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Evaluation of Osteoprotegerin (OPG) levels among Iraqi type2 diabetic patients

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Abstract--Type 2 diabetes mellitus (T2DM) is an increasingly prevalent multifactorial disease that has both genetic and environmental risk factors, resulting in impaired glucose homeostasis. Osteoprotegerin (OPG) is a secretory glycoprotein that belongs to the Tumor Necrosis Factor (TNF) receptor family and involves in the regulation of bone metabolism, ectopic calcification including vascular calcification processes, and endothelium regeneration. The gene encoding OPG is affected by common, functionally important genetic polymorphisms. Serum osteoprotegerin levels were higher in type 2 diabetic subjects than in nondiabetic subjects. OPG may be a potential biomarker in type2 diabetes mellitus OPG concentrations in sera were measured by "enzyme-linked immunosorbent assay (ELISA)" technique using Human-Osteoprotegerin(Bioassay Technology Laboratory). The results of the present study demonstrate that highly significant differences, the OPG levels in the diabetic patients were higher than that of controls (2.7321 ± 0.57), controls (1.5656 ± 0.20104), $P = 0.015$. It is noteworthy that the OPG levels in the current study were higher in females than in males when comparing males patients with females patients 3.2467 ± 1.09578 versus 2.1874 ± 0.28760 with non-significant difference $P = 0.263$. We conclude that there may be a correlation between high levels of "OPG and T2DM.

Keywords---OPG, T2DM , ELISA

Introduction

Type 2 diabetes mellitus (T2DM) is an increasingly prevalent multifactorial disease that has both genetic and environmental risk factors, resulting in

impaired glucose homeostasis (Krentz *et al.*,2020). Osteoprotegerin (OPG) is a secretory glycoprotein that belongs to the Tumor Necrosis Factor (TNF) receptor family and involves in the regulation of bone metabolism, ectopic calcification including vascular calcification processes, vascular tone enhance and endothelium regeneration (Pérez de Ciriza *et al.*,2015). Increased osteoprotegerin plasma levels have been reported in type 2 diabetic patients, and the increased osteoprotegerin levels were associated with microvascular complications (Knudsen *et al.*,2003). serum osteoprotegerin levels were higher in type 2 diabetic subjects than in nondiabetic subjects, and serum osteoprotegerin levels were significantly associated with inflammation and arterial stiffness (Kim *et al.*,2005)

At the present time, there are no studies of Iraqi population groups that investigated or investigated the evaluation of its levels in the sera of those patients. This study aims to evaluation of serum levels of osteoprotegerin in patients with type-2 diabetes mellitus among cases from Wasit province-Iraq.

Method

Materials and Methods

This study included (40) patients with T2DM (20 males, 20 females) whose ages ranged from 40 to 70 years, and (25) apparently healthy individuals(controls) subjects (13 males and 12 females) whose ages ranged from 40 to 70 years. from different regions in Wasit governorate.

Five milliliters of blood were collected from all participants and placed in a tube without anticoagulant and placed in a centrifuge at a speed of 2000 rpm for 10 minutes. After that, the serum was withdrawn into an eppendorff tube 2ml and preserved after being labeled with deep freezing until further processed. OPG concentrations in sera were measured by "enzyme-linked immunosorbent assay (ELISA)" technique using Human-Osteoprotegerin(Bioassay Technology Laboratory)

Results

Serum levels of of Osteoprotegerin (OPG) in patients with T2DM and controls

The results of are shown in Table (3-1). The results reveal highly significant differences, the OPG levels in the diabetic patients were higher than that of T2DM patients (2.7321 ± 0.57), Controls (1.5656 ± 0.20104), $P = 0.015$.

Table1
Serum OPG levels in patients with T2DM and controls

Parameters Groups	Pg/ml Mean+SE
Control	1.5656± 0.20104
T2DM patients	2.7321±0.57
P-value	0.015
LSD	53
Statistical Significant	**

** $P \leq 0.01$

SD: Standard deviation

Pg: Picogram

The same findings of OPG levels in males and females was repeated for the study groups that we previously observed in the Table2. Although there were no significant differences, the OPG levels were elevated among males and females patients with T2DM compared to the control group, (2.1874 ± 0.28760 versus 1.6406 ± 0.05347), $P = 0.54675$. 3.2467 ± 1.09578 versus 1.4906 ± 0.06651), $P = 0.114$ respectively. It is noteworthy that the OPG levels were higher in females than in males when comparing males patients with females patients 3.2467 ± 1.09578 versus 2.1874 ± 0.28760 with non-significant difference $P = 0.263$.

Table2
OPG levels among males and females of studied groups

Parameter s Groups	Pg/ml Mean+SE				
	Male	Female	P-value	LSD	Statistical significance
Control	1.6406±.05347	1.4906±0.06651	0.904	0.1500	NS
T2DM patients	2.1874± 0.28760	3.2467±1.09578	0.263	1.05931	NS
P-value	0.54675	0.114			
LSD	0.54675	1.75607			
<u>Statistical</u> Significant	NS	NS			

NS : Non-significant > 0.005

SD: Standard deviation

Discussion

The results of the present study demonstrate that highly significant differences, the OPG levels in the diabetic patients were higher than that of controls (2.7321 ± 0.57), controls (1.5656 ± 0.20104), $P = 0.015$. These results are in agreement with Casoinic *et al.*, 2015 who found elevated levels of serum OPG in diabetic patients. Moreover, the results of the current study are in concordance with Secchiero *et al.*, 2006 that demonstrated that serum OPG levels are increased in the early onset of diabetes mellitus and progressively increase with the duration of the disease. It is noteworthy that a couple of recent studies have demonstrated that serum OPG is also elevated in patients affected by type 1 diabetes, (Galluzzi *et al.*, 2005; Rasmussen *et al.*, 2006). It is suggested that insulin resistance and inflammatory cytokines might mediate upregulation of the OPG release observed in humans and may reflect the endothelial dysfunction in subjects with diabetes (Secchiero *et al.*, 2006). Patients with type 2 diabetes may have higher systolic blood pressure as a result of arterial stiffness and vascular calcifications, which may be related to the broad matrix changes, including OPG deposition in the arterial wall (Gunes *et al.*, 2021).

It is noteworthy that the OPG levels in the current study were higher in females than in males when comparing males patients with females patients 3.2467 ± 1.09578 versus 2.1874 ± 0.28760 with non-significant difference $P = 0.263$. The results of this study are consistent with Duan *et al.*, 2017 who demonstrated that circulating OPG concentrations were increased in Chinese postmenopausal women with diabetes and prediabetes. In contrast, several studies have shown a negative association between OPG and HOMA-IR in obese African women (Ayina *et al.*, 2015) and Turkish population (Ugur-Altun *et al.*, 2005).

Conclusion

OPG levels are significantly correlated with T2DM and may reflect the proinflammatory state in type 2 diabetes.

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