

Relationship of Serum Ghrelin, Amylase and Lipase with Insulin Level in Type 2 Diabetes Mellitus Patients

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Abstract

Background: Diabetes mellitus (DM) is a metabolic disorder known as hyperglycemia, which is brought on by impaired insulin secretion, inefficient insulin utilization, or both. **Objectives:** This study's aim was to assess the lipase and amylase pancreatic enzymes levels in sera of (T2DM) patients and healthy control subjects. **Materials and Methods:** A case-control research was conducted from December 2021 to March 2022 at the Hilla District Center for Diabetes and Endocrinology in Babylon, Iraq. It included a group of 39 patients with type 2 DM and 39 healthy people between the ages of 35 to 60 years. **Results:** Results were indicating a significant difference in FBS among groups, The mean levels of FBS for DM was (203.7 ± 72.3) mg/dL which was significantly greater than it was for the control group (88.6 ± 7.64) mg/dL, ($P \leq 0.001$). The mean of HbA1c for DM (9.5 ± 2.35) was significantly higher than for control (4.9 ± 0.48) , $P \leq 0.001$. The mean levels of the Amylase and Lipase activity in the DM patients group were (71.4 ± 29.11) and (49.7 ± 14.69) (U/L). When compared to the control group's mean values, which were (72.7 ± 27.19) and (42.0 ± 7.35) (U/L). The mean levels of Lipase activity were shown a significant difference in T2DM patients compared to the healthy control group, ($P < 0.05$). **Conclusion:** Increased serum level of lipase without any symptoms of pancreatitis was indicated in type II diabetes mellitus patients.

Keywords: Amylase, diabetes mellitus type 2, FBS, HbA1c, lipase

INTRODUCTION

Diabetes mellitus (DM), which is brought on by ineffective insulin production, inefficient insulin utilization, or both, is the result of the metabolic disorders known together as diabetes mellitus (DM).^[1,2] (DM) is characterized by immune-mediated (Type 1 diabetes), insulin resistance (Type 2 diabetes), gestational hyperglycemia, or other chronic hyperglycemia; genetic, environmental, infectious, or medication-induced problems; or affects the beta cells of the islets of Langerhans.^[3-5] No country is safe from the diabetes invasion these days since type 2 diabetes mellitus (T2DM) is a significant public health concern or threat in the twenty-first century.^[6] Compared to the proportion of 4.6% in 2000, it is predicted that the anticipated global prevalence of T2DM will rise to 6.4% in 2030. Over the past decade, the prevalence of diabetes has risen rapidly due to an increase in the average age of the community, hereditary background, unhealthy dietary habits, sedentary lifestyle, and increased obesity in line with the growth of urbanization.^[7] The increasing prevalence

of type 2 diabetes in general and in younger people in particular had led to an increasing number of pregnancies with this complication.^[8]

Hyperglycemia develops as the disease develops because insulin secretion can no longer keep glucose levels under control. Patients with T2DM are typically obese or have greater body fat percentages, which are primarily distributed in the abdomen area. Adipokine dysregulation and a rise in the production of free fatty acids are two inflammatory mechanisms used by adipose tissue to enhance insulin resistance in this condition (FFA).^[9]

Population aging, sedentary lifestyles, high-calorie diets, and the global growth in obesity have all contributed to

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a four-fold increase in the incidence and prevalence of T2DM.^[9,10] Overall, men are more likely than women to have diabetes, and individuals 40 and older are the group most likely to have the disease. Additionally, T2DM is becoming increasingly common in adolescents and young adults more quickly. The top five nations with the highest prevalence of T2DM are Japan, Indonesia, China, India, and the United States.^[11,12]

According to a recent study, diseases like “diabetes mellitus” that have subclinical reduction of exocrine pancreatic function frequently have lower serum concentrations of pancreatic enzymes.^[13] The most important enzyme for breaking down dietary fat, decreasing the buildup of fat in adipose tissue, and regulating weight gain is pancreatic lipase, all of which have positive effects on overweight and obesity, which are common in diabetes patients. Triglycerides, which make up 90 to 95% of the ingested fats, are broken down and absorbed by pancreatic lipase. The use of a lipase inhibitor was previously considered as an obesity treatment if there is a way to stop the early transfer of triglycerides from the intestinal lumen. Orlistat, a hydrolyzed version of the lipase inhibitor lipstatin derived from *Streptomyces toxitricini*, is a potent inhibitor of gastric, pancreatic, and carboxyl ester lipase. In treating obesity, a major risk factor for type 2 diabetes, it has showed potential.^[14] The level of C peptide and pancreatic enzyme activity have been found to be significantly correlated by research.^[15] This distinction might be explained by the fact that trypsin is the first enzyme to be lost in the sequence of enzyme loss in the exocrine pancreatic damage linked to human diabetes, and lipase is the last.^[16]

The majority of studies have concentrated on the metabolic disturbance brought on by reduced insulin action and prolonged hyperglycemia. Malnutrition and maldigestion can result from altered pancreatic endocrine activity, amylase, diabetes mellitus, and altered pancreatic endocrine activity. The current study aims to assess exocrine pancreatic function in type 2 diabetics by measuring blood amylase and lipase levels.^[17] In individuals with diabetes mellitus, hyperglycemia and/or insulin inactivity brought on by hypoinsulinemia or insulin resistance may result in pancreatic exocrine dysfunction and the emergence of pancreatic exocrine insufficiency.^[18]

MATERIALS AND METHODS

Patients and controls

The Center for Diabetes and Endocrinology of Hilla District, Babylon, Iraq, conducted a case-control study from December 2021 to March 2022 for the current study. 39 patients with type 2 diabetes and 39 healthy individuals between the ages of 35 and 60 made comprised the study's patient and control groups. Age, gender, and BMI were among the sociodemographic characteristics that were gathered using a self-reporting technique (study

questionnaire). Patients with type 2 diabetes mellitus, who made up 50% of the patient population and had an average age of (35 to 60) years, were included. Diabetes symptoms include frequent urination, intense hunger or thirst, excessive fatigue, blurred vision, wounds or bruises that take a long time to heal, and tingling, discomfort, or numbness in the hands or feet, according to the American Diabetes Association (ADA). Doctors have identified this problem in each case (type 2). About 50% of the participants in the control group were healthy people. None of the individuals showed any disease-related symptoms or indications. Patients with the following conditions were excluded from the study: smokers, pregnant women, Type 1 diabetics, chronic liver disease, heart disease, hypertension, and insulin medication dependency. Quantitative determination of α -amylase in serum was done by kinetic method (CNP3G) and the fasting serum glucose, serum lipase was determined by the colorimetric approach. The turbid metric inhibition immunoassay (TINIA) for hemolyzed whole blood was used to determine the HbA1c level.

Ethical approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients verbal and analytical approval before sample was taken. The study protocol and the subject information and consent form were reviewed and approved by a local ethics committee according to the document number 1050 (including the number and the date in 23/5/2022) to get this approval. The Kerbala Medical College Ethical Committee and the Committee of the Endocrinology Unit of the Center of Diabetes and Endocrinology of Hilla District, Babylon, Iraq, both gave their approval to the study protocol. After receiving patients' or patients' families' agreement, samples were taken.

RESULT

Diabetes mellitus (DM) prevalence is rapidly and steadily increasing worldwide. Diabetes used to be considered a minor disease that mostly affected elderly people, but over the past three generations, it has gained more attention and is now one of the leading causes of morbidity and mortality in middle-aged and young people. Chronic diseases are brought on by functional decline brought on by high blood sugar, insulin sensitivity, and insulin shortage.^[19]

Clinical and demographic characteristics

The clinical demographics of the patients' group were summarized in Table 1. Table illustrated the age range of analysed group which was within (36–59) ^{Years} for patients and (31–58) ^{Years} for healthy control group. The gender distribution was nearly similar in both groups; mostly of the participants were not smokers. The minimum duration

the diabetes was five years; about 56% having Family History of DM and 54% were suffering from hypertensive. More than half of the patients were reporting to use Glucophage and Insulin as a regular medication.

Fasting blood sugar

Generally, patients with type II diabetes mellitus patients were shown an increasing range level of FBS when compared to the healthy control groups. Results were indicating a significant difference in FBS among groups. The means, and standard deviations were presented in Table 2. The mean level of FBS for DM was (203.7 ± 72.3) mg/dL which was significantly greater than for control group (88.6 ± 7.64) mg/dL, ($P \leq 0.001$). The Distribution of serum levels of fasting blood sugar in type II diabetes mellitus patients compared to healthy control group was presented in Figure 1.

Table 1: Baseline characteristics and demographic descriptive of the study population in cases of DM patients

Characteristics		Patients Group	Healthy Control Group
Age Years		36-59	35-60
Gender (No.)	Male	20	19
	Female	19	20
BMI (No.)	Non-obese	15	39
	Obese	24	0
Duration of DM Years	5 – 27 years	/	/
	Yes	Exclude this sample	0
	No	38	39
	Glucophage	15	/
	Insulin	10	/
	Insulin +Glucophage	4	/
HT (No.)	Metformin	4	/
	Other	6	/
	Yes	21	0
	No	18	39
Family History of DM (No.)	Yes	22	/
	No	17	/

HT, Hypertension

Hemoglobin A1C

The hemoglobin A1c (HbA1c) was also examined. The mean levels of serum HbA1c in DM patients were significantly higher than those of healthy individuals ($P < 0.05$), as illustrated in Figure 1 and Table 2. The mean of HbA1C for DM (9.5 ± 2.35) was significantly higher than for Control (4.9 ± 0.48), $P \leq 0.001$.

Serum pancreatic enzyme (amylase) activity (U/L)

The distribution of serum pancreatic enzymes (amylase) was examined as demonstrated in Figure 1. Generally, patients with Type II Diabetes Mellitus were shown an increasing range level of pancreatic enzymes when compared with the healthy control groups. Mean levels of amylase activity in DM patients group were (71.4 ± 29.11) (U/L) whereas the mean values in the control group were (72.7 ± 27.19) (U/L). Lipase activity was shown a significant difference in type II diabetes mellitus patients compared to healthy control group, ($P < 0.05$).

Serum pancreatic enzymes (lipase) activity (U/L)

The distribution of serum pancreatic enzymes (lipase) was examined as demonstrated in Figure 1. Generally, patients with type II diabetes mellitus were shown an increasing range level of pancreatic enzymes when compared with the healthy control groups. Mean levels of lipase activity in the DM patients group were (49.7 ± 14.69) (U/L) respectively, whereas the control group's mean levels were (42.0 ± 7.35) (U/L).

Correlation analysis

The individual Correlation Coefficients of the lipase, and amylase were presented in Table 3.

DISCUSSION

The results for FBS and HbA1c analysis were significant ($P < 0.001$) and indicated Significant variations in FBS were found between the group [Figure 1] and [Table 2] results indicated that diabetic patients (DM) have a significantly higher sugar profile than the healthy control group. Also, mean levels of serum HbA1c in DM patients

Table 2: Descriptive statistics and mean difference of biomarkers level in type II diabetes mellitus patients compared to healthy control group

Variables		Mean $\pm$ SD	SE _M	Mini	Max	Mdn	P value
FBS (mg/dL)	DM patients group	203.7 ± 72.3	11.88	113	363.6	186.8	<0.001
	Control group	88.6 ± 7.64	1.26	70	101	90	
Amylase (IU/L)	DM patients group	71.4 ± 29.11	4.77	30	146	67	0.52
	Control group	72.7 ± 27.19	4.42	26	117	74.5	
Lipase (IU/L)	DM patients group	49.7 ± 14.69	2.41	22.17	92.14	49.95	0.023
	Control group	42.0 ± 7.35	1.12	29.99	62.14	39.93	
HbA1c %	DM patients group	9.5 ± 2.35	0.39	5.9	15	8.9	<0.001
	Control group	4.9 ± 0.48	0.08	4.1	5.9	5	

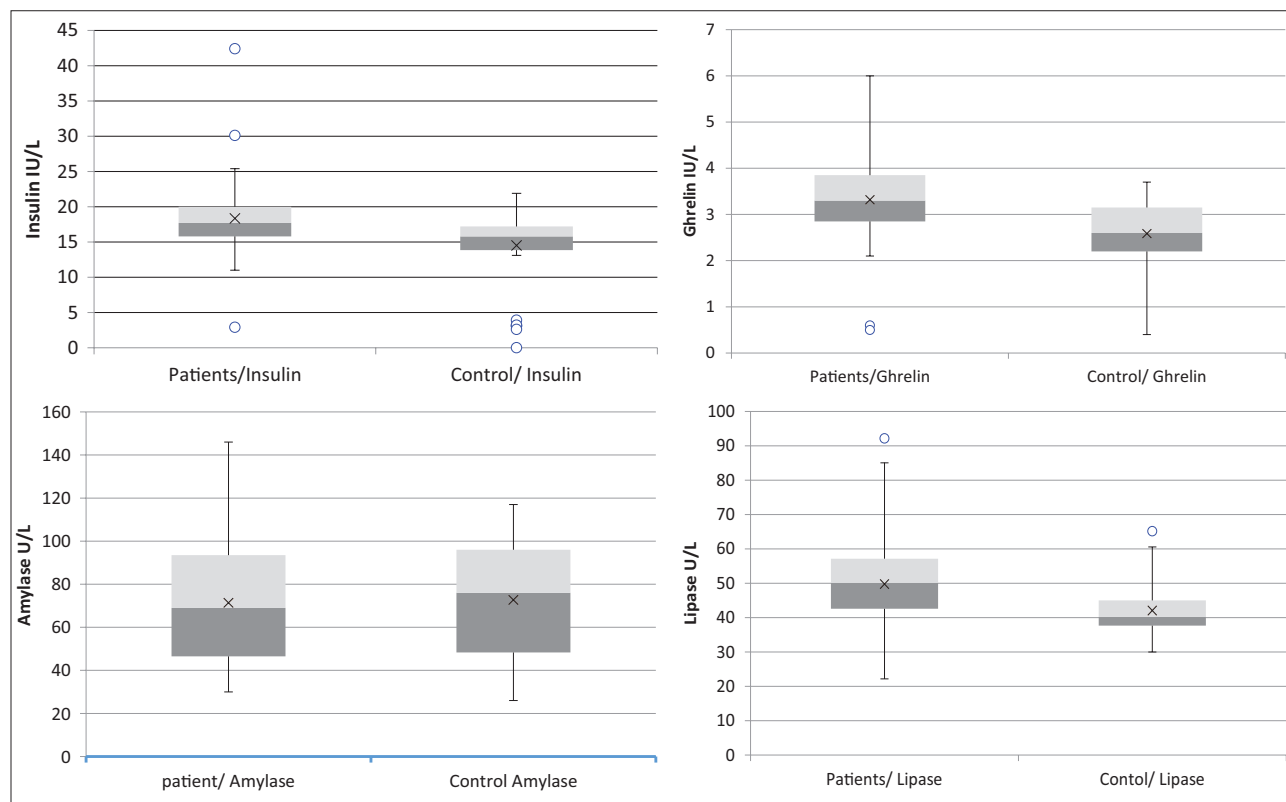


Figure 1: Boxplot of the serum level distribution of (FBS, HbA1c, amylase, lipase) in type II diabetes mellitus patients compared to healthy control group

Table 3: Correlation coefficients of lipase, and amylase and the measured biomarkers in DM patients

Variables		Correlation Coefficient	P value
Lipase	FBS	-0.238	0.14
	HbA1c	0.29	0.76
	Amylase	0.23	0.2
Amylase	FBS	-.328*	0.041
	HbA1c	-0.221	0.1
	Lipase	0.23	0.45

were significantly higher than those of healthy individuals ($P < 0.05$), as illustrated in Figure 1.

Diabetes is characterized by chronic hyperglycemia and causes long-term complications. Since glycated hemoglobin considers a reflection of integrated glycaemia over the entire 120-day lifespan of the red blood cell, HbA1c levels and FBS have a significant correlation. HbA1c is a helpful tool for managing chronic diabetes since it is a reliable predictor of chronic glycemia and correlates well with the risk of acquiring long-term diabetes.^[20] Diabetics have higher blood glucose levels, and glucose binds to hemoglobin in a concentration-dependent method. As hemoglobin becomes glycated with glucose, it forms glucose-bound (glycated) hemoglobin, also known as HbA1c, which measures the average blood glucose levels of a person. It's crucial to

remember that there is an antagonistic relationship between blood sugar levels and HbA1c levels.^[21] Type 2 diabetes mellitus (DM), which is brought on by impaired insulin production, has hyperglycemia as one of its symptoms.^[22] Understanding insulin and insulin resistance completely is made possible by the relevance of the HbA1c test in the diagnosis and prognosis of diabetes patients. Direct links exist between HbA1c and insulin resistance, with HbA1c being more strongly linked to insulin sensitivity in healthy individuals with normal glucose tolerance.^[23]

There are very few human research that have attempted to investigate the biochemical characteristics and underlying mechanisms connecting the exocrine acinar cells and the endocrine islet cells.^[24]

An endocrine problem of the pancreas is indicated by diabetes mellitus (DM), a metabolic illness marked by hyperglycemia and linked with insulin insufficiency or resistance. Enzymes like lipase and amylase are secreted by the pancreas' exocrine part. Diabetes-related endocrine dysfunction may affect the pancreas' exocrine function. As a result of poor insulin action brought on by either insulin resistance or insufficient insulin secretion, reduced serum amylase levels in diabetes were also linked to higher blood glucose levels (negative association).^[24] According to Patel R *et al.*, decreased amylase secretion in the diabetic pancreas may be brought on by a decrease in the amount of

cytosolic free calcium (Ca²⁺) and amylase gene expression as compared to the gene expression for the receptor cholecystokinin (CCK) in pancreatic acinar cells.^[25] Exocrine pancreatic insufficiency has been related to long-term type 2 diabetes (T2D), and T2D patients are more likely to develop acute or chronic pancreatitis. In addition, the main causes of diabetes sequelae such as retinopathy, nephropathy, neuropathy, and other conditions are long-term T2D and insufficient glycemic control.^[26] A different study found that greater serum levels of pancreatic enzymes (amylase and/or lipase) indicated a higher incidence of pancreatitis.^[27] Conditions other than pancreatitis, such as renal illness, hyperglycemia, and ketoacidosis, can exacerbate abnormally high blood lipase activity levels.^[28] Although T2DM was linked to an increased risk of pancreatitis, the pathogenic mechanism is yet unknown.^[27] The pancreas' exocrine-endocrine interactions can be impaired by the elevated serum lipase activity found in individuals who have diabetes and prediabetes. Higher lipase activity is linked to both inadequate insulin secretion and poor insulin action due to insulin resistance in both the diabetes and prediabetes groups because insulin promotes enzyme production and release in the exocrine pancreas.^[29] Inflammatory pancreatic exocrine disease, often known as pancreatitis, is indicated by increased lipase activity in T2D.^[30] An increase in lipase activity, a decrease in insulin levels, an increase in FPG, HbA_{1c}, creatinine, insulin resistance, and a dyslipidaemia profile are all signs of diabetes, according to a previous study (increasing level of total cholesterol, triglyceride, and small dense LDL particles). Based on the study of the fictitious structural model, which demonstrates a significant positive link between the high glucose level and lipase activity, lipase activity does not considerably contribute to the elevation of glucose, nevertheless. As a result, we predict that Indonesian T2D duration or glycemic control impairment are correlated with pancreatitis or a high serum lipase value. Uncontrolled glucose levels can increase triglyceride levels and lipase production, which in turn causes triglycerides to break down into free fatty acids.^[31]

The exocrine function of the pancreas may be affected by the endocrine deregulation seen in diabetes. Diabetes patients with low serum amylase levels have higher blood sugar levels (negative correlation), which was brought on by poor insulin action brought on by either insulin resistance or insufficient insulin production. The lack of pancreatic exocrine acinar cells was the cause of the drop in amylase levels.^[24]

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Conflicts of interest

There are no conflicts of interest.

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