Visfatin Level and its Relation with Obesity and Insulin Resistance In Iraqi Type 2 Diabetes Mellitus Patients.

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Abstract

Background: Obesity is highly associated with insulin resistance and increased risk of type 2 diabetes and cardiovascular disease. Visfatin is adipocytokines that is highly expressed in visceral fat. Its expression in visceral fat is hyperglycemia in insulin deficient diabetes.

Objective: To study the visfatin level in type 2 diabetes mellitus patients and its relation with obesity and insulin resistance.

Patients and methods: This study was done in national diabetes center(NDC),AL -Mustansria University and AL –Yarmok Hospital Teaching ; on a total (120) individuals age range from (33-60) years. (80) patient type 2 diabetes nephropathy, (40) healthy controls . The enrolled patients were divided to three groups according to BMI ,data collection about age, sex ,WHR, BMI and blood samples to estimate serum visfatin levels, fasting plasma glucose(FPG), glycated hemoglobin(HbA1c), lipid profile (TC,TG,HDL-C,and LDL-C), fasting C-Peptide ,and fasting insulin level Furthermore insulin resistance parameters calculated from Homeostasis Model Assessment 2- insulin Resistance were calculated using HOMA2-Calculator software downloaded freely .

Results: The mean FPG,HbA1c, C-Peptide level, fasting insulin level ,HOMA2IR and visfatin level show statistically significantly increased in diabetic patients when compared with control subjects. Serum visfatin level was significantly increased with BMI increased groups. Visfatin level was increased in HOMA2-IR =>3 when compared with HOMA2-IR <3 in diabetic patients. Visfatin level show significant positive coorelation with BMI, WHR,FPG, HbA1c, fasting insulin level , HOMA2-IR , TC,TG,and LDL-C in diabetic patients when compared with control subjects ,and negative correlation between serum visfatin level and HDL-C in diabetic patients when compared with control subjects .

Conclusion: Obesity and Insulin resistance play an important role in the pathophysiology of type 2 diabetes mellitus. Elevated visfatin level in diabetic patients with obesity features of insulin resistance are believed to result in distance clinical characteristics and complications such as atherosclerosis.

Key word: T2DM, Obesity, Insulin resistance, visfatin.

Introduction:

Type 2 diabetes mellitus is considered one of the major metabolic disease of the 21st century [(1)] . Obesity is a chronic disease, conditioned by the multi-factorial influences of genetic, endocrine and environmental factors. Its negative health consequences include high risks of MS, T2DM, CVD and hypertension and more [(2)]. Insulin resistance syndrome refers to a constellation of findings, including glucose intolerance, obesity, dyslipidemia, and hypertension, that promote the development of type 2 diabetes, cardiovascular disease, cancer, and other disorders [(3)]. Visfatin level play role in the development pathogenesis of vascular complications of type 2 diabetes mellitus, insulin resistance, and metabolic conditions such as hypertension and dyslipidemia [(1,4)] . Visfatin is an adipokine identified in 2004(5) and thus named for the suggestion that it would be predominantly produced and secreted in visceral fat. (**vis**ceral **fat** adipok**in**e). Visfatin has a molecular weight of (52 KD) and its gene encodes 491 amino acids, Visfatin/PBEF/ NAMPT was shown to mimic the effects of insulin by binding to the insulin receptor at a site different from that of insulin, was found to be similar compared with that of insulin, and in a competitive binding assay [(5,6)]. As well as visfatin is an endocrine, autocrine and paracrine protein with many functions, including enhancement of cell proliferation, biosynthesis of nicotinamide mono- and dinucleotide and insulin mimetic (hypoglycaemic effect) [(7,8,9,10)]. Increased visfatin level are associated to coronary artery disease (CAD) and acute coronary syndromes even after correction for classic cardiovascular risk factor such as cholesterol, smoking, hypertension diabetes mellitus and obesity[(11)]. Furthermore, the role of visfatin physiology has begun to be described but its role on diabetes and CAD pathophysiology is still controversial

Objective:

This study was designed to evaluate the effect of visfatin level in type 2 diabetes mellitus patients and relation with obesity and insulin resistance.

Materials and Methods:

This study include 120 subjects (80 diabetic patients and 40 controls) age between (33-60) years who were attending in the National Diabetes Center(NDC) AL- Mustansirya University and Al-Yarmok Hospital Teaching. The enrolled patients

were divided to three groups according to Body Mass Index (BMI):Sixteen(16) normal <25 kg/m^2 , than thirty one (31) overweight 25-29.9 kg/m^2 and thirty three (33) obese =>30 kg/m^2 respectively. Blood samples were taken for laboratory investigation which included, Fasting Plasma Glucose (FPG) , Glycated Hemoglobin (HbA1c) lipid profile (Total Colesterol, Triglyceride, High density lipoprotein and Low density lipoprotein), fasting C-Peptide determination by Immuno tech (RIA) kit, fasting insulin level determination by ELISA kit (DRG), visfatin level determination by ELISA kit (CUSABIO). Furthermore insulin resistance parameters calculated from Homeostasis Model Assessment 2- insulin Resistance (HOMA2-IR) were calculated using HOMA2-Calculator software downloaded freely. data processing and statistical analysis was done by the computer SPSS-15 System (Statistical Package for Social Science – version 15).

Results:

A total of (120) individuals (80 diabetic patients and 40 control subjects) has been completed the study successfully without any healthy problems.

The mean Fasting plasma glucose (FPG) , HbA1C, Fasting C-Peptide level, HbA1c,Serum insulin level, and visfatin level was significantly increased for diabetic patients when compared to their level in controls(P< 0.05) table (1).

Table (2) show serum visfatin level (mean±SD) was significantly increased with BMI groups increased. In normal <25 kg/m^2 (16.98±6.77), than overweight 25-29.9 kg/m^2 and obese =>30 kg/m^2 (19.98±7.92) and (20.20±5.78) respectively. Moreover serum level of visfatin showed no significant changes with BMI subgroups in diabetic patients and controls (P=0.176) , (P=0.112) respectively.

Visfatin level was increased in HOMA2-IR =>3(19.17±7.76) when compared with N.I.R <3(18.23±5.86). Moreover, no significant change between HOMA2-IR (mean±SD) for the both subgroups of diabetic patients (I.R=>3 and N.I.R <3) with visfatin level (P=0.588) table(3) .

As shown in table (4), BMI and WHR showed strong positive correlation with serum level of visfatin in both T2DM patients and control subjects (r=0.288,r=0.385,r=0.230, r=0.426) (0.01) respectively.

There is positive correlation between visfatin level and fasting plasma glucose , HbA1c insulin level and HOMA2-IR in T2DM patients (P=0.05, p=0.01) respectively, while not correlated with control subjects. Also there was strong positive significant correlation between visfatin level and total cholesterol , low density lipoprotein and triglyceride in T2DM patients (r=0.604, r=0.536 r= 0.585) respectively was(P=0.01), while there is strong negative significant correlation between visfatin level and high density lipoprotein in T2DM patients (r=− 0.598) (P=0.01) , but it was not correlated with control subjects.

Table(1): comparison of Fasting plasma glucose (FPG), HbA1c, Fasting C-Peptide level, Insulin level,HOMA2-IR and visfatin level between T2DM patients and control subjects**.**

		T2DM	Control	P-value
FBG (mmol/l)	**Mean±SD**	10.78±2.75	5.44±0.29	0.0001
	Range	(7.5-14)	(5-6.1)	
HbA1c %	**Mean±SD**	8.51±1.42	4.79±0.33	0.0001
	Range	(6.3-12.2)	(4.1-5.4)	
C-Peptide (ng/ml)	**Mean±SD**	3.72±1.16	1.81±0.32	0.0001
	Range	(1.8-6.1)	(1.5-2.5)	
Insulin (µIU/ml)	**Mean±SD**	18.58±1.33	10.85±1.04	0.001
	Range	(6.8-45)	(2.5-23.4)	
HOMA2-IR	**Mean±SD**	3.57±1.23	1.40±0.23	0.001
	Range	(1.7-6.2)	(1.1-1.9)	
Visfatin level (ng/ml)	**Mean±SD**	18.86±7.17	9.02±2.33	0.0001
	Range	(7.01-35.73)	(4.04-12.95)	

P<0.05 is significant .

Table(2): visfatin level with Body Mass Index in T2DM patients and control subjects .

		Visfatin level (ng/ml)			
			T2DM		Control
		No	Mean±SD	No	Mean±SD
BMI (Kg/m2)	**Normal (<25)**	16	16.98±6.77	19	8.22±1.57
	Overweight (25-29.9)	31	19.98±7.92	12	9.84±2.92
	Obese (=>30)	33	20.20±5.78	9	9.63±2.51
P-value			0.176		0.112

P<0.05 is significant .

Table(3): visfatin level with HOMA2-IR in T2DM patients .

		No	Visfatin level (ng/ml)
			T2DM (Mean±SD)
HOMA2-IR	**N.I.R (< 3)**	**26**	**18.23±5.86**
	I.R(=> 3)	**54**	**19.17±7.76**
P-value		**80**	**0.588**

Table(4) : Correlation coefficient of Visfatin level in T2DM patients and control subjects with different parameters**.**

correlation	Visfatin level	
	T2DM	control
Age(years)	r=0.016	r=0.164
	P=0.886	P=0.313
BMI(kg/m2)	r=0.288**	r=0.385*
	P=0.010	P=0.014
WHR	r=0.430**	r=0.426*
	P=0.004	P=0.04
FPS(mMol/l /l)	r=0.751*	r=0.209
	P=0.001	P=0.195
HbA1c%	r=0.213*	r=0.378
	P=0.058	P=0.016
TC(mMol/l /l)	r=0.604**	r=0.009
	P=0.005	P=0.955
TG(mMol/l /l)	r=0.585**	r=0.127
	P=0.0001	P=0.435
HDL-C(mMol/l /l)	r=−0.598**	r=−0.369
	P=0.0001	P=0.019
LDL-C(mMol/l /l)	r=0.536**	r=0.003
	P=0.0001	P=0.987
C-Peptide(ng/ml)	r=0.031	r=0.413
	P=0.786	P=0.009
Insulin level (µIU/ml)	r=0.501**	r=0.211
	P=0.001	P=0.401
HOMA2-IR	r=0.296**	r=−0.225
	P=0.008	P=0.162

*Correlation is significant at the 0.05 level.
**Correlation is significant at the 0.01

Discussion:

Diabetes is an important healthy problem since the incidence of diabetes is continuously increased .Greater than 50% of adult with type 2 diabetes mellitus have coronary artery disease (CAD) [12,13]. Recently visfatin was recently described as an adipocytokine with potentially important effects on glucose metabolism and atherosclerosis and visfatin has been linked to several inflammatory conditions, beta cell function and cardiovascular disease [5,14]. EL-Shaer *etal*, 2012 found that visfatin exerts insulin-mimetic effect that are dose dependent and quantitatively similar to those of insulin in stimulating muscle and adipocyte glucose transport and in inhibiting hepatocyte glucose production. In keeping with its insulin memitic effects, visfatin was as effectives as insulin in reducing hyperglycemia in insulin deficient diabetic mice, visfatin was also found to be bound to and activate receptor, causing receptor phosphorelation and the activation of downstream signaling molecule**.**

The present study demonstrated a statistically increased visfatin level in T2DM patients and decreased in control subjects (18.86±7.17) (9.02±2.23) (0.0001) table (1), this is agreement with [9,15,16]. Other study, did not find significant difference in visfatin level between T2DM patients and control subjects [17]. This study shown serum level of visfatin was increased as BMI increased obese (>=30 kg/m^2) (20.20±5.78) , overweight (25-29.5 kg/m^2) (19.98±7.92) in T2DM patients more than normal (<25 kg/m^2) (16.98±6.77) when compared with control subjects table (2), this is agreement with others [18,19].

The preliminary study have shown that plasma level of visfatin increased during obesity because visfatin level are not correlated with the amount of visceral adipose tissue and there was not observed

any difference in expression of visfatin in subcutaneously vs visceral adipose tissue. Even more studies have shown a relationship between visfatin and obesity, its real metabolic role must be clarified [20]. Previous studies showed that, there was no correlation between circulating serum visfatin level with BMI and WHR in subjects [9,21].

In contrast to Sommer *et al*,2008 [9] found a negative correlation between circulating serum visfatin level with BMI and WHR in subjects . Finally, although visfatin's role in the pathogenesis of obesity and T2DM, as yet remains somewhat controversial, it seems that visfatin does not appear to be a meter bystander and its pathological, biological and function state and influence, may depend on the metabolic state in which it is found. Insulin resistance is a common feature of several disorders such as obesity, dislipidemias, T2DM and hypertension. All of which are risk factors for a cardiovascular disease [22].

In the present study a highly significant difference in insulin resistance (HOMA) was observed in T2DM as compared to controls, which was expected because of the increased level of fasting plasma glucose and high level of serum insulin in T2DM patients.

This study showed that there was an increased visfatin level with HOMA2-IR in T2DM table (3), there was positive correlation between visfatin level and HOMA2-IR when compared with control subjects table (4), this is in agreement with [23,24]. In contrast EL-Shaer *et al.*2012.; who did not show any correlation between visfatin level and insulin resistance (HOMA).

Body Mass Index (BMI) and WHR showed strong positive correlation with serum level of visfatin in both T2DM patients and control subjects [9,20,21].

In this study there was shown strong positive correlation between serum visfatin level with fasting plasma glucose , HbA1c and fasting insulin level (P= 0.01) this is agreement with [16,17,23] , while it is not coninicided with previous studies Sommer *et al*,2008.; and GÜrsoy *et al*,2012.; who did not found an association between serum visfatin level and fasting plasma glucose , fasting insulin level in both subjects. The present study show that strong positive correlation between visfatin level and TC,LDL-C and TG in T2DM patients while there is strong negative significant correlation between visfatin level and HDL-C in T2DM patients when compared with control subjects, this is agreement with [25,26]. and disagreement with[6,27] did not found an association between serum visfatin level and lipidprofile.

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