Original
ISSN 2413-0516

Preptin as a Potential Marker in Iraqi Newly Diagnosed T2DM and T2DM with Cardiovascular Disease

Noor Thair Tahir[1*], Shatha M. J. Al-Khateeb[2], Raghda Shams Akram[2]

[1]National Diabetes Center/Mustansiriyah University, Baghdad, Iraq.
[2]Department of Chemistry and Biochemistry, College of Medicine, Mustansiriyah University, Baghdad, Iraq.
*Correspondence to: Noor Thair Tahir (E-mail: dr.noorthair.ndc@uomustansiriyah.edu.iq)
(Submitted: 13 January 2024 – Revised version received: 10 February 2024 – Accepted: 25 February 2024 – Published Online: 26 April 2024)

Abstract

Background: Diabetes mellitus has become one of the world's most typical and costly chronic diseases. Diabetes mellitus and cardiovascular disease, which is the primary reason for morbidity and death among diabetic individuals. The aim of present work is to study the Role of preptin level in Iraqi type 2 diabetes patients and related with other biochemical parameters.

Methods: This study was including (88) partespents, (22) newly diagnosed T2DM, (22) T2DM and (22) ischemic heart disease with T2DM, and (22) as healthy control, age ranged (35–63) years.

Results: The findings indicate that individuals with type 2 diabetes mellitus (T2DM) exhibited markedly elevated levels of FBS, HbA1C, insulin, HOMA-IR, TC, TG, LDL-C, VLDL-C, and preptin in comparison to the control group. These differences were statistically significant ($P < 0.0001$). Moreover, the Pearson correlation analysis revealed that preptin levels were positively associated with FBS, HbA1c, TC, TG, LDL, VLDL, insulin, and HOMA-IR while exhibiting a negative correlation with HDL.

Conclusion: Because preptin plays a critical function in controlling sugar metabolism and, consequently, sugar problems, excessive levels of preptin play a significant role in the patient's inability to control both their level of glycosylated hemoglobin and their blood sugar levels. preptin levels are therefore high in diabetics and those with heart disease, which results in a loss of control over the body's metabolism and exposes a patient to many other ailments.

Keywords: Diabetes mellitus (T2DM), CVD, preptin, lipid profile

Introduction

Diabetes mellitus (DM) is a category of metabolic illnesses characterized by persistently elevated sugar level. Frequent urination, thirst, and hunger are all signs of elevated blood sugar levels. Diabetes can lead to a slew of problems if left untreated.[1,2] Acute consequences include diabetic ketoacidosis, hyperosmolar hyperglycemia, and death[3]. Long-term complications include cardiovascular disease, stroke, chronic kidney illness, foot ulcers, and vision impairment.[2] By 2020, coronary heart disease (CHD), as well as known as ischemic heart disease (IHD), is expected to overtake cancer as the top cause of mortality in emerging countries.[4] Although low-income nations account for more than 80% of worldwide CHD burden, developed countries have a disproportionate amount of knowledge about major risk factors. According to study, South Asians have a higher prevalence of obesity, insulin resistance (IR), T2DM, all of which are important CHD risk factors.[5] Moreover, Preptin, a peptide hormone consisting of 34 amino acids, has been recently identified as being synthesized in pancreatic β-cells and co-secreted with insulin in response to glucose. It has also been detected in the salivary glands, breast tissue, and kidneys.[6] Elevated plasma levels of preptin were observed in individuals diagnosed with type 2 diabetes mellitus (T2DM). Preptin, which is known to stimulate insulin secretion by obstructing ATP-sensitive potassium channels in pancreatic β-cells, exhibits comparable effects on insulin secretion.[7] According to a study by Yang and his team, preptin may contribute to the etiology of type 2 diabetes by enhancing insulin production. Preptin improves insulin secretion induced by glucose.[8]

Materials and Methods

This study was include (88) partespents, (22) newly diagnosed T2DM, (22) T2DM and (22) ischemic heart disease with T2DM, and compared with (22) as healthy control, age ranged from 35 to 63 years, attending to the Mustansiriyah university / National Diabetes Center, during the period from March to December 2021. Age, sex, disease duration, weight, high, and the body mass index (BMI) of each patient was determined by multiplying their kilogram body weight by their squared height in meters (kg/m^2). Participants who had been fasting had their venous blood samples taken, fasting blood sugar (FBS), total cholesterol, triglyceride, high density lipoprotein-cholesterol and low density lipoprotein- cholesterol were estimated by using automated analyzer (BIOLABO Kenza240TX). The Bio-Rad VARIANT hemoglobin A1C use ion-exchange high performance liquid chromatography (HPLC) principles to separate glycated hemoglobin in an automated and precise manner (HbA1c). DRG insulin ELISA kit was used to determine serum insulin concentrations.[9] [fasting insulin (ng/ml)] [fasting glucose (mg/dl)]/405 is the homeostasis model of IR (HOMA-IR).[10] Preptin level was determined by (ELISA) method using.

Statistical Analysis

The SPSS program in version 20.0 and Excel 2016 were both used for the data analysis. A one-way analysis of variance was used to compare differences between the groups (ANOVA). A *P*-value of 0.05 was regarded as significant.

Results

The results shows of biochemical parameters when comparing between patients and control groups (Table 1). The patients with T2DM had significantly higher values for FBS, HbA1C, Insulin, HOMA-IR, TC, TG, HDL-C, LDL-C and VLDL-C ($P < 0.0001$) compared to control group.

Table 1. **Characteristics of clinical parameters in diabetes mellitus group and the control**

Parameters	Control	T2DM	T2DM with IHD	Newly diagnosed T2DM	*P*-value
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
	N = 22	N = 22	N = 22	N = 22	
Sex (M/F)	(11/11)	(10/12)	(11/11)	(10/12)	/
Age (years)	33.64 ± 10.02	50.68 ± 5.78	45.64 ± 7.29	36.32 ± 10.31	0.0001
BMI (kg/m^2)	26.24 ± 3.77	28.34 ± .90	33.80 ± 4.08	25.51 ± 3.21	0.0001
FPS (mg/dl)	89.41 ± 8.96	161.14 ± 27.32	221.77 ± 51.08	116.91 ± 7.48	0.0001
HbA1c%	5.33 ± 0.39	8.74 ± 1.44	9.75 ± 2.07	7.78 ± 1.08	0.0001
Insulin (µU/ml)	9.96 ± 1.33	15.72 ± 4	17.75 ± 3.26	13.88 ± 4.02	0.0001
HOMA-IR	2.19 ± 0.32	6.21 ± 1.70	9.65 ± 2.70	4.03 ± 1.23	0.0001
TC (mg/dl)	143.41 ± 33.11	250 ± 57.14	255.91 ± 36.42	207.14 ± 47.70	0.0001
TG (mg/dl)	99.68 ± 24.86	190.95 ± 63.17	253.64 ± 37.04	154.86 ± 41.20	0.0001
HDL-C (mg/dl)	49.05 ± 7.99	45.59 ± 10.98	38.09 ± 2.86	46.27 ± 6.25	0.0001
LDL-C (mg/dl)	84.59 ± 33.88	166.22 ± 56.88	159.59 ± 37.21	129.89 ± 45.72	0.0001
VLDL-C (mg/dl)	19.94 ± 4.97	38.19 ± 12.63	50.72 ± 7.41	30.97 ± 8.24	0.0001

*The mean differences is significant at the 0.05 level, and highly significant 0.01.

Table 2. **Preptin level in diabetes mellitus group and the control**

Parameter	Control	T2DM	T2DM with IHD	Newly diagnosed T2DM	*P*-value
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
	N = 22	N = 22	N = 22	N = 22	
Preptin (ng/ml)	228.73 ± 23.26	453.55 ± 38.94	676.14 ± 67.11	341.41 ± 25.13	0.0001

*The mean differences is significant at the 0.05 level, and highly significant 0.01.

Table 3. **Correlations between variables in T2DM patients group (r-value)**

Parameters	FPS	HbA1c	TC	TG	HDL	LDL	VLDL	Insulin	HOMAIR	Preptin
FPS	1	.510**	.341**	.540**	–.283*	.265*	.540**	.252*	.863**	.768**
HbA1c	.510**	1	.375**	.346**	–.314*	.354**	.346**	.297*	.560**	.411**
Tc	.341**	.375**	1	.284*	–.031	.972**	.284*	.081	.285*	.310*
TG	.540**	.346**	.284*	1	–.382**	.107	1.000**	.194	.506**	.600**
HDL	–.283*	–.314*	–.031	–.382**	1	–.101	–.382**	–.252*	–.317**	–.363**
LDL	.265*	.354**	.972**	.107	–.101	1	.107	.077	.221	.230
VLDL	.540**	.346**	.284*	1.000**	–.382**	.107	1	.194	.506**	.600**
Insulin	.252*	.297*	.081	.194	–.252*	.077	.194	1	.679**	.369**
HOMAIR	.863**	.560**	.285*	.506**	–.317**	.221	.506**	.679**	1	.742**
Preptin	.768**	.411**	.310*	.600**	–.363**	.230	.600**	.369**	.742**	1

*Correlation is significant at the 0.05 level. ** Correlation is significant at the 0.01 level.

Table 2 shown a highly significant increase of preptin level between study group when compared with control, there is found increased preptin level in T2DM with IHD more than T2DM and Newly diagnosed T2DM.

Using Pearson correlation analysis, it was determined how each parameter included in the current work related to chemical measurements. Table 3 provide a summary of the findings. In the present study preptin level showed a significant positive relation with FPS, HbA1c, TC, TG, LDL, VLDL, Insulin, and HOMA-IR while a significant negative relation with HDL.

The distribution of Study groups by gender as shown in Figure 1 from patients with T2DM shows (42%) male and (58%) female.

The distribution of preptin level according BMI in diabetes mellitus in Figure 2 shown increased levels of preptin in obese (47%) more over weight than (31%) and lean (22%).

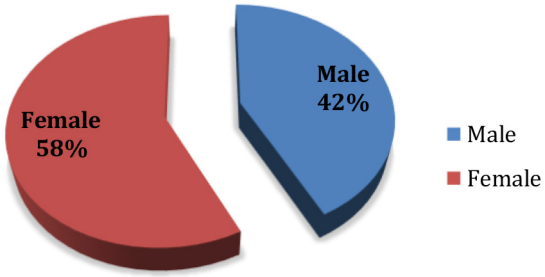

Fig. 1 **Distribution of preptin according to Gender in diabetes mellitus.**

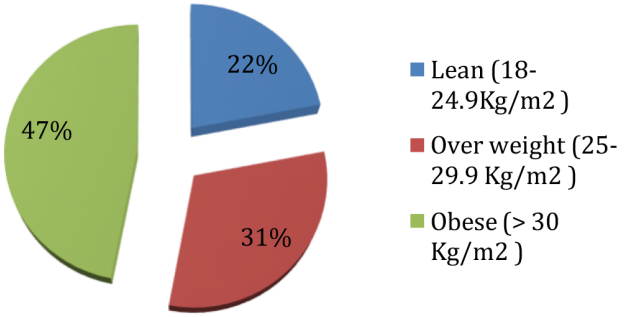

Fig. 2 **Distribution of preptin according to BMI in diabetes mellitus.**

Discussion

Diabetes is a collection from metabolic illnesses defined by hyperglycemia caused by abnormalities in insulin secretion, insulin action, or both, according to contemporary definitions.[11,12] In both normoglycemic and diabetic patients, preptin has been shown to modulate insulin secretion that is glucose-mediated.[13] Preptin acted directly on the -cell, increasing the maximum glucose stimulation insulin production from cultured cells (bTC6-F7 cells). The study conducted by Aiman et al., 2019[14] found that preptin regulation in diabetic patients either may be the outcome of the reduced Preptin metabolism or elevated secretion of preptin. The elevated level of preptin level may redound insulin level secretions. These findings are also consistent with Aslan et al study., who discovered that sera preptin in diabetic subjects was increased more than in a control of healthy people.[15] This agreement to our finding, Earlier studies revealed elevated preptin in diabetic when related with high insulin resistance. Preptin play function in the pathogenesis of T2DM via elevate insulin secretion.[13] There was a high level of preptin detected in patient with DM and glucose test, compared to the control group in an earlier study.[16] According to these findings, IR cases have higher preptin levels. In addition to the relationship between preptin level and age, this study demonstrated a positive relationship between insulin levels and HOMA-IR in T2D. These findings are in line with the research done by Hamzah et al.[17] Hamzah et al.[17] did a study in Iraq and found that preptin levels were considerably greater in T2DM patients compared to healthy people (P = 0.01), which is consistent with our findings. These findings are in line with others. those of Yang et al.,[18] who showed increased preptin level in T2DM patients with CVD compared to the control group. preptin levels have also been found to be higher in investigations of T2DM with CVD, which is consistent with previous findings.[15,19,20] preptin is a physiological booster from glucose-induced insulin secretion.

Recent research has found a link between preptin and insulin resistance in humans.[18] This link was especially important in the case of diabetes mellitus, as evidenced by literature showing that preptin concentrations were higher in DM patients.[21] preptin levels were found to have a substantial positive relationship with insulin and HOMA-IR in the current investigation when compared to healthy controls, which is similar with prior findings that indicated a strong relationship between preptin levels and HOMA-IR in obese participants.[22] In research done by Yang et al., the preptin level was found to have a positive association with insulin, HOMA-IR, glucose, and HbA1c %, similar to our findings.[18] Hypertriglyceridemia and low HDL-C are two examples of abnormal lipid profiles, have been linked to a number of disorders, including obesity, diabetes, and cardiovascular disease. For every 1 mg/dL rise in HDL-C, the risk of cardiovascular disease drops by 2 to 3%.[23] Despite some debate, high triglyceride levels, both fasting and non-fasting, appear to constitute a separate risk factor for IHD.[24,25] Epidemiological evidence suggests that having low HDL-C and high TG level is a substantial risk factor for IHD,[24] which is consistent with our findings, Patients with decreased HDL-C and high TG have the high rate of severe coronary artery, according to postdoctoral analysis of many research.[24] Although whether an elevated level from LDL is an independent risk factor is debatable, it is obviously linked to an increased risk of IHD.[26] In both Europeans[27] and Asians, TC level has been demonstrated to be an established IHD dangers factor[5] LDL-C levels that are high are key IHD risk factors, and treatment with LDL-C medicines has been shown to lower IHD risk, with the reduction proportional to the reduction in LDL-C levels.[27,28]

Conclusion

High levels of preptin play a significant role in the patients lack of control over and the level of glycosylated hemoglobin because it has major role in regulating sugar metabolism and thus controlling sugar complications. Therefore, the high level of preptin in diabetic and people with heart disease leads to lack of control over the body's metabolism and thus exposes a patient diabetes for many other diseases.

Declaration of Interest

No conflict of interest.

References

1. Jedda WAAL, Al-Ali ZAJR, Akram RS. Study the Interferon–γ, C-reactive Protein and Lipid Profile in Iraqi Diabetic Patients With and Without Hypertension. NVEO-NATURAL VOLATILES Essent OILS Journal| NVEO. 2021;8820–32.
2. Ali WM. Factors associated with poor glycemic control in diabetic patients in Kirkuk. Kirkuk Journal of Medical Sciences. 2022 May 1;10(1):87–97.
3. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. Diabetes Care. 2009;32(7):1335–43.

4. Elias NG, Akram RS, Abd Aon YS. Alteration of lipid profile, kidney functions, D-dimer and some anti-inflammatory parameters in samples of Iraqi patients with Covid-19. J Popul Ther Clin Pharmacol. 2023;30(5):515–25.
5. Akram RS, Isaa MQ, Mohammed AA. Fetuin-A levels and Insulin Resistance in Obese and Non-Obese Iraqi Children. J Popul Ther Clin Pharmacol. 2023;30(6):414–20.
6. Faris Rija F, Sulaiman Musa MI, Hamad HT. Some Biochemical Parameters and Level of Preptin in Newly Diagnosed Type 2 Diabetic Women Patients in Tikrit City. J Chem Heal Risks. 2022;12(2):179–82.
7. Smarr T, Clements JN. The Underutilization of Pramlintide as Adjunct Therapy in Type 1 and Type 2 Diabetes. ADCES Pract. 2023;2633559X221150809.
8. Mathiesen DS, Lund A, Holst JJ, Knop FK, Lutz TA, Bagger JI. THERAPY OF ENDOCRINE DISEASE: Amylin and calcitonin–physiology and pharmacology. Eur J Endocrinol. 2022;186(6):R93–111.
9. Nyirjesy SC, Peleckis AJ, Eiel JN, Gallagher K, Doliba A, Tami A, Flatt AJ, De Leon DD, Hadjiliadis D, Sheikh S, Stefanovski D, Gallop R, D'Alessio DA, Rubenstein RC, Kelly A, Rickels MR. Effects of GLP-1 and GIP on Islet Function in Glucose-Intolerant, Pancreatic-Insufficient Cystic Fibrosis. Diabetes. 2022 Oct 1;71(10):2153–2165. doi: 10.2337/db22-0399. PMID: 35796669; PMCID: PMC9501647.
10. Khalili, D., Khayamzadeh, M., Kohansal, K. et al. Are HOMA-IR and HOMA-B good predictors for diabetes and pre-diabetes subtypes?. BMC Endocr Disord 23, 39 (2023). https://doi.org/10.1186/s12902-023-01291-9.
11. Association AD. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2014;37(Supplement_1):S81–90.
12. Tahir NT, Falih IQ, Alkubaisi MR, Alabdaly AR. Apelin as a Potential Marker in Iraqi Children with Type 1 Diabetes Mellitus. J Contemp Med Sci| Vol. 2023,9(6):408–12.
13 Ungureanu, M.-C.; Bilha, S.C.; Hogas, M.; Velicescu, C.; Leustean, L.; Teodoriu, L.C.; Preda, C. Preptin: A New Bone Metabolic Parameter? Metabolites 2023, 13, 991. https://doi.org/10.3390/metabo13090991
14. Abbas A, Ali HA, AL-Rufaie MM, Ali RA. Association of serum preptin levels with insulin resistance in Iraqi women with gestational diabetes mellitus. Int Res J Pharm. 2019;10:49–55.
15. Li B, Li Y, Zhang T, Song L, Lei C, Zhao Y, et al. Preptin is a new predictor of coronary artery calcification. Clin Chim Acta. 2018;485:133–8.
16. Aydin S. Discovery of ghrelin hormone: research and clinical applications. Turk J Biochem. 2007;32:76–89.
17. Hamzah MI, Kareem IAA, Albayati M. Expression of Amylin and Preptinin Iraqi Patients with Type 2 Diabetes Mellitus. Exec Ed. 2020;11(01):1272.
18. Kıraç UI, Demır E, Ozkan H, Sahtıyancı B, Uzun H, Ekıncı I, Buyukkaba M, Durmus S, Akarsu M, Gelisgen R, Tabak O. Maternal serum preptin levels in the pathogenesis and diagnosis of Gestational diabetes mellitus. J Med Biochem. 2023 Mar 15;42(2):311–317. doi: 10.5937/jomb0-36287. PMID: 36987416; PMCID: PMC10040191.
19. Salman Hasan MS, Mashkur MS, Ranaei Siadat SO, Ali HA. Assessment of Serum Afamin and Preptin Levels as a Potential Diagnosis Markers for Cardiovascular Patients Undergoing Catheterization. Medico-Legal Updat. 2020;20(2).
20. Wang H, Wang X, Cao Y, Han W, Guo Y, Yang G, et al. Association of polymorphisms of preptin, irisin and adropin genes with susceptibility to coronary artery disease and hypertension. Medicine (Baltimore). 2020;99(10).
21. Gupta A, Singh SK, Padmavathi BN, Rajan SY, Mamatha GP, Kumar S, et al. Evaluation of correlation of blood glucose and salivary glucose level in known diabetic patients. J Clin diagnostic Res JCDR. 2015;9(5):ZC106.
22. El-Eshmawy M, Abdel Aal I. Relationships between preptin and osteocalcin in obese, overweight, and normal weight adults. Appl Physiol Nutr Metab. 2015;40(3):218–22.
23. Hirata A, Okamura T, Hirata T, Sugiyama D, Ohkubo T, Okuda N, Kita Y, Hayakawa T, Kadota A, Kondo K, Miura K, Okayama A, Ueshima H. Relationship Between Non-fasting Triglycerides and Cardiovascular Disease Mortality in a 20-year Follow-up Study of a Japanese General Population: NIPPON DATA90. J Epidemiol. 2022 Jul 5;32(7):303–313. doi: 10.2188/jea.JE20200399. Epub 2021 Jun 22. PMID: 33456020; PMCID: PMC9189318.
24. Tada H, Nomura A, Yoshimura K, Itoh H, Komuro I, Yamagishi M, Takamura M, Kawashiri MA. Fasting and non-fasting triglycerides and risk of cardiovascular events in diabetic patients under statin therapy. Circulation Journal. 2020 Feb 25;84(3):509–15.
25. Sacks, F. M., & Campos, H. (2003). Low-density lipoprotein size and cardiovascular disease: a reappraisal. The Journal of Clinical Endocrinology & Metabolism, 88(10), 4525–4532.
26. Jung E, Kong SY, Ro YS, Ryu HH, Shin SD. Serum Cholesterol Levels and Risk of Cardiovascular Death: A Systematic Review and a Dose-Response Meta-Analysis of Prospective Cohort Studies. Int J Environ Res Public Health. 2022 Jul 6;19(14):8272. doi: 10.3390/ijerph19148272. PMID: 35886124; PMCID: PMC9316578.
27. Baigent C, Blackwell L, Emberson J, Holland LE, Reith C, Bhala N, et al. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. Lancet (London, England). 2010;376(9753):1670–81.
28. Thair Tahir N, Akram RS, Al-Rubae'i SHN, SH Nsaif A. Vitamin D3 status and insulin resistance in Iraqi patients with osteoarthritis disease in Baghdad governorate-Iraq. In: AIP Conference Proceedings. AIP Publishing LLC; 2022. p. 30015.