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TNF-α as a Predictor of Renal Involvement in Sedentary Obese Individuals

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Abstract

Background: Obesity-related renal dysfunction is a growing health concern, with TNF-α playing a crucial role in inflammation and renal pathology. TNF-α, a pro-inflammatory cytokine mainly produced by adipose tissue, is crucial in driving inflammation and kidney damage associated with obesity. This study aimed to evaluate TNF-α as a predictor of renal involvement in sedentary obese individuals without diabetes, hypertension, or hypothyroidism.

Methods: A cross-sectional observational research was undertaken at the Department of Nephrology, BSMMU, Dhaka. The study period ranged from February 2023 to August 2024. The study population consisted of 67 sedentary obese individuals, according to specific inclusion and exclusion criteria. The sampling method used was purposive sampling. Data were collected using a pre-tested questionnaire through patient history, clinical examination, and laboratory findings. Serum TNF-α levels were measured using the DRG Adiponectin ELISA Kit, which operates on the sandwich principle. Renal involvement was assessed by measuring the urinary albumin-to-creatinine ratio (uACR) and calculating the estimated glomerular filtration rate (eGFR) through the MDRD formula. Correlation analysis and ROC curve analysis were conducted to assess the predictive ability of TNF-α for microalbuminuria.

Results: The participants in the study had an average age of 35.88 ± 8.34 years, who were predominantly male (55.2%), with a significant portion being students (34.3%). Most participants exhibited obesity, with a mean BMI of 34.84 ± 3.47 kg/m², and more than 95% had central obesity. Laboratory results indicated normal glycemic control, with a mean fasting blood sugar of 4.93 ± 0.31 mmol/L and HbA1c of 5.06 ± 0.27%. However, 86.6% of participants had low HDL levels, and a significant number had elevated triglycerides and LDL levels.At enrollment, 8 participants (11.9%) had elevated urinary ACR. After excluding cases of transient microalbuminuria, 7 participants (10.4%) were confirmed to have microalbuminuria, resulting in an overall renal involvement rate of 10.4%. Participants with microalbuminuria exhibited significantly elevated serum TNF-α levels (136.49 ± 26.49 pg/ml, $p<0.001$). Serum TNF-α levels showed a weak positive correlation with BMI, LDL, and urinary ACR. A cut-off value of ≥137.65 pg/ml for TNF-α was identified as a significant predictor of microalbuminuria, demonstrating high sensitivity and specificity.

Conclusion: TNF-α levels demonstrated strong predictive power for early renal involvement, serving as a reliable biomarker for early renal dysfunction in sedentary obese individuals and enabling timely intervention to prevent CKD progression.

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Introduction

Sedentary obesity, marked by excessive body fat and minimal physical activity, is an increasing public health issue closely linked to systemic inflammation and metabolic disorders. Among the numerous pro-inflammatory cytokines, Tumor Necrosis Factor-alpha (TNF-α) plays a pivotal role in the pathophysiology of obesity and its related complications, including chronic low-grade inflammation, dyslipidemia, and insulin resistance. TNF-α, predominantly secreted by adipose tissue in obesity, exerts significant effects on metabolic pathways and contributes to renal involvement through mechanisms like oxidative stress, endothelial dysfunction and glomerular damage. Understanding the association between TNF-α levels and renal dysfunction in sedentary obese individuals may provide insights into early biomarkers and potential therapeutic targets to prevent chronic kidney disease (CKD) progression.

Chronic low-grade systemic inflammation caused by obesity results in systemic metabolic dysfunction, which is associated with both obesity and kidney disease [1]. Albuminuria is viewed as a consequence of widespread endothelial dysfunction, which is intensified by an inflammatory state. Therefore, it is reasonable to propose that the persistent inflammation frequently seen in individuals with obesity contributes to the advancement of microalbuminuria [2].Obesity is considered a potential risk factor of microalbuminuria, particularly in individuals with diabetes and hypertension. It may also contribute to proteinuria in individuals with CKD. Some researchers propose that obesity can negatively impact kidney health even in those without a prior history of diabetes, hypertension, or existing renal conditions [3].

In obesity, the levels of certain inflammatory markers and cytokines, involving tumor necrosis factor-α (TNF-α), C-reactive protein (CRP), macrophage migration inhibitory factor (MIF), and interleukin-6 (IL-6) are increased. Conversely, the levels of adiponectin, a protein hormone with anti-inflammatory properties, are reduced [4]. Adiponectin is a peptide hormone released by anti-atherogenic, possessing anti-inflammatory, adipocytes, and anti-diabetic effects [5]. The pro-inflammatory cytokine TNF-α is mainly produced by macrophages infiltrating adipose tissue but can also be generated by the kidney. This cytokine is pivotal in the development of insulin resistance associated with obesity and the development of inflammation. Oxidized LDL, advanced glycation end-products (AGEs), and angiotensin II (AngII) are known to stimulate TNF-α production in renal cells, leading to local injury. A study demonstrated that TNF-α reduces the expression of a protein named Klotho that is produced by renal cells, via an NF-κB-dependent mechanism, thereby contributing to kidney damage [6]. TNF-α enhances glomerular permeability, impairs podocyte integrity, and plays a significant role in the development of microalbuminuria, an early indicator of renal damage [7]. Higher albumin excretion rates (AER), often observed in obese individuals, suggest an increased risk of early renal impairment and cardiovascular (CV) morbidity and mortality. Overall, the prevalence of microalbuminuria in the general population rises with total and central obesity, mostly impacting nondiabetic and nonhypertensive people [8]. Among moderately obese adolescents, the prevalence is reported at 2.4%. In cases of severe obesity, 3% exhibit proteinuria, 14% have microalbuminuria, and 3% present with a GFR below 60 mL/min/1.73 m^2 [9].

While the prevalence of albuminuria linked to obesity has been documented, this condition is frequently underdiagnosed due to the lack of clinical symptoms and insufficient screening for low-grade albuminuria. Some evidence suggests that in cases of obesity, AER increases due to hemodynamic effects, which include heightened renal blood flow and glomerular pressure. This results in glomerular hyperfiltration and increased permeability to albumin.While abnormalities in renal hemodynamics are likely a significant factor, it is also plausible that inflammatory and metabolic mechanisms play a role. Adipose tissue produces most of the components of the renin-angiotensin-aldosterone system (RAAS). Obese individuals typically exhibit elevated levels of angiotensin-converting enzyme activity, plasma renin activity, angiotensinogen, and circulating angiotensin II. Additionally, non-hemodynamic factors such as hyperinsulinemia, oxidative stress, and inflammation, along with changes in renal hemodynamics, can contribute to or worsen renal damage [10]. Proteinuria may result from these effects, which may also cause focal glomerulosclerosis, glomerular hypertrophy, and hyperfiltration. Visceral fat may also play a role in the production of various renin-angiotensin system (RAS) proteins, affect other hemodynamic factors (such as increased intra-abdominal pressure or cardiopulmonary dysfunction), and disrupt renal blood flow through compression of the renal hilum and/or renal parenchyma. Furthermore, perirenal fat appears to have lipotoxic effects on the kidney, raising glomerular hydrostatic pressure and RAAS activity, which accelerates renal damage [11]. Only a few studies worldwide have investigated the role of serum TNF-α as a predictor of renal involvement in sedentary obese individuals. Against this background, this study aims to evaluate the independent association of TNF-α with renal involvement and to explore its role as a predictor of renal involvement in sedentary obese individuals without diabetes, hypertension, or hypothyroidism.

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Methodology & Materials

Cross-sectional observational research was undertaken at the Department of Nephrology, BSMMU, Dhaka, approximately for 18 months. A total of 67 sedentary obese individuals were taken from the general population, teachers & resident doctor of BSMMU & from Obesity clinic of Endocrinology department, BSMMU. The sampling method was purposive sampling. Those who fulfilled the selection criteria (inclusion and exclusion criteria) were selected and evaluated for this study.

Inclusion Criteria

This study included individuals with a BMI of 30 kg/m² or higher.

Exclusion Criteria

Disorder affecting renal function (e.g. diabetes, hypertension), secondary causes of obesity (e.g. hypothyroidism, cushing's syndrome), conditions affecting adipocytokines e.g. psychiatric disorders, pregnancy, cancer, stroke, acute cardiovascular events or with history of abdominal surgery & all individuals takings steroid, OCP, statins & beta blocker, antidepressants (amitryptyline, mirtazepine), pregabaline, gabapentine & sodium valproate & age < 18 years were not considered for enrollment in the study.

Study procedure

Before enrollment, the objectives, purpose, and procedure of the study were thoroughly explained to the participants. The potential benefits and risks (if any) of the study were clearly outlined, with particular emphasis on how the participants would benefit from their involvement. Informed written consent was obtained in the prescribed format from them when they voluntarily consented to participate. After enrollment, a detailed medical and socioeconomic history was documented in a preformatted data sheet. A full physical examination was performed, and the results were stated.

All study participants had their body mass, height, and waist (measured at the midpoint between the lowest rib and the iliac crest) and hip (measured at the widest point over the greater trochanters) circumferences measured to calculate obesity indices as follows:

- Body mass index: BMI = weight/height (kg/m²).
- Waist-to-hip ratio: WHR = waist circumference (cm)/hip circumference (cm).

Blood pressure was measured using a sphygmomanometer in sitting posture after taking 5 minutes of rest, reducing their anxiety by explaining and reassuring that the sensation of the cuff tightening on their arm is safe.

With all aseptic precautions, 5 ml of venous blood were collected from the ante-cubital vein of the patient in a vacutainer tube and were brought to Kidney Research Laboratory (Department of Nephrology), Department of Laboratory Medicine and Department of Immunology and Microbiology for required tests to be done. Thereafter, the samples were Centrifuged @ 2200-2500 rpm for 15 min, and the obtained serum were kept frozen at -20°C. Different Hematological, biochemical and hormonal test (uACR, serum creatinine, S.TSH, Lipid profile, HbA1C) were done by fully automated SIEMENS (Dimension EXL with LM) machine through spectrophotometry method in Laboratory Medicine Department, BSMMU among the study population. Serum TNF-α level was measured by using The DRG Adiponectin ELISA Kit based on the sandwich principle. Urinary ACR was measured by ELISA method. The estimated glomerular filtration rate (eGFR) for all serum creatinine values was calculated using the Modification of Diet in Renal Disease (MDRD) formula.

Operational Definitions:

BMI:

Body mass index (BMI) is a straightforward and commonly used method for estimating body fat. It is calculated by dividing a person's weight by the square of their height, usually expressed in metric units: Weight in kg / Height in m² [12].

eGFR:

Glomerular filtration rate (GFR) is an indicator of kidney function. This test measures the creatinine level in the blood and uses the result in a formula to calculate a value known as the estimated GFR (eGFR), which reflects the efficiency of kidney function [13].

Microalbuminuria:

Microalbuminuria is defined as an abnormal increase in albumin excretion rate within the specific range of 30–300 mg of albumin/g of creatinine in a spot urine sample that persists over multiple measurements, usually taken over a period of 3 to 6 months [13]. The American Diabetes Association, the National Institutes of Health, and the National Kidney Foundation advise measuring albumin in urine using the albumin-to-creatinine ratio method [14].

Obesity: WHO Criteria for global population [15]. Underweight: BMI < 18.5 kg/m², Normal weight: BMI 18.5–24.9 kg/m², Overweight: BMI 25–29.9 kg/m², Obesity Class I: BMI 30–34.9 kg/m², Obesity Class II: BMI 35–39.9 kg/m², Obesity Class III (Morbid Obesity): BMI ≥ 40 kg/ m².

Central obesity & WHR:

Central obesity is defined by an excess of fat around the

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abdominal region, typically measured using the waist-to-hip ratio (WHR). The World Health Organization (WHO) states that a WHR greater than 0.90 in men and 0.85 in women signifies central obesity, which is linked to higher risks of metabolic and cardiovascular diseases [16].

Sedentary individuals:

All adults should engage in regular physical activity. For substantial health benefits, they should aim for 150–300 minutes of moderate-intensity aerobic exercise, 75–150 minutes of vigorous-intensity aerobic activity, or a combination of both, spread throughout the week. Additionally, adults should perform muscle-strengthening exercises targeting all major muscle groups at a moderate or higher intensity on at least two days each week to gain further health benefits. To achieve even greater health advantages, adults can increase their moderate-intensity aerobic activity to over 300 minutes per week or engage in more than 150 minutes of vigorous-intensity activity, or a combination of both. Those who do not meet these recommendations are considered sedentary [17].

Statistical analysis:

All data were recorded using a pre-defined data collection form. Quantitative data were presented as mean and standard deviation, while qualitative data were shown as frequency distributions and percentages. Statistical analyses were performed using Windows-based software, specifically the Statistical Package for Social Sciences (SPSS-27) (SPSS Inc, Chicago, IL, USA). The Mann–Whitney U test was used to compare two groups for quantitative variables that did not follow a normal distribution. The Chi-square test and Fisher's Exact test were used to compare categorical variables across different groups. Spearman's correlation coefficient (r) was used to evaluate the relationship between two non-normally distributed quantitative variables or between one quantitative and one qualitative variable. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 67 subjects were included in the study. The mean age of the participants was 35.88 ± 8.34 years, with the majority (47.8%) belonging to the >30–40 years age group. Most participants were male (55.2%), and more than one-third were students (Table 1). The systolic and diastolic blood pressure values were normal for all participants, with mean systolic and diastolic blood pressures of 117.52 ± 7.48 mmHg and 75.87 ± 5.23 mmHg, respectively. The mean BMI and waist-to-hip ratio were 34.84 ± 3.47 kg/m² and 0.92 ± 0.03, respectively (Table 2). Among the participants, 13.4% were classified as having morbid obesity, while more than 95% had central obesity (Figure 1). Additionally, 86.6% of the participants had low HDL levels. More than half of the participants had high triglyceride levels, and over one-third had high LDL levels. The total cholesterol level was elevated in 6.0% of the participants (Figure 2). The mean ACR of the participants was 20.93±29.45 with a range of (2.50-209.50). At baseline or enrollment, 8 participants (11.9%) were suffering from high levels of urinary ACR, while approximately 47.8% had elevated eGFR (Table 3). To exclude transient microalbuminuria, the urinary ACR levels of 8 participants with high urinary ACR at baseline were rechecked 3 months after the initial assessment. Of these, only 7 were confirmed to have persistent microalbuminuria. The 8 participants with high urinary ACR at baseline had a median (range) urinary ACR of (22.18–296.34) at 3 months. However, these 7 participants also exhibited high eGFR levels at 3 months. The mean BMI of the participants at 3 months was 36.90 ± 3.02 kg/m² (Table 4).

Overall, 7 participants (10.4%) were found to have microalbuminuria (Figure 3). Table 5 shows that the mean serum TNF-α level was 136.49±26.49 pg/ml in participants with microalbuminuria and 52.49±33.19 pg/ml in participants without microalbuminuria. The mean serum TNF-α level was significantly higher in participants with microalbuminuria (p-value: 0.001). Among the moderately obese participants, 5.9% developed microalbuminuria, while 12.5% of severely obese participants and 22.2% of morbidly obese participants developed microalbuminuria. A gradual increase in the proportion of participants developing microalbuminuria was observed with higher obesity categories. However, no significant association was found between the obesity category and microalbuminuria. Similarly, no significant association was observed between the waist-to-hip ratio and microalbuminuria (Table 6). Furthermore, a significant weak positive correlation was found between BMI, uACR and serum TNF-α (spearman correlation coefficient, r: 0.377, p-value: 0.002) (Figure 4), (spearman correlation coefficient, r: 0.330, p-value: 0.006) (Figure 5). Figure 6 shows the ROC analysis of serum TNF-α for predicting microalbuminuria, with an AUC value of 0.902 (95% CI: 0.760–1.00), which was statistically significant (p-value: 0.001). A cut-off value of ≥137.65 pg/ml demonstrated the highest Youden index (0.824), with 85.71% sensitivity, 96.67% specificity, 95.52% accuracy, and positive and negative predictive values of 75.00% and 98.31%, respectively (Table 7). Table 8 indicates that 6 out of 7 patients with microalbuminuria had a serum adiponectin value of ≥137.65 pg/ml.

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Table 1: Distribution of the participants according to demographic characteristics (N=67)

Demographic characteristics		Frequency	Percentage
Age (years)	18-30	18	26.9
	>30-40	32	47.8
	>40-50	13	19.4
	>50	4	6
	Mean ± SD	35.88±8.34	
	Median (Range)	35.0 (18-58)	
Gender	Male	37	55.2
	Female	30	44.8
Occupation	Housewife	11	16.4
	Business	17	25.4
	Service	14	20.9
	Student	23	34.3
	Others	2	3

SD: Standard deviation, Data was presented as mean± SD, Median (range), Frequency, percentage

Table 2: Distribution of the participants according to the physical parameters (N=67)

Physical parameters		Values
Systolic blood pressure (mm of Hg)	Mean ± SD	117.52±7.48
	Median (Range)	120.0 (100.0-130.0)
Diastolic blood pressure (mm of Hg)	Mean ± SD	75.87±5.23
	Median (Range)	78.0 (70.0-90.0)
Body mass index (kg/m2)	Mean ± SD	34.84±3.47
	Median (Range)	34.60 (30.10-44.90)
Waist Hip ratio	Mean ± SD	0.92±0.03
	Median (Range)	0.93 (0.79-0.98)
Waist circumference (cm)	Mean ± SD	110.93±6.87
	Median (Range)	110.0 (96.0-142)

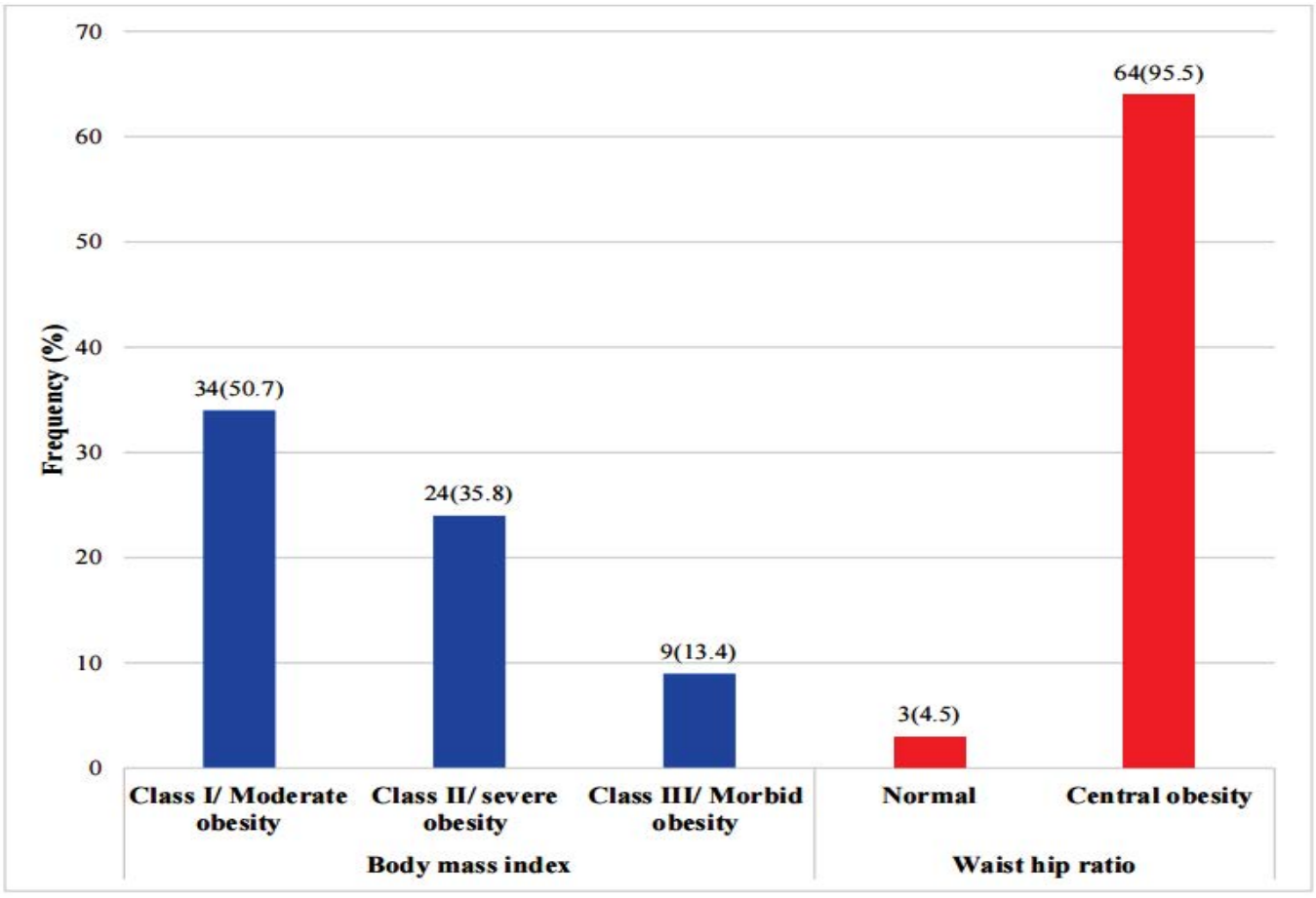

Figure 1: Distribution of body mass index, and waist-hip ratio among the study participants

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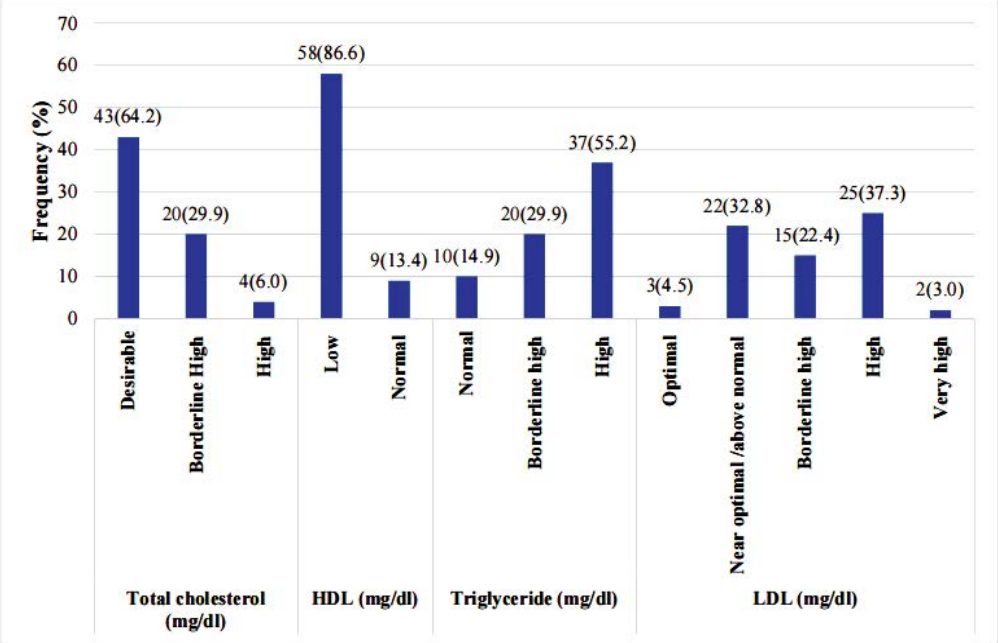

Figure 2: Distribution of the lipid profile of the study participants

Table 3: Assessment of Renal involvement at baseline (N=67)

(A)		
Parameters		**Values**
Urinary ACR	Mean ± SD	20.93±29.45
	Median (Range)	13.0 (2.50-209.50)
S creatinine (mg/dL)	Mean ± SD	1.02 ±0.14
	Median (Range)	1.04 (0.60-1.29)
eGFR	Mean ± SD	120.48±19.54
	Median (Range)	117.0 (92.0-181.0)

(B)			
Parameters		**Frequency**	**Percentage**
Urinary ACR	Normal	59	88.1
	High	8	11.9
eGFR	High	32	47.8
	Normal	35	52.2

Data was presented as mean± SD, Median (range), Frequency, percentage

Table 4: Assessment of body mass index and renal involvement at 3 months (N=8)

(A)		
Parameters		**values**
Urinary ACR (n=8)	Mean ± SD	85.18±89.70
	Median (Range)	44.87 (22.18-296.34)
Serum creatinine (mg/dl) (n=8)	Mean ± SD	0.86±0.19
	Median (Range)	0.90 (0.60-1.10)
eGFR (n=8)	Mean ± SD	154.25±22.30
	Median (Range)	159.0 (118.0-183.0)

(B)			
Parameters		**Frequency**	**Percentage**
Urinary ACR (n=8)	Normal	1	12.5
	High	7	87.5
eGFR (n=8)	High	7	87.5
	Normal	1	12.5

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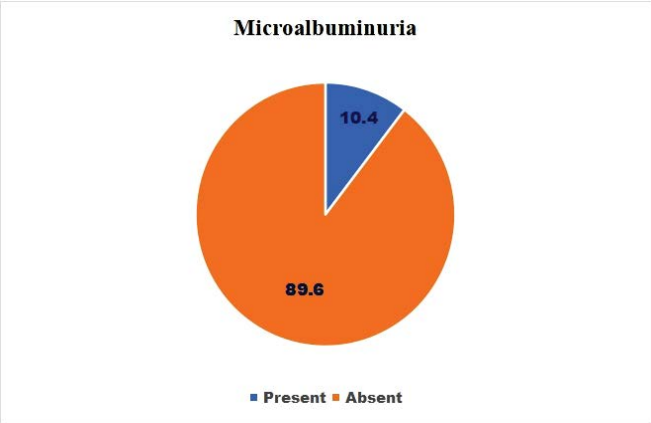

Figure 3: Distribution of microalbuminuria among the study participants

Table 5: Distribution of the Serum TNFα among participants with or without microalbuminuria (n=67)

Parameters		Microalbuminuria		P value
		Yes	No	
		(n=7)	(n=60)	
Serum TNFα (pg/ml)	Mean ± SD	136.49±26.49	52.49±33.19	<0.001
	Median (Range)	145.2 (78.30-157.50)	49.4 (5.50-147.60)	

Mann Whitney U test was done, Data was presented as Mean ± SD, median (range)

Table 6: Association of Body mass index with Microalbuminuria (n=67)

Variables		Microalbuminuria		P value
		Yes	No	
		(n=7)	(n=60)	
Body mass index	Class I/ Moderate obesity	2 (5.9)	32 (94.1)	[a] 0.333
	Class II/Severe obesity	3 (12.5)	21 (87.5)	
	Class III/morbid obesity	2 (22.2)	7 (77.8)	
Waist hip ratio	Normal	0 (0.0)	3 (100.0)	[b]>0.99
	Central obesity/ risk	7 (10.9)	57 (89.1)	

[a] Chi-square test and [b] Fisher's exact test was done, Data was presented as frequency, percentage

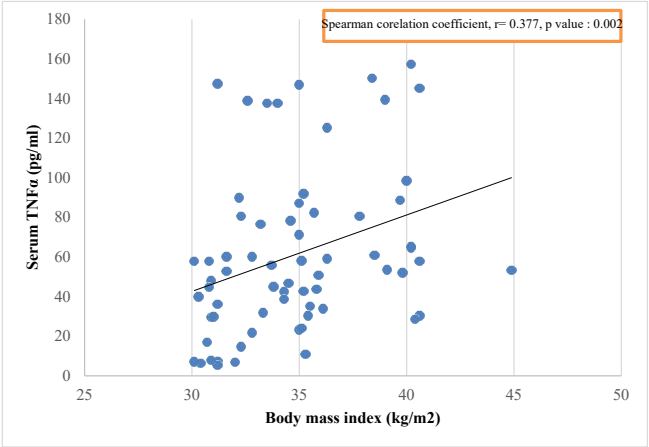

Figure 4: Correlation Of Body Mass Index with Tnfα

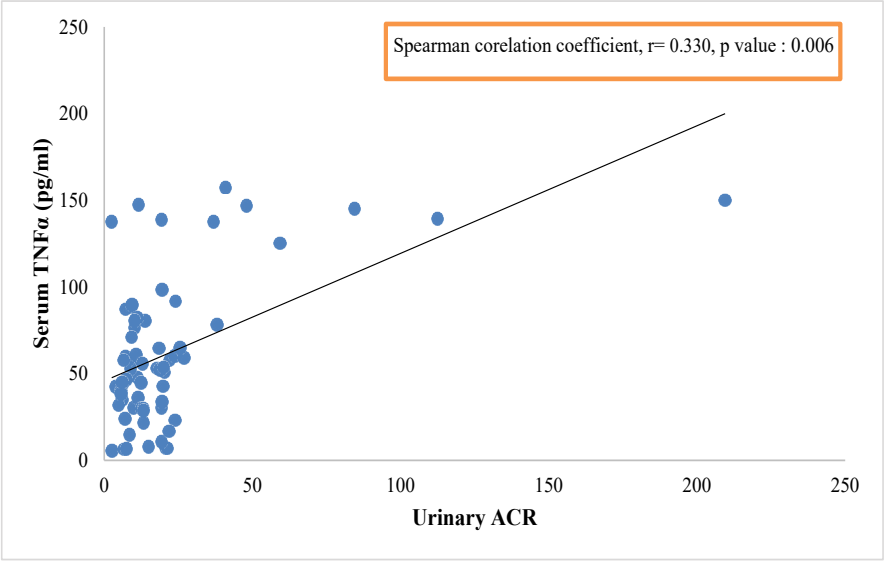

Figure 5: Correlation of urinary ACR with TNFα

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ROC analysis for the Prediction of Microalbuminuria

ROC analysis of serum TNFα to predict microalbuminuria showed an AUC value of 0.960 (95% CI 0.902-1.0) which was statistically significant (P value: <0.001).

Cut-off points

Discussion

This study observed the association between TNFα and microalbuminuria, as well as evaluated the predictive value of TNFα for the presence of microalbuminuria in sedentary obese individuals. This cross-sectional study included 67 sedentary obese individuals without diabetes, hypertension, or hypothyroidism. This study described the demographic characteristics of the participants, with an average age of 35.88 ± 8.34 years. The majority were in the 30–40 years age group (47.8%), with a male predominance (55.2%). Approximately one-third of the participants were students (34.3%), suggesting a population in early mid-life, likely pursuing postgraduate studies. This demographic distribution may indicate a higher risk of metabolic issues in males in early mid-life, potentially due to lifestyle factors such as sedentary behavior or dietary habits.Similar age and sex distributions were observed in a study by de Almeida et al. [18]. Conversely, although male prevalence was observed in studies by Kawamoto et al. [19], Chen et al. [20], and Song et al. [21], the mean age in these studies was significantly higher. In contrast, studies by Mackowiak-Lewandowicz et al. [22] and El-Shaheed et al. [23] focused on a younger demographic, with participants averaging 13.06 ± 2.61 years. This difference could be attributed to variations in target sample selection, as different studies targeted distinct demographic groups. In this study, physical parameters were analyzed, revealing that all participants had normal systolic and diastolic blood pressure levels, with mean values of 117.52 ± 7.48 mmHg and 75.87 ± 5.23 mmHg, respectively. The mean BMI was notably high at 34.84 ± 3.47 kg/m², indicating widespread obesity among the participants. Additionally, the waist-to-hip ratio averaged 0.92 ± 0.03, further suggesting central obesity. This was confirmed by Figure 1, which showed that over 95.5% of participants exhibited central obesity, and 13.4% were classified as morbidly obese.This data underscores the significant burden of obesity-related health risks, potentially exacerbating cardiovascular and metabolic conditions. A similar BMI range (approximately 34.9 ± 7.33 to 37.5 ± 3.88 kg/m²) was reported in comparable studies [18, 23-25].

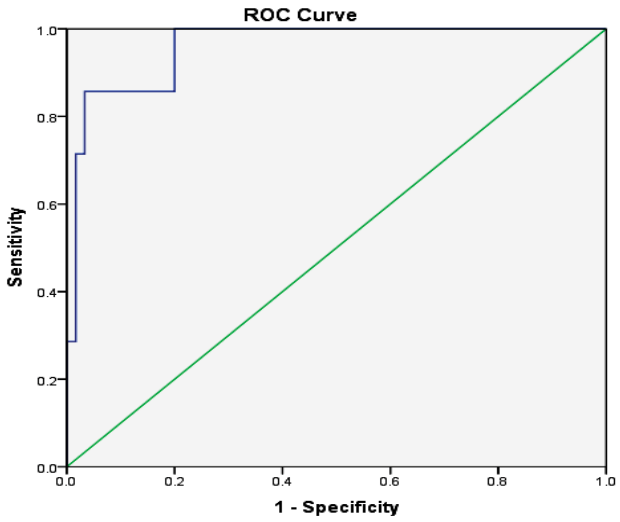

Figure 6: Receiver operator characteristics (ROC) curve of serum TNFα to predict Microalbuminuria

Table 7: Determination of cut-off value with Youden index

Cutoff value	Sensitivity	Specificity	PPV	NPV	Accuracy	Youden index (j=sen+spe-1)
≥131.45	0.8571	0.95	0.6667	0.9828	0.9403	0.807
≥137.65	**0.8571**	**0.9667**	**0.75**	**0.9831**	**0.9552**	**0.824**
≥138.35	0.7143	0.9667	0.7143	0.9667	0.9403	0.681

Table 8: Cross-tabulation of microalbuminuria with serum TNFα value based on derived cut-off value

Serum TNFα (pg/ml)	Microalbuminuria		Total
	Yes	Yes	
≥137.65	6	2	8 (TP+FP)
<137.65	1	58	59 (FN+TN)
Total	7 (TP+FN)	60 (FP+TN)	67 (TP+FP+FN+TN)

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Physical parameters were also consistent with findings from other studies [21,26]. The similarity in physical parameters across studies can be attributed to the fact that individuals with comparable height, weight, and BMI tend to exhibit similar pulse and blood pressure values.

The study also presented laboratory parameters, where the mean fasting blood sugar was within normal limits at 4.93±0.31 mmol/L, and the mean blood sugar two hours after glucose intake was 6.88±0.63 mmol/L. The HbA1c levels were also normal at 5.07±0.27, indicating adequate glycemic control in this population. The median TSH level was 2.9 mIU/L, with a range of 1.15-4.62, suggesting normal thyroid function. However, concerning lipid profiles (Figure 2), 86.6% had low HDL levels, and a significant portion had elevated TGs and LDL levels, with 6.0% exhibiting high total cholesterol. These results indicate a significant prevalence of dyslipidemia, which is a key risk factor for cardiovascular disease. Low HDL and high levels of triglycerides (TG), cholesterol, and LDL were also observed in previous studies [19, 20, 18, 25, 27]. El-Shaheed et al. [23] reported that blood glucose levels were nearly similar between obese and non-obese patients.Another study found that approximately one-third of participants had an elevated albumin-to-creatinine ratio (ACR), while the remaining two-thirds had ACR levels within the normal range. Related studies also reported elevated serum creatinine in overweight or obese patients [19, 20, 25]. Studies by Kawamoto et al. [19] and Chen et al. [20] observed that about 8.78% of patients had decreased eGFR, whereas Mackowiak-Lewandowicz et al. [22] found no decrease in eGFR among their study population. Differences in renal parameters could be attributed to participants being in different categories of obesity, as various obesity categories may affect kidney function differently. The follow-up data at three months included only those participants who were microalbuminuric at enrollment to exclude transient microalbuminuria. Of these, seven out of eight participants with initially high ACR continued to show elevated ACR (median: 22.18–296.34), while one participant became normoalbuminuric, suggesting either transient microalbuminuria or the beneficial effects of weight-loss strategies such as physical exercise and diet control. Additionally, 10.4% developed microalbuminuria, a marker of ongoing renal damage. Notably, participants with microalbuminuria had a higher mean BMI (36.95 ± 3.02 kg/m²) and higher eGFR, indicating that obesity is closely linked to renal stress and subsequent proteinuria. One study identified a significant relationship between microalbuminuria and HbA1c, postprandial blood glucose, and uric acid levels, but no association with ACR, BMI, or eGFR [27]. Only Mackowiak-Lewandowicz et al. [22] found a link between microalbuminuria, eGFR, and BMI z-scores, but their study was conducted in a younger age group. Thus, limited similarities were observed concerning these variables.

This study also highlighted that serum TNF-α levels were significantly higher in participants with microalbuminuria (136.49 ± 26.49 pg/ml) compared to those without microalbuminuria (52.49 ± 33.19 pg/ml), with a p-value of <0.001. Elevated TNF-α, a marker of inflammation, indicates that systemic inflammation may contribute to the development of microalbuminuria, further linking obesity and inflammatory pathways to kidney damage. These findings are supported by several international studies, which have shown that elevated TNF-α levels are associated with microalbuminuria, obesity, and ultimately linked to CKD [18, 24, 25].The present study reported a significant weak positive correlation of BMI (r=0.377, p=0.002), LDL (r=0.359, p=0.003), urinary ACR (r=0.330, p=0.006) and eGFR (r=0.258, p=0.035) with serum TNFα levels. This suggests that increased adiposity and dyslipidemia are associated with higher inflammatory markers, which could contribute to the development of microalbuminuria and other obesity-related complications. Barakat et al. [25] explored the correlation between LDL and TNF-α but found no significant association. Conversely, Lee et al. [24] observed that increased TNF-α is a significant predictor of chronic kidney disease (CKD). The study also examined the relationship between BMI and microalbuminuria, noting that while the prevalence of microalbuminuria increased with the severity of obesity, this association was not statistically significant. This finding suggests that factors beyond BMI may influence renal health. Similarly, the waist-to-hip ratio did not show a significant correlation with microalbuminuria. Additionally, the study determined the optimal cut-off value for TNF-α as a biomarker for predicting microalbuminuria. A serum TNFα level of ≥137.65 pg/ml provided the highest diagnostic accuracy with a Youden index of 0.82, sensitivity of 85.71%, and specificity of 96.67%. This cut-off suggests that high TNF-α levels are strongly predictive of microalbuminuria, emphasizing the role of inflammation and adipokine imbalance in the pathophysiology of renal damage in obese individuals.These findings are unique to this study. To the best of our knowledge, no prior studies have explored predictive cut-off values for TNF-α. Further exploratory studies are recommended to validate and standardize these cut-off points for this biomarker. In the present study, 7 participants (10.4%) were found to have renal involvement in the form of microalbuminuria. The median (range) serum TNFα level was 147.0 (78.30-181.20) pg/ml in participants with renal involvement and 48.0 (5.50-147.60) pg/ml in participants without renal involvement. The serum TNFα level was significantly higher in participants with renal involvement (p-value: <0.001).

Conclusion

This study reveals a strong connection between increased serum TNF-α levels and microalbuminuria in sedentary obese

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individuals, emphasizing the role of systemic inflammation in the development of obesity-related kidney damage. Participants with microalbuminuria exhibited significantly higher TNF-α levels, with a cut-off value of ≥137.65 pg/ml showing strong diagnostic accuracy, sensitivity, and specificity for predicting microalbuminuria. These findings suggest that TNF-α could serve as a valuable biomarker for early detection of renal stress in obese individuals.The high prevalence of dyslipidemia and central obesity among participants further underscores the critical interplay between metabolic dysregulation and kidney health. Although the study did not establish a statistically significant association between BMI and microalbuminuria, the weak positive correlation between BMI, LDL, ACR, eGFR, and TNF-α levels emphasizes the multifactorial nature of obesity-related renal dysfunction.This study uniquely identifies a TNF-α predictive cut-off for microalbuminuria, laying the foundation for future research to validate and standardize its use as a biomarker.

Limitations of the study

The study is limited by a relatively small sample size, which may not have enough statistical power to identify smaller yet potentially significant associations. Furthermore, the cross-sectional design limits the ability to establish causal relationships between obesity, inflammation, and renal dysfunction. Furthermore, the study did not include a detailed and comprehensive assessment of dietary patterns, lifestyle data, physical activity levels, or genetic factors, which may influence both adipocytokine levels and renal outcomes.

Recommendations

Further longitudinal and interventional research is necessary to establish causal relationships and evaluate the effects of targeted therapies on inflammation and renal health in obese populations. Serum TNF-α levels could serve as a valuable biomarker for the early detection of microalbuminuria, particularly in obese individuals at heightened risk of kidney damage. Regular screening for microalbuminuria in obese individuals should be implemented to identify early renal stress and enable timely management. Dyslipidemia should be addressed through lifestyle changes, such as improving diet and increasing physical activity, and supplemented with pharmacological treatments when needed to mitigate metabolic complications. Additionally, promoting weight loss strategies, including consistent exercise and dietary improvements, is crucial for reducing inflammation and enhancing renal health in sedentary obese individuals.

Conflict of Interest: None declared.

Ethical approval: The study was approved by the institutional Ethics committee.

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