



# Food & Health

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## Journal

### Waist-to-Height Ratio and Relative Fat Mass Index Are Predictors of Diabetic Kidney Disease

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#### ARTICLE INFO

##### Original Article

##### Article history:

Received 10 July 2025

Revised 14 September 2025

Accepted 27 September 2025

Available online 29 September 2025

##### Keywords:

Waist-to-height ratio,  
Relative fat-mass,  
Central obesity,  
Diabetic nephropathy,  
Type 2 diabetes mellitus

#### ABSTRACT

This study explored the association between anthropometric indices of central obesity and diabetic kidney disease (DKD). In this study, 206 patients with type 2 diabetes were recruited from the Labafinezhad clinic in Tehran, Iran, using convenience sampling. Dietary variables were assessed using a food frequency questionnaire (FFQ). Waist-to-Height Ratio (WHtR) and relative fat mass index (RFM) were calculated based on their formulas. The associations between WHtR and RFM, and DKD were assessed by logistic regression models. The results of the study showed that waist circumference and diabetes duration were higher in cases, and eGFR and physical activity were lower than in controls ( $p < 0.005$ ). There were no significant differences in age, weight, height, BMI, HbA1C, gender, education level, blood pressure, and smoking status between cases and controls. We found a positive significant association between WHtR and DKD both in the crude (OR: 120.355; 95% CI: 3.037 – 4769.930;  $P = 0.011$ ) and adjusted models (OR: 1984.994, 95% CI: 21.725 – 181366.161);  $p < .001$ ). There was no significant association between RFM and DKD in the crude model (OR: 1.014; 95% CI: 0.982 – 1.048,  $p = 0.392$ ); however, after adjusting for confounders, we found a direct association between RFM and the odds of DKD (OR: 1.154; CI: 1.060 – 1.256,  $p < .001$ ). We found a direct association between RFM and WHtR and DKD risk in type 2 diabetic patients, so they could be used as valuable and simple indicators to predict DKD in this population.

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#### 1. Introduction

Diabetes is one of the global health emergencies and challenges of the 21st century (1). The latest data have shown that the number of diabetic patients rose from 200 million in 1990 to 830 million in 2022(2). Direct health expenditures due to diabetes will increase by 2030 (1).

Diabetic kidney disease (DKD) occurs in 20-40% of patients with diabetes and eventually leads to kidney transplantation and end-stage renal disease (ESRD) (3, 4). Several factors, such as insulin resistance, hyperglycemia, hyperlipidemia, and

hypertension, play a role in the development of DN. Diabetes and being overweight, as well as other issues like hypertension that are part of metabolic syndrome, all tend to work together and lead to the development of kidney problems (5).

Historically, BMI, a commonly used metric, has served as a standard index of obesity; however, it does not fully reflect metabolic health or disease risk (9) and does not differentiate between fat and muscle mass (6). Results of a meta-analysis found that BMI fails to accurately reflect excess body fat percentage in around 50% of people when assessed by reference methods (7).

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It has been shown in a cohort study that abdominal fat assessed through waist circumference, regardless of overall body fat, is a more significant factor in CKD risk for adults than BMI. Moreover, cross-sectional studies have indicated that the waist-to-height ratio (WHtR) outperforms waist circumference (WC) in identifying CKD and CVD risk factors (8, 9). A systematic review showed that the waist-to-height ratio, compared with waist circumference and BMI, is preferred for identifying cardiometabolic risk factors (10). In previous studies, it has been shown that the waist-to-height ratio is associated with metabolic syndrome in patients with type 2 diabetes (11).

The relative fat mass (RFM) index, developed by Woolcott et al., uses waist circumference and height to provide a more precise estimate of total body fat percentage in adults (12). It has been shown that RFM is associated with diabetes (13), chronic kidney disease (CKD) (14), hypertension (15), and heart failure (16).

Based on these results, WHtR and RFM seem to have significant potential as an indicator of chronic disease risk. Nonetheless, the association between WHtR and RFM and DKD is still inadequately examined. It is proposed that WHtR and RFM could act as anthropometric indicators for detecting individuals at risk for DKD.

## 2. Materials and Methods

### 2.1 Study population

This case-control study was performed in Labafinezhad Hospital in Tehran, Iran, during 2023-2024. We utilized a convenience sample method to select the participants. Using Fleiss' formula with a confidence level of 95% and a power of 80%, the sample size was calculated to be 206. Due to incomplete biochemical data, misdiagnosis, incomplete dietary data, and reported energy intakes of more than 4200 kcal per day, 32 participants were excluded. A total of 103 diabetic patients with nephropathy were included in the case group, and 103 diabetic patients without nephropathy from the same center formed the control group for the study. We matched cases and controls for age and gender. An endocrinologist and nephrologist diagnosed diabetes and nephropathy using the diagnostic criteria set by the American Diabetes Association and Kidney Disease: Improving Global Outcomes (KDIGO)(17). The aim of the study was described to all individuals, and informed consent was obtained to enroll in this study. The National Committee for Ethics in Biomedical Research, Iran Ministry of Health and Medical Education, approved the study protocol with the following identification: (IR.IAU.SRB.REC.1401.393).

### 2.2 Inclusion and exclusion criteria

The study included individuals aged 18-65 who had type 2 diabetes mellitus. Individuals with a history of autoimmune diseases, cancer, chronic liver conditions, gastrointestinal issues, coronary artery bypass graft surgery, stroke, dialysis, or who were pregnant or breastfeeding, were excluded from the study. We also omitted participants whose response to the FFQ

was below 80% or whose total energy intake was reported as <800 or >4200 kcal per day (18).

### 2.3 Data collection

General variables such as sex, age, educational attainment, smoking habits, duration of diabetes, and previous medical and medication history were documented. Participants' weight (kg) was recorded while they were in light clothing and without shoes. A tape that does not stretch was utilized to assess height and waist circumference (WC). We assessed height while standing without shoes and WC, measuring from the upper part of the pelvic bone to the lower edge of the ribs. We calculated the body mass index (BMI) by dividing weight by height squared ( $\text{kg/m}^2$ ). WHtR was calculated as: waist circumference/height, RFM was calculated as:  $[64 - (20 \times \text{Height}/\text{WC}) + (12 \times \text{sex})]$ , with sex = 0 (men), and sex = 1 (women)](19).

Blood pressure was assessed in a seated position with a sphygmomanometer. A valid physical activity questionnaire was utilized to assess the participants' physical activity levels (20). Biochemical metrics, such as serum creatinine and HbA1c, were extracted from the patient's medical history. The 2021 CKD-EPI eGFRcr equation from the Chronic Kidney Disease Epidemiology Collaboration was employed to determine eGFR (21).

### 2.4 Dietary intake assessment

A trained dietitian utilized a semi-quantitative FFQ comprising 147 items, which is valid and reliable (30), through direct interviews to assess the dietary intake of the participants. We employed household measurements to convert the consumption frequency of each food into grams.

### 2.5 Assessment of the dietary antioxidant quality score

### 2.6 Statistical analyses

SPSS 27 (SPSS, IBM, USA) was used for statistical analysis. A p-value less than 0.05 was considered significant. Qualitative variables were reported as frequency (%) and were assessed between case and control groups using the Chi-square test. Quantitative variables were presented as mean  $\pm$  standard deviation (SD), and their normality was evaluated using the Kolmogorov-Smirnov test. An independent t-test for the normal quantitative variables, and the Mann-Whitney-U test for variables that were not normally distributed was conducted to compare the variables between two groups. The association between WHtR and RFM, and DKD was evaluated using binary logistic regression.

## 3. Results

### 3.1 General characteristics of participants

The demographic characteristics, anthropometric measurements, and biochemical markers of the case and control groups are presented in detail in Table 1. There were significant

differences in waist circumference and diabetes duration between cases and controls, which were significantly higher in cases ( $p < 0.05$ ). Physical activity and eGFR were significantly lower in the case group ( $p < 0.05$ ). No significant differences

were observed in age ( $p = 0.052$ ), weight ( $p = 0.062$ ), height ( $p = 0.655$ ), BMI ( $p = 0.115$ ), HbA1c ( $p = 0.242$ ), sex ( $p = 0.577$ ), education level ( $p = 0.314$ ), blood pressure ( $p = 0.130$ ), and smoking status ( $p = 0.497$ ) between cases and controls.

**Table 1 . General characteristics of diabetic patients with and without diabetic nephropathy**

variable		Cases (n=103)	Controls (n=103)	p-value
	Age (year)	58.12 $\pm$ 5.702	56.53 $\pm$ 5.916	.052
	Weight (kg)	82.01 $\pm$ 15.693	78.25 $\pm$ 12.904	.062
	Height (cm)	164.02 $\pm$ 9.518	163.41 $\pm$ 10.068	.655
	Waist circumference (cm)	102.42 $\pm$ 12.147	97.38 $\pm$ 10.466	.002
	BMI (kg/m <sup>2</sup> )	30.5905 $\pm$ 5.99563	29.3917 $\pm$ 4.82179	.115
	Diabetes duration (years)	16.09 $\pm$ 8.593	10.78 $\pm$ 8.496	<0.001
	eGFR (mL/min/ 1.73 m <sup>2</sup> )	41.88 $\pm$ 18.210	82.30 $\pm$ 11.951	<0.001
	HbA1c (%)	8.5 $\pm$ 1.8	8.3 $\pm$ 2.0	.242 <sup>1</sup>
	PA (MET/hr/week)	175.7476 $\pm$ 38.67495	198.8328 $\pm$ 58.28104	<0.001 <sup>1</sup>
Sex	Female	52 (50.5%)	56 (54.4%)	.577
	Male	51 (49.5%)	47 (45.6%)	
Education	Illiterate	14 (13.6%)	9 (8.7%)	.314
	Diploma or less	76 (73.8%)	72 (69.9%)	
	Associate degree, BA, BSc	11 (10.7%)	18 (17.5%)	
	MA, MSc, Ph.D.	2 (1.9%)	4 (3.9%)	
Blood pressure	Normal	18 (17.5%)	24 (23.3%)	.130
	Elevated	13 (12.6%)	14 (13.6%)	
	HTN stage 1	14 (17.5%)	23 (22.3%)	
	HTN stage 2	58 (56.3%)	42 (40.8%)	
Smoking status	Yes	24 (23.3%)	20 (19.4%)	.497
	No	79 (76.7%)	83 (80.6%)	

<sup>1</sup> Mann–Whitney test was used.

Statistical significance ( $P \leq 0.05$ ) is bolded

Quantitative variables are presented as: mean  $\pm$  SD

Qualitative variables are presented as frequency (percentage).

Independent sample T test and chi-square were used.

Abbreviations: BA, Bachelor of arts; BSc, Bachelor of Science; BMI, Body mass index; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; HTN, hypertension; MET, metabolic equivalent; MA, master of arts; MSc, master of science; PA, physical activity; PH.D, Doctor of philosophy

### 3.2 The association between the waist-to-height ratio and diabetic kidney disease

The association between waist-to-height ratio (WHtR) and DKD was examined using binary logistic regression in crude and adjusted models. The odds ratios with a 95% confidence interval in the crude and adjusted models are shown in Table 2. We found a significant association between WHtR and DKD in

the crude model (OR: 120.355; 95% CI: 3.037 – 4769.930;  $P = 0.011$ ). In other words, higher WHtR could increase the risk of DKD. In model 1, after adjusting for age, sex, HbA1C, diabetes duration, and energy intake, this association remained significant (OR: 1984.994, 95% CI: 21.725 -181366.161;  $p < .001$ ).

**Table 2. Logistic regression findings for evaluating the association between waist-to-height ratio and diabetic nephropathy**

Wt/Ht	OR (95% CI)	P-value
Crude	120.355 (3.037 – 4769.930)	<b>.011</b>
Model 1	1984.994 (21.725 – 181366.161)	<b>&lt;.001</b>

Resulted from binary logistic regression.

Model 1 adjusted for age, sex, HbA1C, diabetes duration, and energy intake.

Statistically significant differences ( $P \leq 0.05$ ) are bolded.

Abbreviations: CI, confidence interval; OR, odds ratio.

### 3.3 The association between relative fat mass index (RFM) and diabetic kidney disease

The association between RFM and DKD was examined using binary logistic regression in crude and adjusted models. The odds ratios with a 95% confidence interval in the crude and adjusted models are shown in Table 3. We did not find a significant association between RFM and DKD in the crude model (OR: 1.014; 95% CI: 0.982 – 1.048,  $p = 0.392$ ). Although in model 1, after adjusting for age, sex, HbA1C, diabetes duration, and energy intake, this association was significant (OR: 1.154; CI: 1.060 – 1.256,  $p < .001$ ). Higher RFM increased the odds of DKD.

**Table 3. Logistic regression findings for evaluating the association between the relative fat mass index and diabetic nephropathy**

RFM	OR (95% CI)	P-value
Crude	1.014 (0.982 – 1.048)	.392
Model 1	1.154 (1.060 – 1.256)	<b>&lt;.001</b>

Resulted from binary logistic regression.

Model 1 adjusted for age, sex, HbA1C, diabetes duration, and energy intake.

Statistically significant differences ( $P \leq 0.05$ ) are bolded.

Abbreviations: CI, confidence interval; OR, odds ratio.

## 4. Discussion

The association between WHtR and RFM, and DKD in T2DM patients was investigated in this study. WHtR and RFM are more accurate indicators of central obesity compared to BMI. In previous studies, the relationship between WHtR and RFM, and other chronic diseases was mainly assessed, and investigations on the potential correlation between these anthropometric measurements and diabetic nephropathy or DKD are scarce. The findings of the current study suggest that the likelihood of DKD in T2DM patients increased with increasing WHtR and RFM, thus offering novel approaches in the clinical assessment of at-risk populations. These findings support our hypothesis that diabetic people with higher central obesity are more likely to progress to impaired kidney disease and DKD.

Obesity is marked by persistent low-level systemic inflammation, which has been demonstrated to significantly

contribute to the development of chronic kidney disease. WHtR has gained prominence in obesity research due to its ability to reflect central adiposity more accurately than body mass index (BMI), particularly in populations with diabetes (22). Central obesity, characterized by higher visceral fat, is linked to various metabolic disturbances, such as insulin resistance, hypertension, and dyslipidemia—elements that together elevate the risk of DKD (23). Our results were in line with a study on patients with type 1 diabetes that found, strong association between percent visceral fat mass and WHtR and WC (24). Results of a cross-sectional study on 125 type 2 diabetic patients who were overweight showed that WHtR is significantly associated with CKD in this population (25). Another study on 125 obese T2DM patients found that WHtR could be used as a noninvasive method for CKD and peripheral neuropathy detection (26). Moreover, the ease of calculating WHtR, obtained by dividing the waist circumference by height, increases its usefulness in clinical environments, serving as a rapid screening method for healthcare professionals.

RFM provides an improvement in evaluating body fat percentage and distribution without requiring advanced equipment (19). It is calculated using sex, height, and waist circumference, making it accessible for routine clinical use. Our results align with a cohort study, that RFM was associated with cardiometabolic multimorbidity in older adults (27). In other cross-sectional studies, there was a direct association between RFM and CKD (14, 28, 29). Integrating RFM into clinical evaluations allows practitioners to obtain deeper insights into health risks associated with adiposity and kidney function.

In previous studies, the association between RFM and DKD risk has not been explored well. We selected cases and controls in the same period and from the same hospital. To evaluate dietary consumption, we utilized a well-established and reliable FFQ that accurately reflects long-term dietary habits, and a skilled dietitian conducted interviews with patients to collect the food frequency information, thereby reducing potential errors compared to self-administration by patients. We encountered certain restrictions that could affect the understanding. Due to the case-control design utilized in this study, we were unable to establish any causal link between RFM and WHtR and DKD. It must be acknowledged that FFQ relies on memory, and potential under- or over-reporting should be considered.

## 5. Conclusion

The current research contributed new insights to the limited investigations about the link between RFM and DKD. In summary, our results indicated that in T2DM patients, higher abdominal obesity, assessed by simple indicators as well as RFM and WHtR, is associated with a higher risk of DKD. Additional prospective studies are recommended to validate these results.

## Acknowledgement

None.

Declarations

## Funding

The authors did not receive support from any organization for the submitted work.

### Competing interests

The authors have no relevant financial or non-financial interests to disclose.

## Ethics approval

The National Committee for Ethics in Biomedical Research, Iran Ministry of Health and Medical Education, approved the

study protocol with the following identification: (IR.IAU.SRB.REC.1401.393).

## Consent to participate

We described the aim of the study to all individuals, and informed consent was signed to enroll in this study.

## Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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