Relationship Between Insulin and Dopamine2 Receptors in Diabetes Mellitus Patient

Mustafa Sultan Enad
Clinical Biochemistry, Wsit Health Department, Al-azeziya Hopspital.
Corresponding author E-mail: **nazarnazar909@yahoo.com**

Abstract

Dopamine D2 receptors play key roles 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 diabetes patients better regulate their glucose metabolism. There was a significant lower mean and standard deviation of Dopamine2 in the patient group in in comparison to the control group. In addition, the patient group's insulin mean and standard deviation were greater than those of the control group. 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. Fasting blood sugar (FBS) concentrations were considerably higher in the patient group compared to the controls, pointing to a decreased metabolism of glucose in this group. A similar pattern was seen in HbA1c values, which were considerably higher in the patient group in comparison to the controls, suggesting a poor long-term glucose management in the patient group.

Keywords: *Insulin, Dopamine, Diabetes mellitus, receptors.*

العلاقة بين مستقبلات الأنسولين والدوبامين 2 لدى مريض السكري

م.م. مصطفى سلطان عناد

الخلاصة

تلعب مستقبلات الدوبامين D2 دورًا رئيسيًا في التحكم في مقاومة الأنسولين ومستويات السكر في الدم. نظرًا لأن مستويات الببتيد C ودوبامين 2 ترتبطان بشكل إيجابي، فإن زيادة تركيزات الببتيد C قد تؤدي أيضًا إلى تركيزات أعلى من الدوبامين 2، مما قد يساعد مرضى السكري على تنظيم استقلاب الكلوكوز بشكل أفضل. كان متوسط الدوبامين 2 والانحراف المعياري أقل بكثير في مجموعة المرضى مقارنة بمجموعة السيطرة. بالإضافة إلى ذلك، كان متوسط الأنسولين والانحراف المعياري لمجموعة المرضى أكبر من لمجموعة السيطرة. ووفقا لهذه الدراسة، فإن أولئك الذين يعانون من هذا الاضطراب لديهم مستويات أعلى من الببتيد C مقارنة بالأشخاص في مجموعة السيطرة، وهو مقياس لإنتاج الأنسولين. وكانت تركيزات السكر في الدم للصائم (FBS) في مجموعة المرضى أعلى بكثير مما كانت عليه في مجموعة السيطرة، مما يشير إلى انخفاض استقلاب الكلوكوز في هذه المجموعة. ولوحظ نمط مماثل في قيم السكر التراكمي HbA1c، والتي كانت أعلى بكثير في مجموعة المرضى عنها في مجموعة السيطرة، مما يشير إلى أن مجموعة المرضى كانت تعاني من ضعف إدارة الكلوكوز على المدى الطويل.

P-ISSN: 2664-0562
E-ISSN:2664-0554

الكلمات المفتاحية: الأنسولين، الدوبامين2، داء السكري، المستقبلات.

Introduction

The insulin hormone is produced by the pancreas, and this hormone plays an important role in allowing blood glucose to enter into the body cells to be used as energy [1]. Insulin resistance occurs when there is no reaction of the body cells towards insulin as they should in patients with type2 diabetes [2].

As the condition increases, insulin secretion becomes unable to keep glucose levels under control, resulting in hyperglycemia [3] . The overweight or great body fat percentage, especially in the abdominal area, are the major characteristics of patients with type 2 DM [4]. Insulin resistance when The adipose tissues promote insulin resistance via various inflammatory mechanisms, such as the release of high free fatty acid (FFA) or adipokine dysregulations [5]. The incidence and prevalence of type-2 diabetes have tripled as a consequence of human aging, inactive lifestyle, a high calorie diet, and worldwide obesity rate [5]. The chronic metabolic disease known as diabetes mellitus is characterized by persistent hyperglycemia [6]. It might have resulted from increased insulin resistance, decreased insulin productions, or both. About 415 million people aged 20 to 79 had DM in 2015, in accordance with the International Diabetes Federation (IDF) [7]. The primary catecholamine neurotransmitter in the brain is dopamine (DA). Locomotion, memory, emotional and motivated behaviours, and neuroendocrine modulation are just a few of the processes it takes part in. Numerous psychiatric & neurological conditions, e.g. Parkinson disease, Huntington disease, schizophrenia, bipolar disorder, attention deficit hyperactivity disease and Tourette's syndrome, have been linked to elevated DA levels [8].

Materials and Methods

Every patient involved in the present research had 8 ml of venous blood drawn from them between 9 and 11 AM after a long fast (8 to 12 hrs). The blood samples were divided into 2 aliquots and placed in EDTA and gel tube, respectively. Human Insulin ELISA kits & Human Dopamine-2 receptor ELISA kits were used at the Bioassay Technology Laboratory (BT Lab) to assess the biochemical tests (insulin and dopamine 2). The Roche/Hetachi Diagnostics Ltd Company utilized the HbA1c, urea, and creatinine kits. 180 patients in the study project, whose ages varied from 20 to 65, received evaluations between 1st November 2022 and 1st March 2023. The participants have been divided into two groups: a control group of 60 healthy individuals, which included 30 men and 30 females, and 120 patients with type 2 diabetes mellitus.

P-ISSN: 2664-0562
E-ISSN:2664-0554

All individuals gave written, informed permission before having their blood collected for this research. The committee on ethics of the Canadian Hospitals & Specialized Centre for Diabetes & Endocrinology in Baghdad gave its clearance to this research on the 9th of March / 2022.

Statistical analysis

The quantitative variable were presented as means, standard deviation minimums & maximums, whereas the qualitative variable were presented as percentages and frequencies. The Kolmogorov Smirnov test was used to examine the distribution normality. The one-way independent sample's t-test was used for performing the inferential statistics, Mann Whitney test, Pearson correlations and ROC curves. The results were considered statistically significant when ($P \leq 0.05$).

Result and discussion

Table 1 suggests that the mean (SD) BMI for the patient and control groups was, respectively, 28.49 (5.11) and 27.17 (5.18). Additionally, this table displays non-significant BMI difference between the patients and controls at ($p \leq 0.05$).

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

Parameters			Group		Total	P-value
			Patients	Controls		
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

The means (SD) of FBS for the patient and control groups are shown in table 2 to be 228.04 (110.77) and 100.52 (9.44), respectively. Additionally, this data suggests an important difference in FBS between patients and controls at 52 (9.44), respectively. Additionally, this data suggests an important difference in FBS between patients and controls at a ($p \leq 0.05$). HbA1c's mean (SD) for the patient and control groups, respectively, was 9.07 (2.53) and 4.96 (0.54). At a p-value of ≤ 0.05, this table additionally shows significant differences in HbA1c concentration between patients and controls.

P-ISSN: 2664-0562
E-ISSN:2664-0554

Moreover, important differences in urea level between patients and controls. For the patients, the mean (SD) of creatinine was shown to be 0.75 (0.17) while for the controls, it was 0.66 (0.15). Additionally, this data shows an important difference in levels of creatinine between patients and controls at ($p \leq 0.05$).

In terms of cholesterol, the mean (SD) values were 169.22 (29.04) and 173.28 (21.17) for the patient and control groups, respectively. Additionally, this data indicates that at a s were 169.22 (29.04) and 173.28 (21.17) for the patient and control groups, respectively. Like that, this data indicates that at a p-value of ≤ 0.05, there have been no overall changes in cholesterol levels between the patient and control groups. The mean (SD) of Tri for patients and controls, as shown in the table, was 131.30 (57.96) and 92.37 (26.09). Also, this data demonstrates a significant difference in Tri between patients and controls at ($p \leq 0.05$).

Also, this table shows that the mean (SD) of urea for patients and control groups was 27.48 (7.01) and 25.54 (5.67), respectively. Also, this table shows significant difference between patients and controlss regarding urea at ($p \leq 0.05$). While the mean (SD) of creatinine for patients and control groups was 0.75 (0.17) and 0.66 (0.15), respectively. Also, this table shows significant difference between patients and controls regarding creatinine at ($p \leq 0.05$).

In relation to cholesterol, the mean (SD) of cholesterol for patients and control groups was 169.22 (29.04) and 173.28 (21.17), respectively. Also, this table shows non-significant difference between patients and controls regarding cholesterol at ($p \leq 0.05$). This table shows that the mean (SD) of Tri for patients and control groups was 131.30 (57.96) and 92.37 (26.09), respectively. Also, this table shows significant difference between patients and controls regarding Tri at ($p \leq 0.05$).

This table shows that the mean (SD) of HDL for patients and control groups was 39.28 (6.006) and 45.22 (8.59), respectively. Also, this table shows significant difference between patients and controls regarding HDL at ($p \leq 0.05$).

Regarding the mean (SD) of L D L for patients and control groups, they were 104.20 (27.86) and 109.59 (17.06), respectively. Also, this table shows non-significant difference between patients and controls regarding LDL at ($p \leq 0.05$). This table shows that the mean (SD) of V L D L for patients and control groups was 26.28 (11.56) and 18.47 (5.21), respectively. Also, this table shows significant differences between patients and controls regarding VLDL at ($p \leq 0.05$). As shown in table (2).

P-ISSN: 2664-0562
E-ISSN:2664-0554

Table (2): The mean difference of chemical aspect among the study groups.

		N	Min.	Max.	Means	SD	p-values
FBS	Patient	120	90.00	545.00	228.04	110.77	.000*
	Controls	60	88.90	140.00	100.52	9.44	
HbA1c	Patient	120	4.50	16.00	9.07	2.53	.000*
	Controls	60	4.00	6.20	4.96	.54	
Urea	Patient	120	13.80	42.60	27.48	7.01	.048**
	Controls	60	15.86	36.20	25.54	5.67	
Creatinine	Patient	120	.50	1.30	.75	.17	.001*
	Controls	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	
Tri	Patients	120	45.10	340.00	131.30	57.96	.000*
	Control	60	53.40	147.60	92.37	26.09	
H D L	Patients	120	27.20	62.00	39.28	6.006	.000*
	Control	60	35.00	66.00	45.22	8.59	
L D L	Patients	120	50.94	194.00	104.2	27.86	.100
	Control	60	72.24	139.82	109.59	17.06	
V L D L	Patients	120	9.20	68.00	26.28	11.56	.000*
	Control	60	10.68	29.52	18.47	5.21	

The mean (SD) of C. peptide for the patient and control groups was 1.55 (.22) and 1.19 (.22), respectively, as shown in the table. Additionally, this data shows an essential difference in C. peptide levels between patients and controls at ($p \leq 0.05$). For the patient and control groups, the mean (SD) levels of dopamine2 were 2.48 (1.17) and 102.71 (543.30), respectively. Additionally, the dopamine2 levels in both the sick and control groups vary significantly ($p \leq 0.05$) from one another.Insulin levels for the patient and control groups were 262.39 (47.13) and 130.50 (39.41), respectively, in proportion to the mean (SD) of insulin. Additionally, this data shows an essential difference in insulin use between patients and controls at ($p \leq 0.05$), As shown in table 3.

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

	Group	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 ($P \leq 0.05$)

P-ISSN: 2664-0562
E-ISSN:2664-0554

The cutoff values, sensitivity, and specificity of insulin and dopamine 2 in patient groups might vary based on the specific test or assay employed, as well as other elements including the population being tested and the presence of additional co-morbidities. As sows in table 4 and figure 1 and 2

Table (4): Cuts-off values, sensitivity, and specificity of dopamine 2 and insulin in the patient groups.

	Cutoff point	Sensitivity	Specificity	Area	Sig.
Dopamine2	**0.923**	**1.00**	**0.03**	**.414**	**.044**
Insulin	**209.3**	**0.93**	**0.96**	**.990**	**.000**

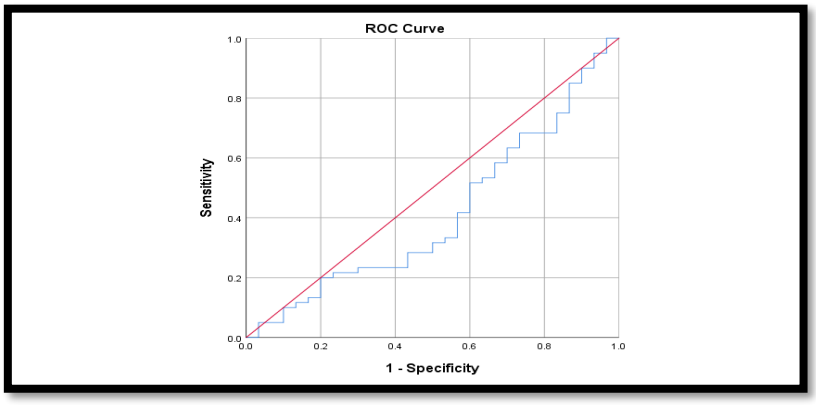

Fig. (1): Receiver Operating Characteristics curve regarding of dopamine2.

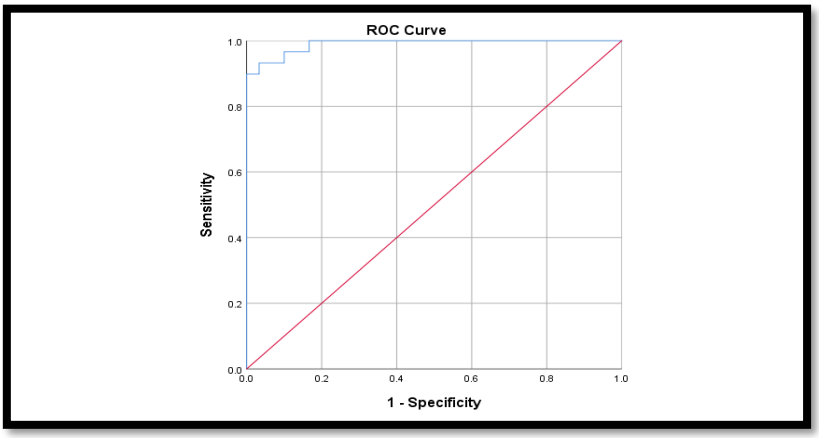

Fig. (2): Receiver Operating Characteristics curve regarding of insulin.

Discussion

According to the results there were non-significant BMI difference between patients and controls at ($p \leq 0.05$). Chen *et al*. 2021 [9] study involving Chinese participants indicated no correlation between BMI and the incidence of T2DM. In a meta-analysis of 21 prospective cohort studies, BMI was shown to be highly correlated with the risks of developing T2DM; however, the intensity of the

P-ISSN: 2664-0562
E-ISSN:2664-0554

association differed across different groups. (2002). Tang *et al*. [10] found that BMI was strongly associated with the incidence of T2DM in a study of Chinese individuals (Wen *et al*., 2020) [11], but this association was stronger in females than in males. It is essential to point out, however, that BMI is only one of a number of variables that can play important roles in T2DM development, and the absence of a statistically significant differences in BMI between patients and controls does not rule out 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. According to a study via Godman et al. (2020), [12] on human beings with T2DM, the patient group had impaired glucose metabolism and poor long-term glucose management, as seen by substantially higher FBS and HbA1c levels as compared to the control group. In addition, levels of FBS and HbA1c were considerably higher in patients in comparison with the controls in Omazi et al. (2021), [13] research on Turkish people with T2DM, showing impaired glucose metabolism and subpar long-term glucose management in the patient group. In addition, levels of FBS and HbA1c were considerably higher in patients in comparison with the controls in a research by Morieri et al. (2020), [14] on Italian individuals with T2DM, showing impaired glucose metabolism and subpar long-term glucose management in the patient group.

Furthermore, the sick group's urea levels were considerably higher than those in the controls (mean SD: 25.54 (5.67)), suggesting that their renal function was compromised. Similar to creatinine levels, which were considerably higher in the patients when compared with the controls (mean SD: 0.75 (0.17) vs. 0.66 (0.15)), further pointing to the patient group's reduced kidney function. This result is consistent with research by Salem et al. (2022), [15] which examined Egyptian people with type-2 DM. They revealed that patients had significantly higher concentrations of urea and creatinine than in controls, indicating compromised renal functions. According to research by Diniz et al. in 2021 [16] on Brazilian people with T2DM, where the patients had substantially higher concentrations of urea and creatinine than in controls, indicating compromised renal functions. In a more recent investigation of people with type-2 DM, Feldman & Ryndina revealed that patients had significantly higher concentrations of urea and creatinine than in controls, indicating compromised renal functions. 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.

P-ISSN: 2664-0562
E-ISSN:2664-0554

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. According to Kawahito et al. (2009), [17] this may cause urea and creatinine to build up in the blood.

However, there was no noticeable difference in cholesterol levels between the patient and control groups (mean SD: 169.22 (29.04) vs. 173.28 (21.17). However, the patient group's triglyceride (Tri) values were notably higher than those in the control group (mean SD: 92.37 (26.09) compared to 131.30 (57.96), 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 (mean SD: 39.28 (6.006)) compared to the control group's (mean SD: 45.22 (8.59)) levels. These outcomes concur with non-significant differences were detected in cholesterol levels between patients and controls in a study by Chen et al., 2020, [18] on Chinese adults with T2DM, but the patient group had significantly higher triglyceride levels and significantly lower HDL levels, indicating dyslipidemia and a poor lipid profile. No significant difference was found in cholesterol levels between the patient and control groups in the study of Kuchay et al, 2020, (19) on Indian adults with T2DM, but the patient group had significantly higher triglyceride levels and lower HDL levels, indicating dyslipidemia and a poor lipid profile. Non-significant differences were detected in cholesterol levels between patients and controls in a study by Bakkar et al., 2020, [20] 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.

According to study by Bazyar et al. (2020), [21] on people with T2DM, there was no significant difference in LDL levels between the patient and control groups, but the patient group had considerably higher VLDL levels, suggesting impaired lipid metabolism. The lipid profile, which includes the amounts of triglycerides, LDL cholesterol, and total cholesterol in the blood, might rise as a result of diabetes.

The results of this study agree with the results reported by Sabre et al., 2021 [22], who discovered that the sick control's mean serum C-peptide level was considerably greater than that of the control group, suggesting hyperinsulinemia and showed that the individual in the study group's mean blood C-peptide level was considerably greater than that of the control group, suggesting hyperinsulinemia [22]. According to Rickels et al., 2020, [23] the patient group's mean serum C-peptide level was considerably greater than that of the control group, suggesting hyperinsulinemia [23].

P-ISSN: 2664-0562
E-ISSN:2664-0554

With a p-value of 0.05, it may be determined that the variations in mean C-peptide value, Dopamine-2 and Insulin between patients and controls may be utilized to distinguish between them. 2019 [24]. 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. Di Giuseppe and others, [25]. 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 [26].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) [27].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 [28].

However, the decreased levels of the neurotransmitter dopamine2 in the sick group may point to poor glucose metabolism [29]. Dopamine2 regulates the breakdown of glucose. In the patients, high levels of insulin may indicate insulin resistance, which is a characteristic of type-2 DM [30]. The hormone (insulin) is responsible for controlling blood sugar level. Thus, such indicators can be used to determine diabetes severity, and to track the measures of diabetes treatment’s effectiveness [31]. To validate these results and look into the underlying causes of these relationships, more study is required. Levels of Dopamine2 were shown to be considerably lower in patients in comparison with controls in Lin and Qu's 2020 research on Korean individuals with T2DM, suggesting poor glucose metabolism. Levels of insulin were shown to be considerably higher in patients in comparison with controls, suggesting insulin resistance, in a research by [32] on Chinese individuals with T2DM. Insulin resistance and blood sugar management are closely regulated by dopamine D2 receptors. 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 (Chien et al., 2023) [18].The development of insulin resistance and type 2 diabetes, however, may be facilitated by long-term

P-ISSN: 2664-0562
E-ISSN:2664-0554

exposure to high dopamine levels or a decline in the availability of dopamine D2 receptors. The ability of dopamine D2 receptors to influence the activity of crucial enzymes involved in glucose metabolism, such as glycogen synthase and phosphatidylinositol-3-kinase (PI3K), may be the cause of this impact. Inflammation and oxidative stress, which are linked to insulin resistance and type 2 diabetes, may be reduced by activating dopamine D2 receptors [33].

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.

P-ISSN: 2664-0562
E-ISSN:2664-0554

References

1. Campbell JE. Newgard CB. Mechanisms controlling pancreatic islet cell function in insulin secretion. Nature reviews Molecular cell biology. 2021;22(2):142-58.

2. Dev K, Ali M, Prakash S. COMPARATIVE STUDY. OF INSULIN RESISTANCE IN RURAL AND URBAN IN TYPE 2 DIABETES PATIENTS OF MUZAFFARNAGAR DISTRICT. 2020.

3. Del Prato S, Tiengo A. The importance of first-phase insulin secretion: implications for the therapy of type 2 diabetes mellitus. Diabetes/metabolism research and reviews. 2001;17(3):164-74.

4. Ekpor E, Akyirem S, Adade Duodu P. Prevalence and associated factors of overweight and obesity among persons with type 2 diabetes in Africa: a systematic review and meta-analysis. Annals of Medicine. 2023;55(1):696-713.

5. Chatterjee S, Khunti K, Davies MJ. Type 2 diabetes. The lancet. 2017;389(10085) :2239-51.

6. Farooqui R, Afsar N, Afroze IA. Role and significance of hematological parameters in diabetes mellitus. Ann Pathol Lab Med. 2019;6(3):A158-62.

7. Yates T, Khunti K. The diabetes mellitus tsunami: worse than the'Spanish flu'pandemic? Nature Reviews Endocrinology. 2016;12(7):377-8.

8. Xia Q-P, Cheng Z-Y, He L. The modulatory role of dopamine receptors in brain neuroinflammation. International Immunopharmacology. 2019;76:105908.

9. Chen X, Duan M, Hou R, Zheng M, Li H, Singh M, et al. Prevalence of abdominal obesity in Chinese middle-aged and older adults with a normal body mass index and its association with type 2 diabetes mellitus: a nationally representative cohort study from 2011 to 2018. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy. 2021:4829-41.

10. Tang M, Zhou Y, Song A, Wang J, Wan Y, Xu R. The relationship between body mass index and incident diabetes mellitus in Chinese aged population: a cohort study. Journal of Diabetes Research. 2021;2021.

11. Wen J, Wang A, Liu G, Wang M, Zuo Y, Li W, et al. Elevated triglyceride-glucose (TyG) index predicts incidence of Prediabetes: a prospective cohort study in China. Lipids in Health and Disease. 2020;19(1):1-10.

12. Godman B, Basu D, Pillay Y, Mwita JC, Rwegerera GM, Anand Paramadhas BD, et al. Review of ongoing activities and challenges to improve the care of patients with type 2 diabetes across Africa and the implications for the future. Frontiers in pharmacology. 2020;11:108.

13. Omazić J, Viljetić B, Ivić V, Kadivnik M, Zibar L, Müller A, et al. Early markers of gestational diabetes mellitus: what we know and which way forward? Biochemia medica. 2021;31(3).

P-ISSN: 2664-0562

E-ISSN:2664-0554

14. Morieri ML, Frison V, Rigato M, D'Ambrosio M, Tadiotto F, Paccagnella A, et al. Effectiveness of dulaglutide in the real world and in special populations of type 2 diabetic patients. The Journal of Clinical Endocrinology & Metabolism. 2020;105(7):e2617-e25.

15. Salem IM, Ismail MI, Ghorab AA, Fouad R, Mosbah O, Khalifa G, et al. Study of Lipoprotein-Associated Phospholipase A2 as a Potential Biomarker for Diabetic Kidney Disease in Type 2 Diabetes. The Egyptian Journal of Hospital Medicine. 2022;88(1): 4062-7.

16. Diniz CO, McKenna Z, Canuto L, Magalhães F, Machado-Moreira CA, Shibuya E, et al. A preliminary evaluation of the kidney function of sugarcane cutters from Brazil. Journal of Occupational and Environmental Medicine. 2021;63(2):e53-e8.

17. Kawahito S, Kitahata H, Oshita S. Problems associated with glucose toxicity: role of hyperglycemia-induced oxidative stress. World journal of gastroenterology: WJG. 2009;15(33):4137.

18. Chien H-Y, Chen S-M, Li W-C. Dopamine receptor agonists mechanism of actions on glucose lowering and their connections with prolactin actions. Frontiers in Clinical Diabetes and Healthcare. 2023;4.

19. Kuchay MS, Krishan S, Mishra SK, Choudhary NS, Singh MK, Wasir JS, et al. Effect of dulaglutide on liver fat in patients with type 2 diabetes and NAFLD: randomised controlled trial (D-LIFT trial). Diabetologia. 2020;63:2434-45.

20. Bakkar N-MZ, Dwaib HS, Fares S, Eid AH, Al-Dhaheri Y, El-Yazbi AF. Cardiac autonomic neuropathy: a progressive consequence of chronic low-grade inflammation in type 2 diabetes and related metabolic disorders. International journal of molecular sciences. 2020;21(23):9005.

21. Bazyar H, Hosseini SA, Saradar S, Mombaini D, Allivand M, Labibzadeh M, et al. Effects of epigallocatechin-3-gallate of Camellia sinensis leaves on blood pressure, lipid profile, atherogenic index of plasma and some inflammatory and antioxidant markers in type 2 diabetes mellitus patients: A clinical trial. Journal of Complementary and Integrative Medicine. 2020;18(2):405-11.

22. Saber AM, Mohamed MA, Sadek AA, Mahmoud RA. Role of umbilical cord C-peptide levels in early prediction of hypoglycemia in infants of diabetic mothers. BMC pediatrics. 2021;21(1):1-7.

23. Rickels MR, Evans-Molina C, Bahnson HT, Ylescupidez A, Nadeau KJ, Hao W, et al. High residual C-peptide likely contributes to glycemic control in type 1 diabetes. The Journal of clinical investigation. 2020;130(4):1850-62.

24. Korner J, Cline GW, Slifstein M, Barba P, Rayat GR, Febres G, et al. A role for foregut tyrosine metabolism in glucose tolerance. Molecular Metabolism. 2019;23:37-50.

25. Di Giuseppe G, Ciccarelli G, Soldovieri L, Capece U, Cefalo CM, Moffa S, et al. First-phase insulin secretion: can its evaluation direct therapeutic approaches? Trends in Endocrinology & Metabolism. 2023.

P-ISSN: 2664-0562

E-ISSN:2664-0554

26. Ziolkowska S, Binienda A, Jabłkowski M, Szemraj J, Czarny P. The interplay between insulin resistance, inflammation, oxidative stress, base excision repair and metabolic syndrome in nonalcoholic fatty liver disease. International Journal of Molecular Sciences. 2021;22(20):11128.

27. Washburn RL, Mueller K, Kaur G, Moreno T, Moustaid-Moussa N, Ramalingam L, et al. C-peptide as a therapy for type 1 diabetes mellitus. Biomedicines. 2021;9(3):270.

28. Foteinopoulou E, Clarke CA, Pattenden RJ, Ritchie SA, McMurray EM, Reynolds RM, et al. Impact of routine clinic measurement of serum C-peptide in people with a clinician-diagnosis of type 1 diabetes. Diabetic Medicine. 2021;38(7):e14449.

29. Dekkers IA, Jiang J, Lamb HJ, Jansen P. Obesity and the brain: structural and functional imaging studies, and opportunities for large-scale imaging genetics. Visceral and Ectopic Fat: Elsevier; 2023. p. 281-93.

30. Kolodziejski PA, Leciejewska N, Chmurzynska A, Sassek M, Szczepankiewicz A, Szczepankiewicz D, et al. 30-Day spexin treatment of mice with diet-induced obesity (DIO) and type 2 diabetes (T2DM) increases insulin sensitivity, improves liver functions and metabolic status. Molecular and Cellular Endocrinology. 2021;536:111420.

31. Wang H, Peng L, Chai Y, Yuan R. High-sensitive electrochemiluminescence C-peptide biosensor via the double quenching of dopamine to the novel Ru (II)-organic complex with dual intramolecular self-catalysis. Analytical chemistry. 2017;89(20):11076-82.

32. Zhou Y, Yang G, Qu C, Chen J, Qian Y, Yuan L, et al. Predictive performance of lipid parameters in identifying undiagnosed diabetes and prediabetes: a cross-sectional study in eastern China. BMC Endocrine Disorders. 2022;22(1):1-9.

33. Park SY, Gautier J-F, Chon S. Assessment of insulin secretion and insulin resistance in human. Diabetes & Metabolism Journal. 2021;45(5):641-54.

P-ISSN: 2664-0562

E-ISSN:2664-0554