

Evaluation of (HbA1c, Creatinine, Dopamine receptor2, Insulin, Glutathione, Lipidperoxidase) in type 2 diabetes mellitus patients

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Abstract: The dopamine receptor, often known as DA, is crucial in the body's regulation of insulin production. The patient group had significantly lower mean and standard deviation values for Dopamine receptors than the control group. In this study, regarding the Dopamine receptor mean (SD), patients with type 2 diabetes mellitus and control groups had values of 2.48 (1.17) and 102.71 (543.30), respectively. The insulin means (SD) for the patient and control groups were 258.0601 (44.35) and 119.8709 (37.075), respectively. The insulin concentration between the patients with type 2 diabetes mellitus and control groups differ significantly, as indicated by a p-value of < 0.05. Based on this research, individuals with the illness exhibited reduced concentrations of Dopamine receptor 2. The significant disparity, as evidenced by a p-value below 0.05, suggests that this divergence is highly unlikely to be a chance occurrence. This result aligns with the notion that the pancreas secretes insulin when blood glucose levels are elevated. The liver enzymes are AST ALT and T2DM patients. The mean values of ALT and AST were considerably higher in the T2DM group than in humans without T2DM (P= 0.001). The findings of this study demonstrate a significant reduction in Dopamine receptor 2 levels and an increase in insulin concentrations in patients with type 2 diabetes mellitus (T2DM) compared to control groups. The elevated levels of liver enzymes AST and ALT in T2DM patients further suggest a potential link between altered biochemical factors and the disease's pathophysiology. These disparities, confirmed by statistically significant p-values, underscore the critical role of Dopamine receptor and liver enzymes in the regulation of insulin production and glucose metabolism.

Keywords: Diabetes mellitus; Dopamine receptor 2 receptors; insulin; T2DM.

1. Introduction

Diabetes is caused by high levels of sugar in the blood, known as hyperglycemia, occurring either during periods of fasting or after eating. Diabetes mellitus (DM) can cause damage, dysfunction, and failure in various organs and tissues such as the retina, kidney, nerves, heart, and blood vessels [1, 2].

The human body depends on various interconnected systems and pathways to work together harmoniously in order to achieve and sustain a state of optimal physiological well-being. The fundamental basis of these

processes is the organism's capacity to preserve a consistent and stable condition known as homeostasis. An abnormality in the balance of internal conditions within the body, known as homeostasis, can result in the occurrence of an injury or a pathological condition in different organs. Obesity diminishes an individual's capacity to control the concentration of glucose in the bloodstream, leading to many significant and small issues [3].

The control of glucose levels in the blood operates through a negative feedback loop and is mediated by the secretion of insulin and glucagon. High blood glucose levels stimulate the B cells of the islet of Langerhans in

the pancreas to secrete insulin. Insulin is a polypeptide consisting of 51 amino acids, with two chains (A and B) linked by disulfide bridges. Insulin is produced from pro-insulin by the activity of pro-hormone convertases (PC I and PC2) and exo-protease carboxypeptidase. These enzymes catalyze the conversion of pro-insulin to insulin and C-peptide [4].

Insulin is a naturally present hormone produced by the pancreas that is crucial for facilitating the utilization of glucose as an energy source in the body. Insufficient production of insulin by the pancreas or improper utilization of insulin by the body results in elevated amounts of glucose in the bloodstream, a condition known as hyperglycemia. This leads to the development of diabetes [4]. The dopamine receptor is a natural catecholamine neurotransmitter in the central nervous system, and a precursor to both epinephrine and norepinephrine (NE). It exerts its action through alpha, beta, and Dopamine receptors. Intermediate dosing (5–10 mcg/kg/min) mostly results in chronotropic and inotropic effects through beta-receptor agonism, such as increased heart rate and systolic blood pressure. As the Dopamine receptor dose is increased, it interacts with alpha-receptors, causing an increase in systemic vascular resistance [3, 6]. Ahat, F. (2023)., Research demonstrates that heightened HbA1c levels are associated with inadequate metabolic regulation and an increased risk of complications, such as diabetic nephropathy, as shown by the correlation between HbA1c and creatinine levels [5].

Vani, K., and Renuka. A., (2023), The correlation between HbA1c and fasting blood glucose (FBS) is also significant, reinforcing HbA1c's utility as a reliable marker for glycemic control [6].

In this study, we evaluate the fasting blood glucose, HbA1c, insulin, Dopamine receptor, and other biochemical factors, such as HbA1c, Creatinine, Insulin, Glutathione, and Lipid peroxidase, to diagnose all patients with T2DM.

2. Materials and Methods

Samples

All of the people in the current study provided a venous blood sample of 10 ml. The blood collection took place between 8 - 10 AM, following an overnight fasting period of 10-12 hours. The Human Insulin ELISA kit, Roche/Hitachi Diagnostics Ltd, and Human Dopamine receptor Bioassay Technology Laboratory (BT Lab) China were utilized to perform biochemical testing.

Study design

From April 2023 to December 2023, a total of 150 people, aged between 20 and 60, were subjected to evaluation as part of a study. The participants were

categorized into two groups: a group of 90 individuals diagnosed with type 2 diabetes mellitus, consisting of 45 males and 45 females, and a control group of 60 healthy individuals, consisting of 30 males and 30 females.

Ethical approval

Before the collection of their blood samples for this study, all participants supplied written informed consent. This study was approved by the ethics committee of the Baghdad laboratory on December 12, 2023.

Statistical analysis

SPSS 26.0 (Chicago) and Excel 2016 were used for statistical analysis. Simple frequency, percentage, mean, and standard deviation measures will be used. Chi-square is used for categorical variables, and a t-test is used for continuous variable tests to determine the difference between two independent means, or a paired t-test is used for the difference of paired observations. If the p-value was below 0.05, statistical significance was assessed.

3. Results and Discussion

Determination of age, gender, smoking, and blood pressure among patients, control group, and p-value in study groups

The study's initial objectives were to determine the prevalence of depression among type 2 diabetic patients. So, all study participants had their depression diagnosed using the Hamilton test, and it was revealed that 90 of type 2 diabetics, or over 75%. A global study has found that as the duration of diabetes increases, the management of the condition deteriorates [7]. The most prevalent complication is neuropathy, followed by cardiovascular, renal, retinopathy, and foot ulcers. [8].

The age means (SDs) for the patient with type 2 diabetes mellitus and control groups are shown in Table 1 to be 90 and 60, respectively. Moreover, this data indicates no age-related variations among the patients with type 2 diabetes mellitus and control groups. This table illustrates that the ratio of males to females in both the sick and control groups was equivalent.

Table 1: Evaluate the variations of different factors among patients with T2DM and the control group.

Data			Patient group (n=90)	Control group (n=60)	p-value
	20-29	F	22	14	.728

Age	30-39	F	16	5	
	40-49	F	25	19	
	50-59	F	16	18	
	60 and more	F	11	4	
	Total	F	90	60	
		%	100.0%	100.0%	
	Mean $\pm$ SD		46.42 $\pm$ 12.87	46.82 $\pm$ 14.53	
	Min- Max		20-65	20-65	
Gender	Male	F	45	30	.400
	Female	F	45	30	
Total		F	90	60	
		%	100.0%	100.0%	
Blood Pressure	No	F	59	60	
	Yes	F	31	0	
Total		F	90	60	
		%	100.0%	100.0%	
Smoking		No	78	60	
		Yes	12	0	

Table 1 reveals that 78 of the sick group did not smoke, compared to 60 of the control group. According to the research, the majority of the individuals in the sick group did not smoke, but none of the people in the control group smoked agreed with the study Mahmood, A. R. (2016) [9].

This study suggests that smoking may increase the risk of developing type 2 diabetes (T2DM). Research conducted by Yeh, H.-C., et al., [10] has established a robust correlation between smoking and a heightened susceptibility to Type 2 Diabetes Mellitus (T2DM). Willi, C. et al., (2007) [11] conducted research that revealed a significant association between smoking and an increased susceptibility to type 2 diabetes mellitus (T2DM), particularly among women. A study conducted

by Consortium et al., (2014) [12] demonstrated a strong correlation between smoking cessation and a significantly reduced risk of developing Type 2 Diabetes Mellitus (T2DM). Śliwińska-Mossoń, M., et al., (2017) [13] conducted research that found a significant association between exposure to secondhand smoking and an increased susceptibility to acquiring type 2 diabetes.

Estimation of biochemical

The mean $\pm$ SD of fasting blood sugar (FBS) for the patient and control groups explained in Table 2 as 219.33 (113.58) and 100.18 (9.73), respectively. Furthermore, this data indicates an important difference in FBS (fasting blood sugar) levels between the patient and control groups, with a p-value of 0.05. The mean (SD) HbA1c levels for the patient and control groups were 10.14 (2.19) and 5.91 (0.55), respectively. At a level of significance of 0.05, this table also demonstrates a significant difference in HbA1c values between the patient and control groups, which agreed with the study Chiu, W. C., (2020) [14]. The mean (SD) of creatinine were 0.75 (0.75) and 0.77 (0.152) for the patient with type 2 diabetes mellitus group and control group, respectively. Furthermore, the data clearly shows a substantial disparity in creatinine levels between the patient and control groups, with a p-value of 0.05. The mean and standard deviation (SD) values for a range of biochemical markers in the treatment and control groups are shown in Table 2.

Table 2: Evaluates the variations in chemical factors between patients with T2DM and control groups.

Analysis Type		N	Min imum	Max imum	Mean	SD	p-value
FBS	Patients	90	90.00	540.00	219.33	113.58	.00*
	Control	60	85.50	150.00	100.18	9.73	
Hb A1c	Patients	90	5.00	18.00	10.14	2.19	.001*
	Control	60	4.00	10.00	5.91	0.55	
Cre atinine	Patients	90	0.50	1.40	0.75	0.75	.001*

	Cont rol	6 0	0.40	1.10	0.6 3	0.1 52	
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The patient's group's Fasting Blood Sugar (FBS) levels were substantially higher than those of the untreated group (mean SD: 219.33 (113.58) vs. 100.18 (9.73)), suggesting that the patient's glucose metabolism was compromised. In a similar vein, the patient group's HbA1c values (mean SD: 10.14 (2.19)) were greater than the control group's (mean SD: 5.91 (0.55)), indicating significantly worse long-term glucose management.

In a study by Post, A., (2021) [15], A study was conducted on patients with T2DM, and it was observed that the patients had significantly elevated creatinine levels compared to the control group; males had lower plasma creatine concentrations ($36.7 \pm 17.6 \mu\text{mol/L}$) compared to females (30.4 ± 15.1 vs. 42.7 ± 17.7 ; $p < .001$). In 7.3 [6.2–7.7] years of follow-up, 235 (5.4%) individuals acquired type 2 diabetes. Higher plasma creatine levels were linked to a higher risk of type 2 diabetes (HR per SD change: 1.27 [95% CI: 1.11–1.44]; $p < .001$), despite possible confounders. Sex significantly impacted this connection (p interaction $< .001$). Higher plasma creatine levels were linked to a higher incidence of type 2 diabetes in men (HR: 1.40 [1.17–1.67]; $p < .001$) but not in females (HR: 1.10 [0.90–1.34]; $p = .37$). The results showed dopamine receptors and insulin, and most diabetic patients had dopamine receptors and insulin. Regarding Dopamine receptor mean (SD), both groups had values of 2.87 (1.53) and 103.5 (532.89), as shown in Table 3.

Table 3: Evaluates the variations of hormones among patients with T2DM and the control group.

	Grou ps	N	Mean	SD	p- val ue
Dopamine receptor 2	Patie nts	9 0	2.874 7	1.531 8	0.0 38
	Contr ol	60	103.51 95	27.027 66	
Insulin	Patie nts	9 0	258.0 601	44.35 651	0.0 0
	Contr ol	60	119.87 09	37.075 18	
Glutathion e	Patien ts	90	5.88	1.32	0.00 1
	Contr ol	60	19.84	5.65	
Lipidperox	Patien	90	6.04	1.56	0.00

idase	ts				1
	Contr ol	60	1.61	0.54	

The results of Glutathione were higher in the control group, and the opposite of Lipid peroxidase was higher in the patient group. Additionally, this data demonstrates a statistically significant difference in Dopamine receptor2 levels between the patient and control groups ($p < 0.05$).

The mean (SD) insulin readings for both groups were 258.0601 (44.35) and 119.8709 (37.075), respectively. With a p-value of 0.05, this table provides evidence of a statistically significant disparity in insulin levels between the patient with T2DM and control groups (without T2DM), which agreed with the glutathione result agreed with study Dworzański, J., (2020) [16]. The study suggests that those with the condition exhibited a reduced concentration of Dopamine receptor 2. This discrepancy is likely not coincidental, as evidenced by the substantial disparity with a p-value below 0.05. Lipid peroxidase increased in patients more than the control group, agreed with the study of Jiang Y., et al., (2020) [17].

The average and variability of insulin levels in the sick group were higher than those in the human without T2DM. This outcome is consistent with the pancreas releasing insulin in response to increased amounts of glucose in the blood. This discrepancy is likely not coincidental, as evidenced by the substantial disparity with a p-value of less than 0.05.

Reduced levels of Dopamine receptor 2, a neurotransmitter responsible for regulating glucose absorption, may impact individuals with diabetes. Elevated insulin concentration observed in humans with T2DM may indicate the presence of insulin resistance, a defining feature of type 2 diabetes. Insulin is a hormone responsible for regulating blood glucose levels. These markers can be used to identify the severity of diabetes, and they can also be used to track the effectiveness of diabetic treatment strategies.

Furthermore, certain medications that target Dopamine receptor receptors, such as antipsychotics prescribed for schizophrenia, can cause metabolic side effects resulting in weight and T2DM.

In this study, table 4 shows a significant correlation between the liver enzymes AST and ALT and T2DM patients. The mean values of ALT and AST were considerably higher in the T2DM group than in humans without T2DM ($P = 0.001$).

Table 4: Results of Liver Function Tests in the Study Groups.

	Groups	N	Mean	SD	p-
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					value
AST (U / L)	Patients	90	31.70	5.86	0.001
	Control	60	23.27	4.10	
ALT (U / L)	Patients	90	29.78	8.75	0.001
	Control	60	21.64	4.97	
ALP (U / L)	Patients	90	88.64	21.66	0.001
	Control	60	97.53	13.43	

Conclusion

The patient group's reduced Dopamine receptor² levels (the D2 receptor is on chromosome 11) are shown by the data, suggesting possible problems with glucose metabolism. The elevated insulin levels in the patient group may indicate insulin resistance. The availability of Dopamine receptor D2 receptors or prolonged exposure to high levels of Dopamine receptors could impact the sensitivity of insulin and raise the likelihood of developing T2DM. These factors are critical in regulating insulin resistance and glucose concentration in the blood. The results of Glutathione were higher in the control group, and the opposite of Lipid peroxidase was higher in the patient group. T2DM patients had higher mean ALT and AST readings than non-T2DM patients. The findings of this study demonstrate a significant reduction in Dopamine receptor 2 levels and an increase in insulin concentrations in patients with type 2 diabetes mellitus (T2DM) compared to control groups. The elevated levels of liver enzymes AST and ALT in T2DM patients further suggest a potential link between altered biochemical factors and the disease's pathophysiology. These disparities, confirmed by statistically significant p-values, underscore the critical role of Dopamine receptor and liver enzymes in the regulation of insulin production and glucose metabolism.

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According to the authors, a conflict of interest is absent.

Author's Contributions

May Ridha Jaafar¹ is writing and collecting samples, Farah Thamer Samawi², Asmaa A. Jawad³, and Nany Hairunisa⁴ Conceived and designed the analysis, and this review

Ethics

This study was conducted under approval by the medical ethics committee at Al-Nahrain University (2024). Parents and agreement provided verbal and written consent for publication, which was obtained from both participants and researchers.

References

1. Al-Khaqani, Z. M., & Al-Turaihi, T. S. A.-D. (2024). Estimate the prevalence of depression in type 2 diabetes patients. *Kufa Medical Journal*, 20, 158-167.
2. Aboghunaim, T. N., & Al-Koofee, D. A. (2021). Genotyping study of CTLA-4 gene polymorphism (Rs2319775) in a sample of type 2 diabetes mellitus with and without hypertensive Iraqi patients. *Journal of Kufa for Chemical Sciences*, 2, 165-175.
3. Alhamdany, M. H. A. (2018). Antibiotic susceptibility of bacteria isolated from patients with diabetes mellitus and recurrent urinary tract infections in Babylon Province, Iraq. *Medical Journal of Babylon*, 15, 63-68.
4. Abusaib, M., Ahmed, M., Nwayyir, H. A., Alidrisi, H. A., Al-Abbood, M., Al-Bayati, A., et al. (2020). Iraqi experts consensus on the management of type 2 diabetes/prediabetes in adults. *Clinical Medicine Insights: Endocrinology and Diabetes*, 13, 1179551420942232.
5. Li, M., Chi, X., Wang, Y., Setrerrahmane, S., Xie, W., & Xu, H. (2022). Trends in insulin resistance: Insights into mechanisms and

- therapeutic strategy. *Signal Transduction and Targeted Therapy*, 7, 216.
6. Khalaf, M. A., & Ali, D. S. (2022). Evaluation of thyroid hormones, kidney function and lipids profile in sera patients with type II diabetes mellitus in Iraqi population. *Journal of Kufa for Chemical Sciences*, 2, 246-261.
7. Shaik, J., & Ibrahim, S. (2018). Study of 24 hours urinary proteins, creatinine, & serum total protein and creatinine in diabetic and hypertensive patients. *The Pharma Innovation Journal*, 7, 18-21.
8. Al-Daghri, N. M., Al-Attas, O. S., Wani, K., Sabico, S., & Alokail, M. S. (2017). Serum uric acid to creatinine ratio and risk of metabolic syndrome in Saudi type 2 diabetic patients. *Scientific Reports*, 7, 1-8.
9. Mahmood, A. R. (2016). Estimation of oxidative stress and some trace elements in Iraqi men patients with type 2 diabetes mellitus. *Iraqi Journal of Pharmaceutical Sciences*, 25, 17-22.
10. Yeh, H.-C., Duncan, B. B., Schmidt, M. I., Wang, N.-Y., & Brancati, F. L. (2010). Smoking, smoking cessation, and risk for type 2 diabetes mellitus: A cohort study. *Annals of Internal Medicine*, 152, 10-17.
11. Wili, C., Bodenmann, P., Ghali, W. A., Faris, P. D., & Cornuz, J. (2007). Active smoking and the risk of type 2 diabetes: A systematic review and meta-analysis. *JAMA*, 298, 2654-2664.
12. Consortium, I., Spijkerman, A. M., van der A, D. L., Nilsson, P. M., Ardanaz, E., Gavrila, D., et al. (2014). Smoking and long-term risk of type 2 diabetes: The EPIC-InterAct study in European populations. *Diabetes Care*, 37, 3164-3171.
13. Śliwińska-Mossoń, M., & Milnerowicz, H. (2017). The impact of smoking on the development of diabetes and its complications. *Diabetes and Vascular Disease Research*, 14, 265-276.
14. Chiu, W.-C., Lai, Y.-R., Cheng, B.-C., Huang, C.-C., Chen, J.-F., & Lu, C.-H. (2020). HbA1C variability is strongly associated with development of macroalbuminuria in normal or microalbuminuria in patients with type 2 diabetes mellitus: A six-year follow-up study. *BioMed Research International*, 2020.
15. Post, A., Groothof, D., Schutten, J. C., Flores-Guerrero, J. L., Swarte, J. C., Douwes, R. M., et al. (2021). Plasma creatine and incident type 2 diabetes in a general population-based cohort: The PREVEND study. *Clinical Endocrinology*, 94, 563-574.
16. Dworzański, J., Strycharz-Dudziak, M., Kliszczewska, E., Kielczykowska, M., Dworzańska, A., Drop, B., et al. (2020). Glutathione peroxidase (GPx) and superoxide dismutase (SOD) activity in patients with diabetes mellitus type 2 infected with Epstein-Barr virus. *PLOS ONE*, 15, e0230374.
17. Jiang, Y., Tan, S., Wang, Z., Guo, Z., Li, Q., & Wang, J. (2020). Aerobic exercise training at maximal fat oxidation intensity improves body composition, glycemic control, and physical capacity in older people with type 2 diabetes. *Journal of Exercise Science & Fitness*, 18, 7-13.