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Factors Associated with Microalbuminuria in Patients with Type 2 Diabetes: A Cross-sectional Study from Eastern India

ABSTRACT

Objective: The current cross-sectional study determines the prevalence and associated factors of microalbuminuria in a focused population in Eastern India.

Methods: The study was conducted in Kolkata from June to December 2022 among type 2 diabetes mellitus (T2DM) patients. Patients with T2DM aged more than 18 were included in the study, and those with overt albuminuria (>300 mg/day), congestive cardiac failure, urinary tract infection, pregnancy, human immunodeficiency virus, hepatitis B, or hepatitis C infection were excluded.

Results: Among 297 T2DM patients, 130 (43.8%) had high albumin creatinine ratio (> 30 mg/g). Diabetic patients with elevated blood pressure (BP > 130/80 mm Hg) were 1.68 times (95% CI, 1.12-2.53) at risk of developing microalbuminuria. Similarly, patients with a diabetes duration of 5 years or more were 1.48 (95% CI 1.09-2.02) times more likely to develop microalbuminuria. Logistic regression also concluded that elevated blood pressure (BP > 130/80 mm Hg, $P = .027$) and duration of diabetes (>5 years, $P = .016$) were predictive of microalbuminuria.

Conclusion: The current study observes a high prevalence of microalbuminuria among diabetes patients. This indicates the need for the implementation of preventive strategies for diabetic nephropathy, especially among patients with long-standing diabetes and elevated blood pressure.

Keywords: Diabetes mellitus, high blood pressure, diabetic nephropathy, microalbuminuria

Introduction

Diabetic nephropathy (DN) is a growing health concern and poses a significant risk of progressing into chronic kidney disease (CKD) and end-stage renal failure.

The Indian Chronic Kidney Disease 2022 study consolidating the numbers from all parts of India reports that about 37% of the patients with CKD have diabetes.[1] International Diabetes Federation 2021 observes an increased global incidence rate of 46%, surmounting about 780 million people affected by DN.[2] The reported prevalence of DN among the Indian population, from studies over the last 15 years, has varied largely from 0.9% to 62.3%.[3] The vast difference in the estimates could be attributed to the large variation in the socio-demographic factors and setbacks in diagnosis and screening processes.

Hemodynamic and structural changes in renal glomeruli precede the development of DN. However, their predictive value remains uncertain.[4] The multifactorial pathogenesis of DN involves common pathways such as the Renin Angiotensin Aldosterone System, Protein Kinase C, and increased Transforming growth factor β expression, leading to reactive oxygen species generation and renal fibrosis.[5] Microalbuminuria (albumin to creatinine ratio; ACR >30-≤ 299 µg/min) is widely recognized as an early indicator of DN.[6] Risk factors of DN include poorly controlled diabetes, hypertension, and genetic predisposition.[7] American Diabetes Association "Standards of Medical Care in Diabetes" recommends routine screening for microalbuminuria in patients diagnosed with diabetes.[8] Despite ongoing research, due to the alarming increase in the incidence of diabetes and its complications, economic considerations, and limited access to resources in certain regions of the country, it remains challenging to prevent or reduce the incidence of DN among patients with diabetes. Focused population-level observational studies reporting the prevalence and investigating the associated factors will have contemporary value in evaluating the impact of preventive measures taken over the past years to subsidize the issue.

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Therefore, based on a population in East India, the current study was conducted to estimate the prevalence of microalbuminuria among T2DM patients and to understand the associated factors.

Materials and Methods

The cross-sectional study was conducted among type 2 diabetes mellitus (T2DM) individuals at a medical institute in Kolkata from July 2022 to December 2022. Informed consent was obtained from the patients, and ethical approval for the study was obtained from the Clinical Research Ethics Committee of School of Tropical Medicine, Kolkata (IEF ref. number: 2022-AS06; date: July 18, 2022). Patients with T2DM aged more than 18 years were included in the study, and those with overt albuminuria (>300 mg/day), congestive cardiac failure, urinary tract infection, pregnancy, HIV, Hepatitis B, and Hepatitis C infection were excluded.

An ACR value of >30 mg/g was considered a high ACR, and an estimated glomerular filtration rate (eGFR) value less than 90 mL/min/1.73 m^2 was considered a sign of impaired renal function.[6] Participants with an hemoglobin A1C (HbA1c) value of less than 7% were considered to have well-controlled diabetes.

Taking the prevalence of microalbuminuria in T2DM patients as 25.6%,[9] the minimum sample size for our study was 293, which yielded a power of 80% for a significance level of 5% and absolute precision of 5%.

Demographic variables (including age, body mass index, and duration of diabetes), clinical parameters (including systolic and diastolic blood pressure), blood sugar parameters (including fasting blood sugar, postprandial blood sugar, and HbA1c), kidney parameters (urea and creatinine), and lipid parameters (including serum cholesterol, low-density lipoprotein, high-density lipoprotein, and triglycerides) were collected.

Categorical variables were represented as n (%), and continuous variables were expressed as mean ± SD. Data were analyzed with R Software version 4.3.1 by R Foundation for Statistical Computing. Fisher's exact test was used to compare categorical variables. A *t*-test was used to compare continuous variables. Pearson's correlation coefficient was used to find a correlation between study parameters. A *P*-value less than or equal to .05 was considered significant. A logistic regression model was used to find predictors of microalbuminuria.

Results

The total number of study participants was 297. Among them, 130 participants had an ACR of more than 30 mg/g. The prevalence of microalbuminuria (ACR > 30 mg/g) among people with diabetes was calculated as 43.8% (95% CI, 38%-49.6%). Table 1 compares different parameters between the participants with high ACR and those with normal ACR.

Table 1. Comparison of Different Parameters Between High and Low Albumin Creatinine Ratio Participants

	ACR ≤ 30 mg/g (n = 167)	ACR > 30 mg/g (n = 130)	*P*
Age (years)	51.3 ± 9.7	54.4 ± 10.1	.009
Body mass index (kg/m^2)	23.3 ± 3.3	23.3 ± 3	.992
Systolic blood pressure (mm Hg)	137.7 ± 18.4	143.6 ± 20.6	.018
Diastolic blood pressure (mm Hg)	81.7 ± 9.6	83.7 ± 11.4	.141
Duration of diabetes (years)	8.3 ± 6.9	10.6 ± 7.3	.012
Fasting blood sugar (mg/dL)	136.8 ± 44.6	147.4 ± 51.1	.070
Post-prandial blood (mg/dL)	201.6 ± 75.8	221.1 ± 88.5	.101
HbA1c (%)	8.5 ± 2.1	8.6 ± 3.1	.885
Urea (mg/dL)	24.9 ± 8.4	26.7 ± 11.5	.221
Creatinine (mg/dL)	0.9 ± 0.2	0.9 ± 0.4	.216
Serum cholesterol (mg/dL)	168.4 ± 38.7	167.8 ± 49.5	.937
Low-density lipoprotein (mg/dL)	97.1 ± 25.6	98.6 ± 34.5	.792
High-density lipoprotein (mg/dL)	47.6 ± 18.1	45 ± 10.1	.302
Triglyceride (mg/dL)	150.1 ± 69.4	150.6 ± 64.7	.961

We found a significant association between raised blood pressure (systolic > 130 mm Hg or diastolic > 80 mm Hg) and high ACR. Diabetic patients with systolic blood pressure above 130 mm Hg or diastolic blood pressure above 80 mm Hg were at 1.68 times (95% CI, 1.12-2.53) higher risk of having high ACR in comparison to those without.

We also found a significant association between the duration of diabetes and microalbuminuria. Patients who had been diabetic for more than 5 years were 1.48 times (95% CI, 1.09-2.02) more likely to have microalbuminuria than those with shorter durations of diabetes.

When comparing the groups with and without microalbuminuria, we found a significant difference in age (*P* = .009), systolic blood pressure (*P* = .018), and duration of diabetes (*P* = .012).

Among the study participants, 104 (35%) were on insulin, and the rest were on oral hypoglycaemic agents. We also found a significant association (*P* = .050) between medications (oral hypoglycaemic agents or insulin) and high ACR, but this is probably due to confounding by the duration of diabetes.

We did not find any association between the control of diabetes and high ACR (*P* = .758).

We calculated the eGFR in 236 patients, and among them, 53% participants had an eGFR value more than or equal to 90 mL/min/1.73 m^2, 35.6% were between 60 to 89 mL/min/1.73 m^2, 9.3% were between 45 and 59 mL/min/1.73 m^2, 0.8% were between 30 to 44 mL/min/1.73 m^2,

MAIN POINTS

- Individuals with diabetes and elevated blood pressure (BP > 130/80 mm Hg) are at a higher risk (1.68 times) of developing microalbuminuria.
- Diabetes individuals with a duration of diabetes > 5 years or more were also more likely (1.5 times) to develop microalbuminuria.
- Multivariate analysis also concluded that elevated blood pressure (BP > 130/80 mm Hg) and duration of diabetes (> 5 years) were predictive of microalbuminuria.

and 1.3% were between 15 and 29 mL/min/1.73 m^2. There was no association between impaired renal function and high ACR ($P = .340$).

There was a significant correlation between ACR and the duration of diabetes (correlation coefficient = 0.168, $P = .008$), as shown in Figure 1. A significant correlation was also found between ACR and both systolic (correlation coefficient = 0.124, $P = .021$) and diastolic blood pressure (correlation coefficient = 0.128, $P = .037$), as shown in Figures 2 and 3, respectively.

On logistic regression analysis, we found that increased blood pressure (systolic above 130 and diastolic above 80, $P = .027$) and a longer duration of diabetes (more than 5 years, $P = .016$) were predictive of microalbuminuria (Table 2).

Discussion

Type 2 diabetes mellitus is a widespread metabolic disorder, and its complications, including DN, pose significant health challenges and economic burdens. Further, in a country like India, with vast socio-demographic variability and disparity in the distribution of resources between urban and rural populations and between various locations, it is imperative to have focused studies on identifying factors associated with microalbuminuria in individuals with type 2 diabetes mellitus. Our study, involving 297 participants from East India with T2DM, revealed a significant 43.8% prevalence of microalbuminuria. This aligns with a central Indian study of 212 T2DM patients, which reported a 38.2% prevalence of microalbuminuria, indicating early markers for DN.[10] Another South-Indian study observed a microalbuminuria prevalence of 36.3%, which had an increasing trend with the duration of diabetes.[11] In comparison, our study reports a higher prevalence of microalbuminuria (43.8%) among type 2 diabetic patients in Eastern India. Our findings emphasize elevated blood pressure and longer duration of diabetes as significant predictors of microalbuminuria. As there was no similar study from Eastern India before, our study enhances the existing knowledge by confirming the high prevalence of microalbuminuria found in other regions of India, suggesting that this may be a widespread issue across different Indian

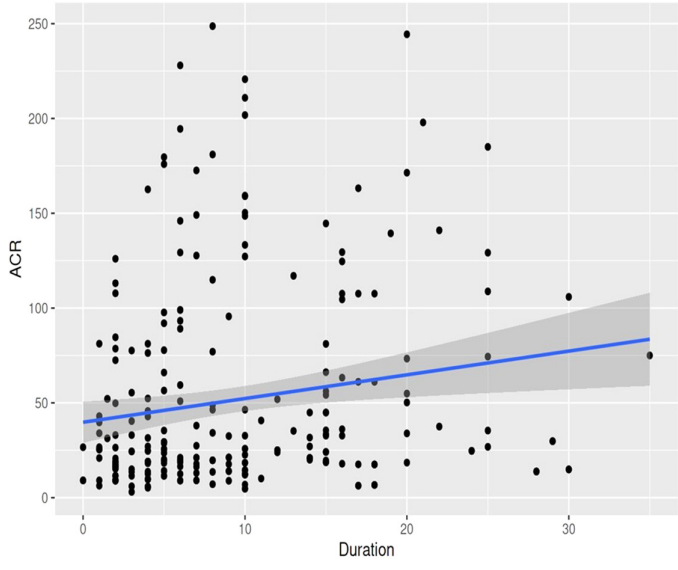

Figure 1. Correlation between albumin creatinine ratio (ACR) and duration of diabetes (correlation coefficient = 0.168).

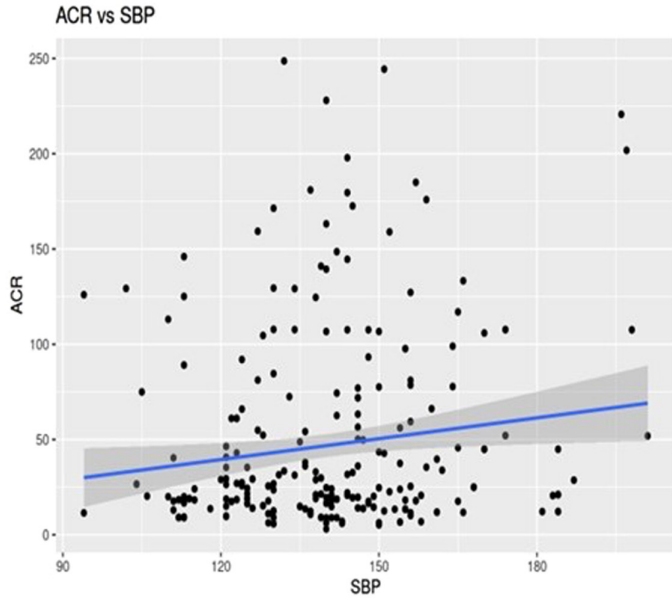

Figure 2. Correlation between albumin creatinine ratio (ACR) and systolic blood pressure (SBP) (correlation coefficient = 0.124).

demographics. It specifically identifies elevated blood pressure as a significant predictor, reinforcing the need for targeted blood pressure management in diabetic patients to prevent nephropathy. The findings are crucial for healthcare settings in Eastern India and can be compared with data from other regions to understand broader implications.

We observed significant differences in key parameters when comparing groups with and without microalbuminuria. Age was notably different between the 2 groups ($P = .009$, Table 1), supporting previous findings of an increased risk of microalbuminuria with advancing

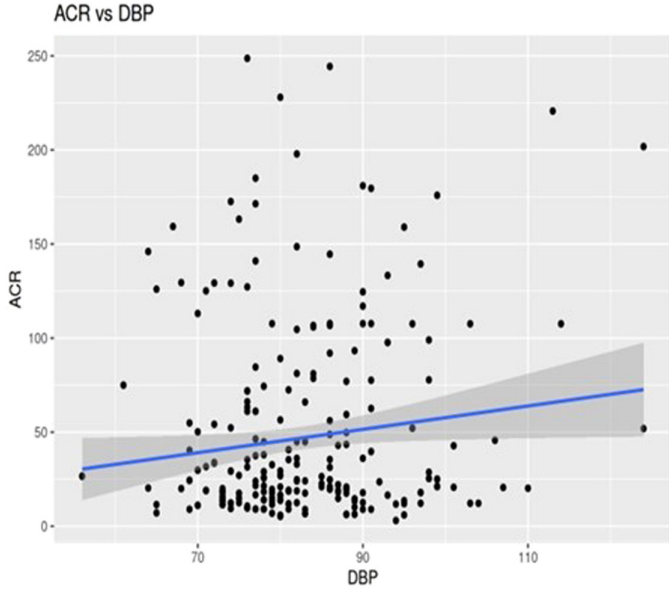

Figure 3. Correlation between albumin creatinine ratio (ACR) and diastolic blood pressure (DBP) (correlation coefficient = 0.128).

Table 2. Logistic Regression Model Showing the Effect of Uncontrolled Hypertension and Duration of Diabetes on the Presence of High Albumin Creatinine Ratio (>30 mg/dL)

Variable	Coefficients	Standard Error	*Z*	*P*	Odds Ratio	95% CI
Intercept	−1.315	0.323	−4.075	<.001	0.268	0.138-0.494
Uncontrolled hypertension (SBP > 130 mm Hg, DBP > 80 mm Hg)	0.723	0.327	2.212	.027	2.061	1.098-3.980
Duration of diabetes> 5 years	0.709	0.295	2.406	.016	2.033	1.147-3.655

age.[10,12] Consistent with the well-established association between hypertension and DN, individuals with microalbuminuria exhibited significantly higher systolic blood pressure ($P = .018$, Table 1). Abdelwahid et al[13] observed that the association of T2D and essential hypertension increased the prevalence of microalbuminuria from 31.2% to 68.5%.[13] A significant correlation between ACR and both systolic (correlation coefficient = 0.124, $P = .021$) and diastolic blood pressure (correlation coefficient = 0.128, $P = .037$) was noted. These patients were also 1.68 times more at risk of developing microalbuminuria (Figures 2 and 3).

Our study found a significant association between the duration of diabetes and microalbuminuria ($P = .012$, Table 1). Patients with microalbuminuria showed a longer duration of diabetes, with those with diabetes for more than 5 years having a 1.48 times higher risk than those with a shorter duration (Figure 1). This has been corroborated by several other studies,[9,11,14] such as the study by Muhammad Ahsan Sana et al, revealing a positive correlation between the duration of diabetes and urinary albumin-to-creatinine ratio.

In contrast, our study did not find a significant association between glycemic control, measured by HbA1c levels, and high ACR ($P = .758$, Table 1). The reasoning could be attributed to the complex interplay of anti-diabetes medications, the extent of glycemic control, duration of diabetes, social habits, and genetic predisposition.[15]

Our study reveals a diverse eGFR distribution, with 53% having values ≥90 mL/min/1.73 m^2. Importantly, no significant association was found between impaired renal function and high ACR ($P = .340$). Albumin creatinine ratio may precede rising creatinine as an early marker of nephropathy.[16]

Regarding medication usage, 35% of our study participants were on insulin, and the rest were on oral hypoglycemic agents. A significant association ($P = .050$) was observed between medication usage and high ACR. However, this association may be confounded by the duration of diabetes, highlighting the complex interplay between treatment modalities and diabetic complications.[11]

The high prevalence of microalbuminuria observed among a T2DM population in Eastern India suggests the need to implement preventive strategies. These findings provide valuable insights for crafting effective strategies to mitigate the risk of DN in this population, emphasizing the importance of multifaceted approaches in diabetes management. Our findings highlight the correlation between prolonged diabetes duration and elevated blood pressure with the presence of microalbuminuria in individuals with T2DM. Early screening incorporating these parameters may help detect the disease and its progression. Specifically, patients with over 5 years of diabetes may benefit from routine screening for microalbuminuria. Moreover, maintaining blood pressure below 130/80 mm Hg is crucial for delaying nephropathy progression in individuals with type 2 diabetes.

Availability of Data and Materials: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: This study was approved by the Clinical Research Ethics Committee of School of Tropical Medicine, Kolkata (approval number: 2022-AS06; date: July 18, 2022).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

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Declaration of Interests: The authors have no conflicts of interest to declare.

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