Assessment of serum and urinary levels of neutrophil gelatinase-associated lipocalin in correlation with albuminuria in nondiabetic obese patients

Nearmeen M. Rashad[a], Nora M. Said[b], George Emad[a], Ahmed F. Gomaa[a], Heba M. Kadry[c]

Departments of [a]Internal Medicine, [b]Clinical Pathology, [c]Medical Microbiology & Immunology, Faculty of Medicine, Zagazig University, Zagazig, Egypt

Correspondence to Nearmeen M. Rashad, MD, Department of Internal Medicine, Faculty of Medicine, Zagazig University, 44519, Zagazig, Egypt. Tel: +20 122 424 8642; e-mail: nrashad78@yahoo.com, n.rashad@zu.edu.eg

Received 8 February 2019
Accepted 7 April 2019
Published: 18 August 2020

The Egyptian Journal of Internal Medicine 2019, 31:642–651

Background
Obesity, a new pandemic, is associated with an increased risk of death and morbidity. Obesity-related glomerulopathy is an increasing cause of end-stage renal disease. Neutrophil gelatinase-associated lipocalin (NGAL) is a neutrophil-expressed inflammatory protein that is increased in different diseases. The objective of the current study was to evaluate the predictive performance of serum and urinary NGAL in obese patients and to clarify its possible relationship with different stages of albuminuria in nondiabetic patients.
Patients and methods
This cross-sectional study was conducted on 55 obese patients and 40 healthy individuals as a control group. The enrolled patients were divided into three groups according to the level of albuminuria. Serum and urinary NGAL (ng/ml) were measured by enzyme-linked immunosorbent assay kits.
Results
Serum and urinary NGAL levels were significantly higher in obese (354.44±121.2 and 213.22±10.8, respectively) compared with healthy controls (44.21±11.2 and 13.9±6.3, respectively; $P<0.001$). Moreover, there were higher significant values of serum NGAL in patients with macroalbuminuria (488.65±44.53) and microalbuminuria (264.33±25.53) compared with patients with normoalbuminuria (122.48±4.53, $P<0.001$) and higher significant values of urinary NGAL in patients with macroalbuminuria (363.84±32.53) and microalbuminuria (112.19±26.53) compared with patients with normoalbuminuria (32.17±10.53, $P<0.001$). Serum and urinary NGAL levels were statistically significant predictors of albuminuria among obese patients. In addition, our results observed that BMI, waist/hip ratio, urinary albumin, estimated glomerular filtration rate, and urinary albumin-creatinine ratio were independently correlated with serum NGAL, whereas BMI, waist/hip ratio, and urinary albumin were the only variables that were independently correlated with urinary NGAL.
Conclusion
The higher levels of serum and urinary NGAL in obese patients compared with healthy group were strongly correlated with urinary albumin-creatinine ratio and cardiometabolic risk factors.

Keywords:
albuminuria, estimated glomerular filtration rate, neutrophil gelatinase-associated lipocalin, obesity

Egypt J Intern Med 31:642–651

1110-7782

Introduction

Accumulating evidence indicates the worldwide prevalence of obesity and its metabolic complications has increased substantially in recent decades. Accumulating evidence suggests that chronic inflammation in adipose tissue may play a critical role in the development of obesity-related metabolic dysfunction [1]. Excess adipose tissue results in the infiltration of macrophages, which leads to the promotion of inflammation and insulin resistance [2]. Chronic inflammation and insulin resistance result in complex metabolic derangements that contribute to the pathogenesis atherosclerosis, coronary artery disease, and chronic kidney disease (CKD) [3].

Several lines of evidence indicate that CKD is now one of the major public health problems. Early detection of CKD is crucial to prevent its progression, and thereby, to potentially improve its outcome [4]. The histopathology of proteinuric obese patients consists

of glomerulomegaly with or without focal segmental glomerulosclerosis. There is an appealing concept that these glomerular changes are thought to be related to altered renal hemodynamics, namely, increased renal blood flow, hyperfiltration, and increased filtration fraction [5].

Neutrophil gelatinase-associated lipocalin (NGAL) is a 25-kDa glycoprotein belonging to lipocalin superfamily [6]. It is a constituent of specific granules and exists in neutrophil as a part of the NGAL–gelatinase complex [7]. Compelling evidence suggests that NGAL is involved in antimicrobial defense mechanisms and is upregulated in systemic bacterial infection [8,9]. It is a useful biomarker in CKD [10].

Increased inflammation in adipose and kidney tissues promotes the progression of kidney damage in obesity. Adipose tissue, which is accumulated in obesity, is a key endocrine organ that produces multiple biologically active molecules. NGAL is a protein derived from neutrophil whose circulating level is increased by kidney injury, bacterial infection, and obesity, but its metabolic consequence remains elusive. Therefore, the objective of the current study was to evaluate the predictive performance of serum and urinary NGAL in obese patients and to clarify its possible relationship with different stages of albuminuria in nondiabetic patients.

Patients and methods

A total of 55 obese patients (BMI>30) and 40 age-matched and sex-matched apparently healthy lean controls (BMI<25) have been enrolled in this preliminary case–control study. Early morning serum and urine samples have been obtained on the same day from all participants. Obese patients who were attending and being followed up in obesity, endocrinology, and renal outpatient clinics of Internal Medicine Department, Faculty of Medicine, Zagazig University hospitals, were divided into three groups according to urinary albumin excretion, which was calculated as urinary albumin-creatinine ratio (UACR): (a) normoalbuminuria group (UACR < 30 μg/mg), (b) microalbuminuria group (at least two of three consecutive urine samples UACR 30–300 μg/mg), and (c) macroalbuminuria group (UACR > 300 μg/mg) [11]. Patients with type 1 or type 2 diabetes mellites, neoplastic disorders, severe liver disease, active or chronic infection or inflammatory disorders, hematological diseases, pregnancy, or a recent history of acute myocardial infarction, stroke, or occlusive peripheral vascular disease have been excluded. All patients were subjected to thorough medical history taking and full physical examination, including blood pressure and BMI. The study was conducted in accordance with the Ethical Committee of Faculty of Medicine, Zagazig University. All participants provided written informed consent to participate in the study after being informed of its purpose.

Blood samples and biochemical measurements

Blood samples were withdrawn from all participants after an overnight fast and divided into three portions: 1 ml of whole blood was collected into tubes containing EDTA for hemoglobin A1c (HbA1c), 1 ml of whole blood was collected into tubes containing fluoride for fasting blood glucose, and the serum from remaining part of the sample was separated immediately and stored at −20°C until analysis for other biochemical measurement. Fasting plasma glucose concentration was measured using the glucose oxidase method (Spinreact, Girona, Spain). Fasting serum insulin levels were determined by high-sensitivity enzyme-linked immunosorbent assay (ELISA) kit provided by Biosource Europe S.A., Nivelles, Belgium. Insulin resistance was assessed using the HOMA model (homeostasis model assessment index) = fasting insulin (μU/ml) × fasting glucose (mmol/l)/22.5 [12]. Total cholesterol and triglycerides (TG) were measured by routine enzymatic methods (Spinreact). High-density lipoprotein was determined after precipitation of the apoB-containing lipoproteins. Low-density lipoprotein was calculated. Quantitative estimation of serum hypersensitive C-reactive protein was done by means of particle-enhanced immunonephelometry using the BN system (Dade Behring, Deerfield, Illinois, USA).

Urine samples

Urine aliquots were stored at −80°C before being used for measurements of urinary markers. Twenty-four hour urine samples were collected from each participant in sterilized urine containers and used to determine albumin in 24-h urine specimen. The urine levels of the biomarkers were normalized to the urinary creatinine concentration to control for variations in hydration status. Spot urinary albumin and creatinine concentrations were measured (Siemens Healthcare Diagnostics Inc., USA) and expressed as the urinary albumin (μg)/creatinine (mg) ratio (UACR). Estimated glomerular filtration rate (eGFR) was calculated using the four-variable Modification of Diet in Renal Disease GFR formulas (age, sex, race, and serum creatinine), which are as follows: eGFR = 186 × (serum creatinine–1.154) × (age–0.203) × (0.742 if female) [13].

Measurement of serum and urinary neutrophil gelatinase-associated lipocalin (ng/ml)

Serum LCN-2 levels were quantified with the Human Lipocalin-2/NGAL Quantikine ELISA kit (R&D Systems, Minneapolis, Minnesota, USA). Urinary NGAL was measured in duplicate by means of commercial ELISA (R&D System) according to the manufacturer's instructions.

Dual-energy radiography absorptiometry

The accurate and precise values of the body composition parameters were estimated from the dual-energy radiography absorptiometry scan of the total body. They included fat mass, fat-free mass. Additionally, the fat mass index [fat mass/square height (kg/m^2)] and free-fat mass index [free-fat mass/square height (kg/m^2)] were calculated.

Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences, version 22 (SPSS Inc., Chicago, Illinois, USA). Normally distributed continuous values were expressed as means±SD and compared using analysis of variance test followed by Tukey HSD post-hoc test for multiple comparisons. Pearson's correlation coefficient was used to test correlations between serum and urinary NGAL and other variables. Linear regression analysis was applied to allow us to estimate the association between serum and urinary NGAL and other variables after adjusting for potentially confounding variables that have been included in the model. Receiver operating characteristics (ROC) analysis was used to calculate the area under the curve for serum and urinary NGAL and to find the best cutoff values. *P* values were considered significant if less than 0.05.

Results

Clinical, anthropometric, and biochemical characteristics of the studied groups

Among cases, 25% were males and 75% were females, and in control individuals, 27.3% were males and 72.7% were females. The mean age of the case group was 46.95±7.63 years and in controls 47.98 ±7.98 years. The case and control individuals were thus matched in terms of age and sex.

There were significant higher values in obese group compared with healthy group regarding systolic blood pressure, diastolic blood pressure (DBP), BMI, waist–hip ratio, total cholesterol, TG, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), fasting plasma glucose, HbA1c, albuminuria, serum creatinine, and UACR ($P<0.05$). On the contrary, obese had significantly lower values of HDL-C, total protein, serum albumin, and eGFR compared with healthy control group ($P<0.001$) (Table 1).

Clinical, anthropometric, and biochemical characteristics of obese patients stratified according to urinary albumin-creatinine ratio

Macroalbuminuric patients had significantly higher levels of DBP, TG, LDL-C, albuminuria, serum creatinine, and UACR compared with normoalbuminuric and microalbuminuric patients ($P<0.05$). On the contrary, obese had significantly lower values of HDL-C, total protein, serum albumin, and eGFR compared with healthy control group ($P < 0.001$) (Table 2).

Comparison of serum and urinary neutrophil gelatinase-associated lipocalin (ng/ml) in the studied population

Serum and urinary NGAL were significantly higher in obese (354.44±121.2 and 213.22±10.8, respectively) compared with healthy controls (44.21±11.2 and 13.9 ±6.3, respectively, $P<0.001$) (Fig. 1a and b). Moreover, there were higher significant values of serum NGAL in patients with macroalbuminuria (488.65±44.53) and microalbuminuria (264.33±25.53) compared with individuals with normoalbuminuria (122.48±4.53, $P<0.001$) (Fig. 2a) and higher significant values of urinary NGAL in patients with macroalbuminuria (363.84±32.53) and microalbuminuria (112.19±26.53) compared with individuals with normoalbuminuria (32.17±10.53, $P<0.001$) (Fig. 2b).

Pearson's correlation between serum and urinary neutrophil gelatinase-associated lipocalin (ng/ml) and clinical, anthropometric, and biochemical characteristics

Serum NGAL levels were significantly positively correlated with BMI, albuminuria, serum creatinine, and UACR. On the contrary, there was a significant negative correlation between serum NGAL and total protein, serum albumin, as well as eGFR ($P<0.001$) (Table 3).

Urinary NGAL levels were significantly positively correlated with BMI, waist/hip ratio, TG, albuminuria, and UACR. On the contrary, there was a significant negative correlation between urinary NGAL and serum albumin, as well as eGFR ($P<0.001$) (Table 3).

Logistic regression analysis evaluating the association of serum and urinary neutrophil gelatinase-associated lipocalin (ng/ml) with albuminuria among obese patients

After adjusting for the traditional risk factors, logistic regression analysis test was done to evaluate the

Table 1 Clinical and demographic characteristics of the study groups

Variables	Healthy control group (*N*=40)	Obese group (*N*=55)	*P* value
Age (years)	47.98±7.98	46.95±7.63	0.143
Sex [*n* (%)]			
Females	30 (75)	40 (72.7)	0.122
Males	10 (25)	15 (27.3)	
BMI (kg/m^2)	22.2±1.3	33.8±5.09	<0.001*
Waist/hip ratio	0.79±0.04	1.13±0.18	<0.001*
FMI (kg/m^2)	3.76±0.66	8.63± 6.244	<0.001*
FFMI (kg/m^2)	19.0±1.160	24.4±3.286	<0.001*
SBP (mmHg)	117.7±3.84	130±11.7	<0.001*
DBP (mmHg)	75.9±4.10	83.74±10.70	<0.001*
TC (mg/dl)	183.3±18.25	211.04±31.34	<0.001*
TG (mg/dl)	176±13.68	228.69±37.44	<0.001*
LDL-C (mg/dl)	100.4±21.48	128.48±30.64	<0.001*
HDL-C (mg/dl)	47.7±5.99	36.82±5.09	<0.001*
FPG (mg/dl)	87.85±3.69	87.66±7.72	0.342
HbA1c (%)	4.99±0.55	5.01±3.27	0.321
Total protein (g/l)	8.2±1.13	6.6±1.27	<0.001*
Serum albumin (g/l)	4.2±0.23	3.6±.047	<0.001*
Albuminuria (mg/l)	10.6±2.1	341.1±54.3	<0.001*
Serum creatinine (mg/dl)	0.916±0.047	1.31±0.18	<0.001*
UACR	13.74±0.71	174.97±153.9	<0.001*
eGFR (ml/min)	99.19±11.2	69.65±9.52	<0.001*
Serum NGAL (ng/ml)	44.21±11.2	354±121.2	<0.001*
Urinary NGAL (ng/ml)	13.9±6.3	213±10.8	<0.001*

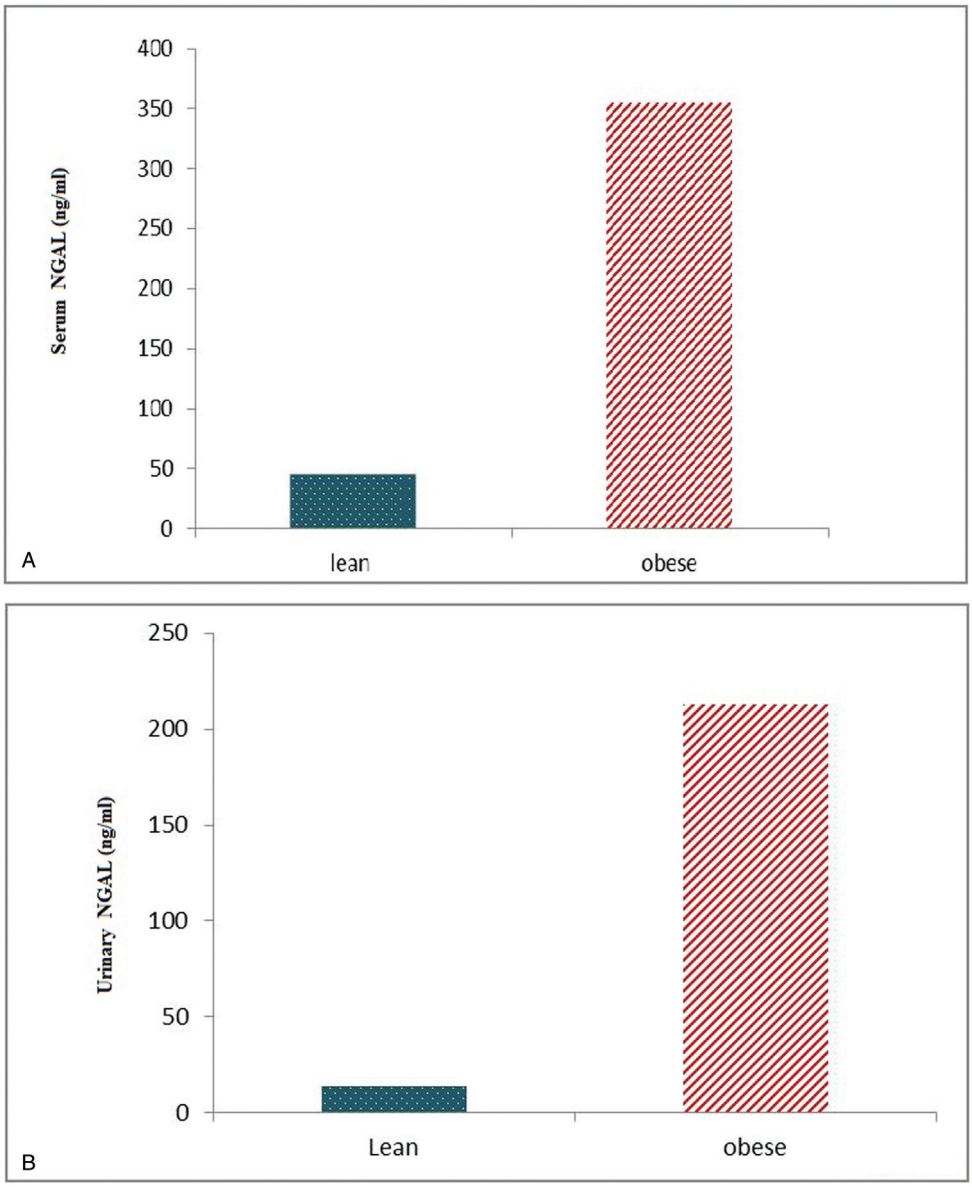
DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FMI, fat mass index; FFMI, free-fat mass index; FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NGAL, neutrophil gelatinase-associated lipocalin; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; UACR, urinary albumin-creatinine ratio. **P* value less than 0.05.

Table 2 Clinical and demographic characteristics of the obese patients

Variables	Normoalbuminuria (*N*=33)	Microalbuminuria (*N*=15)	Macroalbuminuria (*N*=7)	*P* value
BMI (kg/m^2)	31.93±5.27	31.0±5.23	32.71±4.48	0.133
Waist/hip ratio	1.14±0.18	1.10±0.186	1.168±0.16	0.162
FMI (kg/m^2)	8.35±1.348	8.76±1.058	8.9+1.33	0.191
FFMI (kg/m^2)	23.58+3.64	24.7+2.8	25.95+3.29	0.09
SBP (mmHg)	128.30±11.09	129.03±13.26	131.3±11.09	0.121
DBP (mmHg)	85.63±11.10	87.80±9.89	86.04±10.75	0.204
TC (mg/dl)	178.7±40.8	189.4±41.4	184.5±38.9	0.231
TG (mg/dl)	231.32±33.9	229.1±43.36	251.90±37.2	<0.001*
LDL-C (mg/dl)	131.9±27.44	126.47±37.05	153.8±28.23	<0.001*
HDL-C (mg/dl)	39.8±5.27	36.0±5.23	29.7±4.48	<0.001*
FPG (mg/dl)	85.9±9.4	88.49±8.08	88.8±9.3	0.101
Serum albumin (g/l)	3.65±0.95	3.44±0.13	2.91±0.43	<0.001*
Serum creatinine (mg/dl)	1.02±0.18	1.093±0.18	1.337±0.16	<0.001*
Albuminuria (mg/l)	20.3±6.1 2	202.3±72.1	859.6±183.1	<0.001*
UACR	27.32±9.78	69.07±7.86	69.63±8.48	<0.001*
eGFR (ml/min)	28.49±2.53	256.9±23.08	399.61±30.5	<0.001*
Serum NGAL (ng/ml)	122.48±4.53	264.33±25.53	488.65±44.53	<0.001*
Urinary NGAL (ng/ml)	32.17±10.53	112.19±26.53	363.84±32.53	<0.001*

DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FMI, fat mass index; FFMI, free-fat mass index; FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; HDL.c, high-density lipoprotein cholesterol; LDL.c, low-density lipoprotein cholesterol; NGAL, neutrophil gelatinase-associated lipocalin; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; UACR, urinary albumin-creatinine ratio. **P* value less than 0.05.

Figure 1



(a) Comparison of serum NGAL (ng/ml) in the studied group. (b) Comparison of urinary NGAL (ng/ml) in the studied group. NGAL, neutrophil gelatinase-associated lipocalin.

predictors of albuminuria among obese patients. Serum NGAL (odds ratio=0.001, 95% confidence interval=0.000–0.417, $P<0.001$) (Table 4) and urinary NGAL (odds ratio=0.032, 95% confidence interval =0.013–0.051, $P<0.001$) are statistically significant predictors of albuminuria.

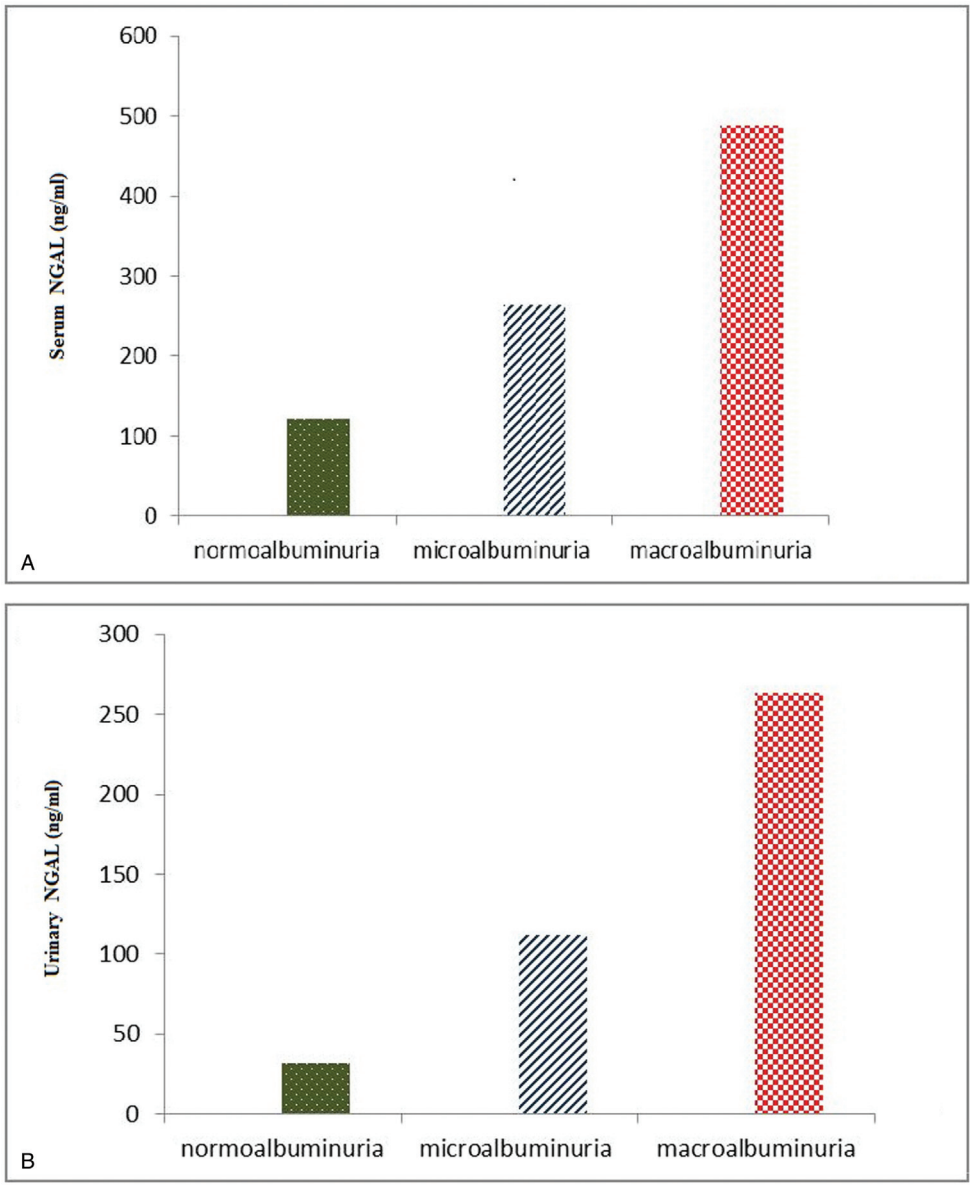
Linear regression analyses in obese patients

A linear regression analysis test was done to assess the main independent parameters associated with serum and urinary NGAL (ng/ml). Our results showed that BMI, waist/hip ratio, urinary albumin, eGFR, and UACR were independently correlated with serum NGAL, whereas, BMI, waist/hip ratio, urinary albumin were the only variables that were independently correlated with urinary NGAL ($P<0.001$) (Table 5).

Discussion

There is strong evidence that the prevalence of obesity and CKD has been increasing throughout the past decades. Although considerable research effort has been focused on obesity and its comorbidities, the pathophysiology of the disease remains incompletely understood. Accumulating evidence suggests that systemic inflammation might be an important mediator [14]. Obesity is a state of low-grade,

Figure 2



(a) Comparison of serum NGAL (ng/ml) in the obese group. (b) Comparison of urinary NGAL (ng/ml) in the obese group. NGAL, neutrophil gelatinase-associated lipocalin.

chronic inflammation characterized by macrophage infiltration in adipose tissue and increased circulating concentrations of proinflammatory molecules [15].

NGAL is expressed in several tissues, including neutrophils, liver, lung, kidney, adipocytes, and macrophages [16–18]. Several inflammatory stimuli, such as lipopolysaccharides and IL-1β, can markedly induce lipocalin-2 expression and secretion in these cells [19]. Nonetheless, the role of NGAL in the pathogenesis of obesity-related diseases has not been investigated to date. Considering that albuminuria and proteinuria are well-recognized risk factors for progressive renal disease as well as cardiovascular disease. This present study aimed to investigate the association of serum and urinary NGAL with susceptibility of albuminuria among obese patients and to clarify its possible relationship with different stages of albuminuria in nondiabetic patients.

As expected, our results revealed that obese patients had significantly higher levels of cardiometabolic risk factors and hypersensitive C-reactive protein as well as serum creatinine, uric acid, and UACR compared with healthy control group. However, eGFR values were significantly lower in obese patients compared with the healthy lean group. Even more importantly, to better evaluate albuminuria among obese patients, we subdivided our obese patients into three subgroups: normoalbuminuria, microalbuminuria, and macroalbuminuria. The

Table 3 Pearson's correlations between neutrophil gelatinase-associated lipocalin (ng/ml) and studied parameters of obese groups

Variables	Serum NGAL (ng/ml)		Urinary NGAL (ng/ml)	
	r	*P*	*r*	*P*
BMI (kg/m^2)	0.938	<0.001*	0.719	<0.01*
Waist/hip ratio	0.029	0.854	0.343	<0.001*
SBP (mmHg)	0.014	0.971	0.006	0.954
DBP (mmHg)	0.088	0.386	0.034	0.734
TC (mg/dl)	0.076	0.452	0.040	0.692
TG (mg/dl)	0.190	0.058	0.232	<0.05*
LDL-C (mg/dl)	0.020	0.286	0.033	0.744
HDL-C (mg/dl)	–0.129	0.201	–0.081	0.423
FPG (mg/dl)	0.029	0.754	0.100	0.325
HbA1c (%)	0.085	0.347	0.189	0.060
Total protein (g/l)	–0.483	<0.001*	–0.597	0.082
Serum albumin (g/l)	–0.850	<0.001*	–0.443	<0.001*
Serum creatinine (mg/dl)	0.744	<0.001*	0.042	0.411
Albuminuria (mg/l)	0.429	<0.001*	0.491	<0.001*
UACR	0.386	<0.001*	0.447	<0.001*
eGFR (ml/min)	–0.838	<0.001*	-0.629	<0.01*

DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NGAL, neutrophil gelatinase-associated lipocalin; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; UACR, urinary albumin-creatinine ratio. **P* value less than 0.05.

Table 4 Logistic regression analysis evaluating the association of serum and urinary neutrophil gelatinase-associated lipocalin (ng/ml) with obesity among studied patients

Variables	*B*	SE	Wald	*P*	Odds ratio	95% CI	
						Lower	Upper
Serum NGAL (ng/ml)	7.028	3.126	5.047	<0.05*	0.001	0.000	0.417
Urinary NGAL (ng/ml)	0.031	0.009	10.799	<0.001	1.032	1.013	1.051
Constant	–13.620	6.675	4.163	<0.05*	0.000		

CI, confidence interval; NGAL, neutrophil gelatinase-associated lipocalin. **P* value less than 0.05.

Table 5 Linear regression analyses test the influence of the main independent variables against serum neutrophil gelatinase-associated lipocalin and urinary neutrophil gelatinase-associated lipocalin (ng/ml) (dependent variable)

Model	Unstandardized coefficients		Standardized coefficients	*t*	*P*	95% CI	
	B	SE	Beta			Lower bound	Upper bound
Serum NGAL							
Constant	1.669	7.634		0.219	0.827	16.78	13.447
BMI	0.189	0.062	0.235	3.025	<0.001*	0.312	0.065
Waist/hip ratio	0.069	0.013	0.346	5.105	<0.001*	0.042	0.096
Urinary albumin (μg/ml)	0.056	0.010	0.363	5.506	<0.001*	0.036	0.076
TG	0.038	0.024	0.171	1.597	0.112		
eGFR (ml/min)	–0.144	.056	–0.186	–2.559	<0.001*	–0.256	–0.03
UACR	0.019	0.009	0.139	2.071	<0.05*	0.001	0.036
Urinary NGAL constant	31.56	13.95		2.263	0.025	59.12	4.017
DBP	0.003	0.008	0.021	–0.355	0.723	0.018	0.013
SBP	0.007	0.004	0.103	1.837	0.068	0.001	0.014
BMI	0.189	0.019	0.702	9.841	<0.001*	0.151	0.227
Urinary albumin (μg/ml)	0.055	0.011	0.425	4.884	<0.001*	0.033	0.078
Waist/hip ratio	4.43	0.895	0.430	4.950	<0.001*	6.200	2.665
TC	0.023	0.027	0.058	0.850	0.397	0.031	0.077
FPG	0.038	0.024	0.171	1.597	0.112	0.009	0.085

CI, confidence interval; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; NGAL, neutrophil gelatinase-associated lipocalin; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; UACR, urinary albumin-creatinine ratio. **P* value less than 0.05.

prevalence of microalbuminuria was 27.2% and macroalbuminuria was 12.7%.

Similar findings were observed by Valensi *et al.* [20]. They observed that daily albumin excretion in urine was significantly higher in obese patients than in healthy patients.

Similar to our results, Rosenstock and colleagues found a relatively high prevalence of albuminuria and proteinuria in obese patients undergoing bariatric surgery. Moreover, they observed that nondiabetic obese patients with hypertension had more albuminuria and proteinuria than those without hypertension, but this did not reach statistical significance. Obese patients who had neither diabetes nor hypertension had higher levels of albuminuria than seen in general population [21].

Serra *et al.* [22] showed that renal pathological changes, mesangial matrix increase, mesangial proliferation, podocyte, and glomerular hypertrophy, could be found in a higher percentage of morbid obese patients undergoing bariatric surgery, despite having no clinical evidence of renal disease. In addition, a study conducted by Chang *et al.* [23] on metabolically healthy obese patients without hypertension or evidence of metabolic syndrome still showed associated with the development of CKD.

On the contrary, a study conducted by Cubeddu *et al.* [24] found that there was a nonsignificant correlation between obesity and microalbuminuria; an interestingly similar finding was observed that there were nonsignificant differences between healthy individuals and obese patients [25,26]. The discrepancies between our findings and the results of these studies could be owing to differences in obese group categorization, as according to our results, obese patients had dyslipidemia and insulin resistance, whereas the obese group of the previous studies was normal and had no insulin resistance. In addition, the study conducted on Turkish population detected higher albumin excretion in 24-h urine samples of obese group compared with healthy individuals but did not reach significant value [26].

The results presented herein are innovative, as this study performs a robust evaluation of NGAL as a diagnostic marker of CKD and albuminuria. Our results confirmed that NGAL was significantly higher in obese patients than healthy individuals. Interestingly, serum NGAL level was positively correlated with BMI, albuminuria, serum creatinine, and UACR. On the contrary, there was a significant negative correlation between serum NGAL and total protein, serum albumin as well as eGFR. Our results detected that BMI, waist/hip ratio, TG, albuminuria, and UACR were positively correlated with urinary NGAL levels. On the contrary, there was a significant negative correlation between urinary NGAL and serum albumin as well as eGFR.

In agreement with our results, Wang *et al.* [27] found that NGAL concentrations were positively correlated with BMI, waist circumference, and fat percentage.

In concordance with our finding, Matthews *et al.* [12] observed that after adjustment for sex and age, serum concentrations of NGAL were positively correlated with waist-to-hip ratio, waist circumference, and fat percentage.

Similar results were obtained by Wafaa *et al.* [28] who observed that the NGAL level was closely related to obesity, metabolic complications, and cardiovascular diseases.

To the best of our knowledge, this study is the first to explore the correlation between serum and urinary NGAL with albuminuria among obese Egyptian patients. To better elucidate the association between NGAL and albuminuria, we subdivided our obese group into three subgroups according to UACR. We found that obese patients with macroalbuminuria had higher values of both serum and urinary NGAL (ng/ml). After adjusting for traditional risk factors, logistic regression analysis test was done to evaluate the predictor of albuminuria among obese patients.

The current results revealed that serum and urinary NGAL levels were statistically significant predictors of albuminuria among obese patients. In addition, our results observed that BMI, waist/hip ratio, urinary albumin, eGFR, and UACR were independently correlated with serum NGAL, whereas, BMI, waist/hip ratio, and urinary albumin were the only variables that were independently correlated with urinary NGAL.

Our findings are in concordance with Lacquaniti *et al.* [29] who found higher levels of serum and urinary NGAL in patients with microalbuminuria compared with the healthy group.

Their results are in agreement with Kaul and colleagues who found a positive correlation between serum and

urinary NGAL and UACR. Even more important, univariate binary logistic regression analysis showed that UACR, serum creatinine, GFR, BMI, duration of diabetes, systolic blood pressure, DBP, and HbA1c were found to be individually significantly associated with serum NGAL [30].Although albuminuria could be used as an noninvasive marker of nephropathy, the need for using new markers is indeed. We aimed to assess the power of serum and urinary NGAL in obese patients. We used ROC to estimate the sensitivity and specificity of serum and urinary NGAL and found that the diagnostic power of urinary NGAL in differentiating macroalbuminuria from normoalbuminuria was stronger than the diagnostic power of serum NGAL in differentiating macroalbuminuria from normoalbuminuria.

Our findings are in concordance with Kaul *et al.* [30] who explored the stronger diagnostic power of urinary NGAL than serum NGAL in the prediction of albuminuria among diabetic patients.

Similar to our result, a study conducted by Lacquaniti *et al.* [29] found that by using ROC analysis, serum and urinary NGAL had good diagnostic values for early prediction of microalbuminuria in diabetic patients.

Conclusion

The higher levels of serum and urinary NGAL in obese patients compared with healthy lean group were strongly correlated with UACR and cardiometabolic risk factors. Therefore, serum and urinary NGAL levels could be used as predictors of microalbuminuria among obese patients.

Acknowledgements

The authors thank members of the Rosen and Kahn laboratories for technical help.

Several studies have shown that increased BMI is an independent risk factor for ESRD. In a cohort of 320 252 adult patients of Kaiser Permanente who were followed for 15–35 years, BMI was found to be a strong and common risk factor for ESRD 10. This relationship between BMI and ESRD persisted even after controlling for baseline blood pressure and diabetes. Similarly, in a population-based, case–control study in Sweden, obesity was shown to be an important and potentially preventable risk factor for ESRD 11.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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