

Assessment of Omentin-1 as a predictor and Renoprotective for type 2 Diabetic Nephropathy

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Abstract:

Background: Diabetic nephropathy is one of the most serious microvascular complications of diabetes, which may lead to chronic kidney disease in diabetic patients.

Objective: to explore correlation of omentin-1 and diabetic nephropathy in type 2 diabetic patients.

Method: Serum omentin-1 levels were measured by enzyme-linked immunosorbent assay (ELISA) in 61 type 2 diabetic patients. These patients were classified into two groups according to their albumin/creatinine ratio (ACR), into patients with normoalbuminuria, group C (ACR< 30 mg/mmol), patients with microalbuminuria, group B (ACR=30-300 mg/mmol), twenty five (25) (10 male and 15 female) apparently healthy matching the Pearson were selected as a control group (group A). In addition, glucose and lipid profile and morphological characters were assessed.

Result: The serum OMT level of group B was much lower than those of group C and group A. While, there was non-difference in OMT level between group C and group A.

Conclusion: Detection of serum OMT level may play an important role in early diagnosis and prevention of diabetic nephropathy in T2DM.

Keywords: diabetic nephropathy, omentin-1, adipose tissue

Introduction:

Diabetic nephropathy develops in 30% to 40% of type 2 diabetic patients and has become the single most common microvascular complications of type 1 and type 2 diabetes mellitus and the leading cause of ESRD worldwide [1]. The development of sustained proteinuria is the major criterion for the diagnosis of DN, the risk of a progressive increase in albumin excretion to overt proteinuria within 6–14 years was 60–80% [2, 3]. Adipose tissue actively participates in neuroendocrine, cardiovascular and immune systems by secreting proteins and other products (called adipokines), as well as responding to neural, hormonal, and nutritional signals [4]. Omentin-1 was shown to be predominantly expressed in visceral adipose tissue, and was among the first molecules known to exhibit such a dramatic difference in gene expression between the two major fat depots. As a secretory factor, omentin-1 may be a novel hormone that is likely to act as both an endocrine factor to modulate systemic metabolism, including insulin action in subcutaneous adipocytes, and an autocrine and paracrine factor to regulate visceral adipose biology locally [5, 6]. Omentin-1 is an adipokine preferentially produced by visceral adipose tissue with insulin-sensitizing effects and its expression was shown to be reduced in obesity, insulin resistance (IR) and type 2 diabetes. Omentin-1 was also found to be positively related with adiponectin, high-density lipoprotein levels and negatively related with body mass index (BMI), waist circumference, IR, triglyceride (TG). Lower plasma omentin levels were suspected to contribute to the pathogenesis of IR, type 2 diabetes and cardiovascular diseases in obese or overweight patients [7-10].

Patient and Methods:

The current study was performed on 61 type 2 diabetic (44 male and 17 female), the age range within 36–64 years, selected sample of patients who attend the National Diabetes Center for Treatment and Research at (AL-Mustansirya University) during the period from February–May 2016. All the patients' height, weight, were measured. Body mass index (BMI) was calculated as the ratio of the weight to the square of height (kg/m²).

Blood assay:

Venous blood samples were collected from all patients in the morning (8:00–9:00) after an at least 8–12 h overnight fast and laboratory analysis of fasting glucose, urea, creatinine, total cholesterol (total-C), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), hemoglobin (Hb), uric acid (UA) were performed with standard methods. Serum samples were transferred into separate eppendorf tubes and frozen at –20°C for later determination of omentin levels and insulin. Patients were classified into two groups according to their albumin/creatinine ratio (ACR), including patients with normoalbuminuria, group C (ACR< 30 mg/mmol), patients with microalbuminuria, group B (ACR=30–300 mg/mmol), twenty five (25) (10 male and 15 female) apparently healthy people, matching with diabetic Pearson were selected as a control group. Determination of Serum omentin-1 levels were measured using a commercial enzyme immunoassay Kit.

Albumin to Creatinine Ratio (A: C ratio)

Measurement of albumin in urine samples. Urine samples were taken for biochemical analyses after an overnight fast of 12 h. Urinary albumin was determined in an early morning spot urine sample.

The urinary ACR was estimated by a using a biochemical analyzer (Combyzer13, Germany).

Statistical Analysis:

All statistical analysis in the study were performed using SPSS version 20.0 for Windows (Statistical Package for Social Science). Descriptive analysis was used to show the mean ± SD of the variables. ANOVA was used to show the differences between variables of differentiated groups. The correlation of serum omentin-1 levels and other clinical variables was assessed by Pearson’s correlation or Spearman’s rank correlation as appropriate.

Results: All the demographic and laboratory findings of the groups were compared and shown in Table 1. BMI, F.P.G, of group B were found statistically higher than the group A and group C (respectively, p=0.0001, p=0.0001, p=0.0001, p=0.0003, p=0.0001,). In group B total cholesterol, TG, VLDL-C, levels were also statistically higher than the group C and group A (respectively, p=0.035,

p=0.0001, p=0.0002). They could not find any difference between the, HDL-C, LDL-C and UA, levels of the study groups. In group B total cholesterol, TG, VLDL-C, levels were also statistically higher than the group C and group A (respectively, p=0.035, p=0.0001, p=0.0002). In group B S. Urea, A:C R (mg/mmol) were also statistically higher than the group C and group A (respectively, p=0.0008, and p=0.0001). The omentin levels of the diabetic patients were statistically lower than the control subjects (Table 1) (p < 0.001). The serum OMT level of group B was much lower than those of group C and control group. While, there was non-difference in OMT level between group C and control group. On correlation analysis of study analyses, omentin-1 was found to correlate negatively with fasting blood glucose, urea, creatinine, cholesterol, albumin/creatinine ratio (ACR).

Table 1: The comparison of antropometric and biochemical parameters among study groups

Variables	Group A	Group B	Group C	P-value
Age Years	45.36±7.038	54.33±7.038	53.71±7.612	0.0001
BMI kg/m2	26.93±3.911	31.74±4.153	29.66±3.476	0.0001
Omentin-1 ng/ml	6.51±1.46	3.86±1.45	5.78±1.52	0.0001
F.P.G mg/dl	92.16±9.754	216.27±66.665	191.94±62.693	0.0001
S.Urea mg/dl	23.76±5.378	29.66±66.665	24.83±5.961	0.0008
S.Cr mg/dl	0.88±0.242	1.1500±0.292	0.959±0.205	0.125
U.Acid mg/dl	3.90±26.036	4.527±1.20842	4.183±1.183	0.0011
T.C mg/dl	166.76±26.036	196.13±50.582	185.48±42.612	0.035
TG mg/dl	163.81±73.162	164.87±82.774	87.04±34.478	0.0001
HDL mg/dl	41.11±11.06699	37.78±8.04328	42.2636±10.158	0.196
LDL mg/dl	108.90±24.473	111.387±38.386	117.2453±53.435	0.719
VLDL mg/dl	17.52±6.977	37.06±21.282	36.60±22.210	0.0002
Hb g/dl	16.68±14.3679	12.72±1.4705	13.661±1.13	0.052
A:CRatio mg/mmol	1.43±0.68	17.98±10.01	1.34±0.67	0.0001

Data are shown in table 1 as mean ± SD, Group A (control), Group B (diabetic patients with microalbuminuria), Group C (diabetic patients with normoalbuminuria). DM diabetes mellitus, BMI Body mass index, (Hb) hemoglobin, (S.Cr) S.Creatinine FG fasting , glucse, LDL= low density lipoprotein, HDL High density lipoprotein, TC total Cholesterol A:CR Albumin creatinine ratio.

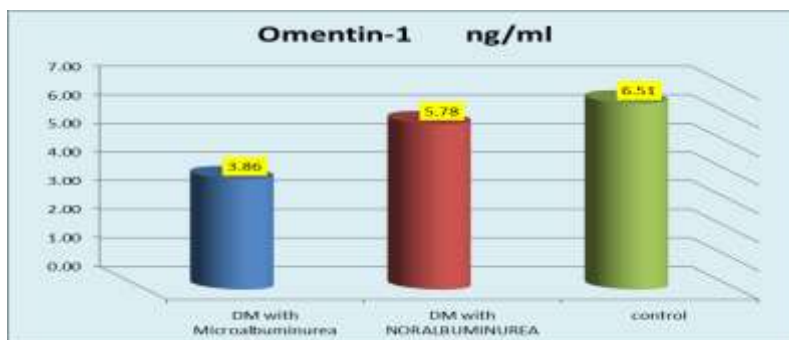


Figure 1:Mean of omentin (ng/ml) of study groups

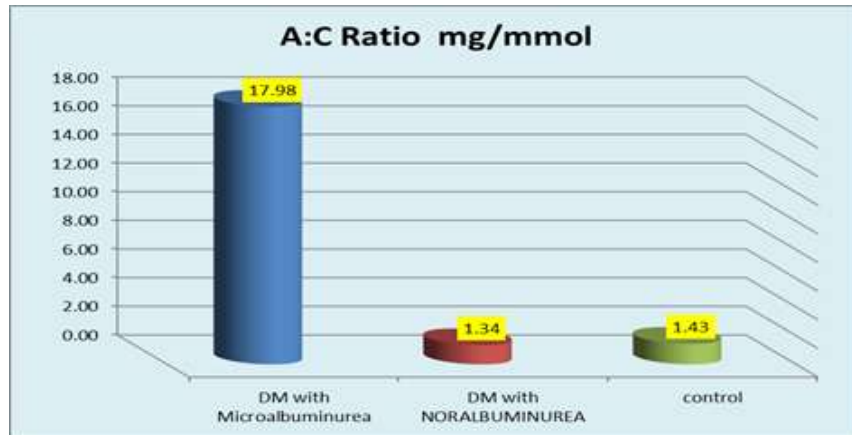


Figure 2: Mean of A:C R mg/mmol of study groups

Correlations Between Omentin-1 and Clinical Parameters

The results of bivariate correlation analyses between serum omentin and various clinical parameters are shown in Table 2. Serum omentin-1 levels showed significant negative

correlations with F. G ($r = -0.299$, $p < 0.01$), S.Urea ($r = -0.280$, $p < 0.01$), S. Cr ($r = -0.244$, $p < 0.05$), T, Cholesterol, U. MA ($r = -0.576$, $p < 0.01$) and A:C Ratio ($r = -0.449$, $p < 0.01$).

Table 2 Correlation of serum omentin levels and other clinical

OMT – Parameters	Correlation (r)	P-value
F.P. G (mg/dl)	-0.299	< 0.01
S.Urea (mg/dl)	-0.280	< 0.01
S.Cr (mg/dl)	-0.244	< 0.05
T,Cholesterol (mg/dl)	-0.242	< 0.05
A:C Ratio (mg/mmol)	-0.449	< 0.01

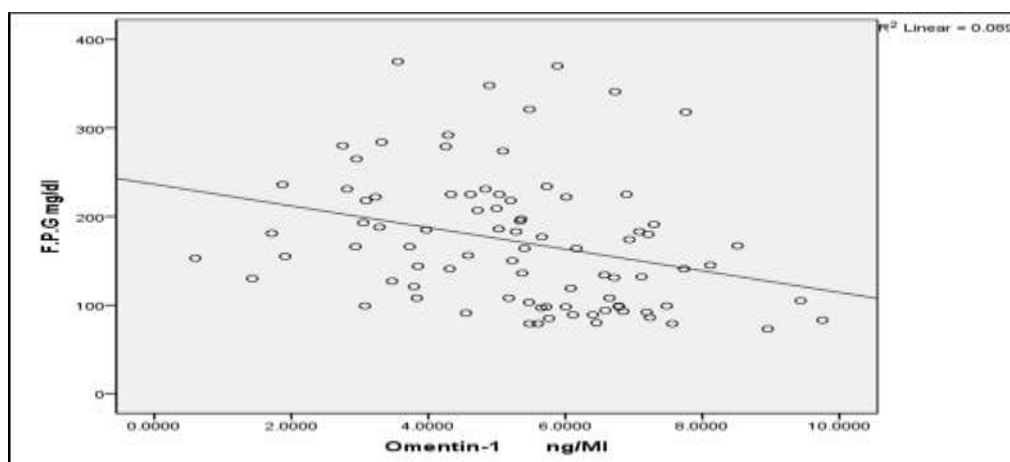


Figure 4:Correlation between F.P.G mg/dl and omentin-1 ng / ml

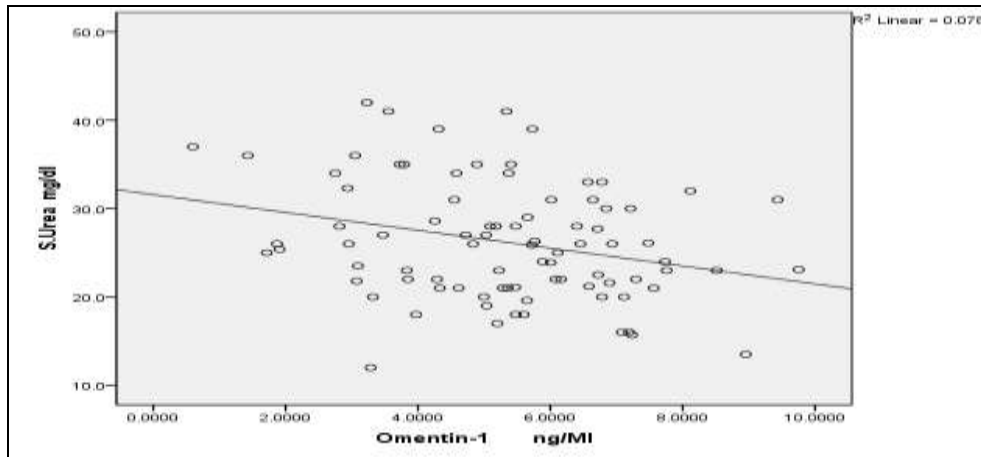


Figure 4: Correlation between Urea mg/dl and omentin-1 ng / ml

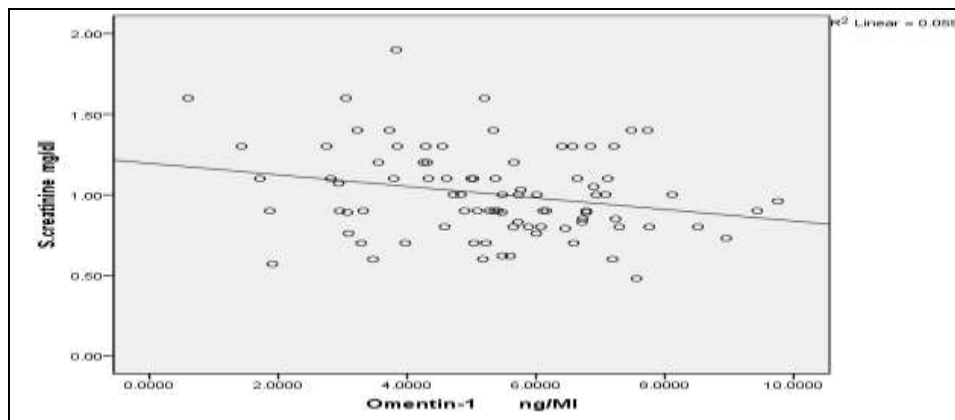


Figure 5: Correlation between S. Creatinine and omentin-1 (ng / ml)

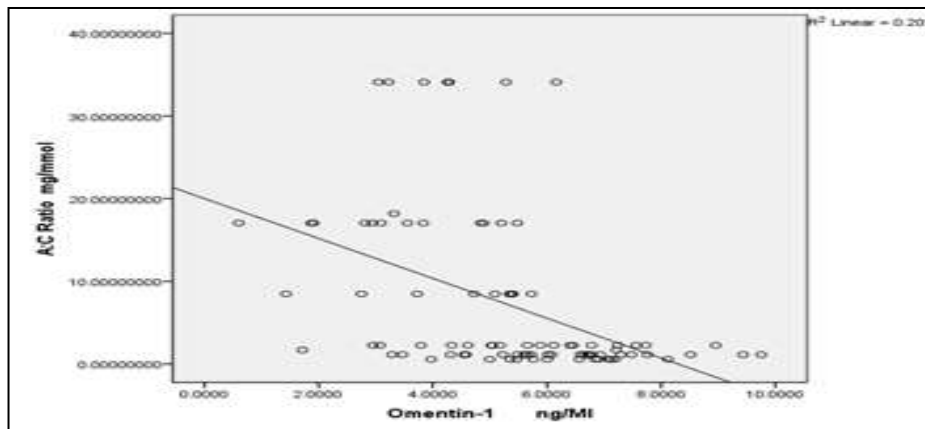


Figure 6: Correlation between A:C Ratio and omentin-1 (ng / ml)

Discussion:

The In this study, we sought to determine the relationship between circulating omentin-1 levels and A: C Ratio in patients with type 2 diabetes. This study revealed that Serum Omentin-1 levels differ between patients (group B and group C). The aim of the present study was to investigate the impact of

inflammation during the early phase of diabetic nephropathy. Recent evidence suggests an important role of inflammation in the pathogenesis and progression of diabetic nephropathy [11]. The present study investigated the correlation between early markers of diabetic nephropathy, such as microalbuminuria and markers of inflammation in

patients with type 2 DM. For this reason, the study consisted of diabetic patients whose main indication of renal impairment was the presence of microalbuminuria. The above results are rather predictable since age and diabetes duration for more than 10 years are well known risk factors for the development of diabetic nephropathy [12, 13]. In the current study, the levels of FPG in the microalbuminuric diabetic group were significantly increased compared to diabetic normoalbuminuric and control groups. These findings are in agreement with the previous studies, which have suggested that hyperglycemia is the driving force for the development of DN [14]. In type 2 diabetic patients with microalbuminuria, the elevated levels of ACR, together with the reduced levels of GFR, fulfill the characteristics of microalbuminuria as reported by Abid et al [15]. Omentin-1 is a novel adipokine mainly expressed in visceral adipose tissue shown to be associated with chronic inflammatory diseases, IR, obesity and carotid atherosclerosis and has been suggested as a biomarker of metabolic disorders [16]. Omentin-1 plays a role in vascular inflammation as it suppresses cytokine-stimulated expression of adhesion molecules in endothelial cells so it was suggested that omentin-1 may be involved in the pathogenesis of atherosclerosis [17]. Similarly in this study, we found that there was difference in serum omentin-1 levels amongst two groups of diabetic patients group A and group B. Serum omentin levels were significantly lower in the diabetic nephropathy subgroup compared to the healthy control group and diabetic without nephropathy subgroup. However, non-significant differences were found between diabetic without nephropathy and control group as reported by Huang X [18]. Several studies have shown that serum omentin levels were negatively correlated with metabolic risk factors and seemed to have anti-inflammatory and insulin-sensitizing effects [16, 19, 20]. The current study found that omentin-1 levels were correlated negatively with obesity, in addition to a significant negative correlation with hyperglycemia. Decreased serum omentin-1 levels observed in Type 2 diabetes may cause a reduction of insulin-stimulated glucose uptake in visceral and subcutaneous adipocytes or other insulin-sensitive tissues [10]. The ability of omentin to reduce insulin resistance in conjunction with its anti-inflammatory and antiatherogenic properties makes it a promising therapeutic target [21].

Conclusion: Detection of serum OMT level may play an important role in early diagnosis and prevention of diabetic nephropathy in T2DM.

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