Evaluations of Omentin as a predictor for type 2 Diabetic Nephropathy

Isam Noori Al-Kirwi* Sarah Salim Mohammed AL-Fahdawi**
*F.F. C.P(UK); D.M:C.A.B: M Consultant physician in National Diabetes Center/Al-Mustansiriya University
**Department of chemistry, College of Education for pure Sciences, University of Anbar

Abstract

Background:

Diabetic nephropathy is the leading cause of chronic kidney disease and accounts for almost 45% of all new patients requiring renal replacement therapy. Omentin novel proteins were suggested to be associated with insulin resistance. Objective to explore correlation of omentin and diabetic nephropathy in type 2 diabetic patients. **Method :** Serum omentin 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 and15 female) apparently healthy matching the socioeconomic status with diabetic 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

Key words: diabetic nephropathy, insulin resistance, omentin

INTRODUCTION

Diabetic nephropathy develops in 30% to 40% of type2 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 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 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 was 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, and waist circumference (WC), hip circumference(HC),thoracic circumference(HC) were measured. Body mass index (BMI) was calculated as the ratio of the weight to the square of height (kg/m^2). Blood pressure was measured patient was considered hypertensive if already on antihypertensive medication or if average blood pressure was 140/90 mmHg, according to the study by Mancia [11].

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 sepa-

rate 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 and15 female) apparently healthy people,matching with diabetic Pearson were selected as a control group. determination of microalbumin and urinary ACR. Serum omentin levels were measured using a commercial enzyme immunoassay Kit (my biosource catalog: MBS726965. USA). Serum insulin was determined using commercially available human enzyme-linked immunosorbent assay kit (Demeditec Catalog: DE2935,Germany) The homeostasis model assessment (HOMA) was used to calculate an index of insulin resistance for each patient, and beta-cell function was estimated from fasting insulin and glucose levels by the homeostasis model assessment (HOMA-β). Using the fasting plasma glucose (mg/ml) and insulin (μIU/ ml), the index for insulin resistance; HOMA IR, was defined as (insulin ×glucose)/ 405 and HOMA β%-cell function= (360 × Insulin/ Glucose – 63) Where FI is fasting insulin concentration (μIU/ml) and F.P.G is fasting Plasma glucose (mg/dl) [12].

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 urine albumin concentration and urinary ACR was estimated by a using a biochemical analyzer (Comblyzer13, 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 ± SE of the variables. ANOVA was used to show the differences between variables of differentiated groups. The correlation of serum omentin levels and other clinical variables was assessed by Pearson's correlation coefficient or Spearman's rank correlation as appropriate.

Results: All the demographic and laboratory findings of the groups were compared and shown in Table 1. SBP, DBP, BMI, WC (cm). 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, HOMA-IR, HOMA-β% and G/I levels were also statistically higher than the group C and group A (respectively, p=0.035, p=0.0001, p=0.0002, P=0.0001, p=0.0001 and p=0.0339). 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, HOMA-IR, HOMA-β% levels were also statistically higher than the group C and group A (respectively, p=0.035, p=0.0001, p=0.0002 P=0.0001, and p=0.0001). In group B S. Urea Microalbuminuria, A:C R (mg/mmol) were also statistically higher than the group C and group A (respectively, p=0.0008, p=0.0001 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 (3.86 ± 0.26, 5.78 ± 0.27, 6.51 ± 0.29ng/ml) respectively. While, there was non-difference in OMT level between group C and control group. On correlation analysis of study analyses, omentin was found to correlate negatively with fasting blood glucose, urea, creatinine, cholesterol ,microalbuminuria, albumin/creatinine ratio(ACR).

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

Variables	Group A	Group B	Group C	P
n(Female/male)	25(10/15)	30(21/9)	31(23/8)	
Age (years)	45.36 ± 1.35	54.24 ± 1.32	53.71 ± 1.36	0.0001
Duration of DM (years)		8.26 ± 0.84	5.58 ± 0.70	0.0483
BMI (Kg/m^2)	26.93 ± 0.78	29.58 ± 0.65	31.75 ± 0.74	0.0001
WC (cm)	89.44 ± 2.02	101.33 ± 2.82	103.83 ± 243	0.0003
Systolic BP (mmHg)	121.00 ± 1.35	140.13 ± 2.12	138.52 ± 2.41	0.0001
Diastolic BP (mmHg)	75.24 ± 3.15	89.57 ± 1.37	87.93 ± 2.01	0.0001
Omentin (ng/mL)	6.51 ± 0.29	3.86 ± 0.26	5.78 ± 0.27	0.0001
F.P.G (ml/L)	92.16 ± 1.95	220.00 ±11.99	191.93 ± 11.25	0.0001
S. Urea mg/dl	23.76 ± 1.07	29.88 ± 0.65	24.83 ± 1.07	0.0008
S. Creatinine (ml/L)	0.885 ± 0.04	1.124 ± 0.04	0.959 ± 0.03	0.125
UA mg/dl	3.90 ± 0.22	4.45 ± 0.21	4.18 ± 0.21	0.0011
Total cholesterol (ml/L)	166.76 ± 5.21	196.86 ± 9.52	185.48 ± 7.65	0.035
LDL-cholesterol	108.91± 4.89	117.70 ± 10.11	111.38 ± 6.89	0.719
HDL-cholesterol (ml/L)	42.26 ± 2.03	41.29 ± 2.08	37.78 ± 1.44	0.196
VLDL- cholesterol	17.52± 0.39	36.72 ± 4.19	37.06 ± 3.82	0.0002
Triglycerides (ml/L)	87.04 ± 6.89	164.58± 15.64	163.81 ± 13.14	0.0001
Hb (g/dl)	19.60 ± 3.81	12.72 ± 0.29	13.66 ± 0.20	0.052
Insulin (fasting) (uIU/mL)	9.63 ± 0.74	19.47 ± 1.96	17.67 ± 1.78	0.0003
HOMA-IR	1.18 ± 0.11	3.26 ± 0.37	3.24 ± 0.31	0.0001
HOMA-β%	105.93 ± 6.07	44.46 ± 5.34	51.77 ± 7.58	0.0001
G/I ratio	10.94 ± 0.82	16.25 ± 1.06	14.08 ± 0.76	0.0339
Microalbuminuria(mg/L)	10.00 ± 0.00	147.67 ± 2.33	10.64 ± 0.64	0.0001
U. Cr (mmol/l)	8.99 ± 0.97	12.94 ± 2.75	10.11 ±0.94	0.304
A:CR (mg/mmol)	1.431 ± 0.13	17.98 ± 1.82	1.336 ± 0.12	0.0001

Data are shown in table 1 as mean ± SE, **Group A** (control), **Group B** (diabetic patients with microalbuminuria), **Group C** (diabetic patients with normoalbuminuria). DM diabetes mellitus, BMI Body mass index, WC waist circumference, BP blood pressure, (Hb) hemoglobin, FG fasting glucose, LDL low density lipoprotein, HDL high density lipoprotein, HOMA-IR homeostasis model assessment-insulin resistance, HOMA-β% - homeostasis model assessment-beta cell function, G/I ratio glucose/insulin ratio, U. Cr urine creatinine , A:CR albumin: creatinine ratio

BIVARIATE CORRELATIONS BETWEEN OMENTIN AND CLINICAL PARAMETERS

The results of bivariate correlation analyses between serum omentin and various clinical parameters are shown in Table 2. Serum omentin 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 variables

OMT - Parameters	Correlation (r)	P value
F.P. G (mg/dl)	-0.299	
S.Urea (mg/dl)	-0.280	
S.Cr (mg/dl)	-0.244	
T,Cholesterol (mg/dl)	-0.242	
Microalbuminuria(mg/L)	-0.576	
A:C Ratio (mg/mmol)	-0.449	< 0.01

S. Cr serum creatinine , A:CR albumin: creatinine ratio

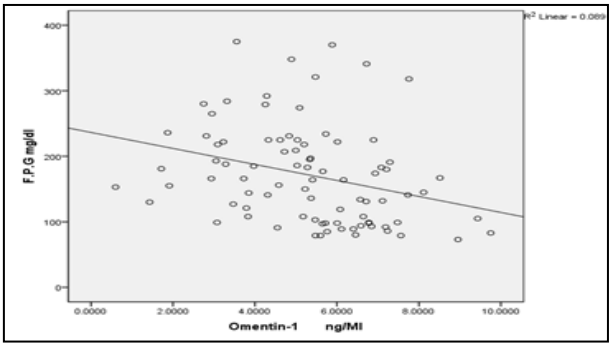

Figure1 correlation between F.P.G mg/dl and omentin(ng/ml)

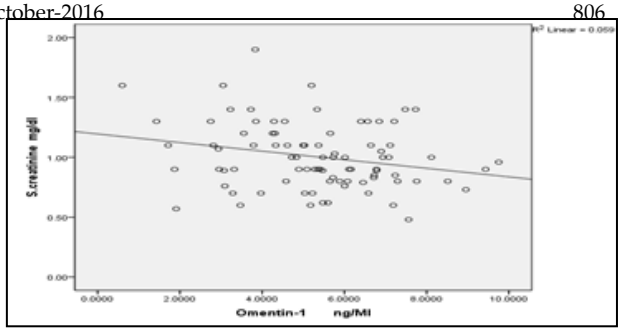

Figure2 Correlation between S.Creatinine and omentin (ng / ml)

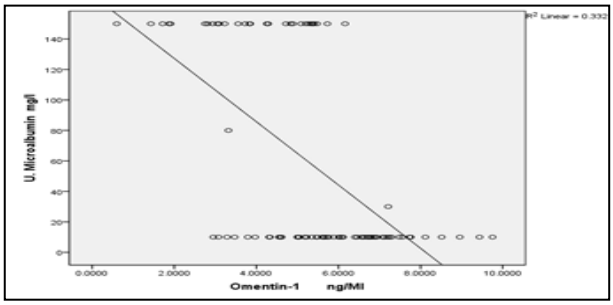

Figure3 Correlation between U.Microalbumin and omentin (ng / ml)

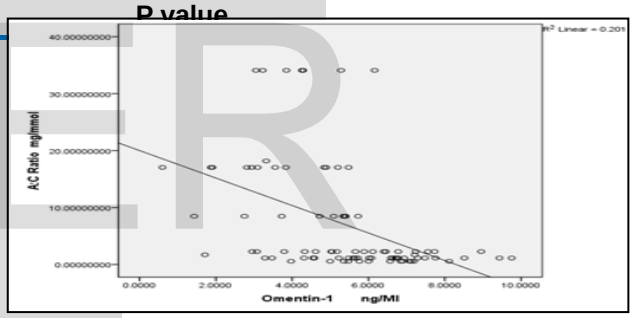

Figure4 Correlation between A:C Ratio and omentin (ng / ml)

5 Discussion

The In this study, we sought to determine the relationship between circulating omentin levels and microalbumin (MA) in patients with type 2 diabetes. This study revealed that Serum Omentin 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 [13].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 [14.15]. 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 [16]· Our findings showed that increased HOMA-IR in type 2 diabetic patients with microalbuminuria and macroalbuminuria was highly significant compared with control and normoalbuminuric diabetic groups. These findings are consistent with the study by Svensson and Eriksson who suggest that IR can occur in the early stages of renal disease and can be detected early at the stage of microalbuminuria. As DN progress, IR may be accelerating the decline in renal function toward end-stage renal disease [17]. IR is believed to be manifest at the cellular level via post-receptor defects in insulin signaling, but the underlying mechanisms still remain unclear. Possible mechanisms include deficiencies or genetic polymorphisms of tyrosine phosphorylation of the insulin receptor, IRS proteins or PIP-3 kinase, or may involve abnormalities of GLUT 4 function [18]. In type 2 diabetic patients with microalbuminuria, the elevated levels of urinary albumin and ACR, together with the reduced levels of GFR, fulfill the characteristics of microalbuminuria as reported by Abid et al [19]. Omentin 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 [20]. Omentin plays a role in vascular inflammation as it suppresses cytokine-stimulated expression of adhesion molecules in endothelial cells so it was suggested that omentin may be involved in the pathogenesis of atherosclerosis [21]. Similarly in this study, we found that there was difference in serum omentin 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 [22]. 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 [23,20 ,24]. The current study found that omentin levels were correlated negatively with obesity, in addition to a significant negative correlation with hyperglycemia, insulin resistance. Decreased serum omentin 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 [26].

Conclusion: Detection of serum OMT level may play an important role in early diagnosis and prevention of diabetic nephropathy in T2DM. Increased insulin resistance give rise to a hyperglycemic state that is a major risk factor for the development of diabetic nephropathy. In addition to increasing urinary protein excretion, increasing insulin resistance and decreased HOMA-β cell % in T2DM with nephropathy.

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