similar to those of Jain et al.[24, 25]confirming that adults above the age of 40 are more likely to develop type 2 diabetes mellitus.

The amylase activity was investigated in this study, and the Karl Pearson's Association Coefficient for it was - 0.078, revealing a negligible negative connection between serum amylase and the duration of diabetes (table-3 & figure-3). Tanvi et al. found the same conclusion in a cross-sectional analysis, in which serum amylase levels exhibited a negative connection with disease duration, but this link was statistically significant.[26] Other researchers arrived to the same conclusion as we did, that serum amylase in individuals with type 2 diabetes mellitus became more seriously affected in long-term diabetes cases.[2]
The results of the present study suggested that both FBS and HbA1c were negatively correlated with the serum amylase levels with (r = -0.156 and p = 0.19) and (r = -0.416 and p<0.001). This finding was in line with the findings of previous researchers, who discovered significantly lower serum amylase levels in type 2 diabetes patients compared to healthy controls ($p \leq 0.001$). This means that people with poorly controlled diabetes had lower serum amylase levels than those with well-controlled diabetes.[9,27] However, one of the studies that calculated overall glycemic levels by blending fasting and postprandial hyperglycemia did not find a link between serum amylase levels and overall glycemic levels.[16]

The mean serum amylase level in cases was substantially lower (56.81 ± 20.65 U/L) than in healthy controls (66.78 ± 21.91 U/L) in this investigation. This results was consistent with the findings of Ewadh et al., who found serum amylase levels in patients with type 2 diabetes mellitus to be 9.2 ± 5.3 and 38.2 ± 3.2 U/L in cases and controls, respectively, with a significant difference at p value < 0.05[2]

These findings were also supported by Nakajima and some investigators from Assam. [28] This could demonstrate that the pancreatic hormones regulate the enzyme synthesis and release in the exocrine pancreas since insulin has trophic

effect on acinar cells whilst glucagon acts vice-versa. So, in type 2 diabetes, insulin insufficiency and an excess of glucagon disrupt the pancreas' internal milieu, resulting in a decrease in pancreatic exocrine secretions.[29] Other studies have also shown reductions in other pancreatic enzymes such as elastase, trypsin, and chymotrypsin, in addition to serum amylase.[30]

Farhood et al.. on the other hand, discovered a substantial rise in serum amylase level in type 2 diabetes mellitus patients (175.35 ± 21.74 U/L) compared to the control group (40.19 ± 10.50 U/L).[31] This conclusion was similar to Shankaraiah and Reddy's findings, which demonstrated that high HbA1c and FBS values exhibited substantially greater alpha amylase activity ($p<0.001$) in individuals with type 2 diabetes mellitus, with Mean±SD, 74.3 ± 4.6 U/L.[14]

Renal impairment or chronic kidney disease were also linked to a significant increase in serum amylase levels.[32]

Although the exact method by which diabetes mellitus makes people more susceptible to greater pancreatic amylase concentrations is uncertain, insulin resistance and hyperglycemia appear to be major factors connected to higher enzyme concentrations in people with type 2 diabetes.[14]

2. Conclusion

In the light of above findings, the present study concluded that there is strong inverse statistically significant correlation of serum amylase activity in the patients of type 2 diabetes mellitus. This could indicate a supposed interplay between the endocrine and exocrine functions of the pancreas owing to their structural vicinity. Low levels of serum amylase may be linked to poor insulin action as a result of insulin resistance and/or insufficient insulin secretion, which leads to a disruption of the exocrine-endocrine axis and, eventually, reduced enzyme production. Therefore, Insulin resistance and hyperglycemia appear to be key contributors in the development of pancreatitis in people with type 2 diabetes.

3. Limitations

The present study has the following limitations:

- Due to the incidence of type 2 diabetes mellitus in different age groups, age and gender matching of patients and controls was not achievable.
- With a longer study period and a larger sample size, more attention to additional pancreatic diseases is needed.
- Aside from that, measuring additional pancreatic enzymes such as elastase, lipase, and trypsin, as well as estimating serum insulin levels, could provide insight into the pancreas' probable endocrine exocrine link in type 2 diabetes patients.

4. Source of Funding

None

5. Conflict of Interest

None

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