

Relation between obesity and diabetic nephropathy among patients with type 2 diabetes

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Abstract

Objective: The most frequent consequence of diabetes mellitus (DM) is diabetic nephropathy (DN), and obesity is a prominent risk factor for DM. This cross-sectional study aimed to investigate the relationship between obesity and diabetic nephropathy in patients with type 2 diabetes mellitus (T2DM).

Methods: This cross-sectional retrospective study included 60 patients with T2DM (32 men and 28 women) aged 44 to 86 years (mean age 62.0 (10.0) years). Those patients included who have had T2DM for more than five years. Anthropometric parameters measured included body mass index (BMI), blood pressure (BP), and blood tests for glucose, glycosylated hemoglobin (HbA1C), total cholesterol, triglycerides, high-density lipoprotein (HDL), and low-density lipoprotein (LDL). The severity of diabetic nephropathy was assessed by the level of microalbuminuria in urine excretion. The patients were categorized into two groups: those with obesity (BMI ≥ 30 kg/m²) and those without (BMI < 30 kg/m²).

Results: The prevalence of microalbuminuria increased ($p < 0.05$) in type 2 diabetic patients with a BMI ≥ 30 kg/m². We frequently observe elevated BP, triglycerides, total cholesterol, low HDL- and high LDL in patients with T2DM who have a BMI greater than 30 kg/m² compared with those who have a BMI less than 30 kg/m².

Conclusion: The development of diabetic nephropathy is significantly influenced by obesity in T2DM. However, in our investigation, no meaningful relation was found between HbA1c, lipid profile, and DN.

Key words: Obesity, type 2 diabetes mellitus, diabetic nephropathy, microalbuminuria

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Highlights:

- When it comes to diabetic nephropathy (DN), obesity is frequently disregarded, which might worsen the clinical and therapeutic results.
- This study confirms that obesity and hypertension in T2DM patients have a significant impact on the development of DN.
- Obesity worsens hemodynamic irregularities at the intrarenal and systemic levels, which affect kidney function and exacerbate the onset of sclerotic changes.

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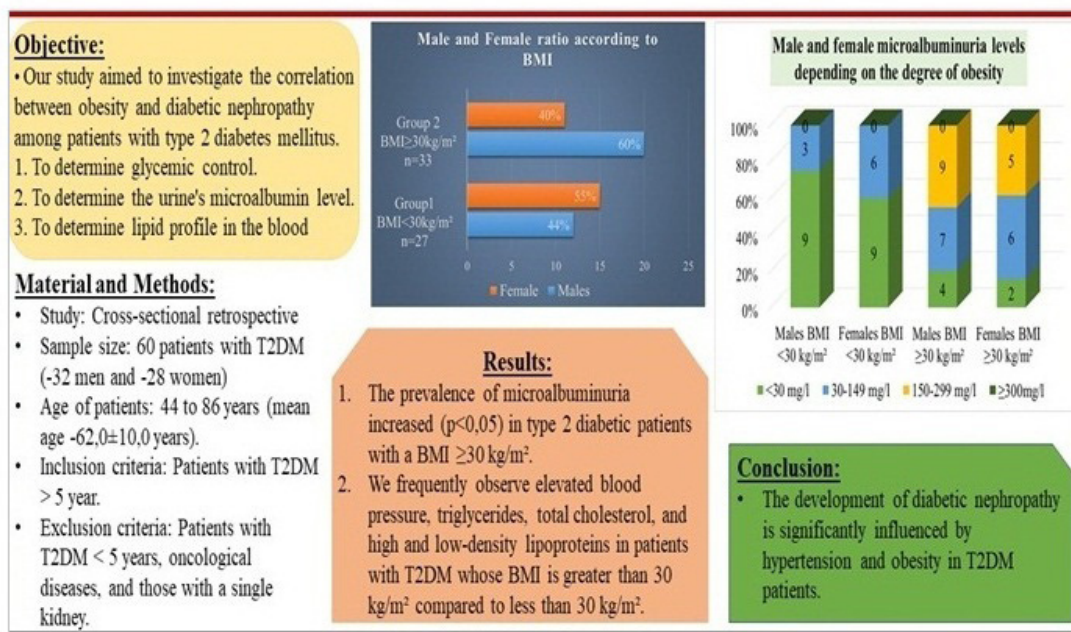
Graphical abstract



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Correlation between obesity and diabetic nephropathy among patients with type 2 diabetes

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Introduction

Type 2 diabetes mellitus (T2DM) is a group of heterogeneous disorders with persistent hyperglycemia (1). According to the International Diabetes Federation (IDF), it is estimated that 589 million people aged 20 to 79 have diabetes. More than 4 out of 5 diabetic adults (81%) reside in low- and middle-income nations (2). Approximately 1.6 million deaths are directly caused by this illness each year (3). The World Health Organization (who) has labeled the recent surge in diabetes and obesity epidemics a "21st Century epidemic" (4).

Diabetic nephropathy (DN) is a common microvascular complication of T2DM and the leading global cause of end-stage renal disease, contributing significantly to morbidity and mortality. It affects nearly 40% of patients after approximately ten years of diabetes duration (5). The most prevalent cause of end-stage kidney disease in developed nations is DN, which affects 20–40% of patients in need of dialysis and/or transplantation (6).

Globally, obesity and chronic kidney disease (CKD) are significant public health issues. The WHO uses the body mass index (BMI) to categorize obesity, which it describes as "an excessive or abnormal accumulation of fat that poses a health

risk." Adipocytes, however, also have strong endocrine roles. They secrete a variety of cytokines and adipokines that cause insulin resistance and a persistent low-grade inflammatory state, which harms the kidneys. The onset of CKD is linked to several metabolic changes that worsen insulin resistance and adipose tissue dysfunction (7, 8). Obesity is a risk factor for CKD-related disability and mortality after adjusting for diabetes and hypertension (9, 10). An estimated 74,801 people in the Kyrgyz Republic have diabetes mellitus as of 2021, making up 12% of the country's total population (11). The onset of albuminuria without renal failure (CKD stages 1-2) and CKD stages 3 and higher is predicted by a high BMI; the effect is significant only in obese persons (12). The progressive loss of kidney function brought on by a reduction in the number of functional nephrons is the hallmark of **CKD**.

Regardless of the cause, CKD is defined by KDIGO (Kidney Disease: Improving Global Outcomes) as a glomerular filtration rate (GFR) of less than 60 mL/min/per 1.73 m² or the presence of kidney damage indicators, or both, for a minimum of three months (13).

Obesity is a recognized contributor to T2DM and has been increasingly implicated in DN; however, the extent to which

obesity independently influences the onset and progression of diabetic nephropathy remains to be fully elucidated. Some studies indicate that metabolic syndrome, including obesity, may be associated with the development of DN.

The aim of study was to investigate the relationship between obesity and diabetic nephropathy among patients with T2DM.

Methods

Study design and population

The study design is retrospective observational study. The data were gathered retrospectively from medical records for the period January 2024 - October 2024 at the Vedanta University Clinic in Bishkek, Kyrgyz Republic.

A total of 60 T2DM patients were included in the study; 32 were men, and 28 were women, with ages ranging from 44 to 86 (mean age 65 (10) years). The WHO's (1998) recommendations were followed in establishing the diagnosis of T2DM.

Patient Selection:

Two patient groups were identified based on BMI:

- Group 1 was considered to be non-obese (BMI < 30 kg/m²).
- Group 2 was considered to be obese (BMI ≥ 30 kg/m²).

Inclusion criteria: patients with T2DM and age >40 years. Exclusion criteria: patients with a single kidney, primary hypertension > 2nd stage, hemodynamically significant stenosis of the renal arteries, primary kidney damage within the context of systemic connective tissue illnesses, chronic glomerulonephritis, oncological diseases, and those with diabetes for less than five years.

Informed consent was obtained from patients for all procedures. The study was retrospective and used anonymized data; therefore, the Institutional Ethics Committee of (IHSM) waived the requirement for ethics approval. The study complies with the principles of the Declaration of Helsinki 2024.

Baseline variables

All patients demographic, disease duration, blood pressure levels, total cholesterol (TCH), triglycerides (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) cholesterol, blood sugar, and creatinine levels were analyzed in the blood serum collected after an overnight fast of 14 hours. Blood pressure (BP) was measured in each patient to check the hypertension stages.

Obesity and body mass index

The formula for calculating BMI is weight in kilograms divided by height in meters squared. Adults with a BMI of 25–29.9 kg/m² were considered overweight or pre-obese, and those with a BMI of ≥ 30 kg/m² were considered obese (14).

Outcome variables

High-performance liquid chromatography was used to determine glycated hemoglobin (HbA1c) levels. The recommended cut point for the diagnosis of diabetes is a HbA1c of 6.5%. A glucose test result of less than 6.5% does not rule out diabetes (15).

Glomerular Filtration Rate (GFR) and albuminuria levels were used to assess kidney damage. CKD was diagnosed according to KDIGO. Hyperfiltration was indicated by a GFR exceeding 130 ml/min/1.73 m², as determined by urine albumin excretion levels.

DN was diagnosed on the basis that urine albumin levels: below 30 mg/L were considered normal, levels between 30–299 mg/L indicated microalbuminuria, and levels exceeding 300 mg/dL that were confirmed on at least 2 occasions, 3–6 months apart, were classified as macroalbuminuria (16).

Statistical analysis

To perform statistical analysis, the 2010 Excel was used for data entrance. SPSS for Windows, version 16 was used for statistical analysis. Mann-Whitney method was used to assess the significance of the differences between the two groups (n) in study variables and microalbuminuria. A p-value of <0.05 was considered reliable.

Results

Baseline characteristics of participants

The baseline characteristics of both groups are summarized in Table 1. Baseline demographics show both groups, which were further divided into male and female, were comparable, with a p-value >0.05. The two groups had similarities in terms of sex, age, T2DM, and its duration.

The average HBA1C levels in males with and without obesity did not differ, according to the study's findings. However, the average HBA1C level in non-obese women was though not significantly lower (6.6 (2.7))% than in obese women (7.3 (0.9))%, (p=0.49).

BP among males with a BMI below 30 kg/m² was significantly (p<0.05) lower than that of males with a BMI of 30 kg/m² or higher. Conversely, the opposite is true for females. The obese group had significantly lower lipid profile readings than the non-obese group, however there were no statistically significant difference.

Relation between obesity and DN

The study's results indicated that obese individuals had a higher rate of kidney injury compared to those who were not obese; notably, microalbuminuria occurred much more often in obese patients (Fig. 1).

Table 1. Baseline characteristics of obese and non-obese patients

Variables	Group 1 BMI <30 kg/m ² (n=27)		Group 2 BMI ≥30 kg/m ² (n=33)		p
	Male (n=12)	Female (n=15)	Male (n=20)	Female (n=13)	
Age, years	65.8 (11.3)		62.4 (8.9)		0.21
BP average value, mmHg	134/86	150/90	142/84	140/84	-
HBA1c, %	7.5 (2.3)	6.6 (2.7)	7.5 (2.1)	7.3 (0.9)	0.49
Total-C, mmol/l	4.1 (1.6)	4.7 (1.6)	4.2 (1.1)	4.8 (1.1)	0.97
TG, mmol/l	1.9 (1.2)	2.0 (1.1)	2.1 (1.3)	1.7 (1.3)	0.95
HDL-C, mmol/l	1.3 (0.5)	1.6 (0.6)	1.5 (0.5)	1.4 (0.4)	0.94
LDL-C, mmol/l	2.3 (1.0)	2.6 (1.2)	2.1 (0.8)	2.9 (1.2)	0.83

Values are shown as mean (standard deviation), except for blood pressure (average)
 Mann Whitney test
 BMI - body mass index, BP - blood pressure, HDL-C - high-density lipoprotein cholesterol, LDL-C - low-density lipoprotein cholesterol, Total-C - total cholesterol, TG - triglycerides

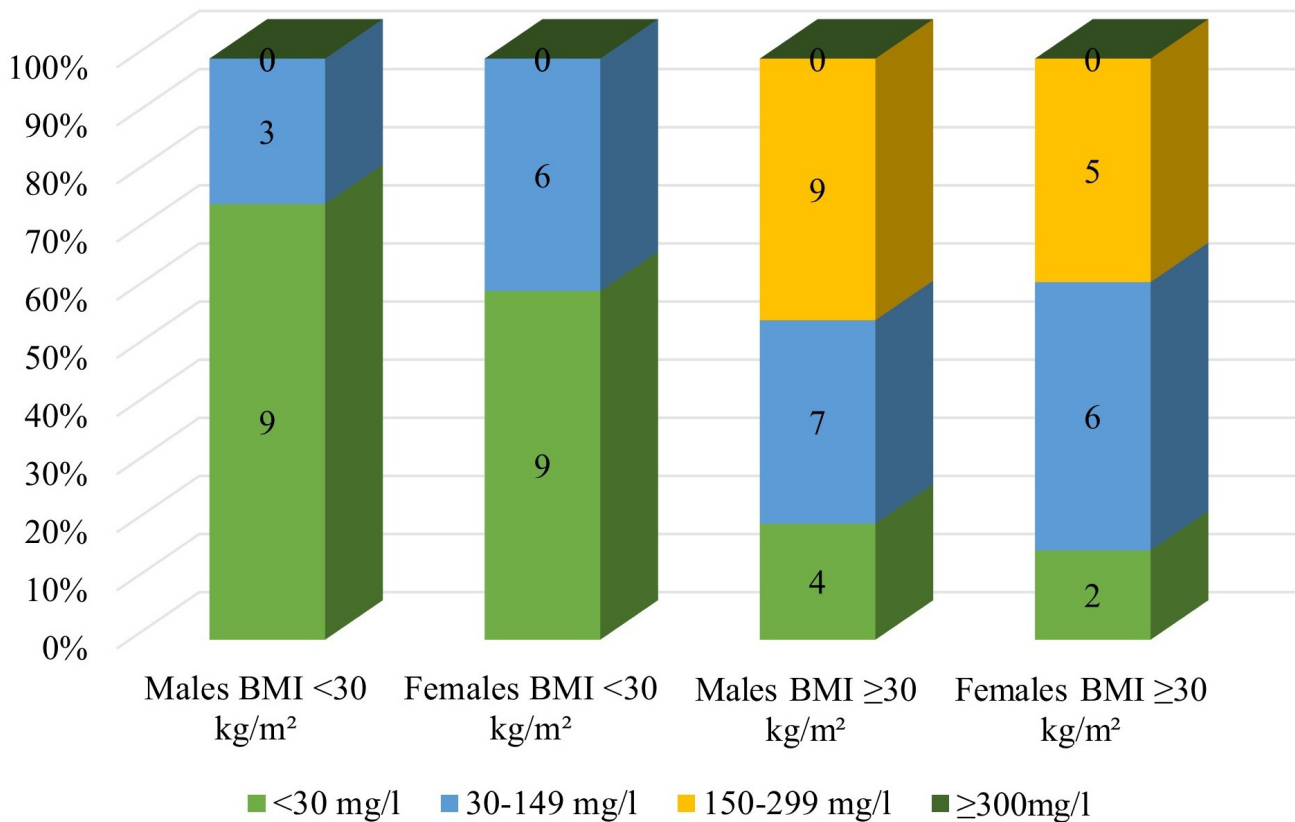


Figure 1. Male and female microalbuminuria levels depending on the degree of obesity

BMI - body mass index

The Mann-Whitney U test found that microalbuminuria was significantly more common in obese subjects than in normal-weight individuals (U = 547.0, p<0.001) (Table 2).

Variables	Normal weight (n=27)	Obesity (n=33)	Mann Whitney U	p
Microalbuminuria	9 of 27	27 of 33	547	<0.001
T2DM – type 2 diabetes mellitus				

Discussion

Our study findings show that obese people irrespective of sex have a significantly higher risk for DN, which will lead to CKD, than non-obese patients. According to our study's findings, people who are obese have a higher frequency of renal injury than those who are not.

The three main risk factors for DN are genetic susceptibility, elevated BP, and hyperglycemia (17). The development or progression of several diseases, including diabetes, heart failure, CKD, and neuropsychiatric disorders, has been studied in relation to sex differences. Male patients had a higher risk of CKD progression and death than female patients, according to a recent study from the Chronic Renal Insufficiency Cohort, which comprised 3,939 people (of whom half had diabetes) (18). In a two-sample Mendelian randomized study, Kjaergaard et al. (19) found similar findings when they investigated the direction and causality of the association between kidney function and obesity. In individuals with T2DM, a high BMI was linked to compromised kidney function (19).

Although the lipid profile varies as nephropathy progresses, blood lipids, notably triglycerides (11, 12), are associated with the onset and course of nephropathy (20–22). DN patients have lower levels of HDL apolipoprotein A-I (ApoA-I) and higher plasma concentrations of triglycerides, cholesterol, and lipoproteins linked to apolipoprotein B (ApoB) very low-density lipoproteins, intermediate-density lipoproteins, LDL, and lipoprotein(a) (Lpa) (23). A more profound comprehension of the mechanisms underlying obesity-induced kidney disease is necessary, given the rising incidence of both conditions (8). At both systemic and intrarenal levels, obesity worsens hemodynamic abnormalities that influence kidney function and speed up the progression of sclerotic changes. Lipid metabolism disorders can also be nephrotoxic. However, in our study, there were no significant differences in lipid profile of patients with and without obesity.

Study limitations

Although this study offers encouraging data on the relationship between obesity and CKD in T2DM patients, it has some limitations. It was carried out at a single center with a limited sample size (n=60), which may restrict how broadly the findings apply. Our findings suggest that further research at the molecular level is needed, especially since leptin levels have been associated with a higher risk of CKD.

Conclusion

Based on our data, the development of diabetic nephropathy is significantly affected by presence of obesity in type 2 diabetes mellitus. However, there was no significant association observed between HbA1c, lipid profile, and DN in our study.

Ethics: Informed consent was obtained from patients for all procedures. The study was retrospective and used anonymized data; therefore, the Institutional Ethics Committee of (IHSM) waived the requirement for ethics approval. The study complies with the principles of the Declaration of Helsinki 2024.

Peer-review: External and internal

Conflict of interest: None to declare

Authorship: M.U. and A.Z.M. equally contributed to the study and manuscript preparation and thus fulfilled all authorship criteria.

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Statement on A.I.-assisted technologies use: During the preparation of this work, the authors used Grammarly (Grammar check) and QuillBot (Paraphraser) as grammar-checking and paraphrasing tools. After using this tool, the authors reviewed and edited the content as needed and took full responsibility for the content of the published process.

Data and material availability: The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request. Any share should be in frame of fair use with acknowledgement of source and/or collaboration

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