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ASSOCIATION OF SERUM INSULIN-LIKE GROWTH FACTOR-1 WITH OBESITY IN TYPE 2 DIABETIC IRAQI PATIENTS AND ACUTE RENAL FAILURE

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ABSTRACT : Diabetes mellitus stands for a set of metabolic diseases that if they are not managed, they can initiate threatening life problems. This study hypothesizes that insulin-like growth factor-1 level can be used as a biomarker for early diagnosing renal problems in patients with type 2 diabetic disease. This study included 30 recently identified type 2 diabetic patients with acute renal malfunction who had an entrance in National Diabetic Center, AL-Mustansiriyah University. They have beenin the Center from October 2018 up to end of April 2019. Their age range has been (40-62) years. Comprehensive clinical investigationhas beencompleted for each patient to discount other diabetic complications like cardiac, neurologic and eye complications. About 30 healthy subjects have beendesignated as a control group that have beencompatible age with patients group. A tester of 10 milliliters venous blood has beenassembledfrom every subject after all nightfasting. Fasting serum glucose, lipid profile, insulin-like growth factor-1 levels were evaluated. A profile of serum lipid has exhibited more significant means except for high-density lipoprotein (HDL) cholesterol in diabetic patients with acute renal failure. As compared to the controls, the concentration of insulin-like growth factor-1 was significantly less in diabetic patients with p-value of 0.0001. Also, there has been a significance for negative correlation amid serum insulin-like growth factor-1 level and body mass index, fasting serum glucose, glycated hemoglobin, triacylglycerol, urea, creatinine and leptin while there has been a weighty positive correlation amid serum insulin-like growth factor-1 level and total cholesterol (TG), HDL cholesterol, and low density lipoprotein (LDL) cholesterol in patients group. Early detection for insulin-like growth factor-1 and lipid profile anomalies have roles to minimalize the hazard for expansion of cardiovascular complications for the patients with type 2 diabetic. Insulin-like growth factor-1 levels can be an advantageous indication for categorizing subjects for dangerous cardiovascular disease in the type 2 diabetics.

Key words : Diabetes mellitus, Insulin-Like Growth Factor-1, acute renal failure.

INTRODUCTION

Diabetes Mellitus (DM) represents the collection of metabolic illnesses categorized by hyperglycemia resultant from imperfections in insulin action, insulin secretion, or together (Sarkar and Meshram, 2017).

Type 2 DM can be resultant from a grouping of resistance to insulin action and a deficient compensatory insulin secretory response. Diabetes is connected with a more significant threat of mortality and morbidity from cardiovascular disease (CVD). Serum lipids are recurrently unusual and are expected to contribute to coronary artery disease risk. Individuals are at threat for the progress of particular complications including retinopathy foremost to sightlessness. Nephropathy generates renal failure and atherosclerotic heart sickness (Grundy, 1999).

Acute renal failure (ARF) stands for an annoying sickness with the great occurrence and unspecific remedial treatment. Though dialysis treatments represent up- to-date treatment basis, no convincing indication that inverses conventional renal injury or stops the expansion of chronic renal failure is found. The occurrence of end-stage kidney sickness secondary to ARF has been nearly 25% that is analogous to diabetic and hypertensive nephropathy (CY, 2007).

Hyperglycemia at the cellular level of vascular tissue makes a significant modifications number which possibly speed up the process of atherosclerotic (Ginsberg, 2000). Insulin resistance (IR) syndrome as well called metabolic syndrome is a gathering of irregularities counting changed glucose tolerance, visceral adiposity, hypertension, small levels of HDL of cholesterol (HDL-C), along with vast levels of triacylglycerol (TAG) are associated with

atherosclerotic CVD (Reaven, 1988).

Generally, growth factors play a vital function in a progress of diabetic vascular problems, and the practical effect of these influences has beentypically correlated to the genetic distribution rather than its level (Sesti *et al*, 2014). It was exposed that insulin-like growth factor-1 (IGF-1) was interrelated to late complications of microvascular diabetes, involving diabetic nephropathy (DN) (Bazzaz *et al*, 2014).

The circulating IGF-1 level possibly does not sufficiently reflect the IGF-1 bioactivity, particularly in pathological situations, owing to the interfering IGF-1-binding proteins so that an another method may be genetic-based investigations. The IGF-1 gene is positioned on an extended arm of chromosome12q22-24.1, and the encoded IGF-1 protein stands for the distinct chain polypeptide with 70 amino acids (Poulaki *et al*, 2004). IGF-1 besides its particular receptor (IGF-IR) possess durable physical homology with proinsulin and insulin receptor. Accordingly, they employnoteworthyinfluences on glucose and protein metabolism besides their mitogenic effects, thus playing a part to foremost paths in the exacerbation as well as progress of complications of diabetic microangiopathic (Rietveld *et al*, 2006).

In obese subjects, the increased adipose tissue generates an increase in serum concentrations of dissimilarchemokines, adipokines, and pro-inflammatory cytokines, that are proteins produced by the visceral adipose tissue. Aninstance of these proteins is leptin (Sood, 2009).

Leptin stands for the 16 kDa protein of 167 amino acids and the resultof the obesity gene (ob gene) in humans (Malli *et al*, 2010). Leptin, a hormone created principally by adipose tissue and as well by skeletal muscle, stomach, and liver has an effect on the hypothalamus to express satiety and normalize continuing energy equilibrium (Mantzoros *et al*, 2011).

Hence, the goal of this research article is to determine the relationship amid IGF-1 and obesity in recently detected type 2 diabetic patients with ARF.

PATIENTS AND METHODS

This study included 30 recently identified type 2 diabetic patients with ARF (15 males and 15 females), who had an entrance in National Diabetic Center, AL-Mustansiriyah University. They have beenin the Center from October 2018 up to end of April 2019. Their age range has been 40-62 years. Comprehensive clinical investigation has been completed for each patient to discount other diabetic complications like cardiac, neurologic and eye complications. About 30 healthy subjects have been designated as a control group that have been compatible age with patients group. A tester of 10 milliliters venous blood has beenassembled from every subject after all night fasting.

Measurements

Height in addition to weight have been measured for all subjects. Accordingly, BMI has been computed by weight (kg) dividing by height (meter). The samples of serum have been employed to calculate approximately the subsequent parameters.

Glucose has beenmeasuredthrough the enzymatic colorimetric technique. The Bio-Rad VARIANT hemoglobin A1C program by using values of ion exchange for high-performance liquid chromatography for automatic and precise separating of glycatedhemoglobin (HbAlc).

By the equation of Friedewald *et al* serum TAG, total cholesterol (TC) and HDL- C have been finalized by the enzymatic colorimetric method. LDL-C has been predicted Serum IGF-1 concentrations were determined by IRMA-Immunotech, France. Serum leptin concentrations have beenrecordedvia DRG leptin ELISA kit.

Statistical analysis

It has been done by an excel program of Microsoft Office. T-test has been employed to evaluate the p-value. A significant difference is indicated in the case of *p*- value is lower than 0.05.

RESULTS

Age distribution of patients is shown in Table 1. The more significant percentage was among the age group 51-60 years. A significant increasing is existing ($p< 0.05$) in age, weight and BMI in patients group as compared with controls as depicted in Table 2.

Glycemic and lipid profile parameters of the investigatedgroups are demonstrated in Table 3. FSG, HbAlc, TC, TAG, LDL-C and VLDL are significantly increased ($p< 0.05$) in patients' collection than controls. There was an elevation in atherogenic index ratios (TC/HDL-C, LDL-C/HDL-C, TAG/HDL-C) in patients group than controls, but they were not significant. Additionally, serum urea and creatinine in patients are significantly bigger ($p< 0.05$) than controls (Table 4).

Table 1 : Distribution of age for patients.

Age group	Patients(n%)
(40-50)	9 (30%)
(51-60)	18 (60%)
> 60 years	3 (10%)
Total	30 (100%)

Table 2 : Anthropometric and clinical parameter of investigated groups.

Parameters	Means ± SE		p-value
	Control (n= 30)	Patients (n= 30)	
Age (years)	38.233±2.08	53.83±1.19	0.001
Height (cm)	168.76±0.99	166.22±1.79	0.15
Weight (Kg)	74.46±3.96	83.96±1.95	0.003
BMI (Kg/m^2)	26.13±0.65	30.45±0.68	0.01

Table 3 : Glycemic and lipid profile parameter of investigated groups.

Parameters	Means ± SE		p-value
	Control (n= 30)	Patients (n= 30)	
FSG (mg/dl)	100.30±1.01	183.63±14.7	0.0001
HbA1c (%)	4.84±0.05	8.87±0.40	0.0001
TC (mg/dl)	159.10±5.29	234.83±9.22	0.0001
TAG (mg/dl)	93.0±1.96	182.06±16.2	0.0001
HDL-C (mg/dl)	52.50±1.03	46.20±0.97	0.003
LDL-C (mg/dl)	84.60±5.54	146.20±5.07	0.0001
VLDL (mg/dl)	18.60±0.33	35.63±3.21	0.0001
TC/HDL-C ratio	3.03±0.90	5.08±0.93	0.17
LDL-C/HDL-C ratio	1.61±0.95	3.164±0.57	0.30
TAG/HDL-C ratio	1.77±0.28	3.94±0.72	0.31

Table 4 : Renal function test of investigated groups.

Parameters	Means ± SE		p-value
	Control (n= 30)	Patients (n= 30)	
Urea (mg/dl)	27.56±1.19	58.33±5.22	0.0001
Creatinine (mg/dl)	0.78±0.05	1.15±0.01	0.0003

Table 5 : Serum IGF-1 and leptin levels of the investigated groups.

Parameters	Means ± SE		p-value
	Control (n= 30)	Patients (n= 30)	
IGF-1	248.3±7.46	105.2±4.08	0.0001
Leptin (ng/ml)	12.50±0.23	26.50±0.95	0.0001

Table 6: Serum IGF-1 levels for males and females in patients group

Parameters	Means ± SE		p-value
	Male (n= 15)	Female (n= 15)	
IGF-1 (ng/ml)	100.82±3.37	110±2.88	0.43

Table 5 shows serum IGF-1 and leptin levels of the studied groups. Serum IGF-1 level is decreased significantly, while serum leptin level is significantly increased in patients group as compared with controls. Furthermore, there has beenaboost in serum IGF-1 level in female as compared with male (Table 6).

Correlation coefficient amid serum IGF-1 and further parameters for patients group are presented in table (7). There has been a weighty negative correlation between serum IGF-1 level and BMI, FSG, HbA1c, TAG, VLDL, urea, creatinine and leptin while there has been a positive correlation significantly amid serum IGF-1 level along with LDL-C, TC, HDL-Cin patients group.

Table 7 : Correlation coefficient amid serum IGF-1 and supplementary parameters for patients group.

IGF-1 (ng/ml)	R	p-value
BMI (Kg/m^2)	-0.022	0.0001
FSG (mg/dl)	-0.093	0.000 1
HbA1c (%)	-0.12	0.000 1
TC (mg/dl)	0.073	0.000 1
TAG (mg/dl)	-0.166	0.0001
HDL-C (mg/dl)	0.157	0.0001
LDL-C (mg/dl)	0.196	0.0001
VLDL-C (mg/dl)	-0.15	0.0001
Urea (mg/dl)	-0.05	0.0001
Creatinine (mg/dl)	-0.14	0.0001
Leptin (ng/ml)	-0.082	0.0001

DISCUSSION

Diabetic nephropathy represents the kidney disease that happens owing to diabetes. Diabetes control has deteriorated with a lengthier period of the disease, with neuropathy as typical complication and subsequently renal complications, CV complications, foot ulcers and retinopathy (Ruggenenti and Remuzzi, 2000). Diabetic nephropathy is possibly happened in type 1 and type 2 DM. The pathology and occurrence of nephropathy differ in the above types of diabetes. Although, the complete presence of nephropathy has been considerably more significant in type 1, previous data recommend in which the renal risk is comparable in all diabetes (Krolewski *et al*, 1985).

As compared with healthy controls, there was an increase in level of FSG, HbA1c levels, lipid profile except for HDL-C in type 2 diabetic patients with ARF (Bamanikar *et al*, 2016).

Based on this study, serum TC, LDL-C and atherogenic ratios (LDL-C/HDL-C, TC/HDL-C, TAG/HDL-C) have been greater significantly while HDL-C has been smaller significantly in ARF patients than resultant values in case of control that is compatible with the study of Anjankar *et al* (2014). There is development a slightly changed and probably more atherogenic lipoprotein profile in ARF patients. Consequently, between patients with CVD, the death risk has been more significant in ARF patients as compared to healthy subjects (Anjankar *et al*, 2014).

In this paper, serum urea and creatinine levels are

statistically increased with significance in diabetic patients group than healthful control subjects.

Hyperglycemia (poor glycemic control) stands for a typical property of DM that is well-accepted fact by scholars and specialists. The reported papers published by numerous scholars have testified an increasing in serum urea levels in addition to creatinine in diabetic patients (Mohan *et al*, 2013; Association, 2010).

There is an increasing in urea level in the case of a damaged kidney, or the case of kidney is not operational appropriately. Increase of blood urea level with increased sugar level specifies that the increased blood sugar level results in the damaged kidney. A study done by Anjaneyulu et al. 2004 had concluded that increased urea and serum creatinine in diabetic rats points to advanced renal damage (Muragundla, 2004).

In this study, serum IGF-1 is significantly decreased in patients than the controls.

The IGF-1 possesses hypoglycemic properties and improves insulin sensitivity in investigational human along with animal subjects. The organic performance of IGF-I is supposed to be arbitrated through its type 1 receptors and hybrid insulin/ IGF-1 receptors (Sesti *et al*, 2001).

Clinical researches have shown the efficacy of recombinant human IGF-1 treating in enhancing insulin sensitivity and metabolic mechanism in patients with type 1 or type 2 diabetes besides in patients with risky IR (Moses *et al*, 1996).

There is an indication that IGF-1 protects in contradiction of the creation of systemic inflammation, P-cell dysfunction, free fatty acids, hypertension, and IR. Accordingly, small IGF-1 supports metabolic syndrome and diabetes development (Rajpathak *et al*, 2009).

It has been suggested that the early and advanced deterioration in serum IGF-1 bioactivity throughout aging in patients with type 2 diabetes can cause insufficient defensive and renewal consequences of IGF-1 on the cardiovascular system. Also, there has beenaboost in serum IGF-1 levels for females patients as compared to males (PH, 2001).

Released adipokines can physiologically control Obesity-induced IR through adipose tissue. Adipokines has control among other inflammation, insulin sensitivity, lipid metabolism and angiogenesis. Adipocytes, all with macrophages are sensitive for adipose tissue, secrete pro-inflammatory cytokines like IL-6 and TNF-α and adipokines like leptin (Kazmi *et al*, 2012).

The current study has shown a significance in increased leptin serum level in patients than the control group. Nevertheless, it proved that BMI only is feasibly been an influential analyst of medical indicators of obesity as significant and a strong correlation amid leptin and BMI in obese diabetic population (Ameen and Muhammad, 2015).

The findings are as follows-serum IGF-1 concentration has correlated with HDL- C, TC, besides LDL-C while adversely correlated with BMI, FSG, HbA1c, TAG, VLDL, urea and creatinine, which is compatible with A (2018).

CONCLUSION

Early detection of insulin-like growth factor-1, lipid profile, along with atherogenic index abnormalities can minimalize the risky expansion of cardiovascular complications in type II diabetic patients. Insulin-like growth factor-1 levels can be an advantageous indicator for detecting risky subjects for cardiovascular illness in the type 2 diabetics.

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