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Correlation Study of Betatrophein and GLP-1 with Some Biochemical Parameters in Iraqi Male Patients with Diabetic nephropathy (DN)

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ABSTRACT

Diabetes mellitus (DM) is one of complications which lead to Diabetic nephropathy (DN). Betatrophin is a hormone secreted by liver and affected lipid and glucose metabolism involving autophagy and adipogenesis. Betatrophin's role in glucose metabolism through regulation glucose level via insulin signaling pathway, glycogen synthesis in addition to inhibit gluconeogenesis. Glucagon-like peptide 1 (GLP-1) is a peptide hormone release from pancreatic α-cells, and intestinal L cells as responding to food intake. GLP-1 increases insulin secretion from pancreatic β-cells and decreases glycaemia through glucagon inhibition from pancreatic α-cells and deduction of satiety by delaying gastric evacuation. Also, GLP-1 decreases plasma glucose levels and maintains normal glycemia. This study was carried out to measure and compare Betatrophin and GLP-1 levels T2DM with DN in 45 Iraqi male patients and 37 control subjects. Betatrophin levels were high significant increase while GLP-1 levels were high significantly decreased compare to the healthy control. Conclusions: High level of betatrophin may be a good biomarker indicated in DN patients and more studies are needed to explain the metabolism of this biomarker in DN.

Keywords: Betatrophin, glucogan like protein 1, HbA1c and diabetes nephropathy.

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INTRODUCTION

Diabetes mellitus (DM) is one of complications which leads to Diabetic nephropathy (DN), besides that a different factors can caused DN such as genetic, diet, lifestyle and health systems(1). DN is related to ethnic as compared to other groups in the society(2), and developed in patients with a family history. DN is defined as a clinical syndrome caused by albuminuria (more than 300 mg/day) that proved at minimal two times separated by 3-6 months(2), loss of glomerular filtration rate (GFR) and arterial hypertension(3,4). DN is known as nodular diabetic glomerulosclerosis, intercapillary glomerulonephritis and Kimmelstiel-Wilson syndrome which they first described the syndrome(5). DM is a main cause of end-stage renal disease (ESRD) in the patients and increase with older people. T2D patients with DN is about 25% while T1D with DN about 40% (6) and developed early to ESRD as compared to T2D.

Betatrophin known as a lipasin and an angiopoietin-like protein 8 (ANGPTL8), is a hormone secreted by liver and affected lipid and glucose metabolism involving autophagy and adipogenesis(7,8,9). Previous studies demonstrated that betatrophin related with circulating high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglyceride (TG) through different mechanisms(10).

The role of betatrophin in postprandial TG regulation through inhibition the activity of lipoprotein lipase (LPL)(11, 7, 12). While betatrophin's role in glucose metabolism through regulation glucose level via insulin signaling pathway, glycogen synthesis in addition to inhibit gluconeogenesis(13). Betatrophin expression increased in brown and white adipose tissue as exposed to high fat diet and decreased in fasting(14). It was observed that betatrophin level associated with renal function and increases with insulin resistance(15, 16).

Glucagon-like peptide 1 (GLP-1) is a peptide hormone consist of a 30 amino acids in its chain, release from pancreatic α-cells, and intestinal L cells as responding to food intake, in addition to central nervous system(17, 18). GLP-1 has metabolic homeostasis through the postprandial period by multiple manners. Through postprandial period, GLP-1 increases insulin secretion from pancreatic β-cells(18,19), while GLP-1 decreases glycaemia through glucagon inhibition from pancreatic α-cells and deduction of satiety by delaying gastric evacuation(20). In addition GLP-1 decreases plasma glucose levels and maintains normal glycemia(21). Recent studies cleared that GLP1 has invaluable physiological actions on a different tissues like cardiovascular and neurological systems therefore GLP1 has high clinical relation with post-diagnosis complications which associated with T2D(18, 19,22, 23-26).

This study was conducted to measure the circulating levels of betatrophin and GLP1 in Iraqi male patients with DN and make correlation study between them compared with healthy control.

METHODS

The serum of total 45 males (patients group) suffering from T2DM and complicated with DN was collected from the diabetic and endocrinology center in Al-Kindy Teaching hospital in Baghdad, for period time September 2019 till January 2020. The average patients' age was (35-45) years old. While 37 volunteer concerned as control group, the average age was (31-43) years old. Others complicated with T2MD and obesity was excluded.

Fasting serum glucose (FSG) levels were determined by using enzymatic colorimetric reactions (commercially available kits Biolabo®, France). Urea, and creatinine were measured by enzymatic method. Glycated

hemoglobin (HbA1C) was measured by immunoassay technique.

Betatrophin and GLP-1 levels were measured by Enzyme Liked Immunoassay (ELISA) technique (the kits supplied from mybiosoruse company, Germany). Also fasting Insulin level was measured by using sandwich principle in ELISA method (DRG, Germany).

Statistical Analysis:

The data was calculated statistically by using SPSS version (prism ® 7 and Microsoft excel 2013) and expressed by (mean±SD). The P <0.01 values were measured by using t-test and considered as high significant. The correlation analysis between betatrophoin with other biochemical variable and r value was calculated for the parameters variants.

RESULTS AND DISSECTION

The obtained data results were listed in (Table1) reveled high significant elevated (P<0.001) in betatrophin level (1327.6±303.19) in patients group when compared with control group (1038.5±190.85).

Table 1: Betatrophin and other biochemical parameters in DN and control groups.

Groups	FSG mg/dL	HbA1C %	Insulin µlU/ml	B.urea mg/dL	creatinine mg/dL	GLP-1 ng/ml	Betatrophin pg/ml
	mean±SD	mean±SD	mean±SD	mean±SD	mean±SD	mean±SD	mean±SD
Patients No. 45	223.09±18.2	9.90±0.36	10.23±0.61	63.41±2.06	1.79±0.35	35.99±7.31	1327.6±303.19
Control No. 37	90.44±5.30	4.46±0.20	3.51±0.21	31.28±2.99	0.87±0.06	48.04±4.37	1038.5±190.85
***P* value**	h.s	h.s	h.s	h.s	h.s	h.s	h.s

Diabetes mellitus (DM) is one of the metabolic syndrome disorder as a result of deficient or defect insulin secretary. Also protein and fat metabolism affected in DM. DN is one of DM complicated and advanced renal disease caused changing in glomerular and tubular function and structure.

The level of betatrophin is still ambiguous in both types of DM and its increased level unknown(27). Previous study revealed the betatrophin level increased significantly with DM in both types patients newly diagnosed(28), other study showed the newly diagnosed T2DM patients had higher betatrophin levels in comparison with the control(29). Although several studies have indicated the concentrations of betatrophin to be higher in T2DM patients(30, 31–33), opposite data study(34). Hu et al., attributed the increasing betatrophin level in T2DM to an attitude of defensiveness which express blood glucose elevated levels or hepatic insulin resistance by increasing insulin secretion via increasing β cell prolifration(29).

This study, finding betatrophin level was highl significant in T2DM patient with nephropathy compared with control group. Most pervious papers on betatrophin are related to DM in both types and no study unclear DN.

Glucagon Glucagon like peptide-1 (GLP-1) was high significant decrease (P<0.001) in DN patients group as compared with control (35.99±7.31) and (48.04±4.37) respectively as in table 1.

The researchers found that GLP-1 significant decrease with T2DM than in control group which in agreement with present results, this attributed to impaired GLP-1 secreted and GLP-1 metabolism accelerated in T2DM(35). While another study showed a significant increase in the level of GLP-1 and insulin in DN and T2DM groups according to control one(36).

Another Studies showed that GLP-1 pathways act in T2DM progression(37,38) and the decreasing GLP-1 level has been attributed to several factors, including impaired secretion of GLP-1, accelerated metabolism of GLP-1 and GIP, and defective responsiveness to both hormones(38).

The correlation study between betatrophin with GLP-1and HbA1c was conducted in DN patients and listed in table 2.

Table 3: The correlation data in DN group.

Parameters	Betatrophin		GLP-1	
	R	*P* value	R	*P* value
HbA1c	0.16	h.s	-0.13	h.s
GLP-1	0.28	h.s	-	-

This study found betatrophin high significant positively correlated with GLP-1 (r=0.28, p=0.000), and with HbA1C (r=0.16, p=0.000) while there was high significant negative correlation between GLP-1 with HbA1c (r=-0.13, p=0.000) in DN patients as in figure 1, 2 and 3.

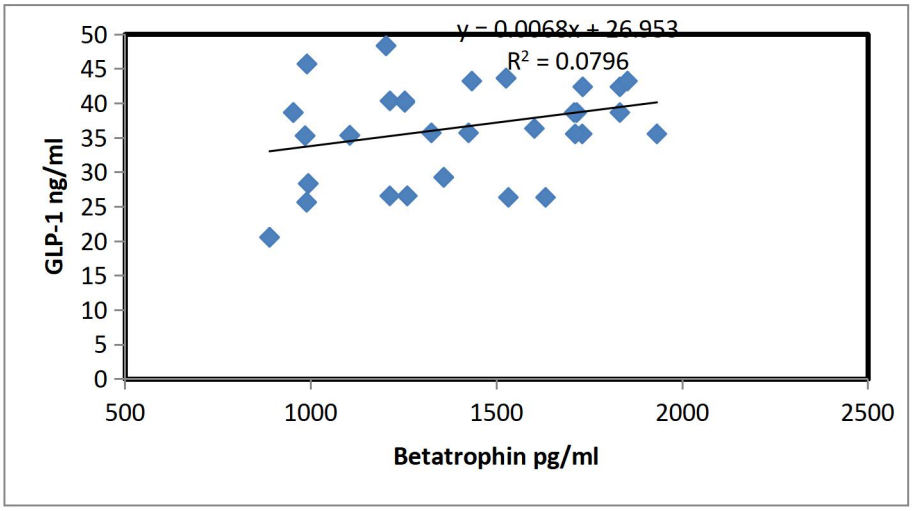

Figure 1: Betatrophin correlation with GLP-1 in DN patients.

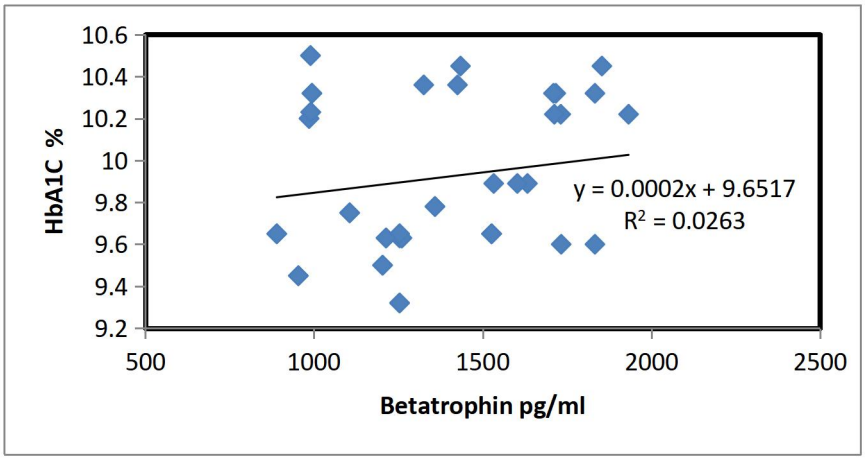

Figure 2: Betatrophin correlation with HbA1C in DN patients.

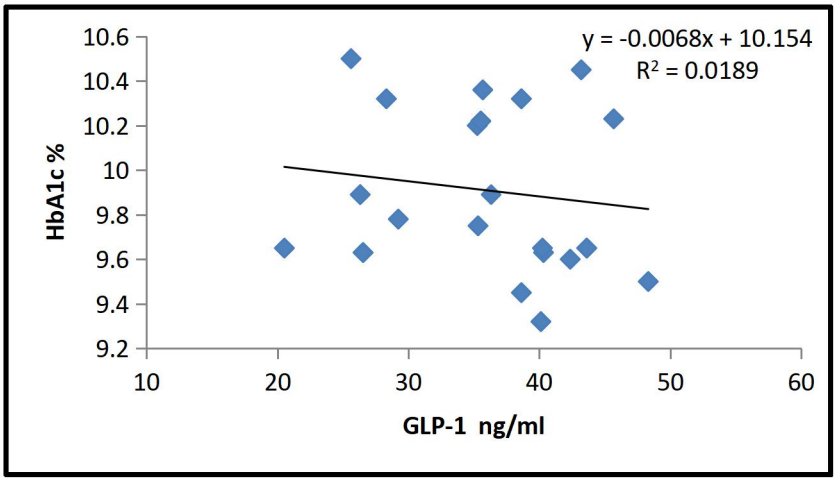

Figure 3: GLP-1 correlation with HbA1C in DN patients.

Previous studies revealed a positive correlation between betatrophin with FSG, HbA1c and insulin in T2DM patients(16)

Conclusions: The level of betatrophin was increased in Iraqi males DN patients compared with control and was correlated positively with GLP-1 and HbA1C, thus betatrophin may be a good biomarker indicated in DN patients.

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