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Correlation between C- peptide, insulin and dopamine2 receptors in diabetic patients

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Abstract

Dopamine D2 receptors play a key role in controlling insulin resistance and blood sugar levels. Because C-peptide and dopamine 2 levels are positively correlated, increased C-peptide concentrations may also result in higher concentrations of dopamine 2, which may help diabetic patients better regulate their glucose metabolism. In this study, results showed that the mean Dopamine2 level was significantly lower in the patient group than in the control group. In addition, the mean insulin level in the patient group washigher than those in the control group. Diabetic patients in our study were shown to have higher levels of C-peptide than healthy individuals in the control group, which is a measure of insulin production. Fasting blood sugar (FBS) concentrations in the patient group were considerably higher than in the control group, pointing to a decreased metabolism of glucose in this group. A similar pattern was seen in the mean HbA1c value, which was considerably higher in the patient group than in the control group, suggesting that the patient group had poor long-term glucose management.

Keywords: T2DM; *Diabetes mellitus*; Dopamine 2 receptors; Insulin.

Introduction

The pancreas produces a hormone called insulin, which functions as a key to allow glucose from the blood to enter the body's cells to be used as energy[1]. Insulin resistance, which occurs when cells don't react to insulin as they should in individuals with type 2 diabetes [2].

As the condition increases, insulin secretion becomes unable to keep glucose levels under control, resulting in hyperglycemia[3]. Being overweight or having a greater body fat percentage, especially in the abdominal area, are the main characteristics of T2DM patients [4]. Through various inflammatory mechanisms, including increased free fatty acid (FFA) release and adipokinedys regulation[5], adipose tissue promotes IR in this situation. The prevalence and incidence of type 2 diabetes (T2DM) have tripled as a result of human ageing, sedentary lifestyles, high-calorie diets and worldwide obesity rates.

The chronic metabolic disease known as *Diabetes mellitus* (DM) is characterized by persistent hyperglycemia[6]. It might have resulted from increased insulin resistance, decreased insulin production, or both. About 415 million people aged 20 to 79 had *Diabetes mellitus* in 2015, according to the International Diabetes Federation (IDF)[7].

The primary catecholamine neurotransmitter in the brain is dopamine (DA). Locomotion, memory, emotional and motivated behaviors, and neuroendocrine modulation are just a few of the processes it takes part in. Numerous neurological and psychiatric conditions, such as Parkinson's disease, Huntington's disease, schizophrenia, bipolar disorder, attention deficit hyperactivity disorder and Tourette's syndrome, have been linked to elevated DA levels [8].

Materials and methods

In the present study, venous blood samples were obtained after 8-12 hour fasting from 180 individuals aged (20-65) years during the period from November 2022 to March 2023at the Canadian Hospital and Specialized Centre for Endocrinology and Diabetes, Baghdad-Iraq. The samples were

divided into two aliquots and placed in EDTA and gel tubes, respectively. The Human Insulin ELISA kit and the Human Dopamine 2 receptor ELISA kit were used at the Bioassay Technology Laboratory (BT Lab) to assess the biochemical tests (insulin and dopamine 2). The Roche/Hetachi Diagnostics Ltd Company kit was used to measure the HbA1c, urea and creatinine kit.

The participants were divided into two groups: The patient group (120) patients (60 males and 60 females) and the control group (60) healthy individuals (30 males and 30 females). All participants gave written, informed permission before having their blood collected for this study. The committee on ethics of the Canadian Hospital and Specialized Centre for Endocrinology and Diabetes in Baghdad gave its clearance to this research on March 9, 2022.

Statistical analysis

The quantitative variables were presented as mean, standard deviation minimum and maximum, while the qualitative variables were presented as frequencies and percentages. The normality of distribution was tested by using Kolmogorov-Smirnov (K.S) test. Inferential statistics were performed using the one-way independent sample t-test (for normal distribution), Mann-Whitney test (for abnormal distribution), Pearson correlation and ROC curve. When the P-value is ≤ 0.05, the results are deemed statistically significant.

Results and discussion

Results in table (1)showed that the mean and (SD) of BMI for the patient and control groups was28.49 (5.11) and 27.17 (5.18) respectively, with a non-significant difference between them (p>0.05).

Table (1): Distribution of BMI among the study groups

			Group		Total	P-value
			Patient group	Control group		
BMI	**Under weight**	F	2	4	6	.105
		%	1.7%	6.7%	3.3%	
	Normal	F	32	22	54	
		%	26.7%	36.7%	30.0%	
	Overweight	F	28	22	50	
		%	23.3%	36.7%	27.8%	
	Obesity	F	58	12	70	
		%	48.3%	20.0%	38.9%	
Total		F	120	60	180	
		%	100.0%	100.0%	100.0%	
Mean± SD			28.49±5.11	27.17±5.18		

*Independent sample t-test, p-value≤ 0.05

In a study by [9], no correlation was found between BMI and the incidence of T2DM. however, in a meta-analysis of 21 prospective cohort studies, BMI was found to be strongly associated with the risk of developing T2DM; the intensity of the association differed across different groups. It was found that BMI was strongly associated with the incidence of T2DM, but this association was stronger in females than in males [10,11].

It is essential to point out, however, that BMI is only one of a number of variables that can play a role in the development of T2DM, and the absence of a statistically significant difference in BMI between the patient and control groups does not rule out the presence of other risk factors in the patient group. Furthermore, the BMI may not be the most accurate measure of body composition because it

does not differentiate between adipose mass and muscle mass, which can have distinct health implications.

Results in the table (2) demonstrated that the mean and SD of FBS for the patient and control group were 228.04 (110.77) and 100.52 (9.44), respectively, with a highly significant difference ($p<0.01$).The mean and SD of HbA1cfor the patients and controls was 9.07 (2.53) and 4.96 (0.54) respectively, with a highly significant difference ($p<0.001$).

In addition results in table (2) showed that the mean and SD of urea for patients and controls was 27.48 (7.01) and 25.54 (5.67) respectively, with a significant difference between the two groups ($p<0.05$). The mean and (SD) of creatinine was 0.75 (0.17) and 0.66 (0.15) for the patients and controls respectively, with a significant difference ($p<0.05$).

In terms of cholesterol, the mean (SD) values were 169.22 (29.04) and 173.28 (21.17) for the patient and controls, respectively, with a non-significant difference ($p>0.05$). The mean and (SD) of Triglyceride for the patient and control groups was (131.30 (57.96) and 92.37 (26.09) respectively, with a highly significant difference between them ($p<0.001$)

This table also showed that the mean and (SD) of HDL for patients and controls was 39.28 (6.006) and 45.22 (8.59), respectively, with a highly significant difference ($p<0.001$).

The mean and (SD) of LDL for patients and control groups was 104.20 (27.86) and 109.59 (17.06), respectively, with a non-significant difference ($p>0.05$).Furthermore, in regard with VLDL, this table showed a highly significant difference between patients and controls 26.28 (11.56) and 18.47 (5.21) respectively ($P<0.001$).

Table (2): Distribution of biochemical parameters among the study groups

		N	Minimum	Maximum	Mean	SD	p-value
FBS	Patients	120	90.00	545.00	228.04	110.77	.000*
	Control	60	88.90	140.00	100.52	9.44	
HbA1c	Patients	120	4.50	16.00	9.07	2.53	.000*
	Control	60	4.00	6.20	4.96	.54	
Urea	Patients	120	13.80	42.60	27.48	7.01	.048**
	Control	60	15.86	36.20	25.54	5.67	
Creatinine	Patients	120	.50	1.30	.75	.17	.001*
	Control	60	.40	1.08	.66	.157	
Cholesterol	Patients	120	104.00	263.00	169.22	29.04	.077
	Control	60	128.20	204.90	173.28	21.17	
Triglyceride	Patients	120	45.10	340.00	131.30	57.96	.000*
	Control	60	53.40	147.60	92.37	26.09	
HDL	Patients	120	27.20	62.00	39.28	6.006	.000*
	Control	60	35.00	66.00	45.22	8.59	
LDL	Patients	120	50.94	194.00	104.2	27.86	.100
	Control	60	72.24	139.82	109.59	17.06	
VLDL	Patients	120	9.20	68.00	26.28	11.56	.000*
	Control	60	10.68	29.52	18.47	5.21	

According to a study conducted by [12] on patients with T2DM, they showed impaired glucose metabolism and poor long-term glucose management, as seen by substantially higher FBS and HbA1c levels when compared with the control group. In addition, FBS and HbA1c levels were found to be considerably higher in the patient group compared to the control group in the study done by [13] on Turkish patients with T2DM, showing impaired glucose metabolism and subpar long-term glucose

management in the patient group. In addition, FBS and HbA1c levels were considerably higher in the diabetic patient group compared to the control group, showing impaired glucose metabolism and subpar long-term glucose management in the patient group [14].

Additionally, the patient group's urea levels were considerably higher than those in the control group, suggesting that their renal function was compromised. Similar to creatinine levels, which were substantially higher in the patient group than in the control group, further indicating to reduced kidney function among the patients. This result is consistent with the findings of[15] and [16] whofound that the patient group had considerably higher urea and creatinine levels than the control group, suggesting compromised kidney function. Higher blood levels of urea and creatinine, two indicators of renal function, may be a sign of impaired kidney health or kidney injury. Diabetic nephropathy, a frequent complication in patients with diabetes, often results in kidney damage. There are a number of factors, including glucose toxicity, that may make it such that persistently high blood glucose levels harm the blood capillaries in the kidneys and reduce their capacity to filter waste from the blood, and this may cause urea and creatinine to build up in the blood [17].

There was no noticeable difference in cholesterol levels between the patient and control groups. However, the patient group's triglyceride (Tri) values were notably higher than those in the control group, suggesting dyslipidemia in the patient group. The patient group had a poor lipid profile, as seen by the considerably lower high-density lipoprotein (HDL) levels compared to the control group. This non-significant difference was found in cholesterol levels between the patient and control group in studies by [18] and [19]on patients with T2DM, but the patient group had significantly higher triglyceride levels and significantly lower HDL levels, indicating dyslipidemia and poor lipid profile. No significant difference was found in cholesterol levels between the patient and control groups on adults with T2DM, but the patient group had significantly higher triglyceride levels and significantly lower HDL levels, indicating dyslipidemia and a poor lipid profile [20].

Finally, there was no discernible change in the levels of low-density lipoprotein (LDL) between the patient and control groups. However, the patient group's very low-density lipoprotein (VLDL) levels were considerably higher compared to the control group, suggesting that the patient group had impaired lipid metabolism.

The mean and (SD) of C. peptide for the patient and control groups was 1.55 (.22) and 1.19 (.22), respectively, with a highly significant difference ($p<0.001$), as shown in the table (3). The mean and (SD) levels of dopamine2 for the diabetic patients and controls was 2.48 (1.17) and 102.71 (543.30), respectively, with a significant difference between them ($p<0.05$).Insulin mean and SD for the patient and control groups was262.39 (47.13) and 130.50 (39.41), respectively, with a highly significant difference ($p<0.05$) as shown in table (3).

Table (3): Distribution of mean C. peptide, dopamine 2 and insulin among the study groups

	Groups	N	Minimum	Maximum	Mean	SD	p-value
C. peptide	Patients	120	1.03	2.77	1.5592	.22466	0.00
	Control	60	.85	1.67	1.1960	.22847	
Dopamine 2	Patients	120	1.01	5.94	2.4828	1.17197	.044
	Control	60	.83	3004.00	102.7185	543.30205	
Insulin	Patients	120	182.09	371.20	262.3902	47.13408	0.00
	Control	60	85.48	212.66	130.5028	39.41824	

*significant ($P\leq0.05$)

The results of this study agreed with the results reported by [21] and [22] whoshowed that the mean blood C-peptide level was considerably higher than that of the control group, suggesting hyperinsulinemia.

C-peptide is a measure of insulin secretion, and higher levels in the patient population may signify an overactive response to hyperglycemia in terms of insulin production [23]. A molecule called C-peptide is produced when the pancreas secretes insulin. Proinsulin, an inactive version of insulin that includes a C-peptide divide, is the thing that is produced when insulin is first made. The active insulin molecule is created from the C-peptide and is subsequently released into the circulation. In cases of insulin resistance, the body's cells become less receptive to insulin, which might cause the pancreas to produce more insulin to make up for it. As a consequence, the generation of C-peptide may also rise [24].

A possible cause for this is that insulin resistance may increase the amount of beta cells in the pancreas that produce both C-peptide and insulin. Additionally, insulin resistance may increase the amount of proinsulin generated, which in turn increases the synthesis of C-peptide [25].

Because it is a more reliable marker than insulin itself, which may be quickly excreted from the circulation, C-peptide can be used as a monitor of insulin production in diabetics. Both type 1 and type 2 diabetics may have their C-peptide levels evaluated to see how well their bodies are producing insulin [26].

Dopamine2 regulates the breakdown of glucose. Increased insulin levels in the patient group may be a sign of insulin resistance, a characteristic of type 2 diabetes [27].

Insulin levels were found to be considerably higher in the patient group compared to the control group, suggesting insulin resistance, in a research [28]on Chinese individuals with T2DM.

Dopamine D2 receptor activation in the pancreas may promote insulin production and aid in lowering blood sugar levels. Additionally, the hypothalamus's dopamine D2 receptors control energy balance and food intake, both of which have an impact on glucose metabolism [18].

Inflammation and oxidative stress, which are linked to insulin resistance and type 2 diabetes, may be reduced by activating dopamine D2 receptors [29].

Results in table (4) showed that C-peptide levels and insulin receptor levels in the patient group had a positive association ($r = 0.278$, $p = 0.002$), while C-peptide levels and dopamine 2 levels had an even larger positive correlation ($r = 0.427$, $p = 0.000$). These findings imply a connection between the concentrations of these biomarkers in individuals with diabetes. In particular, larger concentrations of C-peptide and dopamine 2 may be linked to higher concentrations of the insulin receptor.

In the control group, there is a significant negative association between insulin receptor and dopamine 2 levels ($r = -0.288$, $p = 0.026$) and a high positive correlation between C-peptide and insulin receptor levels ($r = 0.680$, $p = 0.000$). These findings imply that there is a connection between these biomarkers in people who are not diabetic as well. For example, in non-diabetic people, greater levels of C-peptide may be linked to higher levels of insulin receptor, but higher levels of insulin receptor may be linked to lower levels of dopamine 2.

Table (4): Correlation between C. peptide level insulin receptor and dopamine2 in the study groups

C. peptide		**Insulin receptor**	**Dopamine 2**
Patient	Pearson Correlation	.278**	.427**
	Sig. (2-tailed)	.002	.000
	N	120	120
Control	Pearson Correlation	.680**	-.288*
	Sig. (2-tailed)	.000	.026
	N	60	60

**. Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).

Conclusion: According to this study, those with the disorder had greater levels of C-peptide than people in the control group, which is a measure of insulin production. Additionally, urea levels in the patients group was considerably higher than those in the control group, suggesting that their renal

function was compromised. Between the patient and control groups, there was no discernible change in cholesterol levels. However, the patient group's triglyceride (Tri) values were substantially greater than those of the control group. However, the patient group's very low-density lipoprotein (VLDL) levels were considerably higher compared to the control group, suggesting that the patient group had impaired lipid metabolism. The patient group had a poor lipid profile, as seen by the considerably lower high-density lipoprotein (HDL) levels compared to the control groups. There was no discernible change in low-density lipoprotein (LDL) levels between the patient and control groups.

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