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Original Article

Serum leptin in diabetic nephropathy male patients from Gaza Strip

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ABSTRACT

Objective: To assess serum leptin in diabetic nephropathy male patients from Gaza Strip.
Materials and methods: This case-control study comprised 132 type 2 diabetic patients and 44 non-diabetic controls. The diabetic patients were classified into three groups; 44 normoalbuminurics, 44 microalbuminurics and 44 macroalbuminurics. Data were obtained from questionnaire interview, and biochemical analysis of blood and urine samples. Patients and controls were matched for age and body mass index (BMI).
Results: Serum leptin was significantly higher in micro- and macro-albuminuric patients (14.6 ± 11.7 and 15.6 ± 13.5 ng/ml) than controls and normoalbuminurics (5.9 ± 4.0 and 8.1 ± 7.6 ng/ml) with $P < 0.05$. In general, serum glucose, urea, createnine, cholesterol, triglycerides, low density lipoprotein cholesterol (LDL-C), urinary albumin and albumin creatinine ratio (ACR) were increased in diabetic groups compared to non-diabetics, and reaching their maximum increase in macroalbuminurics whereas high density lipoprotein cholesterol (HDL-C), urinary creatinine and glomerular filtration rate (GFR) were decreased reaching its maximum decrease in macroalbuminurics. Serum leptin showed significant positive correlations with diabetes duration ($r = 0.188$, $P = 0.020$), glucose ($r = 0.298$, $P < 0.001$), cholesterol ($r = 0.323$, $P < 0.001$), triglycerides ($r = 0.361$, $P < 0.001$), LDL-C ($r = 0.248$, $P = 0.001$) and urinary albumin ($r = 0.256$, $P = 0.001$) whereas negative significant correlations were found with HDL-C ($r = -0.313$, $P < 0.001$) and urinary creatinine ($r = -0.202$, $P = 0.007$).
Conclusion: The comitant raise of serum leptin with urinary albumin combined with decrease in GFR makes leptin eligible candidate as a biomarker for progression towards diabetic nephropathy in type 2 diabetes.

1. Introduction

The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels. Diabetic nephropathy is a syndrome characterized by the presence of pathological quantities of urine albumin excretion, diabetic glomerular lesions, and progressive decline of glomerular filtration rate (GFR) in diabetics [1]. Microalbuminuria or incipient nephropathy is the earliest clinical evidence of diabetic nephropathy (Albumin Creatinine Ratio: ACR of 30–300 mg/g, equivalent to timed collections of 30–300 mg/24 h). Progression to overt nephropathy (macroalbuminuria) or clinical albuminurea is heralded by a urinary albumin excretion of >300 mg/24 h or ACR > 300 mg/g, and is more likely to be associated with the development of other diabetes-related complications, including retinopathy, cardiovascular disease (CVD) and neuropathy, and finally with the development of end-stage renal disease, ESRD [2,3].

Assessment of kidney function in terms of GFR is another diagnostic modality to identify and monitor diabetic nephropathy [4]. The GFR is considered to be the most reliable measure of the functional capacity of the kidneys and is it has proved to be the most sensitive and specific marker of changes in overall renal function [5]. Increased albuminuria and decreased GFR are both associated with an increased risk of chronic kidney disease and are synergistic [6]. In this context, albuminurea and GFR are now used worldwide as clinical markers of diabetic nephropathy in real practice. Moreover, these markers help to decide whether or not to apply early therapeutic techniques and provide information to assess the risks of CVD and ESRD in diabetic nephropathy [7].

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Leptin is a small peptide hormone (16-kDa protein) that is mainly, but not exclusively, secreted by adipose tissue and the forerunner of a class of molecules collectively called adipokines. Initially discovered in 1994 [8], its crucial role as a central regulator in energy homeostasis has been largely described during the past two decades. Once secreted into the circulation, leptin reaches the central and peripheral nervous systems and acts by binding and activating the long form of leptin receptor, regulating appetite and food intake, bone mass, basal metabolism, reproductive function and insulin secretion, among other processes [9–11].

As a small peptide, leptin is cleared principally by the kidney [12,13]. Not surprisingly, serum leptin concentrations are altered in patients with chronic kidney disease. However, the link of leptin with diabetic nephropathy and its variation with different stages of this life threatening disease is still not fully understood and needs further investigation. Globally, few studies reported hyperleptinemia in micr- and macroalbuminurea stages of diabetic nephropathy in humans [14,15]. To our best knowledge, this study is the first to assess leptin status and its relations in diabetic nephropathy among type 2 diabetic males in Gaza Strip.

2. Materials and methods

2.1. Study design and study population

The present study was a case-control study. The study population comprised 132 type 2 diabetic patients who were referred to Diabetic Care Unit at Al Rimal Medical Center (the representative clinic for diabetic patients in Gaza Strip) and were previously diagnosed according to the current World Health Organization diagnostic criteria for diabetes [16]. The diabetic patients were classified into three groups: Group I included 44 patients with normoalbuminuria (ACR < 30 mg/g), Group II comprised 44 patients with microalbuminuria (ACR = 30–300 mg/g) and Group III included 44 patients with macroalbuminuria (ACR > 300 mg/g). Patients who have urinary tract infection were excluded. A total of 44 healthy individuals with no personal history of diabetes were selected randomly from general population and served as a control group. All patients and controls were males, and matched for age (40–60 years old) and BMI.

2.2. Ethical consideration

The research was undertaken according to the Declaration of Helsinki and after the Local Research Ethics Committee had approved the study. All participants provided written informed consent prior to the study.

2.3. Questionnaire interview

A meeting interview was used for filling in the questionnaire. All interviews were conducted face to face by only one investigator himself. The questionnaire was based on diabetic clinic questions of the Palestinian Ministry of Health with some modifications [17]. Most questions were the yes/no type, which offer a dichotomous choice [18]. A questionnaire was validated, and piloted with 10 individuals not included in the population sample, and modified as necessary. The questionnaire included questions related to age, smoking, family history of diabetes and diet.

2.4. Patients' records

Clinical data including duration of diabetes and diagnosed diabetic complications were obtained from the patients' records. The body weight and height of each individual dressed in light clothing without shoes were measured using a carefully calibrated balance (Detecto, CAP-180 Kg, USA) for weight and vertical measuring rod for height and the BMI was calculated as Kilogram (kg) body mass/height in meter squared [19].

2.5. Urine and blood sampling and processing

Fasting blood samples (about 8 ml each) and random urine samples were collected and centrifuged at 4000 rpm/10 min using a Rotina 46 Hettich Centrifuge, Japan.

2.6. Biochemical analysis

Serum leptin was determined by competitive enzyme immunoassay diagnostic system laboratories, USA [20]. The glucose oxidase/glucose peroxidase (POD) method was used to measure serum glucose using Labkit Kits, Spain [21]. Serum urea and creatinine were determined by the urease glutamate dehydrogenase/UV method and by the alkaline picrate method, respectively, using the BioSystems kit, Spain [22,23]. Serum cholesterol and triglycerides were measured by the cholesterol oxidase/POD method and by the glycerol phosphate oxidase/POD method, respectively, using the BioSystems kit, Spain [24,25]. High-density lipoprotein cholesterol was determined by the precipitating method using Labkit kit, Spain [26]. Low-density lipoprotein cholesterol was calculated using the empirical relationship of Friedewald [27].

2.7. Urine analysis

Urinary albumin was determined by Immunoturbidimetry-Latex method using BioSystems kit, Spain [28]. Urinary creatinine was measured by kinetic test without deproteinization using DiaSys reagent kits [29]. ACR (mg/g) = microalbumin in urine (mg/l) x1000/creatinine in urine (mg/dl) x10. eGFR was calculated by Schwartz equation: eGFR (ml/min/1.73 m^2) = 0.55 x length/serum creatinine.

2.8. Statistical analysis

Data entry and statistical analyses were performed using Statistical Package for Social Sciences Inc., Chicago, IL (SPSS) computer program version 23 for windows. A simple distribution of the study variables and cross tabulation was applied. Chi-square (χ^2) was used to identify the difference between variables. The continuous variables were expressed as mean ± SD and compared using the independent one-way analysis of variance (ANOVA) to test the relationship between different diabetic groups and controls. Bonferroni test was used to examine the difference within various groups. Pearson's correlation test was applied. The results were accepted as statistically significant when $P < 0.05$.

3. Results

3.1. Clinical and demographic characteristics

Table 1 shows no significant differences between various groups for age, BMI and smoking ($P > 0.05$). However, family history of diabetes and diet revealed significant differences among the groups (χ^2=17.810, $P < 0.001$ and χ^2=8.439, $P = 0.038$, respectively). Bonferroni test revealed that family history and diet were significantly higher in groups I, II and III compared to control group, but no significant differences were found among groups I, II and III.

Table 1
Clinical and demographic characteristics of control group, normoalbuminuric diabetic patients (Group I) and diabetic nephropathy patients (Groups II and III).

Characteristic	Control group (n = 44)	Group I Normo-albuminuria (n = 44)	Diabetic nephropathy		Test	P-value
			Group II Micro-albuminuria (n = 44)	Group III Macro-albuminuria (n = 44)		
Age (year)	50.1 ± 7.3	50.6 ± 6.4	51.5 ± 6.5	50.6 ± 6.7	F = 0.393	0.758
BMI (kg/m^2)	28.6 ± 3.5	29.2 ± 4.4	28.5 ± 3.8	28.6 ± 6.2	F = 0.273	0.844
Smoking						
Yes	6 (13.6)	6 (13.6)	10 (22.7)	8 (18.2)	$\chi^2 = 1.768$	0.622
No	38 (86.4)	38 (86.4)	34 (77.3)	36 (81.8)		
Family history						
Yes	12 (27.3)	24 (54.5)[a]	30 (68.2)[a]	28 (63.6)[a]	$\chi^2 = 17.810$	<0.001
No	32 (72.7)	20 (45.5)	14 (31.8)	16 (36.4)		
Diet						
Yes	7 (15.9)	16 (36.4)[a]	18 (40.9)[a]	18 (40.9)[a]	$\chi^2 = 8.439$	0.038
No	36 (84.1)	28 (63.6)	26 (59.1)	26 (59.1)		

kg: kilogram, m: meter, BMI: body mass index: People with BMI = 18.5–24.9 were considered to have normal weight, people with BMI = 25.0–29.9 were classified overweight and people with BMI ≥ 30.0 were considered obese (WHO, 2014).
Values are n (%) except age and BMI where values are expressed as means ± SD.
[a] Significant, P < 0.05): * compares diabetic groups versus control group.

3.2. Duration of diabetes and diabetic complications

Table 2 displays a significantly increase trend in diabetes duration recording mean values of 4.8 ± 4.9, 6.2 ± 5.9 and 8.4 ± 6.2 years in groups I, II and III, respectively (F = 12.901, P < 0.001). Bonferroni test revealed that diabetes duration in groups II and III was significantly longer than that of group I, and in group III it was significantly longer than that of group II. Retinopathy, CVD and neuropathy showed significant differences among the groups ($\chi^2 = 13.459$, P = 0.004; $\chi^2 = 8.664$, P = 0.034 and $\chi 2 = 12.624$, P = 0.006, respectively). Retinopathy and CVD were significantly higher in groups I, II and III compared to control group (P < 0.05). Neuropathy was significantly higher in groups II, and III compared with control group and group I (P < 0.05). On the other hand, recurrent infections and skin lesions showed no significant differences among the groups.

3.3. Serum leptin, glucose, urea, creatinine, and lipid profile

As illustrated in Table 3, serum leptin shows significant difference among various groups (F = 10.227, P < 0.001). Bonferroni test revealed significant increases in leptin of groups II and III compared to control group and group I (P < 0.05). Similarly, significant difference was found for glucose (F = 26.488, P < 0.001), with significant increases in groups I, II and III versus control group as well as in group III versus group I. Serum urea and creatinine also displayed significant differences among the groups (F = 24.077, P < 0.001 and 17.148, P < 0.001, respectively). There were significant decreases in urea and creatinine of group I compared to control group. However, significant increases were found in group II and III compared to group I. In addition, creatinine was significantly higher in group III with respect to group II. Serum cholesterol, triglycerides, HDL-C and LDL-C exhibited significant differences among the groups (F = 13.438, P < 0.001; F = 6.462, P < 0.001; F = 25.892, P < 0.001 and F = 13.479, P < 0.001 respectively). Cholesterol and LDL-C were significantly increased in group II and III versus control group, and in group III versus group I. Significant increase was also found in triglycerides of groups I, II and III than control group. Conversely, HDL-C was significantly decreased in groups I, II and III compared to control group.

Table 2
Duration of diabetes and diabetic complications of control group, normoalbuminuric diabetic patients (Group I) and diabetic nephropathy patients (Groups II and III).

Complication	Control group (n = 44)	Group I Normo-albuminuria (n = 44)	Diabetic nephropathy		Test	P-value
			Group II Micro-albuminuria (n = 44)	Group III Macro-albuminuria (n = 44)		
Diabetes duration (year)	–	4.8 ± 4.9	6.2 ± 5.9≠	8.4 ± 6.2≠¥	F = 12.901	<0.001
Retinopathy						
Yes	2 (4.5)	12 (27.3)*	16 (36.4)*	10 (22.7)*	$\chi^2 = 13.459$	0.004
No	42 (95.5)	32 (72.7)	28 (63.6)	34 (77.3)		
CVD						
Yes	0 (0.0)	8 (18.2)*	4 (9.1)*	6 (13.6)*	$\chi^2 = 8.664$	0.034
No	44 (100)	36 (81.8)	40 (90.9)	38 (86.4)		
Neuropathy						
Yes	0 (0.0)	2 (4.5)	8 (18.2)*≠	8 (18.2)*≠	$\chi^2 = 12.624$	0.006
No	44 (100)	42 (95.5)	36 (81.8)	36 (81.8)		
Recurrent infections						
Yes	0 (0.0)	4 (9.1)	0 (0.0)	2 (4.5)	$\chi^2 = 7.592$	0.055
No	44 (100)	40 (90.9)	44 (100)	42 (95.5)		
Skin lesion						
Yes	0 (0.0)	2 (4.5)	2 (4.5)	4 (9.1)	$\chi^2 = 4.190$	0.242
No	44 (100)	42 (95.5)	42 (95.5)	40 (90.9)		

CVD: Cardiovascular disease.
Values are n (%).
*, ≠, ¥: Significant, P < 0.05: * compares diabetic groups versus control group, ≠ compares groups II and III versus group I, and ¥ compares group III versus group II.

Table 3
Serum leptin, glucose, urea, creatinine, and lipid profile of control group, normoalbuminuric diabetic patients (Group I) and diabetic nephropathy patients (Groups II and III).

Parameter	Control group (n = 44)	Group I Normo-albuminuria (n = 44)	Diabetic nephropathy		F	P-value
			Group II Micro-albuminuria (n = 44)	Group III Macro-albuminuria (n = 44)		
Leptin (ng/ml)	5.9 ± 4.0	8.1 ± 7.6	14.6 ± 11.7*≠	15.6 ± 13.5*≠	10.227	<0.001
Glucose (mg/dl)	86.6 ± 14.2	177.3 ± 91.6*	180.2 ± 88.1*	219.9 ± 69.1*≠	26.488	<0.001
Urea (mg/dl)	30.7 ± 5.8	20.3 ± 6.4*	29.2 ± 7.9≠	32 ± 8.3≠	24.077	<0.001
Creatinine (mg/dl)	0.7 ± 0.3	0.5 ± 0.2*	0.7 ± 0.2≠	0.8 ± 0.1≠¥	17.148	<0.001
Cholesterol (mg/dl)	161.6 ± 47.3	183.6 ± 37.8	195.7 ± 34.5*	220.0 ± 54.0*≠	13.438	<0.001
Triglycerides (mg/dl)	155 ± 129.2	215.5 ± 71.8*	210.2 ± 84.3*	241.5 ± 84.3*	6.462	<0.001
HDL-C (mg/dl)	51.5 ± 8.4	43.3 ± 3.9*	42.7 ± 6.1*	40.8 ± 5.7*	25.892	<0.001
LDL-C (mg/dl)	79.1 ± 36.0	97.2 ± 36.8	111 ± 36.5*	131 ± 47.8*≠	13.479	<0.001

HDL-C: High density lipoprotein cholesterol, LDL-C: Low density lipoprotein cholesterol.
Values are expressed as means ± SD.
*, ≠, ¥: Significant, P < 0.05: * compares diabetic groups versus control group, ≠ compares groups II and III versus group I, and ¥ compares group III versus group II.

3.4. Urinary albumin, creatinine, ACR, and eGFR

Table 4 demonstrates significant differences among different groups for urinary albumin, creatinine, ACR and GFR ($F = 182.438$, $P < 0.001$; $F = 12.704$, $P < 0.001$; $F = 182.438$, $P = <0.001$, and $F = 26.490$, $P < 0.001$, respectively). Bonferroni test showed significant increases in urinary albumin and ACR of groups II and III compared to control group and group I, and in group III than group II ($P < 0.05$). In contrast, urinary creatinine exhibited significant decreases in groups I, II and III versus control group. GFR displayed significant increase in group I compared to control group, whereas significant decreases were found in GFR of group II and III compared to group I.

3.5. Serum leptin in relation to the studied parameters

As indicated in Table 5, Pearson correlation test revealed significant positive correlations of serum leptin with BMI ($r = 0.397$, $P < 0.001$), duration of diabetes ($r = 0.188$, $P = 0.020$), glucose ($r = 0.298$, $P < 0.001$), cholesterol ($r = 0.323$, $P < 0.001$), triglycerides ($r = 0.361$, $P < 0.001$), LDL-C ($r = 0.248$, $P = 0.001$), and urinary albumin ($r = 0.256$, $P = 0.001$). Conversely, significant negative correlations of serum leptin was found with HDL-C ($r = -0.313$, $P < 0.001$) and urinary creatinine ($r = -0.202$, $P = 0.007$).

Table 5
Serum leptin in relation to the studied parameters.

	Serum leptin (ng/ml) (n = 176)	
	Pearson correlation (r)	P-value
Diabetes duration (year)	0.188	0.020
Glucose (mg/dl)	0.298	<0.001
Urea (mg/dl)	−0.037	0.626
Creatinine (mg/dl)	0.076	0.315
Cholesterol (mg/dl)	0.323	<0.001
Triglycerides (mg/dl)	0.361	<0.001
HDL-C (mg/dl)	−0.313	<0.001
LDL-C (mg/dl)	0.248	0.001
Urinary Albumin (mg/g)	0.256	0.001
Urinary creatinine (mg/dl)	−0.202	0.007
GFR (ml/min/1.73m^2)	0.010	0.894

HDL-C: high density lipoprotein cholesterol, LDL-C: low density lipoprotein cholesterol, GFR: glomerular filtration rate.
The correlation was analyzed using Pearson correlation coefficient (normally distributed data).
P < 0.05: Significant, P > 0.05: not significant.

4. Discussion

The incidence of diabetes is escalating worldwide and, consequently, this has become a major health care problem. Type 2 diabetes is associated with significantly accelerated rates of microvascular (retinopathy, nephropathy and neuropathy) and macrovascular (CVD) complications. Diabetic nephropathy is the most common cause of ESRD. Microalbuminuria is the most widely used early clinical indicator of diabetic nephropathy and has been recognized as a predictor of progression to ESRD in type 2 diabetes [30]. Beside this traditional indicator, the present study focused on serum leptin status and its relations in different stages of diabetic nephropathy male patients from Gaza Strip. This may provide a clear view on the progression of the disease and could be useful in its management.

In this study, all the studied groups were matched by sex, age and BMI to avoid the effect of these confounder factors on serum leptin level [31,32]. Family history and diet were significantly higher in normo-, micro- and macroalbuminuric type 2 diabetic patients compared to controls, but no significant differences were

Table 4
Urinary albumin, creatinine, ACR, and eGFR of control group, normoalbuminuric diabetic patients (Group I) and diabetic nephropathy patients (Groups II and III).

Variable	Control Group (n = 44)	Group I Normo-albuminuria (n = 44)	Diabetic nephropathy		F	P-value
			Group II Micro-albuminuria (n = 44)	Group III Macro-albuminuria (n = 44)		
Albumin (mg/g)	10.8 ± 9.3	13.9 ± 5.2	113.7 ± 53.3*#	478.6 ± 210.6*#¥	182.438	<0.001
Creatinine (mg/dl)	156.6 ± 66.4	114.7 ± 39.5*	102 ± 55.1*	99.4 ± 26.6*	12.704	<0.001
ACR (mg/g)	10.8 ± 9.3	13.9 ± 5.2	113.7 ± 53.3*#	478.6 ± 210.6*#¥	182.438	<0.001
eGFR (ml/min/1.73m^2)	127.2 ± 21.6	194.4 ± 63.1*	140.8 ± 48.7#	120.6 ± 25.2#	26.490	<0.001

ACR: Albumin creatinine ratio, GFR, Glomerular filtration rate.
Values are expressed as means ± SD.
*, #, ¥: Significant, P < 0.05: * compares diabetic groups versus control group, # compares groups II & III versus group I, and ¥ compares group III versus group II.

found among patients. It is well recognized that type 2 diabetes is associated with family history [33]. There was an increasing trend in diabetes duration with significant longer duration in micro- and macro-albuminuric patients than normoalbuminurics, and in macro-than micro-albuminurics. This implies that diabetic nephropathy develops in patients with several years' medical history of diabetes. The frequent complications among diabetic nephropathy stages were associated with retinopathy, CVD and neuropathy. Recent studies concluded that long duration of type 2 diabetes, elevated blood pressure, poor glycemic control and presence of retinopathy were significantly associated with the progression of diabetic nephropathy [34,35].

In general, serum leptin was higher in diabetic patients than non-diabetic controls, a finding coincides with that reported by other authors [33,36]. Within diabetic groups, serum leptin was significantly elevated in micro- and macro-albuminuric patients than normoalbuminurics, reaching its maximum value in macro-albuminurics. This suggests that renal leptin degradation is impaired in the early stages of diabetic nephropathy and this impairment increase with the progression of the disease. Therefore, leptin hormone may consider as a new biomarker for progression of kidney disease in diabetic nephropathy patients and may be useful in practical and diagnostic issues. However, this needs further investigation. Nevertheless, hyperleptinemia was found to be related to chronic kidney disease incidence and progression in patients with type 2 diabetes [37,38].

It is not surprisingly that glucose levels are significantly elevated in diabetic groups than controls. In addition, macroalbuminuric patients showed significant raise in glucose levels than normoalbuminurics. Hyperglycemia was reported to be the key modifiable risk factor that promotes the development of diabetic kidney disease in type 2 diabetes [39]. Serum urea and createnine were also significantly increased in micro- and macro-albuminuric patients than normoalbuminurics. Similar result was obtained [40]. The change in serum urea and creatinine may be related to disturbance of kidney function toward the progression of diabetic nephropathy. Cholesterol, triglycerides and LDL-C were progressively increased in the three diabetic groups compared to controls and reaching their maximum increase in macroalbuminuric patients whereas HDL-C was gradually decreased reaching its maximum decrease in macroalbuminuric patients. These findings are in agreement with other studies [40,41]. It is accepted that diabetic patients with hyperlipidemia are more prone to develop diabetic complications [42].

Urinary albumin and ACR showed significant elevation in micro- and macro-albumiuric patients than normoalbuminurics and controls, and in macroalbuminurics than microalbuminurics. Conversely, urinary creatinine and GFR, in general, exhibited significant decreases in micro- and macro-albumiuric patients. Elevation in urinary albumin levels is considered as key characteristics of diabetic nephropathy [43], and explained mostly as a result of impairment of kidney filtration efficiency [44]. This is supported by the observed significant decrease of GFR which is used as an index of chronic kidney disease [45].

In this study, serum leptin showed significant positive correlations with diabetes duration, glucose, cholesterol, triglycerides, LDL-C and urinary albumin whereas negative significant correlations were found with HDL-C and urinary creatinine. Such correlations indicate alterations of serum leptin level in type 2 diabetes and throughout its advancement towards diabetic nephropathy. Similar findings were reported in the literature [14,46]. The comitant raise of serum leptin with urinary albumin combined with decrease in GFR makes leptin eligible candidate as a biomarker for progression to different stages of diabetic nephropathy in type 2 diabetes. To complete this view, further research is recommended to assess serum leptin status and its relations to other biochemical parameters in ESRD patients or even in hemodialysis patients.

5. Conclusions

Serum leptin was significantly higher in micro- and macro-albuminuric patients than controls and normoalbuminurics. In general, serum glucose, urea, createnine, cholesterol, triglycerides, LDL-C, urinary albumin and ACR were increased in diabetic groups compared to non-diabetics, and reaching their maximum increase in macroalbuminurics whereas HDL-C, urinary creatinine and GFR were decreased reaching its maximum decrease in macro-albuminurics. Serum leptin showed significant positive correlations with diabetes duration, glucose, cholesterol, triglycerides, LDL-C and urinary albumin whereas negative significant correlations were found with HDL-C and urinary creatinine.

Conflicts of interest

The authors declare no conflicts of interest.

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