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Evaluation of Lipocalin-2 and Vaspin Levels in In Iraqi Women with Type 2 Diabetes Mellitus

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Abstract

The main objective of this study would be that if serum lipocalin-2 and Vaspin levels may be utilized as indicators for chronic in Type 2 diabetes mellitus (T2DM) patients. T2DM treatment is to maintain a healthy glycemic level. If this goal is not met, diabetes consequences, both acute and chronic, may emerge, one of which is obesity. As a result, researchers have investigated the levels of Lipocalin-2 and Vaspin, as well as their connection to obesity and insulin resistance. In this study, we included 60 T2DM (ages 35 to 65 years) and 30 healthy controls. After an overnight fast, blood serum samples were collected, and routine biochemical parameters such as lipocalin-2, Vaspin, and glucose were measured in all samples. At a P <0.05 level, the data were declared significant. Using an ELISA kit, the levels of serum Lipocalin-2 and Vaspin were measured. The results have shown that patients with T2DM had substantially greater blood serum levels of Lipocalin-2 and Vaspin than normal controls (P <0.001 for all comparisons). Also, results revealed Lipocalin-2 and Vaspin have a high positive correlation with each of BMI and Homeostasis Model Assessment for insulin resistance HOMA-IR and moderate positive correlation between Vaspin and Fasting blood glucose.

Keywords: ***Type*** two Diabetes Mellitus, obesity, Lipocalin-2, Vaspin, HOMA-IR

تقييم Lipocalin-2 وVaspin لدى النساء المصابات بداء السكري من النوع 2 في العراق

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الخلاصة

يهدف علاج مرض السكري من النوع 2 إلى الحفاظ على مستوى طبيعي لنسبة السكر في الدم ، والذي إذا لم يتم الوصول إليه يمكن أن يؤدي إلى مضاعفات مرض السكري الحادة و / أو المزمنة ، أحدها السمنة. السمنة ومرض السكري من الأوبئة المنتشرة في اجزاء كثيرة من العالم. يهدف هذا العمل إلى التحقق من مستويات Lipocalin-2 و Vaspin وعلاقتها بالسمنة ومقاومة الأنسولين ، وتضمنت هذه الدراسة ستون مريضًا تم تشخيص إصابتهم بـ T2DM بأعمار تتراوح بين (35 إلى 65) عامًا وثلاثين من الاصحاء. تم تحديد مستوى Lipocalin-2 وVaspin في الدم باستخدام تقنية ELISA. تم العثور على مستوى

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Lipocalin−2و Vaspin أعلى بكثير في مرضى السكري من المجموعة الصحية. أيضا ، أظهرت النتائج وجود علاقة إيجابية قوية بين Lipocalin−2 و Vaspin مع كل من BMI و HOMA−IR وعلاقة إيجابية معتدلة بين Vaspin و FBG.

Introduction

Diabetes mellitus (DM) is a chronic endocrine and metabolic disease characterized by persistent hyperglycemia (high blood sugar) and abnormalities in protein, lipid, and carbohydrate metabolism caused by insulin action, insulin secretion insufficiency, or a combination of the two [1, 2]. In the human body, DM produces numerous complications, many of which result in significant mortality and morbidity [3, 4]. Obesity and diabetes are closely connected, with around 80% of diabetics being overweight. Obesity is a common occurrence in T2DM patients. Obese adults have lower insulin sensitivity (insulin resistance IR) [5]. Adipokines are a class of bioactive chemicals, that have a role in sensitivity and secretion of insulin, inflammation, appetite, energy expenditure and cardiovascular function [6]. Because adipocyte and adipose tissue dysfunction are essential anomalies in obesity, obesity is associated to type 2 diabetes, insulin resistance, hypertension, fatty liver disease, airway disease, dyslipidemia, dementia, atherosclerosis, and certain cancers [7]. Lipocalin-2, a glycoprotein with a molecular weight of 25 kDa that was initially found in human neutrophil granules and mouse kidney cells [8], is a glycoprotein generated by the body. Innate immunity and apoptosis are two processes that have been connected to this protein. In addition to neutrophils, lipocalin-2 is found in a range of organs, including the kidney, liver, adipocytes, lung, and macrophages [9]. Inflammation, organogenesis, cell differentiation, liver injury, apoptosis, and kidney damage are just a few of the physiological and pathological processes that LCN-2 plays a part with, in contrast to its bacteriostatic qualities, LCN-2 is also suggested to have a role in cancer development and metastasis. [10]. Lipocalin-2 is important for insulin sensitivity and glucose homeostasis [11]. Vaspin is a newly discovered adipokine produced by subcutaneous and visceral adipose tissues [12]. Vaspin is a recently found adipokine with insulin sensitization and appetite suppression properties. A hormonal imbalance can cause diabetesmellitus, Addison's disease, Acromegaly, infertility, and Hashimoto's disease, to name a few. Plasma vaspin levels have been found to be higher in polycystic ovarian syndrome (PCOS), the most common ovarian illness. Vaspin has been discovered as a potential link between obesity and metabolic abnormalities in humans [15]. Vaspin was discovered for the first time in visceral adipose tissue of insulin-resistant obese rats used as a type 2 diabetes model [16]. The aim of the research is how lipocalin-2 and Vaspin concentrations fluctuate in healthy people and people with T2DM. In addition, the level of T2DM patients who are obese against those who are not obese was compared. In addition to that, the sensitivity and specificity of the Lipocalin-2 and Vaspin markers were determined using the receiver operating characteristic curve (ROC) analysis. There was also a link discovered between diabetic characteristics and (lipocalin-2 and Vaspin).

Materials and methods

Studied groups

The current study was a case-control study with 60 women diagnosed with T2DM ranging in age from 35 to 65 years old and 30 healthy controls (35-to 65). The investigation was conducted from August to October 2021 with an age-matched control group.

Exclusion Criteria

Type1DM, pregnant women, women with other diabetic complications

Blood Sample

The blood sample was separated into two portions, the first of which (1mL) was transferred to an EDTA-containing tube to determine the amount of glycated hemoglobin (HbA1C). While the second half was transferred to a gel tube to separate the serum and kept at –20°C until it could be examined, the first part was kept at room temperature.

Experimental

The BMI (body mass index) was determined using the following formula (weight in kilograms divided by height in meters squared). Tosoh's automated glycohemoglobin analyzer HLC-723GX was used to measure glycated hemoglobin (HbA1C). A kenza (240TX) (Biolabs) equipment was used to measure biochemistry (fasting blood glucose (FBG), total cholesterol (TC), total triglycerides (TG), and high-density lipoprotein (HDL)). An ELISA kit was used to assess the quantities of (c-peptide, Vaspin, and Lipocalin-2) (Al-Shkairate establishments, Jordan).

Statistical analysis

The results were tested using IBM SPSS for Windows, Twenty-two edition. To compare the study groups, a T-test was performed. The value of the (correlation coefficient) was determined using (Pearson Correlation) analysis (r). This study also used (ROC curve) analysis to determine the degree of each marker's ability to aid in disease diagnosis.

Results

Table 1: (age, BMI, FBG, HbA1c, c-peptide, HOMA-IR, total cholesterol (TC), triglycerides (TG), High density lipoprotein (HDL), Vaspin, and Lipocalin-2) data (mean SD). Between T2DM patients and control groups, there was a significant rise in BMI (*P* 0.0001), although there was no significant difference in age (*P* >0.871). The amount of FBG and HbA1c, C-peptide, and HOMA-IR in the T2DM Patients group is likewise significantly higher (*P*= 0.0001) than in the control group. Diabetic patients had considerably higher levels of total cholesterol (TC) and triglycerides (TG) than non-diabetic people, *P*=0.0001. Diabetes patients had significantly lower amounts of high-density lipoprotein, according to the findings (HDL). When compared to the controls, the levels of vaspin and Lipocalin-2 in the patients increased significantly (*P* =0.0001).

Table 1: A comparison of clinical parameters between the control and T2DM

Variables	Control (30) healthy patients	T2DM Patients (60) patients	*P*-value
Age	47.03±7.86	46.72±6.89	0.871
BMI kg/m2	25.59±3.58	35.12±5	<0.0001
FBG mg/dl	87.16±8.72	220.56±95.89	<0.0001
HbA1c %	4.82±0.4	8.54±0.76	<0.0001
c-peptide ng/mL	1.44±0.56	3.90±1.39	<0.0001
HOMA-IR	2.18±0.61	5.85±0.68	<0.0001
TC mg/dl	138.72±33.60	290±43.63	<0.0001
TG mg/dl	105.31±22.63	196.51±45.37	<0.0001
HDL mg/dl	49.20±4.02	42.63±4.66	<0.0001
Vaspin ng/mL	64.86±7.05	137.21±12.49	<0.0001
Lipocalin-2 ng/mL	75.86±8.35	126.98±14.31	<0.0001

Table 2 shows a comparison of obese (30 patients) and non-obese (30 patients) T2DM (2). Between obese and non-obese T2DM groups, there was a substantial rise in BMI (P <0.0001). The amount of FBG and HbA1c in the obese patients' group is likewise significantly higher (P <0.0001) than in non-obese T2DM patients. The obese T2DM group had significantly higher levels of C-peptide and HOMA-IR than the non-obesity T2DM group (P <0.0001). Furthermore, obese T2DM with diabetes had significantly higher TC and TG than non-obese T2DM with diabetes, P=0.0001. HDL levels were significantly lower in obese T2DM patients (P <0.0001). When obese T2DM patients were compared to non-obese T2DM patients, vaspain and lipocalin-2 levels increased significantly (P <0.0001).

Table 2: Comparison between (obese and non-obese) T2DM

Variables	Non obese T2DM (30)patients	obese T2DM (30)patients	*P*-value
BMI kg/m2	28.86±4.76	39.21±5.97	<0.0001
FBG mg/dl	180.26±23.76	259.02±42.23	<0.0001
HbA1c %	8.32±1.31	8.91±1.54	<0.0001
c-peptide ng/mL	3.1±1.38	4.72±2.72	<0.0001
HOMA-IR	4.72±0.92	6.89±1.34	<0.0001
TC mg/dl	220.05±41.76	355.21±44.32	<0.0001
TG mg/dl	132.23±32.76	259,02±37.62	<0.0001
HDL mg/dl	47.21±3.92	39.15±2.76	<0.0001
Vaspin ng/mL	129.51±11.63	147.23±14.52	<0.0001
Lipocalin-2 ng/mL	118.51±10.24	135.26±11.56	<0.0001

Table 3: Correlation between (Lipocalin-2 and Vaspain) and the variables of obese T2DM

variables	Lipocalin-2 r	P-value	Vaspain r	*P*-value
BMI kg/m2	0.621	<0.0001	0.536	0.002
FBG mg/dl	0.263	0.023	0.382	0.033
HbA1c %	0.426	0.027	0.439	0.029
c-peptide ng/mL	0.412	0.021	0.365	0.031
HOMA-IR	0.523	0.002	0.618	<0.0001

Lipocalin-2 has a substantial positive connection with (BMI, HbA1c, C-peptide, and HOMA-IR) in obese T2DM patients [(r=0.621, P=0.0001), (r=0.426, P=0.027), (r=0.412, P=0.21), and (r=0.523, P=0.002), correspondingly, whilst FBG had no significant correlation in the same patients group. In the same table, there was also the result of Vaspain level association with (BMI, FBG, HbA1c, C-peptide, and HOMA-IR), which showed significant positive correlation with (BMI, HbA1c, and HOMA-IR) [(r= 0.536, P=0.002), (r= 0.439, P=0.029), and (r= 0.618, P=0.0001)] correspondingly, while moderate positive connection was detected with (FBG and c-peptide) (r= 0.382, P=0.033) and (r=0.365, P=0.031) respectively.

Receiver Operator Characteristics (ROC) Analysis Curve

Receiver operator characteristics (ROC) used to evaluate the area under curve (AUC). In addition, the best cut off value (CV), sensitivity, and specificity were calculated.

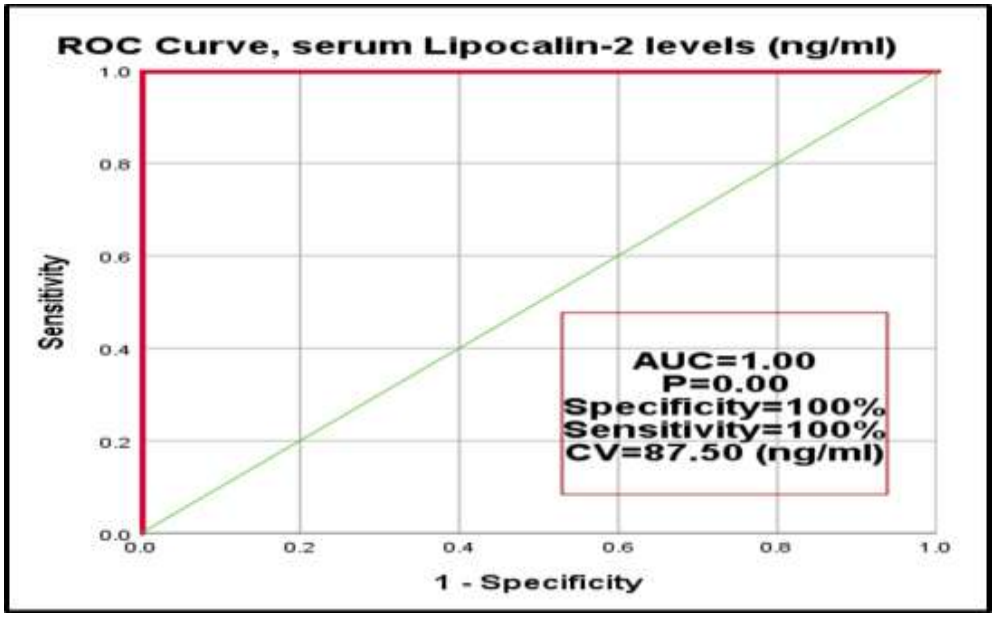

Figure 1: The ROC curve for Lipocalin-2 levels in distinguishing obese T2DM patients from the control group.

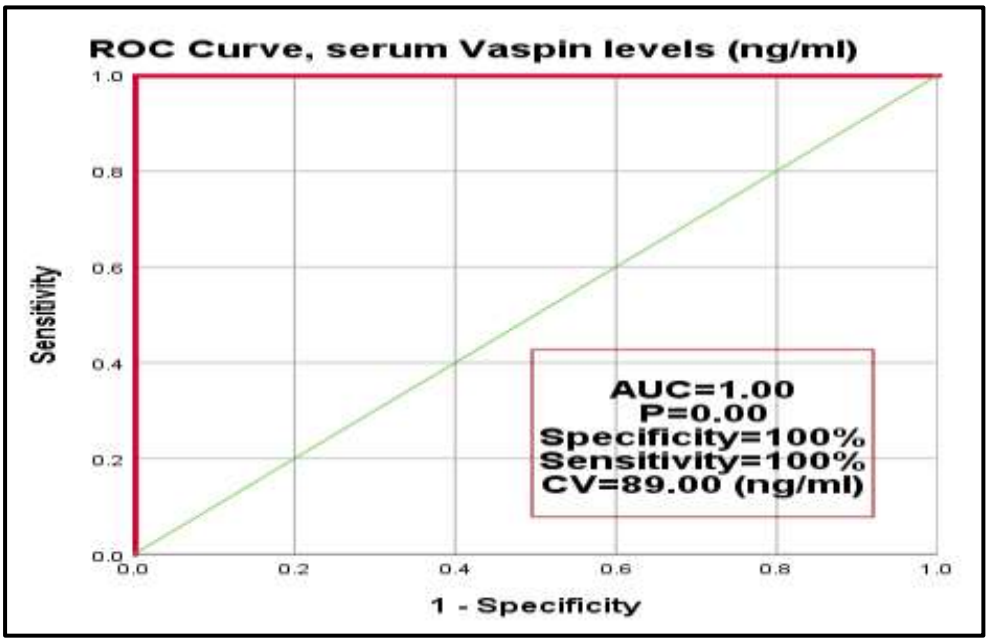

Figure 2: The ROC curve for serum Vaspin levels in discriminating between in discriminating between obese T2DM and control group.

Discussion

When T2DM cases were compared to controls, we discovered that Lipocalin-2 levels were significantly higher in T2DM cases. In obese T2DM [17], higher blood Lipocalin-2 levels have been associated to obesity and insulin resistance [8]. According to a study by Choi *et al.*, there is no significant difference in Lipocalin-2 serum levels between obese and non-obese T2DM patients [18]. Lipocalin-2 levels were observed to be considerably higher in diabetic patients than in healthy persons in the study. This was also confirmed by studies in Hong Kong and Egypt [8, 19].

By inhibiting insulin's metabolic effects in peripheral tissues, lipocalin-2 can promote glucose intolerance and insulin resistance [20, 21]. This study found a robust link between obesity and Lipocalin-2, as evaluated by BMI, in contrast to Areej E. Elkhidir *et al.*, study's which found no link between Lipocalin-2 and BMI [11].

In this study, patients with T2DM had significantly higher HbA1c levels than controls. Furthermore, obese T2DM patients had a significantly higher HbA1c than non-obese T2DM patients, with a *P*-value of 0.0001. Obese T2DM exhibited worse glycemic control compared to non-obese T2DM, which could be ascribed to a poorly regulated diet.

Lipocalin-2 was found to have a strong relationship with HbA1c in obese T2DM patients. This finding is in line with prior Chinese study that found a strong positive connection between Lipocalin-2 and HbA1c [8]. Serum Lipocalin-2 (LCN-2) was discovered to have substantial relationships with FBG and HbA1c in T2DM patients by Wu *et al.*, [17].

Lipocalin-2 levels were found to have a strong positive connection with HOMA-IR in obese T2DM women in this investigation. Similar to our findings, previous studies [22,23] demonstrated substantial relationships between Lipocalin-2 levels and HOMA-IR. Lipocalin-2 levels have not been linked to HOMA-IR in previous studies [24,25].

Increased vaspin levels have been associated to obesity and insulin sensitivity [7, 26]. Many studies [27, 28] contradicted these findings, demonstrating no connection between vaspin levels and insulin sensitivity or obesity. Vaspin levels, interestingly, were shown to be strongly linked with HOMA-IR in this study [29]. In contrast to these findings, as well as our own previous research [29], vaspin levels in BMI, insulin-resistant, and obese people were indistinguishable [30].

Vaspin levels were higher in obese patients, implying a link between vaspin, insulin resistance, and obesity-related diseases. Vaspin levels were higher in people with BMIs greater than 25 kg/m2, indicating that higher blood vaspin levels in T2DM patients lead to obesity and/or insulin resistance. HOMA-IR has also been associated to serum vaspin in diabetics with long-term illness and the obese [31].

In the correlation analysis, we discovered a strong positive association between vaspin and HOMA-IR in the obese diabetic group, which was similar to the findings of other studies [32].

According to Tan *et al.*, Vaspin levels are closely linked to BMI [33]. Loeffelholz *et al.*, observed a link between Vaspin levels and BMI [27]. Chang *et al.*, (2010) reported a strong link between levels of Vaspin and HOMA-IR in studies looking at the relationship between blood vaspin concentrations and abdominal obesity [34]. Obese women had higher plasma

vaspin than women of average body weight, according to Saboori *et al.*, [35]. Vaspin and HOMA-IR levels have a positive association, according to our findings. This association was observed in a study including a larger number of elderly patients [36]. According to another study, there is no link between Vaspin levels and HOMA-IR [37]. Although the exact mechanism by which vaspin improves insulin sensitivity is unknown, studies have demonstrated that vaspin can mitigate the effects of up-regulated proteases in insulin resistance [38]

Conclusion

Vaspin and Lipocalin-2 level considers as new predictor of IR and obesity in type2 diabetes mellitus females' Iraqi patients. The results have revealed increased levels of Lipocalin-2 and Vaspin in obese T2DM patients (FBG, HbA1c, c-peptide, BMI). In diabetic individuals with obesity, Lipocalin-2 and Vaspin are the most specific and sensitive markers.

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