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Role of serum osteoprotegerin and hs-CRP levels in obese diabetic patients

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ABSTRACT: Obesity is thought to be the primary environmental factors that may be contributed to the development of Type 2 diabetes mellitus (T2DM) and insulin resistance. Osteoprotegerin (OPG) has been assessed as a novel non-invasive inflammatory biomarker that directly contributes to inflammatory processes. This study aimed to elucidate the role of osteoprotegerin and high sensitivity C-reactive protein (hs-CRP) in obese diabetic patients and to explore their possible involvement in the pathogenesis of T2DM. Ninety participants divided in two group (45) T2DM obese patients compared with (45) healthy control, aged between 40-55 years. Results showed that there was a highly significant increase in the levels of hs-CRP and osteoprotegerin in obese diabetic patients compared with controls. Results also demonstrated that a positive significant correlation were exist between osteoprotegerin and body mass index, waist, systolic blood pressure, diastolic blood pressure, total cholesterol, triglyceride and low-density lipoprotein-cholesterol and a highly significant positive correlation with fasting blood sugar, hemoglobin A1c and hs-CRP, whereas negative correlation was obtained between osteoprotegerin and High-density lipoprotein cholesterol in obese diabetic patients. It was concluded that high levels of hs-CRP and OPG in obese diabetic patients and thought to be risk factors for the development of CVD which can increase the mortality rate in association with patient's incapacity to control his blood sugar levels and the imbalance in his fat contents.

KEYWORDS: Type 2 diabetes mellitus; Obesity; Osteoprotegerin; high sensitivity C-reactive protein; Lipid profile.

1. INTRODUCTION

One of the most environmental factors that may contributed to the emergence of Type 2 diabetes mellitus (T2DM) and insulin resistance are thought to be the obesity and a sedentary lifestyle [1]. T2DM is a polygenic illness, and abnormalities in numerous molecular routes have been found or suggested. Recent data points to shared molecular mechanisms between the insulin and inflammatory signaling pathway [2]. Chronic low-grade inflammation, increasing -cell failure, and increased apoptosis are all linked to obesity conditions. Proinflammatory mediators with endocrine qualities are expressed in adipose tissue [3], which have been linked to insulin resistance and have been found to be more prevalent in obese people. These mediators may serve as mediators of the ongoing process of -cell destruction that occurs in T2DM, as well, according to one study [4]. Vascular compliance is also known to be decreased by obesity [5,6]. By increasing blood flow impedance, increasing cardiovascular (CV), and causing left ventricular hypertrophy, an increase in vascular stiffness has long-term adverse effects on the CV system [7]. Osteoprotegerin (OPG) is a soluble member of the tumor necrosis factor (TNF) receptor superfamily, which affects endocrine function, vascular inflammation, and bone metabolism in a variety of ways. Receptor Activator for Nuclear Factor B Ligand (RANKL) uses OPG as a decoy receptor in the RANK/RANKL/OPG axis to inhibit bone resorption and osteoclastogenesis [8,9]. It is released by several tissues, such as the kidney, lung, immunological system, and CV system [10,11]. This study aimed to elucidate the role of osteoprotegerin and high sensitivity C-

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reactive protein (hs-CRP) in obese diabetic patients and to explore their possible involvement in the pathogenesis of T2DM.

2. RESULTS

According to the results tabulated in Table 1, waist circumference (WC), body mass index (BMI), diastolic blood pressure (DPB), and systolic blood pressure (SBP) in obese diabetic patient who subjected to the current work showed to be significantly (p≤0.05) higher than those of healthy subjects with significant elevations (p≤0.05) in the levels of hemoglobin A1c (HbA1c), triglyceride (TG), cholesterol (TC), and low-density lipoprotein-cholesterol (LDL-C), in obese diabetic patients comparing with controls. There was also a highly significant increase (p≤0.001) in fasting blood sugar (FBS) in patients comparing with controls, while the levels of High-density lipoprotein cholesterol (HDL-C) in patients were significantly lower than those of healthy control.

Table 1. Clinical parameters between patients and control.

Parameters	Mean ± SD		p-value
	Patients (N=45)	Control (N=45)	
Age (Years)	44.56 ±3.14	42.87±4.30	0.107
Sex (M/F)	23/22	21/24	/
BMI (kg/m2)	31.1±2.22	23.13±2.0	0.05
WC (cm)	103.08 ±6.14	86.10± 6.15	0.05
DBP (mmHg)	110.00 ±10.00	15.10± 5.25	0.05
SBP (mmHg)	150.00 ±10.25	15.0± 5.25	0.05
FBS (mg/dL)	171.62 ±7.22	75.23± 8.30	0.001
HbA1c	9.25±2.58	5.23±0.59	0.05
TG (mg/dl)	188.22±16.81	95.14 ±19.14	0.01
TC (mg/dl)	260.12± 11.10	164.12 ±14.92	0.01
LDL-C (mg/dl)	115.77± 10.26	82.83 ±8.56	0.05
HDL-C (mg/dl)	38.55± 3.09	52.80± 3.55	0.05

P value is statistically significantly at P≤0.05, and high significant at P≤0.001.

There was a highly significant increase (P≤0.001) in the levels of hs-CRP and OPG in patients comparing with controls as illustrated in Table 2.

Table 2. Inflammatory markers and osteoprotegerin between patients and control.

Parameters	Mean±SD		p value
	Patients (n=45)	Control (n=45)	
hsCRP (ng/dL)	14.32 ± 2.05	3.22 ± 4.33	0.0001
OPG (ρg/mL)	56.41 ± 2.10	14.61 ± 1.30	0.0001

P value is statistically significantl at P≤0.05, and high significant at P≤0.001.

As shown in Table 3, OPG had a positive, significant correlation (p≤0.05) with BMI, WC, SBP, DPB, TC, TG, and LDL-C and a highly significant (p≤0.001) positive correlation with FBS, HbA1c, and hs-CRP. On the other hand, results illustrated that there was a significant negative correlation between OPG and HDL-C in diabetic obese patients.

3. DISCUSSION

In the current investigation, we showed that diabetic obese patients had higher circulating OPG concentrations. Numerous cells in the CV system, such as endothelial and vascular smooth muscle cells, can release OPG, a vascular system protective factor [10,11]. OPG has been shown to promote the endothelial cell proliferation of human blood vessels, in a manner akin to the effects of growth factors on endothelial cells, such as fibroblast growth factor and vascular endothelial growth factor. Extracellular signal-regulated kinases1/2 and protein kinase B activation in those cells may be the cause of this [12]. OPG concentrations were found to have a strong correlation with DBP and systolic blood pressure (SBP), suggesting that serum OPG concentrations may be an indicator of hypertension. Recent research by two different study teams revealed that patients with hypertension had a significant increase in serum of OPG than healthy individuals [13]. Individuals with diabetes and hypertension also had significantly greater OPG serum levels than

individuals with hypertension who were not diabetic or who were diabetic but did not have hypertension [14].

Table 3. Correlation Coefficient between osteoprotegerin and other parameters in diabetic obese patients.

Parameters	OPG
BMI	0.338*
Waist(cm)	0.302*
SBP(mmHg)	0.331*
DBP(mmHg)	0.315*
FBS (mg/dl)	0.565**
HbA1c	0.578**
TG (mg/dl)	0.369*
TC (mg/dl)	0.361*
LDL-c(mg/dl)	0.581**
HDL-c(mg/dl)	-0.364*
hs-CRP (ng/ml)	0.758**

P value is statistically significantly at P≤0.05, and high significant at P≤0.001.

Results of the current research showed a strong relationship between blood OPG levels and FBS, HbA1C, and insulin resistance (IR), but the underlying processes are yet unknown [15]. It is believed that OPG and insulin resistance may be related to inflammation. Type II diabetes mellitus is characterized by IR, which is thought to represent a persistent, low-grade systemic inflammation [16]. Inflammatory pathogenesis was shown to be caused by OPG, which was shown to be favorably linked with inflammatory markers [17]. According to specific reports, dyslipidemia and an increase in OPG cause proinflammatory alterations in adipose tissue [18]. OPG has been suggested as a potential biomarker of lipid disease since it is secreted by endothelial cells in response to a proinflammatory environment, hyperglycemia, and hyperinsulinemia, which define dyslipidemia. Even after taking into account factors including age, gender, ethnicity, blood sugar, and microvascular problems, OPG has been shown to be an accurate predictor of DM [19]. Dyslipidemia characterized by increased triglycerides and decreased HDL values is associated with obesity. There is substantial evidence linking this dyslipidemia to a higher risk of type 2 diabetes, and after long periods of diabetes, the patient has been experiencing problems such as diabetic nephropathy. Diabetic individuals' abnormal lipoprotein levels [20].

According to the current findings, elevated blood lipid levels are consistent with the association between lipid and obesity dysfunction, which is indicated by higher levels of the serum lipid profile in T2DM. Patients with elevated triglycerides and lower HDL levels are more likely to be obese diabetics. Other comprehensive studies in T2DM that discovered a high connection between improved dyslipidemia and other markers [21] have corroborated the current findings. In the Terekeci et al. study [22] there was a significant correlation found between serum OPG levels and total cholesterol, HDL cholesterol, lipoprotein(a), apolipoprotein B, and hs-CRP. A correlation has been shown between OPG and inflammatory biomarkers (CRP, fibrinogen and erythrocyte sedimentation rate) in a number of previous studies [14, 23, 24] involving both the general population and patients with cardiovascular diseases (CVD). While OPG was linked to CRP in both diabetic and healthy patients, Vik et al. [25], OPG was favorably connected with total cholesterol, HDL-cholesterol, and fibrinogen among participants in a community health study [26].

4. CONCLUSION

It was concluded that high levels of hs-CRP and OPG in obese diabetic patients and thought to be risk factors for the development of CVD which can increase the mortality rate in association with patient's incapacity to control his blood sugar levels and the imbalance in his fat contents. This underscores the importance of monitoring these biomarkers in clinical practice to assess cardiovascular risk in this population.

5. MATERIALS AND METHODS

A case control study was conducted on ninety participants aged between 40-55, who were divided into two groups: A 45 T2DM obese patients compared with 45 healthy controls. Participants recruited from the national diabetes center, Baghdad –Iraqi from October 2023 to end of March 2024. The age for both groups were close to each other as it was 44.56 ±3.14 years for patients and 42.87±4.30 for controls as illustrated in Table 1. Weight, age, SBP, DPB, and BMI were all recorded. Body Mass Index (BMI) were

calculated using the formula of BMI = kg/m² where kg is a participant's weight in kilograms and m² is their height in metres squared given that the participant with a BMI of 30 kg/m² considered as an indicator of obesity. Blood samples were obtained from all participants and serum were separated and stored at -20 °C until the end of sample collection period that followed by measuring of levels of fasting blood sugar (FSG), glycated hemoglobin (HbA1c), lipid profile (total cholesterol, triglycerides, high-density lipoprotein, and low-density lipoprotein) and osteoprotegerin level using an ELISA kit according to instruction provided by manufacturer (fine company catalog).

6- STATISTICAL ANALYSIS

All the obtained data were stored and analyzed using version 22 of Statistical Package for the Social Sciences (SPSS) software. The data was displayed as Mean ± standard deviation (SD). Correlations between all variables were assessed by using Pearson correlation test to assess the strength of these association given that the coefficient of 0-0.5 indicate a weak correlation whereas a coefficient of more than 0.5 considered as a strong correlation. The statistical analysis was conducted use the LSD method, with a significant threshold of ($P \leq 0.05$) and highly significant at $p \leq 0.001$. [27,28].

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