Original Article

Prevalence of Microalbuminuria in Type 2 Diabetes Mellitus

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ABSTRACT

Introduction: Microalbuminuria manifests ten to fourteen years before overt diabetic nephropathy. It is possible to stop the progression of diabetic nephropathy or reverse it at this point. Diabetic nephropathy, the primary cause of morbidity and death in patients with T2DM, is strongly predicted by microalbuminuria. Additionally, proliferative retinopathy, peripheral neuropathy, and vascular hypertension are more common in people with microalbuminuria.

Aims/ objective: To determine the prevalence of microalbuminuria in type-2 diabetic patients and to evaluate the relation between microalbuminuria and glycaemic control, age, sex, duration of diabetes, body mass index (BMI), and creatinine clearance.

Materials and Method: On the day after the visit, the patients were asked to provide a clean catch, mid-stream urine sample from their initial morning void, and the samples were sent for Urine Albumin-Creatinine Ratio (UACR). Normal urinary protein excretion was defined as UACR less than 30mg/g; microalbuminuria as UACR between 30 and 300 mg/g; and macroalbuminuria as urinary protein excretion more than 300 mg/day or 300 mg/g. Patients were also investigated for fasting & post-prandial blood sugar; HbA1c (glycated haemoglobin), lipid profile, and serum creatinine.

Results: A total of 130 patients, were included in the study. Overall prevalence of microalbuminuria in the present study was 35.38% (46 cases). We found significant association between older age, greater duration of diabetes, high body mass index and lower creatinine clearance with respect to microalbuminuria ($p<0.05$). We found significant association between poor glycaemic control and prevalence of microalbuminuria with 50% of microalbuminuric patients with HbA1c > 7.5% as compared to only 25% in normoalbuminuric patients ($p<0.05$).

Conclusion: For every diabetes patient, the UACR should be included in standard practice. Microalbuminuria signals to the doctor to take timely ACE inhibitors and adjust risk factors in order to stop progression towards chronic kidney disease.

Keywords: Microalbuminuria, Type 2 Diabetes Mellitus, Diabetic Retinopathy, HbA1c.

INTRODUCTION

Both the prevalence of T2DM (type 2 diabetes mellitus) and the complications linked to the disease are rising globally. In developing nations, the premature mortality rate due to T2DM surged by 5% from 2000 to 2016.[1] Chronic complications of T2DM significantly increase the risk of death and morbidity. T2DM can cause macro-vascular or micro-vascular complications. Micro-vascular complications consist of diabetic nephropathy, retinopathy, peripheral and autonomic neuropathy whereas macro-vascular complications consist of coronary artery disease, transient ischemic attack, stroke, and lower limb ischemia. Glycaemic handling must be sufficient to postpone or avoid these problems.

Due to the rising prevalence of type 2 diabetes, diabetic kidney disease is one of the most prevalent causes of CKD (chronic kidney disease), which can develop to ESRD (end-stage renal disease).[2] The American Diabetic Association (ADA) advises patients with T2DM to be screened for microalbuminuria once a year in order to diagnose diabetic nephropathy earlier[3]. Urinary albumin excretion had previously been measured using a 24-hour urine sample. For the purpose of screening for microalbuminuria, a spot morning sample for the urine albumin: creatinine ratio (UACR) is now utilized. It is practical and closely aligns with 24-hour urine collection in adults.[3, 4]

The quantity of albumin that is discharged into the urine as a result of malfunctioning of the filtration barrier of glomerular basement membrane is noteworthy.[5] As of right now, a urine albumin level that is both higher than average and lower than what a traditional dipstick test can detect is considered microalbuminuria. Thus, in microalbuminuria, the rate of UAE (urine albumin excretion) is 30 to 300 mg/day. It may also indicate 20–200 micrograms/minute on two of the three urine collections, or 30–300 microgram per 1 gram of creatinine. Although this reference range is established from studies in adult patients, it may be also be applicable to the paediatric patients.[6, 7] On the other side, more than 100 mg per 12 hours or 300 mg per day albumin excretion is categorized as macroalbuminuria. Diabetic retinopathy with consistently increased albuminuria (more than 300 mg per day), and lack of other kidney illnesses are necessary for determining the presence of diabetic kidney disease in individuals with type 1 or type 2 diabetes mellitus.

UACR ranging from 30 to 300 milligrams per gram are also included in the current diagnostic of microalbuminuria.[8]

Microalbuminuria manifests ten to fourteen years before overt diabetic nephropathy. It is possible to stop the progression of diabetic nephropathy or reverse it at this point. Use of an ACE inhibitor, together with stricter glycaemic management, are among the therapeutic approaches that can reverse microalbuminuria.[9]

Microalbuminuria prevalence in patients with type 2 diabetes mellitus can vary between 8 to 47%.[10, 11] Diabetic nephropathy, the primary cause of morbidity and death in patients with T2DM, is strongly predicted by microalbuminuria. Additionally, proliferative retinopathy, peripheral neuropathy, and vascular hypertension are more common in people with microalbuminuria. Research published in the Western literature has shown a linear association between the level of microalbuminuria and blood pressure, diabetes duration, and body mass index (BMI). In T2DM, there was no gender link observed in microalbuminuria.[12, 13]

UACR and glycaemic control are directly correlated, and an effective way to measure glycaemic control is with glycosylated haemoglobin, or HbA1c. Diabetes mellitus can be diagnosed with HbA1c levels ≥6.5%, and people with diabetes are advised to have levels < 7.0%.[14, 15] This study was aimed to determine the prevalence of microalbuminuria in type-2 diabetic patients and to evaluate the relation between microalbuminuria and glycaemic control, age, sex, duration of diabetes, body mass index (BMI), and creatinine clearance.

MATERIALS AND METHODS

This was a cross-sectional study conducted on patients of type 2 diabetes mellitus in outpatient Department of General Medicine of tertiary care hospital of eastern India from January 2023 to June 2023. Data collection was started after taking the approval of institutional ethics committee and after taking written informed consent from the study participants who were provided with participant information sheet in their local language. Rights and confidentiality of recruited type 2 diabetes patients were taken care of as per guidelines of Good Clinical Practice.

Inclusion Criteria: Patients of either sex aged more than 18 years diagnosed with type 2 diabetes mellitus as per American Diabetic Association (ADA) guidelines. [16]

Exclusion Criteria: Patients of type 1 diabetes mellitus or with any life-threatening disease or with active infection or with diagnosis of chronic kidney disease or with diagnosis of hypertension or having macroalbuminuria or with obesity (BMI ≥ 30 kg/m^2) were excluded from our study.

Sample Size: For a confidence level of 95% and margin of error of 5% the sample size has been calculated as patients of either sex who are more than 30 years and above (taking the prevalence of Type 2 diabetes in India is 9.3% using cochran's formula. [17]

$n=z^2xp(1-p)/e^2$

$n=1.96^2x0.093(1-0.093)/0.05^2$ =130 patients

METHODOLOGY

During patient interviews, demographic and clinical information was documented, including age, sex, time since T2DM diagnosis, and type of anti-diabetic therapy. During the clinic visit, measurements of blood pressure, weight, and height were taken. The formula for calculating body mass index (BMI) is to divide weight in kilograms by height in meters squared. On the day after the visit, the patients were asked to provide a clean catch, mid-stream urine sample from their initial morning void, and the samples were sent for UACR.

Normal urinary protein excretion was defined as UACR less than 30mg/g; microalbuminuria as UACR between 30 and 300 mg/g; and macroalbuminuria as urinary protein excretion more than 300 mg/day or 300 mg/g. [8]

Patients were also investigated for fasting & post-prandial blood sugar; HbA1c (glycated haemoglobin), lipid profile, and serum creatinine. Glycaemic control was graded based on HbA1c levels as follows:

- Good: <7.0%
- Average: 7.0%-7.5%
- Poor: > 7.5%

Statistical Analysis

Data collected from patients in case record form were presented in tabular form using Microsoft Excel 365 and then transferred to IBM SPSS version 24 for further statistical analysis. Descriptive statistics were used to interpret the result in form of number, percentage, and mean ± SD (standard deviation). Age, BMI, duration of diabetes, creatinine clearance, FBS, PPBS and lipid parameters were expressed as mean ± SD and unpaired t-test was used to test statistical significance of difference between normoalbuminuric and microalbuminuric. Fisher's exact test and chi-square test were used to test statistical significance of difference with respect to sex, type of anti-diabetic therapy, HbA1c levels between two groups.

RESULTS

A total of 130 patients, 73 males and 57 females, were included in the study. Overall prevalence of microalbuminuria in the present study was 35.38% (46 cases). Among the patients with microalbuminuria, 25 (54.35%) were males and 21 (45.65%) were females. Baseline characteristics of the type 2 diabetes patients are shown in Table 1.

We found significant association between older age, greater duration of diabetes, high body mass index and lower creatinine clearance with respect to microalbuminuria ($p<0.05$). However, there was no significant association of microalbuminuria with gender and insulin therapy ($P>0.05$) [Table 1].

Table 1: Comparison of Baseline characteristics between normoalbuminuric and microalbuminuric patients

Parameters	Patients with normoalbuminuria (n=84)	Patients with microalbuminuria (n=46)	P-Value
Age in years (mean ± SD)	52.39 ± 6.36	59.58 ± 6.25	<0.001*
Sex, n (%)			
Male	49 (66.22)	25 (54.35)	0.71**
Female	35 (41.67)	21 (45.65)	
Body Mass Index in kg/m^2 (mean ± SD)	22.73 ± 2.34	23.97 ± 3.17	0.01
Duration of Diabetes in years (mean ± SD)	6.30 ± 2.13	9.75 ± 3.13	<0.001
Creatinine Clearance in ml/min/m^2 (mean ± SD)	91.33 ± 11.27	79.52 ± 10.68	<0.001
Therapy for T2DM			
Oral antidiabetic drug	71 (84.52)	35 (76.09)	0.47***
Insulin	3 (3.57)	2 (4.34)	
Oral antidiabetic + Insulin	10 (11.90)	9 (19.56)	

*Unpaired t-test, **Fisher's exact test, ***Chi-square test

Table 2: Association of HbA1c with prevalence of microalbuminuria

HbA1c	Number of Patients with normoalbuminuria (n=84)	Number of Patients with microalbuminuria (n=46)	Total
<7.0%	22 (26.19)	6 (13.04)	48
7.0-7.5	41 (48.81)	17 (36.96)	64
>7.5	21 (25.00)	23 (50.00)	38
P-Value (Chi-Square Test)	0.01		

We found significant association between poor glycaemic control and prevalence of microalbuminuria with 50% of microalbuminuric patients with HbA1c > 7.5% as compared to only 25% in normoalbuminuric patients (p<0.05) [Table 2].

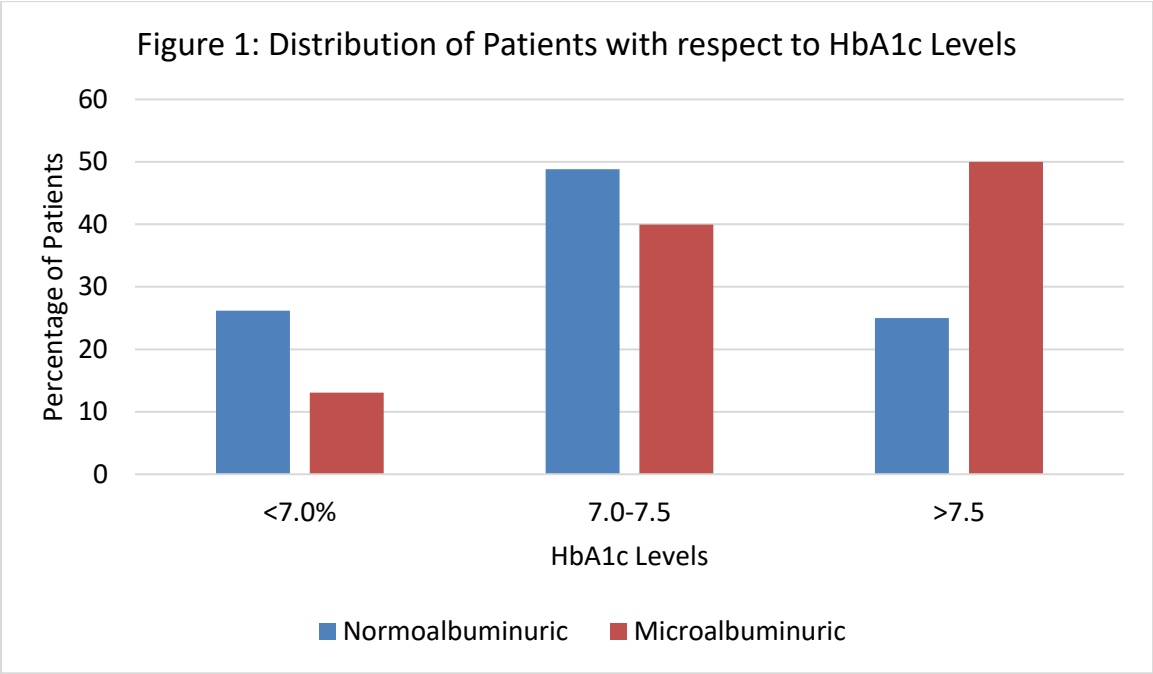

Table 3: Association of Glycaemic Control with Prevalence of Microalbuminuria

Parameters	Patients with normoalbuminuria (n=84)	Patients with microalbuminuria (n=46)	P-Value (Unpaired t test)
FBS in mg/dl (mean ± SD)	173.48 ± 18.33	195.53 ± 25.50	<0.0001
PPBS in mg/dl (mean ± SD)	246.06 ± 23.28	281.01 ± 31.59	<0.0001
HbA1c in % (mean ± SD)	7.13 ± 0.72	8.09 ± 1.32	<0.0001

Fasting blood sugar, post-prandial blood sugar and HbA1c was significantly elevated in microalbuminuric patients as compared to normoalbuminuric patients.

Table 4: Association of Lipid Parameters with prevalence of microalbuminuria

Lipid Parameters in mg/dl (mean ± SD)	Number of Patients with normoalbuminuria (n=84)	Number of Patients with microalbuminuria (n=46)	Total -Value (Fisher's Exact Test)
Total Cholesterol	197.18 ± 18.72	207.83 ± 21.86	0.004
Triglyceride	155.40 ± 13.17	173.72 ± 15.63	<0.0001
LDL	126.86 ± 10.84	129.67 ± 11.71	0.17
HDL	32.55 ± 3.63	29.14 ± 3.51	<0.0001

There was significantly elevated level of triglyceride and low level of HDL in microalbuminuric patients as compared to normoalbuminuric patients (p<0.0001) [Table 4].

DISCUSSION

Findings on the prevalence and correlations between microalbuminuria and several parameters in patients with T2DM are presented in this cross-sectional study. In contrast to the research conducted by Ghai et al., which found a prevalence of twenty-five percent, the current study reports a prevalence of 35.38% for microalbuminuria.[18]

Within this subcontinent, a study conducted in Bangladesh found that 29.72% of diabetic patients had microalbuminuria.[19] Microalbuminuria was found in 25.5% of patients with T2DM in North India, according to Kanakamani et al. and 20% of T2DM patients in Nepal, according to Thakur et al. [20, 21]

The majority of the patients in this study had erratic treatment with inadequate glycemic control, which may have contributed to the higher prevalence. Additionally, the limited sample size may have had a role. Ethnic differences and the methodology used to estimate microalbuminuria may have contributed to the increased prevalence found in this study. The most significant factor driving the shift from normoalbuminuria to microalbuminuria appears to be the degree of glycaemic control.

Among the variables that affect the development of kidney disease are blood pressure, blood sugar regulation, and heredity. Strict diabetes management has a greater influence on prognosis when a patient has microalbuminuria. [22] Microalbuminuria was found to be significantly correlated with higher HbA1c levels. The findings published by Showail et al., Amini et al., Al-Shaikh et al., and Patel et al. were identical to this. [23, 24]

The degree of albuminuria shows a statistically significant linear connection with age, according to the current study. Previous research has also demonstrated a positive relationship between patients' ages and microalbuminuria. [25, 26] In contrast to other research that revealed a male predominance in the prevalence of microalbuminuria, our study did not demonstrate a gender-wise correlation of microalbuminuria. Our investigation also found significant association between BMI and microalbuminuria, as has been documented in numerous other studies. [25, 26] Possibility of confounding factors that would have contributed significantly to the development of microalbuminuria, such as the length of diabetes and glycaemic management couldn't be ruled out.

Although not statistically significant, the current study's findings indicate a minor negative connection between eGFR (creatinine clearance) and microalbuminuria. All of the patients' serum creatinine and eGFR were within acceptable limits. It is easy to divide diabetic nephropathy into several phases based on renal hemodynamic, systemic blood pressure, urine results, and responsiveness to treatment. Albuminuria is absent and glomerular filtration is higher during the first stage of renal hyperperfusion. Albuminuria will not be seen and glomerular filtration will be high and normal during the second stage (clinical delay). The following stage is called incipient nephropathy, in which microalbuminuria is present but glomerular filtration will be within normal range. It often manifests five to fifteen years after T2DM is diagnosed.

In the next phase, macroalbuminuria and nephropathy's clinical signs emerge, and glomerular filtration falls. It ultimately culminates in severe albuminuria and decreased

glomerular filtration, indicating ESRD (end-stage renal disease). [27] Consequently, microalbuminuria may not be linked to aberrant serum creatinine levels or creatinine clearance, but it can be a crucial warning indicator that, if disregarded, could cause permanent kidney injury.

Consistent with other prior publications, the current investigation has demonstrated a positive association between the duration of diabetes mellitus and microalbuminuria. Diabetes for an extended period of time significantly increases the risk of developing microalbuminuria due to the buildup of advanced end products of glycosylation brought on by hyperglycemia. Diabetic nephropathy development is significantly influenced by glycaemic control with consistent treatment. [28–30]

The current study's limitations must also be taken into account. The results of our study may have been impacted by selection bias because it was not based on the broader population. It might be necessary to use a larger sample size in the general population to validate the findings of this investigation.

CONCLUSION

Diabetic nephropathy is one of the main ESRD precursors. Sensitive markers such as the UACR allow for the determination of both disease progression and early identification. Furthermore, our research demonstrates a correlation between greater UACR and poor glycaemic control in T2DM. For every diabetes patient, the UACR should be included in standard practice. Microalbuminuria signals to the doctor to take timely ACE inhibitors and adjust risk factors in order to stop progression towards chronic kidney disease.

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