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RESEARCH ARTICLE - MEDICAL TECHNIQUES

Biochemical Assessment of Insulin and Dopamine 2 Receptors in Patients with Type 2 Diabetes

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Abstract

Dopamine (DA) plays a key role in the body's regulation of insulin production. This study aimed to estimate insulin and dopamine 2 receptors in type 2 diabetic patients. The study included 180 subjects aged (20-65) years during the period from November 2022 to March 2023. They were divided into two groups: 120 patients with type 2 Diabetes mellitus (60 males and 60 females), and 60 healthy individuals (30 males and 30 females) as a control group. The biochemical tests (insulin and dopamine 2) were measured by the Human Insulin ELISA kit and Human Dopamine 2 receptor ELISA kit in Bioassay Technology Laboratory. The HbA1c, urea, and creatinine were measured by the kit from Roche/ Hetachi Diagnostics Ltd Company. The fasting blood glucose and HbA1c were measured to diagnose all patients with T2DM and controls to confirm the subjects with T2DM. The samples were obtained from the AL Kinday Hospital and Endocrine Center in Baghdad, Iraq.

The results of this study explained that the patients and controls were comparable in age, gender, and smoking status with no significant differences (P> 0.05). while results reported that there was a greater significant difference ($p<0.01$) in levels of the mean for fasting blood sugar (FBS), glycated hemoglobin (HbA1c), and a significant difference ($p<0.05$) in urea and creatinine levels between the type 2 diabetic patients and the controls there was a significant difference detected in values of insulin and dopamine 2($p<0/05$) between the patient and control groups.

It can be concluded from our study that those who had type 2 diabetes mellitus had higher levels of dopamine and insulin when compared with the control group.

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1. Introduction

Diabetes mellitus (DM) is a disease in which the human body does not make enough of the hormone insulin or cannot respond to it properly [1], leading to excessively high levels of glucose in the blood, defects in the action of insulin, or excessive glucagon release [2]. Both type 1 and type 2 diabetes are chronic forms of diabetes [3]. Reversible diabetic issues include gestational diabetes and prediabetes [4]. When glucose levels in the blood are higher than normal, prediabetes develops. However, the blood glucose levels are not sufficiently elevated to qualify as diabetes. Furthermore, if no preventive measures are implemented, prediabetes may develop into diabetes [5].

The main nervous system is thought to be responsible for the dopamine 2 receptor agonist bromocriptine's therapeutic benefits in type 2 diabetes [6]. However, lipid metabolism in adipose tissue (AT) and glucose absorption in insulin-sensitive tissues are both directly influenced by peripheral dopamine [7]. Individuals with T2D may have decreased dopaminergic function in their adipose tissue, and that bromocriptine's therapeutic effects may include altering metabolism in this tissue [8].

Normally, the pancreas "beta-cells" respond to glucose by producing insulin [9], a process known as "glucose-stimulated insulin secretion (GSIS)". DA, which causes brief fluctuations in human insulin concentrations, negatively regulates GSIS [10]. The aim of the study estimates dopamine 2 receptors and insulin in type 2 diabetes mellitus patients. The creatinine blood test measures the level of creatinine in the blood. This test is done to see how well your kidneys are working. A blood urea nitrogen (BUN) test measures the amount of urea nitrogen found in your blood. Urea nitrogen is a waste product made when your liver breaks down protein [9]. In this study, we detected differences in biochemical

Nomenclature & Symbols			
DM	Diabetes Mellitus	AT	Adipose Tissue
FBS	Fasting Blood Sugar	GSIS	Glucose-Stimulated Insulin Secretion
T2D	Type 2 Diabetes	Dm	Dopamine
SD	Standard Deviation	HBA1C	HEMOGLOBIN A1C
D2R	Dopamine D2 Receptor	EDTA	Ethylenediaminetetraacetic Acid

parameters such as HbA1c, creatinine, and urea in addition to differences in biochemical parameters of dopamine 2, and insulin among the patient and control group.

2. Materials and Methods

2.1. Sample collection

In the current study, venous blood samples were collected from all subjects enrolled in the study between 9 -11 AM after overnight fasting (8-12) hours. The samples were divided into two aliquots EDTA tubes a Gel tubes. The biochemical tests (insulin and dopamine 2) were measured by the Human Insulin ELISA kit and Human Dopamine 2 receptor ELISA kit in Bioassay Technology Laboratory. The HbA1c, urea, and creatinine were measured by the kit from Roche/ Hetachi Diagnostics Ltd Company. The fasting blood glucose and HbA1c were measured to diagnose all patients with T2DM and controls to confirm the subjects with T2DM. The samples were obtained from the AL Kinday Hospital and Endocrine Center in Baghdad, Iraq.

2.2. Study design

In this study, 180 subjects aged (20-65) years, were enrolled during the period from November 2022 to March 2023. They were divided into two groups: 120 with type 2 *Diabetes mellitus* (60 males and 60 females), and 60 healthy individuals (30 males and 30 females) as a control group.

2.3. Ethical approval

Before beginning this study, all participants provided written consent. AL Kinday Hospital and Specialized Center for Endocrinology and Diabetes in Baghdad's ethics committee approved the study on March 9, 2022.

2.4. Statistical analysis

The quantitative variables were presented as mean, standard deviation minimum, and maximum, while the categorical (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.

3. Results and Discussion

3.1. Demographic Characteristics of patients and controls

The mean age and (SD) of the patient and control groups are shown in Table 1 to be 43.86 (14.67) and 43.16 (13.77), respectively, suggesting that there are no significant differences between the patient and the control groups p>0.05. This table demonstrated that the percentage of males and females was (50%) for each with no significant gender difference between the patient and control groups P>0.05. Regarding smoking status, Table 1 revealed that the majority 112 (93.3%) of the patient group were non-smokers, compared to 60 (100%) of the control group with no significant difference p>0.05.

Table 1. Distribution of age, gender, and smoking among patient and control groups

Demographical data			Patient group (n=120)	Control group (n=60)	p-value
Age	20-29	F	28	16	.759
		%	23.3%	26.7%	
	30-39	F	10	6	
		%	8.3%	10.0%	
	40-49	F	26	16	
		%	21.7%	26.7%	
	50-59	F	38	16	
		%	31.7%	26.7%	
	60 and more	F	18	6	
		%	15.0%	10.0%	
	Total	F	120	60	

			%	100.0%	100.0%	
		Mean ±SD		43.86±14.67	43.16±13.77	
		Min- Max		16-65	16-65	
Gender		Male	F	60	30	
			%	50.0%	50.0%	
		Female	F	60	30	
			%	50.0%	50.0%	.400
	Total		F	120	60	
			%	100.0%	100.0%	
Smoking		No	F	112	60	
			%	93.3%	100.0%	
		Yes	F	8	0	
			%	6.7%	0.0%	.051
	Total		F	120	60	
			%	100.0%	100.0%	

Although non-significant variation was observed in our study regarding smoking between the diabetic patients and the control group, many studies indicated that smoking poses a danger to type 2 diabetes (T2DM) and is regarded as an important risk factor for its development. [11], authors stated that smoking is strongly linked to an elevated risk of T2DM. In addition, another study performed by Wang *et al*. (2020) [12], found that smoking was linked to a higher risk of T2DM, with a greater connection shown in women patients [13]. They also showed that quitting smoking was linked to a significantly lower chance of acquiring T2DM. Moreover, it was reported that exposure to smoking was shown to be a higher risk for developing type 2 diabetes [14].

Smoking can increase the risk of developing diabetes or worsen the disease in people who are already diabetic. This is because smoking can lead to a condition called insulin resistance, and this decreases the sensitivity of cells to the hormone insulin. Insulin is a hormone that helps the body use and store glucose from the food we eat, and when cells become resistant to insulin, glucose levels in the blood can rise, leading to type 2 diabetes. In addition to insulin resistance, smoking can also increase inflammation in the body, which can further worsen insulin resistance and development and contribute to type 2 diabetes. Furthermore, smoking is known to increase the risk of other health complications that are associated with diabetes, such as cardiovascular disease, kidney disease, and nerve damage [11].

3.2. Estimation of biochemical parameters

There was a highly significant difference p <0.001 in the mean FBS between the patient and control groups, 228.04 (110.77) and 100.52 (9.44), as shown in Table 2. Also, there was a highly significant difference p<0.001 in mean HbA1c levels between the patient and control groups, 9.07 (2.53) and 4.96 (0.54) respectively. Additionally, the results indicated a significant difference p<0.05 in mean urea levels between the patient and control groups, 27.48 (7.01) and 25.54 (5.67) respectively. The mean creatinine was 0.75 (0.17) for the patient group and 0.66 (0.15) for the control group, indicating a significant difference between the two groups p<0.05.

Table 2. Mean differences of biochemical parameters between patient and control group

Analysis Type		N	Minimum	Maximum	Mean	SD	p-value
FBS(mmol/l)	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(mmol/l)	Patients	120	13.80	42.60	27.48	7.01	.048
	Control	60	15.86	36.20	25.54	5.67	
Creatinine(mmol/l)	Patients	120	.50	1.30	.75	.17	.001
	Control	60	.40	1.08	.66	.157	

The mean Fasting Blood Sugar (FBS) levels were substantially higher in the patient group than in the untreated group (mean SD: 228.04 (110.77) opposing 100.52 (9.44), which suggests that the patient group was experiencing impaired glucose metabolism. A similar pattern was

seen for HbA1c levels, which showed substantially worse long-term glucose management in the patient group (mean SD: 9.07 (2.53) compared to the control group (mean SD: 4.96 (0.54)). These results of urea and creatinine were consistent with [15], who studied Egyptian patients with T2DM, and discovered that the patient group had considerably higher urea and creatinine levels than the control group, suggesting compromised kidney function. Additionally, another study conducted by [16] on Brazilian people with T2DM found that the levels of urea and creatinine among type-2 diabetic patients were considerably higher than those of the control group, suggesting decreased kidney function.

Urea and creatinine are both markers of kidney function, and higher levels of these substances in the blood can indicate reduced kidney function or kidney damage. In people with diabetes, kidney damage is a common complication known as diabetic nephropathy. Several factors, including glucose toxicity, mean that elevated blood glucose levels over an extended period can damage the blood vessels in the kidneys, impeding their ability to filter debris from the blood. This can lead to an accumulation of urea and creatinine in the blood [17, 24].

3.3. Estimation of dopamine 2 and insulin

Regarding Dopamine2, the data in Table 3 revealed that the mean dopamine2 values in patient and control groups were 2.48 (1.17) and 102.71 (543.30), respectively, with a statistically significant difference ($p < 0.05$). There was also a significant difference $p<0.05$ in mean Insulin values between the patient and control groups 262.39 (47.13) and 130.50 (39.41) respectively. This study implies that individuals with diabetes had lower levels of dopamine 2, a neurotransmitter linked to motivation and reward, than those in the control group. This divergence is probably not accidental, as shown by the significant difference with a p-value of less than 0.05. The differences in mean values of dopamine2 and Insulin levels between the patient and control groups can be used to differentiate between the two groups [18, 25]. On the other hand, dopamine is a neurotransmitter that is involved in the regulation of glucose metabolism, and its lower levels in the patient group may indicate impaired glucose metabolism [19, 26]. Insulin is a hormone that controls the level of glucose in the blood circulation, and its higher levels in the patient group may indicate insulin resistance, which is a hallmark of type-2 diabetes [20, 28].

Table 3. Mean differences of dopamine 2, and insulin among patient and control group

	Groups	N	Minimum	Maximum	Mean	SD	p-value
Dopamine 2(ng/ml)	Patients	120	1.01	5.94	2.4828	1.17197	.044
	Control	60	.83	3004.00	102.7185	543.30205	
Insulin receptor(ng/ml)	Patients	120	182.09	371.20	262.3902	47.13408	0.00
	Control	60	85.48	212.66	130.5028	39.41824	

The patient group's mean insulin was higher than those of the control group. This result suggests that the pancreas secretes insulin in response to elevated blood glucose levels.

Dopamine 2, a chemical found in neurons that regulates the absorption of glucose, may be affected in people with diabetes due to reduced levels seen in that population [21, 28] Increased insulin levels in the patient group may be a sign of insulin resistance, a characteristic of type 2 diabetes [22, 28-30] Insulin is a hormone that controls blood glucose levels. The severity of diabetes may therefore be determined using these indicators, and the efficacy of diabetes treatment measures can be tracked [23, 31-34].

Also, a few drugs that attack dopamine D2 receptors, including antipsychotics utilized for the treatment of schizophrenia, may have metabolic adverse effects that lead to weight gain, type 2 diabetes, and insulin resistance.

4. Conclusions

The study revealed that dopamine 2 levels in the patient group were lower than controls. which may signify poor glucose metabolism. The patient group's elevated insulin levels ARE SUGGESTED AS A sign of insulin resistance. The high amounts of dopamine 2 RECEPTORS may affect insulin sensitivity and increase the risk of type 2 diabetes. These receptors are crucial in the control of blood glucose levels and insulin resistance.

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