ORIGINAL RESEARCH

Correlation of Serum Amylase and HbA1c Levels in Type II Diabetes Mellitus – A Case Control Study

[1]Dr. Vishwanath H.L, [2]Dr. Anitha M, [3]Dr. Roshiny Rajendran, [4]Dr. K Chandrakala, [5]Dr. Pushpanjali H

[1,4,5]Professor, [2]Assistant Professor, [3]Postgraduates, Department of Biochemistry, Bangalore Medical College and Research Institute, India

Corresponding Author
Dr. Roshiny Rajendran
Postgraduates, Department of Biochemistry, Bangalore Medical College and Research Institute, India
Email: roshmedico@gmail.com

ABSTRACT
Background: Diabetes mellitus, a growing epidemic in India, currently affects over 62 million individuals. Pancreatic alpha-amylase, primarily secreted by acinar cells, plays a critical role in starch hydrolysis. Recent studies suggest a relationship between low serum amylase and metabolic syndrome, including type 2 diabetes mellitus. This study aims to evaluate the correlation between HbA1C, an established marker for glycemic control, and serum amylase in patients with type II diabetes mellitus.
Objectives: To determine blood glucose, HbA1C, serum amylase in type II diabetes mellitus patients and to compare and correlate type 2 diabetes with normal healthy individuals
Methods: In a Case Control study of 41 type II diabetes mellitus patients and 40 healthy controls , fasting blood glucose, serum amylase, and HbA1C levels were measured.
RESULTS: Statistical analysis, including Unpaired T-test and Pearson correlation, revealed significantly lower serum amylase in diabetic patients ($p < 0.03$) and no significant correlation between amylase and HbA1C ($r = -0.13$).
Conclusion: The study concludes that serum amylase may be considered as a prognostic factor in type 2 diabetes mellitus due to its association with glycaemic control.
Key words: Amylase , Blood glucose, Diabetes mellitus, HbA1C, Pancreas

INTRODUCTION

Diabetes has become an epidemic in India with more than 62 million diabetic individuals currently diagnosed with the disease. The prevalence of diabetes is predicted to double globally from 171 million in 2000 to 366 million in 2030 with India experiencing the maximum growth.[1]

Type II Diabetes mellitus accounts for approximately 90 percent of all cases. Type II Diabetes mellitus is due to beta cell deficiency or dysfunction or insulin resistance[1]

Pancreas is a mixed gland, with 84% made up of exocrine portion while the endocrine part comprises 2% and remaining portion is connective tissue. Alpha amylase is an enzyme of hydrolase class that catalyses the hydrolysis of 1,4-alpha glycosidic linkages in polysaccharides. In pancreas the enzyme p type is synthesized by acinar cells and then secreted into the intestinal tract by way of pancreatic duct system. It is the main enzyme responsible for cleaving starch into maltose, maltriose and alpha limit dextrin[2,3].

Glycated hemoglobin is formed by non enzymatic linkage of glucose to hemoglobin. The concentration of HbA1c depends on the concentration of glucose in blood and the erythrocyte life span.

HbA1c is used to diagnose diabetes, monitor glycemic control, evaluate the need to change therapy and predict the development of microvascular complication. Recently some studies showed that low serum amylase values are associated with metabolic syndrome and diabetes [2,3].

High value of amylase is seen in pancreatitis, pancreatic cancer and pancreatic duct obstruction. Animal and cellular studies showing the relationship between the endocrine and the exocrine pancreas have persistently observed that insulin affects amylase secretion via islet acinar cell axis[4,5]. Limited Indian studies are available regarding serum amylase and its

association with type 2 diabetes. The current study was used to evaluate the HbA1C and serum amylase of type II diabetes mellitus patients and to find the correlation.

OBJECTIVES

To determine blood glucose, HbA1C, serum amylase in type II diabetes mellitus patients between35-65 years.

To compare and correlate type 2 diabetes with normal healthy individuals of age group of 35-65years

METHODS

- A case control study was done in 81 subjects who visited Infosys central lab ,Victoria hospital, Bangalore medical college between February 2022 to March 2023. A total of 81 subjects included in the present study, were both male and female of age group ranging between 35-65years. Among them 41 were considered as Cases, diagnosed to have type 2 diabetes mellitus patients (<5 years onset) , according to American Diabetes Association Criteria (ADA) and 40 were considered as Controls , age and gender matched

Healthy individuals. The subjects fulfilling the inclusion criteria were enrolled for the study after obtaining informed consent and after obtaining ethical clearance from the institute. Subjects with history of recent acute abdomen, hepatic disorders, chronic renal insufficiency, parotid disorders and patient not willing to give informed consent were excluded from the study. About 8 ml of venous blood was collected into two separate vacutainers, red and purple from each individual under sterile conditions from phlebotomy section of Infosys central lab Victoria Hospital.

The collected sample was centrifuged at 3200rpm for 15 minutes , serum was separated and analysed for the following parameters in both controls and cases.

1. FBS- Hexokinase method
2. PPBS-Hexokinase method
3. Amylase- Colorimetric method by Roche cobas 6000 Fully automated integrated analyzer.

In whole blood HbA1c was analysed by Biorad D10 HbA1c analyser. Study reporting was in accordance to the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines.

STATISTICAL ANALYSIS

Statistical methods have been used to analyse the collected data for the present study. The collected data was entered in Microsoft excel 2021 and analyzed using SPSS v21.0. The quantitative variables were expressed as mean and standard deviation . The difference in the mean values between the two groups was assessed using unpaired T -test and p -value of less than 0.05 was considered significant. The correlation between serum amylase levels and HbA1C levels in cases were assessed using Pearson Correlation coefficient (r) and the value of p less than 0.05 was considered as significant. Graphs have been used to help analyze categorical variables, in comparison with time factors and quantitative variables.

RESULTS

The study was conducted on 41 cases who were diagnosed as type 2 diabetes mellitus and 40 healthy controls.

[Table 1] shows mean± SD values, and p-values of serum amylase in type 2 DM patients and controls . [Table2] shows that FBS level was significantly increased in type 2 diabetes patients as compared to control group. [Table 3] shows mean± SD values, and p-values of HbA1c levels in cases and controls. There was no significant correlation between FBS and amylase (r =0.091) and HbA1C and amylase (r =-0.13).

Table 1: Comparison of Serum Amylase between cases and controls

Groups	Serum Amylase levels (IU)		p-value
	Mean	Standard deviation	
CASES	61	27.2	0.03*
CONTROLS	79.2	36.6	
Values are expressed in mean and SD. p-value is from unpaired t test. p-value <0.05 is considered significant. *significant.			

**Table 2: Comparison of Fasting Blood Sugar (FBS) between cases and controls**

Groups	Serum Fasting Blood Sugar levels (mg/dL)		p- value
	Mean	Standard deviation	
CASES	220.9	106.6	<0.00001***
CONTROLS	96.68	16.09	
Values are expressed in mean and SD. p-value is from unpaired t test. p-value <0.05 is considered significant.*** highly significant			

Table 3: Comparison of HbA1c levels between cases and controls

Groups	HbA1c levels (%)		p- value
	Mean	Standard deviation	
CASES	9.55	1.22	
CONTROLS	4.94	0.41	
Values are expressed in mean and SD .p-value is from unpaired t test. p-value <0.05 is considered significant *** highly significant			<0.00001***

Table 4: Correlation of serum Amylase with fasting blood sugar levels in cases

Correlation of Serum Amylase with	Pearson's Correlation Co-efficient (r)	p- value
Fasting Blood Sugar (mg/dL)	0.091 Positive correlation	0.57 Not significant
HbA1c (%)	-0.13 Negative correlation	0.40 Not significant
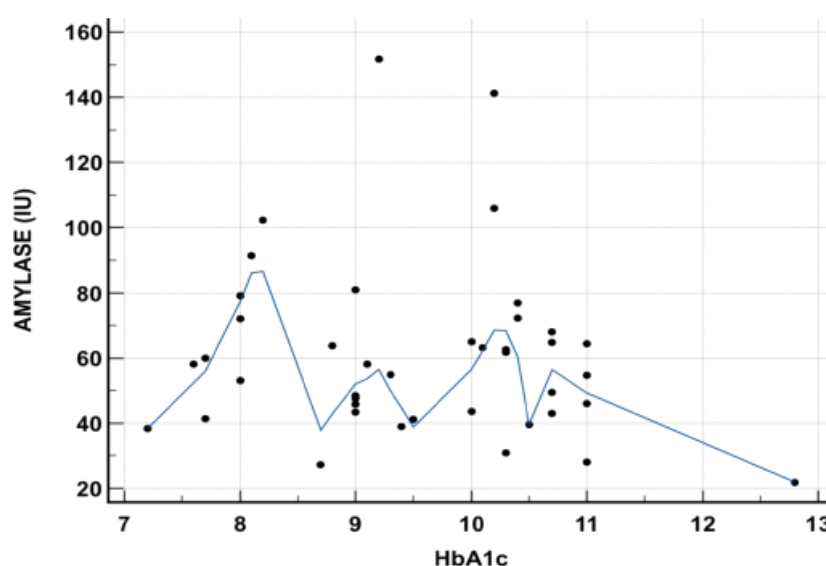
Figure 2: Scatter plot of correlation between Amylase and HbA1C

DISCUSSION

We found significantly low amylase level in type 2 diabetic groups as compared to that of healthy controls. In our study, the levels of fasting blood sugar and HbA1c was high in cases compared to controls but both the parameters didn't show any significant correlation with serum amylase levels. Our study highlights the usefulness of measuring serum amylase levels for the early detection and monitoring of type 2 diabetes mellitus (T2DM) patients. Yadav R et al [6] in 2013 did a study in New Delhi that the patients with poorly controlled diabetes had lower serum amylase level as compared to well controlled diabetic patients. In diabetes mellitus there will be excess of glucagon and insulin deficiency, this might be postulated to lower the volume of pancreatic contents and secretion of enzyme amylase[7].

Zhao Y, et al in his study in chinese population observed that low serum amylase levels are significantly associated with an increased prevalence of metabolic syndrome and diabetes. Obese and people with type 2 diabetes mellitus tend to have hyperinsulinemia to compensate for insulin resistance.

Future studies which measure serum insulin might be helpful to confirm these findings. [8]

In a study by Anil kumar et al they observed low serum amylase level in Type 2 DM group compared to non-diabetic group and they found a negative correlation between HbA1c of diabetes and serum amylase level [9]

The study by Ata N et al , suggested that in diabetes mellitus, hyperglycemia may cause cellular damage of the exocrine pancreas and it leads to impaired synthesis of pancreatic digestive enzymes[10]

This was similar to the findings of study by Augusteen et al [11] where FBS and HbA1C levels were higher in type 1 and type 2 diabetic patients . The levels of serum amylase in type 2 diabetes patients were higher in patients with longer duration of illness and low serum insulin value.

A study conducted by Zhuang L et al[12] concluded that serum amylase levels are positively associated with integrated islet β cell function in patients with early type 2 diabetes

Low serum amylase is also associated with insulin deficiency in patients with diabetes mellitus also

associated with the pathogenesis of insulin resistance in many animal based studies[11,12,13]

A study by Barreto SG et al suggested that islet-derived hormones like insulin and somatostatin, along with other humoral factors ghrelin and pancreastatin and neurotransmitters like nitric oxide, peptide YY, galanin regulate the activity of acinar cells, which are responsible for secreting digestive enzymes like amylase.[13]

A community based study done by Nakajima K et al [14] showed low serum amylase levels diabetes, suggesting a possible exocrine-endocrine relationship. Another study by Frier BM et al in juvenile onset diabetics showed that residual insulin secretion, had a strong correlation with amylase output also gives evidence of exocrine-endocrine relationship [15]

Many animal studies showed evidence of lower amylase activity in obese rats , suggesting insulin resistance a factor contributing to decrease in amylase levels [16].

A study by Dandona P et al showed that serum pancreatic enzyme concentrations were not related to glycosylated haemoglobin concentrations, the dosage of insulin, or the age of onset of diabetes[17].

A cohort study by Izumi Ikeda et al showed that the decrease in amylase level was a consistent finding independent of age , BMI and HbA1C .The possible etiology suggested by many studies is that pancreas is atrophic in patients with type 2 diabetes mellitus[18,19,20,21].

Limitations
The study was a case control study with a small sample size. Large sample size with adequate follow up study is required to establish the role of serum amylase as prognostic marker

An estimation of the serum insulin levels, along with the measurement of the other pancreatic enzymes e.g. lipase, would be able to provide more explanation into the endocrine-exocrine relationship of the pancreas in the patients of diabetes.

CONCLUSION
In our study, subjects with type 2 diabetes mellitus have lower serum amylase levels compared to healthy controls . However, no significant correlation was observed between serum amylase and HbA1C levels, suggesting that serum amylase may not directly reflect glycaemic control. Further research is recommended to explore the exocrine-endocrine relationship in diabetes.

Data availability

REFERENCES
1. Kaveeshwar SA, Cornwall J. The current state of diabetes mellitus in India. AMJ. 2014;7(1):45–8.
2. Marshall WJ, Lapsley M, Day AP, Shipman K. Clinical chemistry. 9th ed. St Louis(O): Elsevier; 2021.
3. Rifai N, Horvath AR, Wittwer CT, Tietz NW. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 6th ed. St Louis(Missouri): Elsevier; 2018.
4. Czako L, Hegyi P, Rankonczay ZJ, Wittmann T, Otsuki M. Instructions between the endocrine and exocrine pancreas and their clinical relevance. Pancreatology. 2009;9(4):351–9.
5. Tanvi NE, Akhter QS, Nahar S, Sumi MN, Hosen M. Serum amylase and lipase levels in type 2 diabetes mellitus. J Bangladesh Soc Physiol. 2017;12(2):52–6.
6. Yadav R, Bhartiya JP, Verma SK, Nandkeoliar MK. The evaluation of serum amylase in the patients of pe 2 diabetes mellitus, with a possible correlation with the pancreatic functions.*JClin Diagn Res*. 2013 Jul;7(7):1291-4. doi: 10.7860/JCDR/2013/6016.3120. Epub 2013 Jul 1. PMID: 23998048; PMCID: PMC3749618.
7. Singh J, Yago MD, Adeghate E. The role of insulin, glucagon, somatostatin, cholecystokinin, acetylcholine and nerve stimulation in the interactions between the endocrine and exocrine pancreas in normal and diabetic conditions in rats. Int J Diabetes. 1999;7(1):114–9.
8. Zhao Y, Zhang J, Zhang J, Wu J, Chen Y. Metabolic syndrome and diabetes are associated with low serum amylase in a Chinese asymptomatic population. Scand J Clin Lab Invest. 2014 Apr;74(3):235-9. doi: 10.3109/00365513.2013.878469. Epub 2014 Jan 23. PMID: 24456421.
9. Anil Kumar, Avinash S Itagi, T. L Chetan, Sanjay Neeralagi. Study of Serum Amylase Levels in Patients with Type 2 Diabetes Mellitus in a Tertiary Care Hospital Asian Journal of Medical 21.
10. Ata N, Dal K, Kucukazman M, Yeniova AO, Karakaya S, Unsal O et al. The effect of glycemic control on CEA, CA 19-9, amylase and lipase levels. Open Med. 2015.Research 99Volume 11 99Issue 2 99April -June 2022
11. 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(1):73–7.
12. Zhuang L, Su J bin, Zhang X lin, Huang H yan, Zhao L hua, Xu F, et al. Serum Amylase Levels in Relation to Islet β Cell Function in Patients with Early Type 2 Diabetes. PLOS ONE. 2016 Sep 8;11(9):e0162204.
13. Barreto SG, Carati CJ, Toouli J, Saccone GT. The islet-acinar axis of the pancreas: more than just insulin. Am J Physiol Gastrointest Liver Physiol.2010;299(1)–22.

14. Nakajima K, Nemoto T, Muneyuki T, Kakei M, Fuchigami H, Munakata H. Low serum amylase in association with metabolic syndrome and diabetes: A community-based study. Cardiovasc Diabetol. 2011 Apr 17;10:34. doi: 10.1186/1475-2840-10-34. PMID: 21496338; PMCID: PMC3102610.

15. Frier BM, Faber OK, Binder C, Elliot HL. The effect of residual insulin secretion on exocrine pancreatic function in juvenile-onset diabetes mellitus. Diabetologia. 1978 May;14(5):301-4. doi: 10.1007/BF01223020. PMID: 348540.

16. Schneeman BO, Inman MD, Stern JS. Pancreatic enzyme activity in obese and lean Zucker rats: a developmental study. J Nutr. 1983 Apr;113(4):921-5. doi: 10.1093/jn/113.4.921. PMID: 6187904

17. Dandona P, Freedman DB, Foo Y, Perkins J, Katrak A, Mikhailidis DP, Rosalki SB, Beckett AG. Exocrine pancreatic function in diabetes mellitus. J Clin Pathol. 1984 Mar;37(3):302-6. doi: 10.1136/jcp.37.3.302. PMID: 6699193; PMCID: PMC498704.

18. Macauley M, Percival K, Thelwall PE, et al. Altered volume, morphology and composition of the pancreas in type 2 diabetes. PLoS One. 2015;10

19. Mossner J, Logsdon CD, Goldfine ID, et al. Regulation of pancreatic acinar cell insulin receptors by insulin. Am J Physiol. 1984;247

20. Silva ME, Vezozzo DP, Ursich MJ, et al. Ultrasonographic abnormalities of the pancreas in IDDM and NIDM patients. Diabetes Care . 1993;16:1296–7.

21. Ikeda I, Fujihara K, Osawa T, Takeda Y, Hatta M et al Retrospective cohort study to examine the association between serum amylase and the incidence of type 2 diabetes mellitus, Toranomon Hospital Health Management Center Study 23 (TOPICS 23). BMJ Open Diabetes Res Care. 2023 Jul;11(4):e003482. doi: 10.1136/bmjdrc-2023-003482. PMID: 37437950; PMCID: PMC10347468

22. Zhuang L, Su J bin, Zhang X lin, Huang H yan, Zhao L hua, Xu F, et al. Serum Amylase Levels in Relation to Islet β Cell Function in Patients with Early Type 2 Diabetes. PLOS ONE. 2016 Sep 8;11(9):e0162204.

23. Barreto SG, Carati CJ, Toouli J, Saccone GT. The islet-acinar axis of the pancreas: more than just insulin. Am J Physiol Gastrointest Liver Physiol.2010;299(1)–22.

24. Nakajima K, Nemoto T, Muneyuki T, Kakei M, Fuchigami H, Munakata H. Low serum amylase in association with metabolic syndrome and diabetes: A community-based study. Cardiovasc Diabetol. 2011 Apr 17;10:34. doi: 10.1186/1475-2840-10-34. PMID: 21496338; PMCID: PMC3102610.

25. Frier BM, Faber OK, Binder C, Elliot HL. The effect of residual insulin secretion on exocrine pancreatic function in juvenile-onset diabetes mellitus. Diabetologia. 1978 May;14(5):301-4. doi: 10.1007/BF01223020. PMID: 348540.

26. Schneeman BO, Inman MD, Stern JS. Pancreatic enzyme activity in obese and lean Zucker rats: a developmental study. J Nutr. 1983 Apr;113(4):921-5. doi: 10.1093/jn/113.4.921. PMID: 6187904

27. Dandona P, Freedman DB, Foo Y, Perkins J, Katrak A, Mikhailidis DP, Rosalki SB, Beckett AG. Exocrine pancreatic function in diabetes mellitus. J Clin Pathol. 1984 Mar;37(3):302-6. doi: 10.1136/jcp.37.3.302. PMID: 6699193; PMCID: PMC498704.

28. Macauley M, Percival K, Thelwall PE, et al. Altered volume, morphology and composition of the pancreas in type 2 diabetes. PLoS One. 2015;10

29. Mossner J, Logsdon CD, Goldfine ID, et al. Regulation of pancreatic acinar cell insulin receptors by insulin. Am J Physiol. 1984;247–60.

30. Silva ME, Vezozzo DP, Ursich MJ, et al. Ultrasonographic abnormalities of the pancreas in IDDM and NIDM patients. Diabetes Care . 1993;16:1296–7.

31. Ikeda I, Fujihara K, Osawa T, Takeda Y, Hatta M et al Retrospective cohort study to examine the association between serum amylase and the incidence of type 2 diabetes mellitus, Toranomon Hospital Health Management Center Study 23 (TOPICS 23). BMJ Open Diabetes Res Care. 2023 Jul;11(4):e003482. doi: 10.1136/bmjdrc-2023-003482. PMID: 37437950; PMCID: PMC10347468