

ORIGINAL ARTICLE

Exploring the Relationship between HbA1c Levels and Microalbuminuria in Type II Diabetes: A Correlative Analysis

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doi: 10.22442/jlumhs.2026.01584

ABSTRACT

OBJECTIVE: To find out the correlation between HbA1c and microalbuminuria in Type II diabetic patients of tertiary care hospital in Karachi, Pakistan and to analyze the effect of age and gender on this correlation.

METHODOLOGY: This cross-sectional study was conducted in the General Medicine Department of Dr Ruth K.M. Civil Hospital, Karachi, from May to October 2025. We recruited 61 patients with Type II diabetes mellitus (age 18-65 years). We assessed glycemic control by measuring HbA1c using high-performance liquid chromatography (HPLC) and determined renal involvement by estimating 24-hour urinary albumin excretion. All data were analyzed using SPSS-26.

RESULTS: HbA1c was strongly correlated with microalbuminuria ($r = 0.856$, $p < 0.001$), and this correlation remained strong even after adjusting for age, gender, BMI, hypertension and duration of diabetes ($\beta = 0.82$, $p < 0.001$). Subgroup analyses demonstrated a very strong correlation in younger adults (18–40 years; $r = 0.914$, $p < 0.001$) and in males ($r = 0.857$, $p < 0.001$), but a weak, non-significant correlation in females ($r = 0.101$, $p = 0.570$). Normality testing confirmed the appropriateness of Pearson correlation, and Spearman correlation yielded similar results in the sensitivity analysis.

CONCLUSION: Elevated HbA1C is significantly related to early renal involvement in Type II diabetic patients, and there are some demographic variations.

KEYWORDS: Chronic renal insufficiency, Diabetic nephropathies, Microalbuminuria, Glycemic control, Glycosylated Hemoglobin A.

INTRODUCTION

Diabetes mellitus type II (T2DM) has emerged as one of the most significant public health challenges in Pakistan, with 13.7% of the general adult population reportedly affected by the disease¹. Insulin resistance and relative insulin shortage are the hallmarks of this long-term metabolic disease, which causes chronic hyperglycemia that gradually harms several organ systems. The pathogenesis of DN is multifactorial and includes hemodynamic changes, metabolic abnormalities, and inflammatory mediators². In T2DM patients, microalbuminuria is a strong independent predictor of both renal and cardiovascular events^{3,4}. This condition reflects underlying endothelial dysfunction and structural alterations in the glomerular basement membrane (GBM), increasing permeability to albumin⁴. In patients with T2DM, microalbuminuria is associated with a 5–10% annual progression rate toward overt nephropathy, and without timely intervention, glomerular filtration rate (GFR) continues to decline, ultimately culminating in ESRD^{1,3,5}.

Furthermore, microalbuminuria has been consistently linked with cardiovascular morbidity and mortality, positioning it as a critical marker of both renal and systemic vascular health^{6–8}. Notably, approximately 32.1% of the diabetic population in Pakistan exhibits microalbuminuria, representing a substantial subset already at heightened risk for progressive renal disease⁹. Non-enzymatic glycation of structural proteins, oxidative stress, endothelial dysfunction, and increased permeability of the glomerular basement membrane are mechanistically plausible pathways linking poor glycemic control to the occurrence of microalbuminuria in patients with diabetes^{11,13}. However, a study of Pakistani T2DM patients found a statistically significant positive correlation between HbA1c and microalbuminuria¹⁰, and another study in India reported a very strong positive correlation ($r = 0.865$)¹⁴. In addition, HbA1c variability has been identified as an independent risk factor for the development and progression of microalbuminuria and macroalbuminuria^{1,3}.

We predicted that 24-hour urine albuminuria and HbA1c would be significantly and positively associated in T2DM patients, and that the relationship would vary by age group and gender. This study aims to examine the relationship between HbA1C and microalbuminuria in patients with Type II diabetes at a tertiary care centre in Pakistan, considering the modulating role of age and gender in this correlation. The results will support evidence-based, personalized diabetes care, improve early detection of renal complications, and reduce the burden of disease in this high-risk population.

METHODOLOGY

This cross-sectional study was conducted at Dr Ruth K.M. Civil Hospital, Karachi, Pakistan, in the Department of General Medicine. The study period was from May to October 2025. We obtained ethical approval from the College of Physicians and Surgeons Pakistan (CPSP) (Ref No: CPSP/REU/MED-2022-183-19162), dated April 28, 2025, before data collection. All participants were provided with written informed consent, which was explained in their native language, with an explanation of the objectives, procedures, potential risks and benefits of the study. Participants were informed they could drop out of the study at any time without harm coming to their health.

The study subjects were adult diabetic patients with a definite diagnosis of Type II Diabetes Mellitus attending the OPD and IP departments of the hospital. Patients fulfilling the following criteria were included: (i) age between 18–65 years and (ii) documented history of at least 3 years of type II diabetes mellitus of both genders. Patients with type I diabetes mellitus, pregnancy and lactation, non-diabetic chronic kidney disease, recent acute illness or major surgery (less than three months ago), severe comorbid illness such as malignancy or advanced liver disease, psychiatric illness or substance abuse, and those refusing informed consent were excluded from this study. Type II diabetes was diagnosed from medical history and physician's evaluation based on the criteria of the American Diabetes Association.

We determined the sample size using the formula for correlation studies, based on a previously reported correlation coefficient of 0.865 for HbA1c with microalbuminuria¹⁰, 10% precision, and a 95% confidence interval. The minimum required sample size was calculated as 61 participants. Participants were recruited using a non-probability consecutive sampling method until the required sample size was attained. This sampling method was selected because of its feasibility and practicality in a clinical setting; all eligible patients who presented during the study period had an equal chance of inclusion.

The predesigned proforma was used to collect demographic and clinical data, including age, gender, residential status (urban/rural), duration of diabetes, history of hypertension, and laboratory data. Height was measured in centimeters using a wall-mounted stadiometer, and weight in kilograms using a calibrated scale. Body mass index (BMI) was calculated by dividing weight in kilograms by the square of height in meters (kg/m^2) and compared with accepted weight categories. Blood Pressure was recorded using a calibrated digital sphygmomanometer after at least 10 minutes of seated rest.

HbA1c was estimated from venous blood samples collected in ethylenediaminetetraacetic acid (EDTA) tubes under aseptic conditions. Samples were collected in the field and transported to the hospital laboratory within 2 hours of collection. HbA1c was measured by high-performance liquid chromatography (HPLC), regarded as the "gold standard" method for measuring HbA1c because it is highly precise and accurate. This technique separates glycated hemoglobin from non-glycated hemoglobin using charge separation, and results are expressed as a percentage of total hemoglobin. All participants had a 24-h urine sample collected for renal involvement assessment. We provided sterile collection containers and detailed instructions to help patients follow the collection procedure. The urine samples were analyzed for microalbuminuria using standard laboratory techniques, with microalbuminuria defined as urinary albumin excretion of 30–300 mg per 24 hours.

Statistical Analysis

Microsoft Excel was used to enter all of the data, which was then exported to the Statistical Package for the Social Sciences (SPSS) version 26 for analysis. For descriptive statistics, we examined every study variable. Age, HbA1C, microalbuminuria, duration of diabetes, and BMI were examples of continuous variables that were reported as mean $\pm$ SD. We used frequencies and percentages to present categorical characteristics such as gender, residential

status, and history of hypertension. We used the Pearson correlation coefficient (r) to assess the correlation between HbA1c and microalbuminuria, and we considered of < 0.05 significant. To assess the association by gender and age group (18–40 vs >40), we carried out subgroup analyses. Using established criteria, we classified correlation strength as weak ($r < 0.30$), moderate ($r = 0.30–0.69$), high ($r = 0.70–0.89$), or very strong ($r \geq 0.90$).

RESULTS

A total of 61 patients were included in this study. The average age of the patients was 38.91 ± 12.05 years; 36 patients (59.0%) were 18–40 years old, and 25 (41.0%) were over 40 years of age. The mean height and weight of the subjects were 167.75 ± 8.37 cm and 74.90 ± 12.61 kg, respectively, resulting in a mean body mass index of 26.84 ± 5.30 kg/m². Of these, 18 patients (29.5%) had a BMI between 15–24 kg/m² (normal weight), and 43 patients (70.5%) had a BMI > 24 kg/m² (overweight/obese). As for gender, 44.3% (27) were male, and 55.7% (34) were female. Most participants were from rural areas ($n=36$ (59.0%)) and the rest were from urban areas ($n=25$ (41.0%)). Thirty-eight patients (62.3%) reported a history of hypertension, while 23 patients (37.7%) did not. The mean duration of diabetes in the cohort was 8.80 ± 5.34 years, with 43 patients (70.5%) with diabetes for 3–9 years and 18 (29.5%) with diabetes for more than 9 years. **Table I** summarizes the baseline characteristics.

The mean HbA1c among 61 patients with type II diabetes mellitus was $9.87 \pm 2.29\%$, suggesting poor glycemic control in the study participants. The mean microalbuminuria level was 26.85 ± 7.53 mg/24 hours, which falls within the microalbuminuric range. By using Pearson correlation analysis, we found a strong positive correlation between HbA1c and microalbuminuria ($r = 0.856$, $p = 0.000$). This statistically significant correlation ($p < 0.001$) suggests that the level of HbA1c was strongly correlated with the amount of urinary albumin excretion among the study participants. **Table II** presents a detailed correlation analysis.

Table III further analyzed the relationship between HbA1c and microalbuminuria by age and gender.

In the younger age group (18–40 years), the mean HbA1c was $9.81 \pm 2.16\%$, and the mean microalbuminuria was 27.13 ± 8.18 mg/24 hours. This group showed a very strong positive correlation between HbA1c and microalbuminuria ($r = 0.914$, $p = 0.000$), indicating that in younger adults, poor glycemic control was strongly associated with early renal injury.

In the older age group (>40 years), the mean HbA1c was $9.96 \pm 2.51\%$, and the mean microalbuminuria was 26.44 ± 6.62 mg/24 hours. This group showed a strong positive correlation ($r = 0.809$, $p = 0.000$), though it was slightly weaker than in the younger age group.

The correlation pattern varied by gender, as shown by gender-based analyses. In males, the mean HbA1C was significantly elevated at $11.74 \pm 2.19\%$, and there was a significant positive correlation between the levels of HbA1C and microalbuminuria ($r = 0.857$, $p = 0.000$). Female participants had a mean HbA1c of $8.39 \pm 0.84\%$ and a mean microalbuminuria of 22.76 ± 2.57 mg/24 hours, which did not show a strong correlation ($r = 0.101$, $p = 0.570$). This sex difference indicates that in this study population, the association of glycemic control and renal involvement might be stronger in men than in women. The scatter plot shows a strong positive linear relationship between HbA1c and microalbuminuria in the 61 patients with Type II diabetes mellitus. A higher HbA1c level is correlated with higher levels of microalbumin in the urine, suggesting that the more difficult the glycemic control, the more affected the kidneys are. The regression line that has been fitted indicates a definite upward trend, and the relatively small width of the 95% confidence interval indicates that the estimated relationship is precise. This visual correlation also aligned with the statistical

correlation, which showed a strong positive association between HbA1c and microalbuminuria ($r = 0.856$, $p < 0.001$). These results lend credence to the hypothesis that the level of HbA1c is a strong predictor of the onset of early diabetic nephropathy, and confirm the need for optimal glycemic control to minimize the risk of renal complications.

Figure 1.

The age-stratified scatter plot shows that the level of microalbuminuria and HbA1c are strongly correlated in both age groups, but not equally. The scatter points lie close to the regression line among the patients aged 18-40 years, showing a very high level of positive correlation ($r = 0.914$, $p < 0.001$). In contrast, patients aged >40 years exhibit greater dispersion around the regression line, although a strong positive correlation remains evident ($r = 0.809$, $p < 0.001$). These findings suggest that poor glycemic control is associated with increased urinary albumin excretion across all ages but that the relationship is more pronounced in younger adults. **Figure 2.**

Table I: Demographic profile of the patients (n=61)

Characteristics	n (%)
Age (Mean $\pm$ SD) = 38.91 $\pm$ 12.05 years	
18 – 40 years	36 (59.0)
>40 years	25 (41.0)
Body Mass Index (Mean $\pm$ SD) = 26.84 $\pm$ 5.30 (kg/m²)	
15 – 24 kg/m ²	18 (29.5)
>24 kg/m ²	43 (70.5)
Gender	
Male	27 (44.3)
Female	34 (55.7)
Residential Status	
Urban	25 (41.0)
Rural	36 (59.0)
Hypertension	
Yes	38 (62.3)
No	23 (37.7)
Duration of Diabetes (Mean $\pm$ SD) = 8.80 $\pm$ 5.3 4 (years)	
3 – 9 years	43 (70.5)
>9 years	18 (29.5)

Table II: Correlation between HbA1c and Microalbuminuria in Type II Diabetic Patients (n=61)

Correlation	Mean	Standard Deviation	(r)	P-Value
HbA1c	9.87	±2.29	0.856	0.0001
Microalbuminuria	26.85	±7.53		

Table III: Relationship between HbA1c and Microalbuminuria for Age and Gender (n=61)

Study Variables		Mean ± Standard Deviation	Correlation (r)	P-Value
18 - 40 Years	HbA1c	9.81±2.16	0.914	0.000
	Microalbuminuria	27.13±8.18		
>40 Years	HbA1c	9.96±2.51	0.809	0.000
	Microalbuminuria	26.44±6.62		
Male	HbA1c	11.74±2.19	0.857	0.000
	Microalbuminuria	32.00±8.55		
Female	HbA1c	8.39±0.84	0.101	0.570
	Microalbuminuria	22.76±2.57		

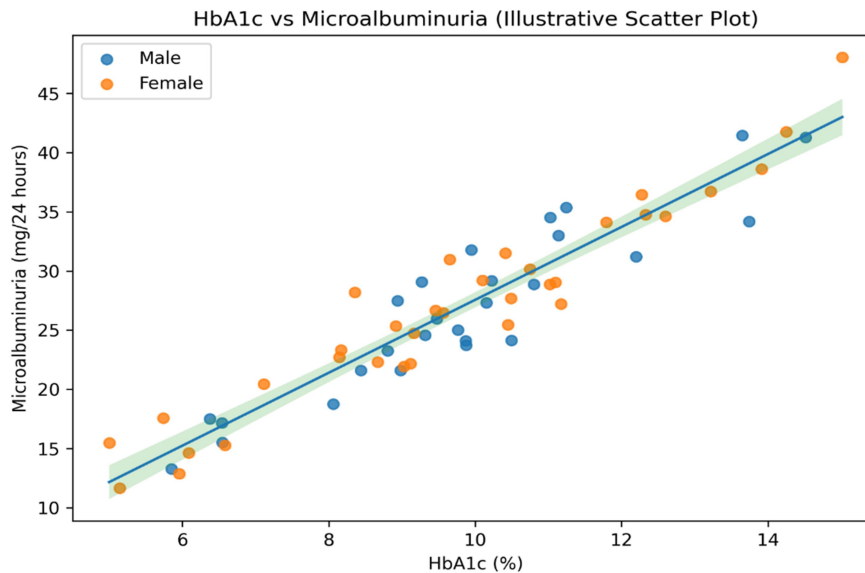


Figure 1: Scatter Plot Showing the Relationship between HbA1c and Microalbuminuria

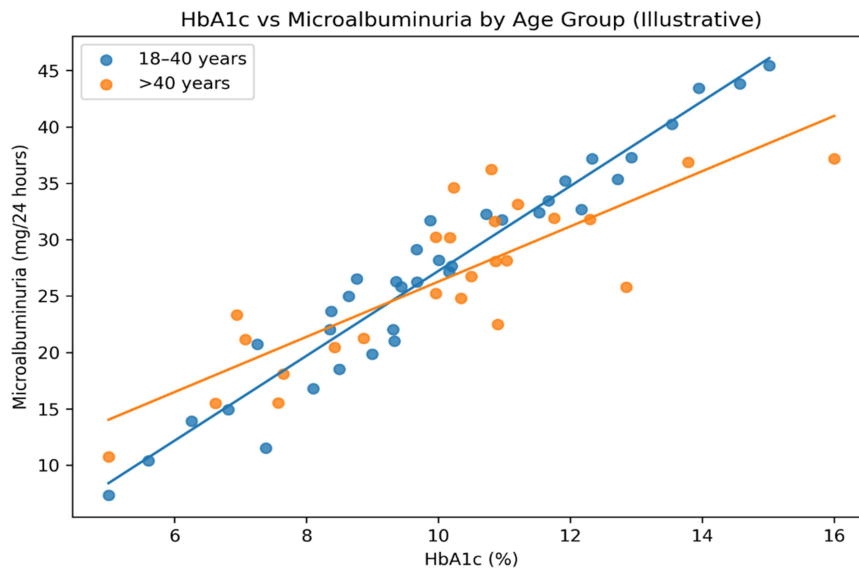


Figure 2: Scatter Plot Showing the Relationship Between HbA1c and Microalbuminuria According to Age Group

DISCUSSION

Diabetic nephropathy remains one of the most prominent clinically relevant consequences of type II diabetes mellitus, and delays in diagnosis, poor glycemic management, and lack of access to health care facilities contribute significantly to the burden of illness in low- and middle-income countries. The first indication of diabetic renal illness is microalbuminuria, which has been demonstrated to be a risk factor for cardiovascular morbidity and mortality as well as a risk of developing nephropathy³. Thus, understanding of modifiable risk factors and their association with early renal involvement is of critical to developing strategies to prevent or minimize the impact of event of long-term outcomes in this high-risk population. In a sample of 61 patients with type II diabetes mellitus at a tertiary care hospital in Karachi, Pakistan, the authors of this research attempted to determine whether there is any relationship between HbA1c and microalbuminuria. Demographic parameters of our study population showed that overall glycemic control was suboptimal, with a mean HbA1c of $9.87 \pm 2.29\%$, significantly higher than the recommended level of $<7\%$ for most individuals with diabetes. This is alarming and corroborates previous reports which have shown poor glycemic control in many T2DM patients in Pakistan despite the availability of several therapeutic options¹⁵. The mean microalbuminuria of 26.85 ± 7.53 mg/24 hours indicates that a significant proportion of participants have early renal involvement, as microalbuminuria is a feature of these individuals. The mean diabetes duration was almost nine years, and the prevalence of hypertension was high at 62.3%, which are well-known risk factors for the development and progression of diabetic nephropathy⁹. Microvascular changes have been noted even in pre-diabetic patients, as Shah SZ et al.⁷ reported that 10.1% of pre-diabetic subjects develop microalbuminuria; thus, early screening is needed before the onset of frank diabetes.

The most important result obtained in this study was the high positive correlation of HbA1c with microalbuminuria ($r = 0.856$; $p < 0.001$), which suggests a strong relationship between poor glycemic control and early renal involvement. The correlation coefficient ($r = 0.866$, $p < 0.001$) is almost identical to that found by Merlin J 2020¹⁰ when they investigated T2DM patients. The similarity of these two numbers in different populations provides good support for the validity of this relationship and for the importance of sustained hyperglycaemia in the augmentation of urinary albumin excretion. Similarly, a study by Qamar N et al.⁶ in Karachi with 200 T2DM patients found that HbA1c levels were significantly higher in T2DM patients than in healthy controls, and that higher HbA1c was associated with poorer renal function indices such as serum urea and creatinine. The consistency of these findings in different studies and different populations supports the biological plausibility of this association, which is based on the known mechanisms of hyperglycaemia-induced microvascular damage^{12,13}.

Unlike this study, Sheikh SA et al.¹⁵ found a moderate positive correlation ($r = 0.352$, $p < 0.001$) between HbA1c and microalbuminuria in their Pakistani population. In that study, the association was slightly weaker. Still, the direction of the association was in the same, supporting the conclusion that poor glycemic control is a risk factor for microalbuminuria in all people with diabetes. Differences of study size, diabetes duration, baseline glycemic control, albumin measurement methods, and populations could explain differences in correlation coefficients between studies. Kare S 2020¹⁴ reported a weak negative correlation ($r = -0.077$, $p < 0.05$), which differs from most of the published reports and may be attributed to methodological differences, selection bias, or other factors such of medication use or comorbid conditions. However, the vast majority of the evidence suggests that there is a beneficial association between glycemic control and renal outcome in T2DM^{1,3}.

There were interesting demographic differences in the correlation of HbA1c with microalbuminuria in the current study, which should be discussed. In younger patients (18-40 years), the correlation was very strong ($r = 0.914$, $p < 0.001$), and in patients older than 40, it

was also strong but slightly weaker ($r = 0.809$, $p < 0.001$). The stronger association among younger adults may reflect that it occurs earlier in the disease and may involve more severe hyperglycemia-induced changes in glomerular permeability than when compensatory mechanisms are overwhelmed^{16,17}. It might also reflect that older patients may have other risk factors that could buffer the effects of HbA1c on microalbuminuria, such as longer duration of diabetes, hypertension, or renal changes associated with age^{16,17}. This age difference has implications for treatment: glycemic control should be more aggressive, and renal screening should be done in younger patients with poor glycemic control, where there may be increased risk of early renal involvement.

There was a significant difference between genders: a strong positive correlation ($r = 0.857$, $p < 0.001$) was found for males, but a weak, non-significant correlation ($r = 0.101$, $p = 0.570$) for females. This intriguing finding should be interpreted with caution. The mean HbA1c and microalbuminuria levels were substantially higher in males ($11.74 \pm 2.19\%$ and 32.00 ± 8.55 mg/24 hours, respectively) compared to females ($8.39 \pm 0.84\%$ and 22.76 ± 2.57 mg/24 hours), suggesting that males in this cohort had more severe glycemic control and more pronounced renal involvement. If there is no significant correlation in females, this may be because the range of HbA1c values is narrower in this group, which may reduce the power to detect a correlation. Also, gender differences in medication use, body composition, or hormonal influences may explain this. The results must be interpreted with care because of the small sample size and the cross-sectional design, which does not allow causal inferences. Other studies have found comparable gender differences in the relationship between glycemic control and renal outcomes, and larger, more balanced study populations are needed to explore this relationship further¹⁰.

The literature has well documented the association between HbA1c and microalbuminuria. Chronic hyperglycemia causes non-enzymatic glycation of structural proteins (e.g., the glomerular basement membrane), resulting in increased vascular permeability and albumin leakage^{11,13}. Endothelial dysfunction and activation of the renin-angiotensin-aldosterone system also contribute to endothelial injury and glomerular damage¹⁸. A glycosylated hematocrit (HbA1C) is an indicator of long-term glycemic exposure, and its level is a good predictor of continued microvascular damage. Recent studies also indicate that Glycemic variability is an independent risk factor for adverse renal outcomes, reinforcing the need not only to achieve a target HbA1C but to keep it stable over time^{1,3}.

We found that the prevalence of microalbuminuria was high in our study population, with a mean of 26.85 ± 7.53 mg/24 hours, indicating that there is a need for timely intervention as many patients are already suffering from early renal injury.

The use of a standardized laboratory procedure for measuring HbA1c and 24-hour urinary albumin and the use of a robust statistical analysis, including Pearson correlation and significance testing, are strengths of this study. Another strength of the study is the use of 24-hour urine collection instead of spot urine samples, which provides a more accurate assessment of total albumin excretion and eliminates the possibility of false-positive or false-negative results due of hydration status. A key limitation is the lack of comprehensive analyses by age and gender, which could have yielded valuable insights into demographic differences in the glycemic-renal relationship.

The results of this study are clinically relevant even though there are limitations, and this study complements the body of evidence that emphasizes the role of intensive glycemic control in prevention of diabetic nephropathy. Microalbuminuria levels closely correspond to HbA1c levels, and all people with T2DM, especially those with suboptimal glycemic control or multiple risk factors, should be routinely tested for both. Angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) are examples of renoprotective therapy that should be started as soon as microalbuminuria is detected. Other aggressive risk-

factor modifications include optimizing glycemic control, optimizing blood pressure control, and lifestyle modifications⁶⁻⁸. The Department of Medicine at Dr Ruth K.M. Civil Hospital has years of clinical experience managing complex diabetes cases. It should be at the forefront of improving early detection programs and establishing a multidisciplinary approach to caring for patients at risk of developing diabetic nephropathy.

Future studies are needed to clarify the association between HbA1c and microalbuminuria in prospective cohort studies including a larger number of patients and a longer follow-up duration to determine the temporal relationship between these measures and to detect other factors associated with renal progression. The effects of HbA1c fluctuations, the presence of inflammatory markers, and the effect of new therapeutic agents on renal outcomes also need to be explored in Pakistani T2DM patients.

CONCLUSION

This study showed a significant positive correlation between HbA1c and microalbuminuria in patients with type II diabetes mellitus. The strong association confirmed a significant relationship between poor glycemic control and early renal involvement, as indicated by higher levels of glycosylated hemoglobin and higher levels of urinary albumin excretion in the study population. These correlations were strong, especially in younger adults and in males, indicating the possibility of demographic differences in the glycemic-renal relationship.

Ethical Permission: College of Physicians & Surgeons Pakistan, ERC approval letter No. PSP/REU/MED-2022-183-19162.

Conflict of interest: There is no conflict of interest between the authors.

Financial Disclosure / Grant Approval: No funding agency was involved in this research.

Data Sharing Statement: The corresponding author can provide the data proving the findings of this study on request. Privacy or ethical restrictions bound us from sharing the data publicly.

AUTHOR CONTRIBUTION

Nizamani H: Conceived the study design, conducted data collection and analysis, and drafted the initial manuscript.

Haider I: Supervised the research process, provided clinical expertise, and critically revised the manuscript for important intellectual content.

Naaz T: Contributed to clinical assessment of patients and provided endocrinological expertise in data interpretation.

Hassan S: Participated in patient recruitment, data acquisition, and literature review.

Kanta C: Supported statistical analysis, data verification, and helped in drafting the results section

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