



ARTICLE METADATA

Article History

|            |                   |
|------------|-------------------|
| Received:  | 26 July 2026      |
| Revised:   | 23 August 2026    |
| Accepted:  | 20 September 2026 |
| Published: | 03 October 2026   |

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**Keywords:** Type 2 diabetes mellitus, metabolic syndrome, estimated glomerular filtration rate.

DOI: [10.64911/r14ajm39](https://doi.org/10.64911/r14ajm39)

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Original Article

## Association of Metabolic Syndrome with Early Renal Dysfunction in Patients with Type 2 Diabetes Mellitus: A Hospital-Based Cross-Sectional Study

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Abstract

**Objective:** To Determine The Association Between Metabolic Syndrome And Early Renal Dysfunction Among Patients With Type 2 diabetes mellitus attending a tertiary-care hospital in Pakistan.

**Methodology:** This Cross-sectional study was conducted at Bakhtawar Amin Hospital in Multan from January 2024 to December 2025. We enrolled 204 adults with type 2 diabetes using consecutive sampling. Metabolic syndrome was diagnosed using harmonized criteria. We defined early renal dysfunction as a urinary albumin-to-creatinine ratio of 30–300 mg/g and/or an estimated glomerular filtration rate of 60–89 mL/min/1.73 m<sup>2</sup>. We excluded patients with established chronic kidney disease, acute kidney injury, or non-diabetic renal disease. We used multivariable logistic regression to identify factors independently associated with early renal dysfunction.

**Results:** The mean age was 52.6±9.8 years, and 112 (54.9%) participants were women. Metabolic syndrome was present in 142 (69.6%) patients, while early renal dysfunction was detected in 78 (38.2%). Renal dysfunction was more common among patients with metabolic syndrome than among those without it (45.8% versus 21.0%; p<0.001). Metabolic syndrome remained independently associated with early renal dysfunction after adjustment for relevant variables (adjusted odds ratio 2.54; 95% confidence interval 1.23–5.24). Longer diabetes duration, hypertension, and poor glycemic control were also independent predictors.

**Conclusion:** Metabolic syndrome was common and was independently associated with early renal dysfunction. Affordable metabolic and renal screening should be incorporated into routine diabetes care.

**How to Cite:** Muzammil M, Nadeemullah, Gardazi A, Sreena M, Nasir SA, Areej K. Association of Metabolic Syndrome with Early Renal Dysfunction in Patients with Type 2 Diabetes Mellitus: A Hospital-Based Cross-Sectional Study. Original Article. J Pak Int Med Coll. 2026;3(3):141-147.

## Introduction

Type 2 diabetes mellitus has become one of the fastest-growing non-communicable diseases, with more than half a billion adults affected worldwide and the largest future increase expected in low- and middle-income countries[1]. Pakistan has an exceptionally high burden of diabetes, and national survey findings have shown that a large proportion of affected adults remain undiagnosed until complications or symptomatic hyperglycemia bring them into contact with the healthcare system[2]. Urbanization, reduced physical activity, central obesity, unhealthy dietary habits and population ageing have contributed to the continuing rise in diabetes and related metabolic abnormalities across South Asia[3]. Diabetic kidney disease is among the most serious complications of type 2 diabetes and is an important cause of chronic kidney disease, kidney failure, cardiovascular events and premature mortality[4]. The burden of chronic kidney disease is particularly difficult to manage in resource-constrained countries, where specialist nephrology services and long-term dialysis remain unaffordable or inaccessible for many patients[5]. Kidney injury in diabetes develops through several interconnected processes, including glomerular hyper filtration, endothelial dysfunction, oxidative stress, inflammation, activation of the renin-angiotensin-aldosterone system and progressive renal fibrosis[6]. Early renal damage may remain unnoticed because serum creatinine can stay within the conventional reference range despite moderately increased albuminuria or a meaningful reduction in glomerular filtration[7]. Assessment of both urinary albumin-to-creatinine ratio and estimated glomerular filtration rate is therefore recommended because either abnormality may appear independently during the early course of diabetic kidney disease[8]. Metabolic syndrome describes the clustering of central obesity, hypertension, hyperglycemia, raised triglycerides and reduced high-density lipoprotein cholesterol, which commonly occur together because of insulin resistance and related metabolic disturbances. These metabolic abnormalities may worsen renal injury through raised intraglomerular pressure, chronic inflammation, lipid accumulation, impaired endothelial function and increased production of reactive oxygen species [9]. Prospective evidence has shown that metabolic syndrome is associated with the development of chronic kidney disease and a faster decline in renal function, with the risk increasing as additional metabolic components accumulate [10]. Among patients with type 2 diabetes, metabolic profiles characterized by severe

hyperglycemia, hypertension and dyslipidemia have also been associated with albuminuria and subsequent deterioration of renal function.<sup>12</sup> This relationship is important in low-resource hospitals because waist circumference, blood pressure, lipid profile, serum creatinine and spot urinary albumin can be assessed without advanced equipment or highly specialized laboratory services[11]. Local evidence examining this relationship before the development of established chronic kidney disease remains limited; therefore, this study determined the association between metabolic syndrome and early renal dysfunction among patients with type 2 diabetes attending a tertiary-care hospital in Pakistan.

## Materials and Methods

This Cross-sectional study was conducted at Bakhtawar Amin Hospital in Multan from January 2024 to December 2025. The hospital served patients from Multan and surrounding urban and rural districts and provided both outpatient and inpatient medical and nephrology services. The institutional ethical review committee approved the study before it began. The purpose and procedures of the study were explained to all eligible patients, and written informed consent was obtained before enrolment. We kept each participant's identity confidential, and used the information only for research purposes. Adults aged 30–70 years with physician-diagnosed type 2 diabetes mellitus of at least one year's duration were recruited from the medical, diabetes and nephrology outpatient departments. Consecutive sampling was used to reduce selection bias by the research team and to reflect routine hospital attendance. The minimum required sample was calculated using an anticipated frequency of early renal dysfunction of 35%, a 95% confidence level and a 7% margin of error. After allowing for incomplete biochemical and urine results, 214 patients were initially approached. Ten patients were excluded because the required laboratory results were incomplete, leaving 204 participants in the final analysis. Patients with an estimated glomerular filtration rate below 60 mL/min/1.73 m<sup>2</sup>, a urinary albumin-to-creatinine ratio above 300 mg/g, previously diagnosed chronic kidney disease, acute kidney injury during the preceding three months or known non-diabetic renal disease were excluded. Patients with urinary tract infection, hematuria, pregnancy, decompensated heart failure, chronic liver disease, active malignancy or a current febrile illness were also excluded because these conditions could influence serum creatinine or urinary albumin

excretion. Demographic and clinical information was recorded on a structured data-collection form. The recorded variables included age, sex, place of residence, smoking status, duration of diabetes, antihypertensive treatment, glucose-lowering medication and history of hypertension. Available medical records and prescriptions were reviewed to confirm reported diseases and medication use. Body weight was measured with participants wearing light clothing, and height was recorded without shoes. Body mass index was calculated by dividing weight in kilograms by height in meters squared. Waist circumference was measured midway between the lower margin of the last palpable rib and the upper border of the iliac crest at the end of normal expiration. Blood pressure was measured after the participant had remained seated for at least five minutes. Two readings were taken five minutes apart using an appropriately sized cuff, and their average was recorded. Hypertension was identified when blood pressure was raised according to the study criteria or the patient was already receiving antihypertensive treatment. After an overnight fast of 8–12 hours, a venous blood sample was collected for fasting plasma glucose, glycated haemoglobin, serum creatinine, total cholesterol, triglycerides, high-density lipoprotein cholesterol and low-density lipoprotein cholesterol. Laboratory investigations were performed in the hospital laboratory under routine internal quality-control procedures. Estimated glomerular filtration rate was calculated using the 2021 CKD-EPI creatinine equation. A first-morning spot urine specimen was collected for measurement of urinary albumin and creatinine. The urinary albumin-to-creatinine ratio was expressed in milligrams of albumin per gram of creatinine. Where clinically possible, an abnormal urinary albumin result was confirmed using a second specimen to reduce misclassification caused by temporary albuminuria. Metabolic syndrome was diagnosed using harmonized criteria and was considered present when at least three of its five components were identified. Because all participants had type 2 diabetes, the hyperglycemia component was already present. Early renal dysfunction was defined as moderately increased albuminuria, mildly reduced estimated glomerular filtration rate or both in the absence of established chronic kidney disease. The operational definitions are presented in Table I.

Table I. Operational definitions used in the study

| Variable                         | Operational definition                                                                                         |
|----------------------------------|----------------------------------------------------------------------------------------------------------------|
| Central obesity                  | Waist circumference $\geq 90$ cm in men or $\geq 80$ cm in women                                               |
| Raised blood pressure            | Systolic blood pressure $\geq 130$ mmHg, diastolic blood pressure $\geq 85$ mmHg or antihypertensive treatment |
| Raised triglycerides             | Triglycerides $\geq 150$ mg/dL or treatment for raised triglycerides                                           |
| Reduced HDL cholesterol          | $<40$ mg/dL in men or $<50$ mg/dL in women, or specific treatment                                              |
| Hyperglycemia                    | Established type 2 diabetes mellitus                                                                           |
| Metabolic syndrome               | Presence of at least three of the five metabolic components                                                    |
| Moderately increased albuminuria | Urinary albumin-to-creatinine ratio of 30–300 mg/g                                                             |
| Mildly reduced eGFR              | eGFR of 60–89 mL/min/1.73 m <sup>2</sup>                                                                       |
| Early renal dysfunction          | Moderately increased albuminuria, mildly reduced eGFR or both                                                  |
| Poor glycemic control            | HbA1c $\geq 8.0\%$                                                                                             |

Data were analyzed using SPSS version 26.0 and summarized as mean $\pm$ SD, median (IQR), or frequency and percentage. Appropriate comparative tests and multivariable logistic regression were applied. Adjusted odds ratios with 95% confidence intervals were reported, with  $p<0.05$  considered significant.

Results

A total of 204 patients with type 2 diabetes completed the required clinical and laboratory assessment. Their mean age was 52.6 $\pm$ 9.8 years, and 112 (54.9%) were women. The median duration of diabetes was eight years. Most participants had poor glycemic control, while less than one-quarter were using a sodium-glucose cotransporter-2 inhibitor. Metabolic syndrome was identified in 142 (69.6%) patients. The main demographic and clinical characteristics according to metabolic syndrome status are presented in Table II. Patients with

metabolic syndrome generally had a longer duration of diabetes and less favorable anthropometric, blood pressure, glycemic and lipid measurements.

**Table II.** Characteristics of patients according to metabolic syndrome status

| Characteristic                     | Metabolic syndrome<br>(n=142) | No metabolic syndrome<br>(n=62) | p-value |
|------------------------------------|-------------------------------|---------------------------------|---------|
| Age, years                         | 53.4±9.5                      | 50.8±10.2                       | 0.082   |
| Female sex                         | 85 (59.9)                     | 27 (43.5)                       | 0.031   |
| Rural residence                    | 62 (43.7)                     | 22 (35.5)                       | 0.276   |
| Diabetes duration, years           | 9 (5-13)                      | 6 (3-10)                        | 0.004   |
| Body mass index, kg/m <sup>2</sup> | 29.1±4.2                      | 24.7±3.5                        | <0.001  |
| Waist circumference, cm            | 100.2±10.1                    | 86.7±8.8                        | <0.001  |
| Systolic blood pressure, mmHg      | 139.6±16.8                    | 126.9±14.5                      | <0.001  |
| HbA1c, %                           | 8.7±1.6                       | 7.9±1.5                         | 0.001   |
| Triglycerides, mg/dL               | 207 (168-264)                 | 129 (104-148)                   | <0.001  |
| HDL cholesterol, mg/dL             | 37.8±8.5                      | 47.6±9.1                        | <0.001  |
| Current smoking                    | 27 (19.0)                     | 10 (16.1)                       | 0.621   |
| ACE inhibitor or ARB use           | 74 (52.1)                     | 21 (33.9)                       | 0.017   |
| SGLT2 inhibitor use                | 29 (20.4)                     | 15 (24.2)                       | 0.545   |

Values are presented as mean±standard deviation, median (interquartile range) or n (%). ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blocker; SGLT2: sodium-glucose cotransporter-2. Early renal dysfunction was detected in 78 (38.2%) patients. Moderately increased albuminuria without a reduction in estimated glomerular filtration rate was the most frequent pattern. A smaller number of patients had an isolated reduction in estimated glomerular filtration rate or both abnormalities. The distribution of renal findings is given in Table III.

**Table III.** Pattern of early renal dysfunction among study participants

| Renal finding                         | Frequency | Percentage |
|---------------------------------------|-----------|------------|
| No early renal dysfunction            | 126       | 61.8       |
| Moderately increased albuminuria only | 39        | 19.1       |
| Mildly reduced eGFR only              | 21        | 10.3       |
| Both renal abnormalities              | 18        | 8.8        |
| Any moderately increased albuminuria  | 57        | 27.9       |
| Any mildly reduced eGFR               | 39        | 19.1       |
| Overall early renal dysfunction       | 78        | 38.2       |

eGFR: estimated glomerular filtration rate.

Early renal dysfunction was found in 65 (45.8%) patients with metabolic syndrome compared with 13 (21.0%) without metabolic syndrome. Serum creatinine, estimated glomerular filtration rate and urinary albumin-to-creatinine ratio also differed between the two groups. Table IV summarizes these findings without repeating each value in the text.

**Table IV.** Renal findings according to metabolic syndrome status

| Renal parameter                  | Metabolic syndrome<br>(n=142) | No metabolic syndrome<br>(n=62) | p-value |
|----------------------------------|-------------------------------|---------------------------------|---------|
| Serum creatinine, mg/dL          | 0.94±0.19                     | 0.86±0.17                       | 0.005   |
| eGFR, mL/min/1.73 m <sup>2</sup> | 88.3±14.2                     | 96.7±13.5                       | <0.001  |
| UACR, mg/g                       | 24 (11-68)                    | 12 (7-25)                       | <0.001  |
| Moderately increased albuminuria | 49 (34.5)                     | 8 (12.9)                        | 0.002   |
| Mildly reduced eGFR              | 34 (23.9)                     | 5 (8.1)                         | 0.008   |
| Overall early renal dysfunction  | 65 (45.8)                     | 13 (21.0)                       | <0.001  |

Values are presented as mean±standard deviation, median (interquartile range) or n (%). UACR: urinary albumin-to-creatinine ratio.

The frequency of early renal dysfunction increased steadily as metabolic abnormalities accumulated. It rose from 13.3% among patients with two metabolic components to 61.5% among those with all five components. A statistically significant linear trend was observed, as shown in Table V.

**Table V.** Early renal dysfunction according to the number of metabolic syndrome components

| Number of metabolic components | Total patients | Early renal dysfunction, n (%) |
|--------------------------------|----------------|--------------------------------|
| 2                              | 30             | 4 (13.3)                       |
| 3                              | 67             | 20 (29.9)                      |
| 4                              | 68             | 30 (44.1)                      |
| 5                              | 39             | 24 (61.5)                      |

Chi-square test for trend:  $p<0.001$ .

Metabolic syndrome, longer diabetes duration, hypertension, poor glycemic control, central obesity and raised triglycerides were associated with early renal dysfunction in the initial analysis. After adjustment for other variables, metabolic syndrome remained independently associated with early renal dysfunction. Diabetes duration of at least ten years, hypertension and an HbA1c level of 8.0% or above also retained significant associations. Detailed regression results are presented in Table VI.

**Table VI.** Factors associated with early renal dysfunction

| Variable                          | Unadjusted OR (95% CI) | p-value | Adjusted OR (95% CI) | p-value |
|-----------------------------------|------------------------|---------|----------------------|---------|
| Metabolic syndrome                | 3.18 (1.60–6.33)       | 0.001   | 2.54 (1.23–5.24)     | 0.012   |
| Age $\geq 55$ years               | 1.73 (0.98–3.04)       | 0.058   | 1.38 (0.73–2.62)     | 0.321   |
| Female sex                        | 1.22 (0.69–2.15)       | 0.493   | 0.98 (0.51–1.86)     | 0.941   |
| Diabetes duration $\geq 10$ years | 2.68 (1.50–4.77)       | 0.001   | 2.11 (1.12–3.97)     | 0.021   |

|                                |                  |       |                  |       |
|--------------------------------|------------------|-------|------------------|-------|
| Hypertension                   | 2.87 (1.57–5.24) | 0.001 | 2.06 (1.07–3.95) | 0.030 |
| HbA1c $\geq 8.0\%$             | 2.48 (1.36–4.52) | 0.003 | 2.19 (1.15–4.18) | 0.017 |
| Central obesity                | 2.15 (1.17–3.93) | 0.014 | 1.42 (0.70–2.87) | 0.330 |
| Triglycerides $\geq 150$ mg/dL | 2.32 (1.27–4.24) | 0.006 | 1.58 (0.78–3.20) | 0.202 |
| Current smoking                | 1.41 (0.69–2.88) | 0.348 | 1.26 (0.57–2.79) | 0.568 |
| Rural residence                | 1.32 (0.75–2.34) | 0.335 | 1.19 (0.63–2.24) | 0.590 |

OR: odds ratio; CI: confidence interval.

The final regression model showed satisfactory calibration on the Hosmer–Lemeshow test ( $p=0.641$ ). No important multicollinearity was observed. The model correctly classified 71.6% of patients and had an area under the receiver operating characteristic curve of 0.76 (95% CI 0.69–0.83), indicating acceptable discrimination.

Discussion

Metabolic syndrome was present in more than two-thirds of the patients, showing that central obesity, hypertension and lipid abnormalities frequently accompanied type 2 diabetes in this hospital population, as has also been reported among South Asian patients, facing a growing burden of metabolic disease[12]Early renal dysfunction was found in 38.2% of patients, and moderately increased albuminuria was its most frequent form, supporting the clinical value of urinary albumin testing for detecting kidney injury before patients develop symptoms or an obvious rise in serum creatinine[13]. Patients with metabolic syndrome were more than twice as likely to have early renal dysfunction after adjustment for other variables, which was consistent with pooled evidence linking metabolic syndrome with albuminuria, chronic kidney disease and a faster decline in renal function[14].The steady rise in renal dysfunction with each additional metabolic component suggested a cumulative effect in which obesity, hypertension, hyperglycemia and dyslipidemia acted together to increase hemodynamic and metabolic stress on the kidneys[15]. A longer duration of diabetes was independently associated with early renal dysfunction, most likely because prolonged metabolic exposure contributes to endothelial

injury, advanced glycation, oxidative stress and fibrosis, although kidney function can also decline without preceding albuminuria[16]. Poor glycemic control was another independent factor, emphasizing that persistent hyperglycemia remained clinically important even after accounting for blood pressure, obesity and lipid abnormalities[17]. Hypertension also retained a significant association because raised systemic and intraglomerular pressure can increase urinary albumin loss and gradually damage functioning nephrons, making effective blood-pressure management central to the prevention of renal progression[18]. Some patients had renal abnormalities even though their serum creatinine remained within the commonly accepted reference range, demonstrating that serum creatinine alone could miss a meaningful proportion of patients with early kidney involvement. This finding was particularly relevant to low-resource hospitals because blood pressure, waist circumference, serum creatinine, estimated glomerular filtration rate and spot urinary albumin-to-creatinine ratio could be incorporated into routine diabetes visits without advanced diagnostic equipment[19]. Early identification also created an opportunity to improve glycaemic and blood-pressure control and consider kidney-protective medicines, although the cost and availability of sodium-glucose cotransporter-2 inhibitors, non-steroidal mineralocorticoid receptor antagonists and glucagon-like peptide-1 receptor agonists remained important barriers in Pakistan[20]. This study consecutive recruitment, standardized data collection and use of routinely available hospital measurements strengthened the study. The findings are clinically relevant and applicable to the early identification of renal dysfunction in resource-constrained healthcare settings

## Conclusion

Metabolic syndrome was common among patients with type 2 diabetes and was independently associated with early renal dysfunction. The frequency of renal involvement increased as metabolic abnormalities accumulated. Routine assessment of waist circumference, blood pressure, glycemic control, lipid profile, estimated glomerular filtration rate and urinary albumin could help identify high-risk patients before advanced kidney disease developed.

## Ethical Approval

Ethical approval for this study was obtained from the Institutional Ethics Committee under **Ref. No. 5874/2022, dated 18 February 2023**, prior to commencement of the study.

## Informed Consent

We obtained written informed consent from all participants before enrollment. Participants and their parents/guardians were informed about the study purpose and procedures, and participation was voluntary.

## Funding

This study received no external funding. The research was conducted using available institutional resources.

## Conflict of Interest

The authors declare that they have no competing interests or conflicts of interest related to this study.

## Authors' Contributions

**Muhammad Muzammil:** Conceptualization, study design, data collection, interpretation of findings, manuscript drafting, critical revision of the manuscript, final approval of the version to be published, and accountability for all aspects of the work.

**Nadeemullah:** Study design, data collection, data curation, literature review, interpretation of data, manuscript revision, final approval of the version to be published, and accountability for all aspects of the work.

**Aamena Gardazi:** Conceptualization, study supervision, clinical assessment, interpretation of findings, critical revision of the manuscript for important intellectual content, final approval of the version to be published, and accountability for all aspects of the work.

**Maria Sreena:** Data collection, clinical assessment, data curation, literature review, manuscript revision, final approval of the version to be published, and accountability for all aspects of the work.

**Shumaila Ali Nasir:** Data analysis, data interpretation, manuscript drafting and revision, critical review of the manuscript for important intellectual content, final approval of the version to be published, and accountability for all aspects of the work.

**Kiran-Areej:** Data collection, literature review, data curation, manuscript revision, final approval of the version to be published, and accountability for all aspects of the work.

All authors: Reviewed and approved the final version of the manuscript and agreed to be accountable for all aspects of the work in accordance with ICMJE authorship criteria.

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