Original Article

Prevalence and Spectrum of Albuminuria among Type 2 Diabetic Patients in a Tertiary Health-care Facility in Southern Nigeria

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Abstract

Background: Diabetic nephropathy (DN) is a life-threatening microvascular complication often leading to progressive renal failure and death. Microalbuminuria is an early marker of DN and a major risk factor for endothelial dysfunction. Routine screening for albuminuria will improve health outcomes in these patients. **Materials and Methods:** A cross-sectional study comprising 150 consecutive adults with type 2 diabetes mellitus (DM) (WHO criteria) attending the medical outpatient clinic of our hospital from December 2017 to December 2018. The study was done in accordance with the Declaration of Helsinki. Ethical approval was sought and obtained from the Ethical and Research Committee of the hospital before the commencement of the study. Written informed consent was obtained from individual participants after a careful explanation of the study. Samples for spot urine albumin-to-creatinine ratio were collected for analysis. Results were analysed with the Statistical Package for the Social Sciences (SPSS)-23 software. **Results:** The study involved 94 (62.7%) females and 56 (37.3%) males with a mean age of 55.87 ± 10.96 years. The mean duration of diabetes was 9.45 ± 6.94 years and 56 (37.3%) have had diabetes for 6–10 years. The mean urine albumin-to-creatinine ratio (uACR) was 153.54 ± 146.28 mg/g, with 66.7% having values between 30 and 299 mg/g while 15.3% had values ≥ 300 mg/g. The prevalence of albuminuria was 82% among participants. The relationship between the duration of Type 2 DM and UACR categories was not statistically significant, with $P = 0.473$. **Conclusion:** Routine screening for albuminuria in type 2 DM patients will improve health outcomes.

Keywords: Albuminuria, prevalence, spectrum, type 2 diabetes mellitus, urine albumin-to-creatinine ratio

Introduction

Diabetes mellitus (DM) is a global epidemic reportedly affecting about 451 million (8.4% of global prevalence) in 2017, with an estimated increase to 642 million people worldwide by 2040.[1] Recent systematic reviews predict an expected rise in global prevalence, with about 49.7% of this population undiagnosed[2] and the developing economies of Africa and Asia contributing a significant fraction of this figure.

Diabetic Nephropathy (DN) is a chronic complication of uncontrolled diabetes and the single most common cause of the end-stage renal disease (ESRD) worldwide.[3] In the United States, DN accounts for about 15%–40% of new cases of ESRD,[4] with a prevalence of 30%–40% of all cases of ESRD. In Sub-Saharan Africa, including Nigeria, it is the third-most common cause of ESRD, with chronic glomerulonephritis and hypertension being more prevalent.[5]

DN is defined as a clinical syndrome characterised by persistent albuminuria (≥300 mg/day or > 200 µg/min) that is confirmed on at least two occasions 3–6 months apart, a progressive decline in the glomerular filtration rate (GFR) and an elevated systemic arterial blood pressure (BP).[6] DN can also be defined based on urine albumin-to-creatinine

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ratio ≥ 30 mg/g of creatinine in the absence of other renal diseases.[7]

Routine screening, therapeutic interventions, and efforts to prevent the progression of nephropathy have the greatest impact if instituted early in the course of the disease.[8] Research to identify biomarkers (such as transferrin, ceruloplasmin, and urinary collagen IV) with potential for earlier diagnosis and risk stratification in DN are currently ongoing, yet to date, none have outperformed microalbumin on a larger scale.[9]

Materials and Methods

This was a cross-sectional study carried out between December 2017 and December 2018 from a tertiary centre in southern Nigeria. Ethical approval for this study was obtained from the Ethical and Research Committee of the hospital before the commencement of the study. The study population comprised adults (≥18 years) living with type 2 diabetes attending medical consultant clinics (Endocrine/Metabolic clinic). They were screened, and all those eligible for the study were recruited. Diabetic patients who were pregnant were excluded from the study.

The cost of the necessary investigation for the purpose of the study was borne by the investigator. All data collected from participants were kept confidential and their names were not included on the study forms. Participants were informed of the benefits of the study and were allowed to withdraw at any stage without negative repercussions. Participants found to have deranged results were referred to appropriately.

A total of 150 recruited patients for this study were subjected to a detailed history, physical examination, and assessment of the spot urine albumin-to-creatinine ratio. Furthermore, a fasting venous blood sample for serum total protein, serum albumin as well as HbA1c estimation was done. Clinical information retrieved from the above exercise were entered into a pro forma and data sheet for this study.

DM was diagnosed based on previous history and treatment of diabetes and/or using the WHO guideline[10] of fasting plasma glucose of ≥ 7.0 mmol/L (126 mg/dl) or a 2 h postprandial or oral glucose tolerance test of 11.1 mmol/L (≥200 mg/dl) or HbA1c of ≥ 6.5%. In this study, good glycemic control was defined as HbA1c of < 6.5%, while poor glycemic control as HbA1c of l ≥ 6.5%.

BP was measured using Vintage Accoson® mercury sphygmomanometer with the patient in both supine and sitting positions after a 5–10-min rest and confirmation that the patient avoided exercise, caffeine, and smoking 30 min before measurement. A cuff of appropriate size was wrapped around the proximal two-thirds of the upper arm (supported at heart level) and inflated 20 mmHg above the level where the radial pulse could no longer be palpated. Systolic and diastolic BP levels were taken at the first and fifth Korotkoff sounds, respectively. Hypertension was defined as BP ≥ 140/90 mmHg using the JNC-7 guideline for diagnosis and classification of hypertension.[11]

Five millilitres of random spot urine of each participant were collected into a sterile urine bottle for assessment of their urine albumin-to-creatinine ratio (UACR) determined using MICROALBUMIN (Immunoturbidimetric) test kit (Fortress diagnostics limited, Antrim, Northern Ireland, United Kingdom). UACR was calculated as albumin (mg)/creatinine (g). Normo-albuminuria (A1), microalbuminuria (A2), and macroalbuminuria (A3) were defined as UACR of < 30 mg/g, 30–300 mg/g, and > 300 mg/g, respectively. All urine samples were analysed in the Research laboratory of the hospital by the investigator and the laboratory scientist.

Five millilitres of fasting venous blood was collected from the cephalic vein of either the right or left cubital fossa. Three milliliter of blood sample was transferred into a lithium heparin bottle for estimation of serum total protein and albumin, while the remaining 2 ml was transferred into an ethylenediaminetetraacetic acid bottle for HbA1c estimation. All blood samples were analysed in the Research laboratory of the hospital.

Data collected were entered into an Excel spreadsheet and thereafter transferred into IBM statistical package for the social sciences version 23 (SPSS Inc., Chicago, Illinois, USA.) where it was checked for data entry errors, coded and analysed. Descriptive statistics was conducted, and continuous variables were summarised using mean ± standard deviation for parametric measurements, while categorical variables were summarised as frequency and percentages. Inferential statistics was conducted with means (standard deviations) of continuous variables compared using the Students *t*-test, while categorical variables were compared with the Chi-square test or Fisher's exact test as appropriate. A value of $P < 0.05$ was considered statistically significant. All results were presented in tables or graphs as appropriate.

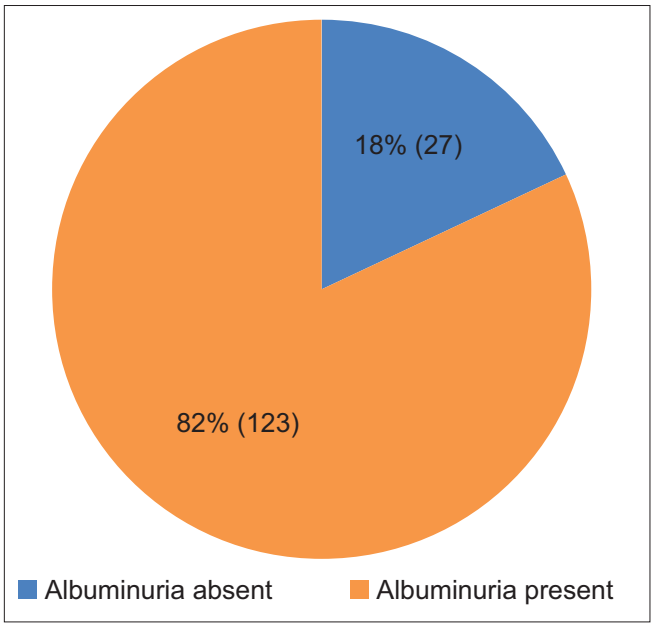

Figure 1: Pie chart illustrating the prevalence of albuminuria among study participants

Results

More females were recruited for the study with a female-to-male ratio of 1.68: 1 and a mean age of 55.87 ± 10.96 years. All participants had formal education. The mean duration of DM was 9.45 ± 6.94 years, while the most common symptoms at diagnosis of DM were frequent urination, tiredness, and frothiness of urine, constituting 125 (88.0%), 55 (38.7%) and 17 (11.6%), respectively. Participants with co-existing hypertension were 99 (69.7%). Meanwhile, 94.4% of the participants had a significant family history of diabetes. About 13.4% of participants consumed alcoholic beverages, while 2.8% used tobacco products occasionally. Oral hypoglycemic agents (OHA) were the most common medications used by participants, with 97.2% (138) exclusively on OHA, while 28.9% (41) used insulin regimen concurrently with OHA.

Participants recruited for this study had a mean body mass index (BMI) of 28.03 ± 5.46 kg/m^2, with 93 (65.5%) being overweight or obese, and 2 (1.3%) being underweight. There was a difference in BMI categories between male and female participants (X^2 = 24.097, P = 0.0001). The mean systolic BP among participants was 135.75 ± 18.83 mmHg, with a corresponding mean diastolic BP of 80.98 ± 10.90 mmHg. Table 1 summarises the biochemical parameters of the participants.

It was observed that 80.0% of the participants had suboptimal glycemic control. Summary statistics of HbA1c levels are highlighted in Table 2.

The KDIGO 2012 staging criteria for chronic kidney disease using albuminuria categories (UACR values) showed that 66.7% of the participants had microalbuminuria (A2) or incipient nephropathy, while 15.3% had macroalbuminuria (A3) or overt nephropathy [Table 3]. The calculated mean UACR was 153.54 ± 146.28 mg/g.

A total of 123 (82.0%) of the participants had moderate-to-severe degree of albuminuria. This is illustrated in Figure 1.

Assessing the relationship between the level of education and degree of albuminuria among participants did not show any statistical difference, where X^2 = 8.872, P = 0.064. Figure 2 shows the frequency of albuminuria categories among participants of different educational levels.

One-way analysis of variance test between UACR categories and mean age of participants show no statistically significant difference, where F = 0.729, P = 0.484, as shown in Table 4.

Although more females were recruited for this study and the middle age group was more representative, the association between UACR categories with sex and age of respondents [Table 5] presents no statistically significant difference, with P > 0.05 (alpha level).

There was no difference in UACR values observed among participants with co-existing hypertension compared to those without hypertension (X^2 = 0.852, P = 0.653). There was, however, a significant difference in the mean values of UACR and serum albumin (P = 0.0001), UACR, and eGFR (P = 0.0001) among study participants. Relationship between duration of Type 2 DM and UACR categories was not statistically significant with P = 0.473 [Table 6].

Table 1: Summary of biochemical profile of participants

Variable	Minimum value	Maximum value	Mean±SD
FBG (mmol/L)	3.7	23.0	8.36±3.69
HbA1c (%)	5.0	15.9	8.32±2.31
Total serum protein (g/dL)	58.0	90.0	69.78±4.87
Serum albumin (g/dL)	24.0	54.0	36.58±4.29

FBG: Fasting blood glucose, HbA1c: Glycated hemoglobin, SD: Standard deviation

Table 2: Glycated hemoglobin levels among participants

Variable	Frequency, *n* (%)
HbA1c	
Poor control (≥6.5)	120 (80.0)
Good control (<6.5)	30 (20.0)
Mean HbA1c	8.32±2.31

HbA1c: Glycated hemoglobin

Table 3: Renal function status of participants using urine albumin-to-creatinine ratio categories

Variable	Frequency, *n* (%)
UACR categories (mg/g)	
Normal to mildly increased (<30)	27 (18.0)
Moderately increased (30–299)	100 (66.7)
Severely increased (≥300)	23 (15.3)

UACR: Urine albumin-to-creatinine ratio

Table 4: Relationship between urine albumin-to-creatinine ratio categories with mean age of participants

Variable	Age (mean±SD)	ANOVA	
		F	*P*
UACR categories			
A1	54.67±10.27	0.729	0.484
A2	55.64±11.48		
A3	58.26±9.36		

ANOVA: Analysis of variance, UACR: Urine albumin-to-creatinine ratio, SD: Standard deviation, A1: Normoalbuminuria, A2: Microalbuminuria, A3: Macroalbuminuria

Discussion

DM remain a global health challenge, but recent advances in screening for chronic complications such as DN have changed the landscape in therapeutic guidelines. Albuminuria remains the earliest clinical sign of DN and is a marker of endothelial dysfunction which heralds DN. This study set out to identify the prevalence and spectrum of albuminuria among T2DM patients in our tertiary health facility.

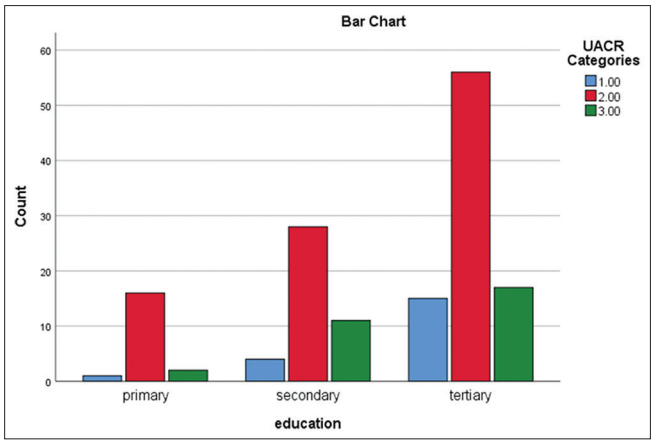

Figure 2: Bar chart showing frequency of albuminuria among participants of different levels of education. UACR: Urine albumin to creatinine ratio; 1.00 – normal levels; 2.00 – microalbuminuria; 3.00 - macro albuminuria

This study cohort comprised more females than males [Table 1] although it is known that DN affects males and females equally with no sexual predilection.[12] Interestingly, despite having more females recruited, our study did not find any significant difference in the prevalence of DN between males and females. (X^2 = 0.584, P = 0.747) which agrees with previous reports.[12] The middle age group constituted the highest majority making up 58.6% (88) of the study population [Table 1]. Age at onset and duration of diabetes are associated with the development and progression of DN, especially in the presence of chronic hyperglycemia from β cell exhaustion and poor glycemic control.[13] DN is reported to affect adults with a mean age of 60 years[12,13] with a higher risk in blacks, Pima Indians, and Native Americans. All participants of this study were Nigerians and majority fall within and above the middle age group; however, our study did not find a statistically significant difference between the age groups of participants and albuminuria (P = 0.29). This could be explained by the study design and methodology used.

Onovughakpo-Sakpa *et al*.[14] reported mean significant increases in UACR with the duration of diabetes (4.17 ± 0.63 years) among diabetic patients (type 1 and type 2) with their age- and sex-adjusted controls; our study was, however, a cross-sectional descriptive study and there was no statistical difference between UACR categories with age and sex of study participants [Table 5]. Furthermore, our study did not find any statistical association between the duration of diabetes and the development of albuminuria [Table 6]. Thus the development of DN may not be directly associated with the duration of DM but with chronic uncontrolled hyperglycemia. Several studies have highlighted the relationship between chronic hyperglycemia and the development and progression of DN[15,16] and our study observed that 80.0% of participants had suboptimal glycemic control with their HbA1c values above 6.5% [Table 2], which may explain the high prevalence of albuminuria recorded.

Table 5: Relationship between urine albumin-to-creatinine ratio categories with sex and age group of participants

Variable	UACR categories			Test of association	
	A1, *n* (%)	A2, *n* (%)	A3, *n* (%)	χ^2	*P*
Sex					
Female	18 (66.7)	62 (62.0)	14 (60.9)	0.235	0.889
Male	9 (33.3)	38 (38.0)	9 (39.1)		
Age group (years) merged					
<45	7 (25.9)	21 (21.0)	1 (4.3)		0.29+
>45-64	16 (59.3)	57 (57.0)	15 (65.2)		
65 and above	4 (14.8)	22 (22.0)	7 (30.4)		

+Fisher's exact. A1: Normoalbuminuria, A2: Microalbuminuria, A3: Macroalbuminuria, UACR: Urine albumin-to-creatinine ratio

Table 6: Relationship between duration of type 2 diabetes mellitus and urine albumin-to-creatinine ratio categories

Variable	Duration of DM (years)		Test of association	
	≤10	>10	Fisher's exact	*P*
UACR categories (mg/mmol)				
Normal to mildly increased (<30)	21 (20.8)	6 (12.2)	1.604	0.473
Moderately increased (30-299)	65 (64.4)	35 (71.4)		
Severely increased (≥300)	15 (14.9)	8 (16.3)		

UACR: Urine albumin to creatinine ratio, DM: Diabetes mellitus

In our study, we classified participants into various stages of albuminuria using spot urine albumin-to-creatinine ratio levels in staging DN[10] [Table 3]. It was observed that 66.7% had incipient nephropathy or moderate albuminuria (30–299 mg/g) while 15.3% had overt nephropathy or severe albuminuria (≥300 mg/g) levels. It can therefore be inferred that 123 (82.0%) of the participants had moderate-to-severe degrees of albuminuria of at least 30 mg/g [Figure 1] with a mean UACR value of 153.54 ± 146.28. This prevalence is similar to the findings of Janmohamed *et al*.,[17] who reported a prevalence of 80% in Tanzania using similar criteria. The index study presents a slightly higher prevalence than that reported by various other authors[18,19] in southern Nigeria, with values ranging between 58% and 72.63%. Patel *et al*.[20] reported a prevalence rate of DN as high as 43% in newly diagnosed type 2 DM patients. Our study, however, included both old and newly diagnosed patients with type 2 DM, which may explain the difference in prevalence values.

There have been reports suggesting that metabolic risk factors such as obesity are associated with the development of diabetic kidney disease.[21] Our study found a statistical difference in BMI categories between male and female participants (X^2 = 24.097, P = 0.0001); however, there was no significant difference in the prevalence of DN between males and females (X^2 = 0.584,

$P = 0.747$). Second, there was no statistical difference in the degree of albuminuria among participants with and without co-existing hypertension. This could be as a result of medications such as angiotensin-converting enzyme inhibitors or angiotensin receptor blockers used by 111 (74.5%) of the participants and their medications were not stopped before the study was conducted.

These findings buttress the need for spot UACR measurement as an early assessment tool for DN to promote early diagnosis and treatment with consequent retardation of progression to end-stage kidney disease from DN.

Limitations

Our study was a cross-sectional observational study, and so the conclusion of the diagnosis of DN could not be made based on a single-point sampling and analysis of the subjects. Second, this study was hospital based and all recruited participants received medications for DM, which may have influenced some values. Finally, this was a single-centre study; therefore, findings cannot be generalised to the entire Nigerian patients living with type 2 DM.

Conclusion

Our study observed a high prevalence of albuminuria (82%) among participants; we, therefore, suggest that all type 2 DM patients be routinely screened for micro/macro-albuminuria using spot UACR for categorisation at the point of diagnosis, and then yearly to enhance better health outcome.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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