

SJMLS - 10(1) - 008

**Prevalence of Microalbuminuria and Associated Risk Factors Among Type 2 Diabetic Patients Attending Some Selected Hospitals in Kano State, Nigeria**Suleiman, J.I.<sup>2\*</sup>, Babale, N.S.<sup>1</sup>, Ahmad, M. B.<sup>2</sup>, Idris, Y.M.<sup>3</sup>, Adamu, F.<sup>4</sup>

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**Abstract**

Diabetes mellitus is a major health problem accompanied by severe oxidative stress as well as acute metabolic and late systemic complications. Diabetic nephropathy as one of the late systemic complications is increasing steeply along with diabetes epidemic. Microalbuminuria (MA) as a biomarker plays an important role in the early detection of diabetic nephropathy (DN). The aim of the study was to check the prevalence of microalbuminuria risk factors associated with micro-albuminuria in type 2 diabetic patients. The study recruited 84 normotensive type 2 diabetic patients with and without MA and 84 age and gender-matched apparently healthy individuals as control group. Anthropometric measures including age, height, BMI and weight were assessed among the study participants. Plasma glucose, urea, creatinine, Glycated haemoglobin (HbA1c), urinary creatinine, urinary albumin and microalbuminuria were analyzed. The prevalence of MA among the diabetic patients was 22.6%. The measured anthropometric and biochemical parameters were significantly higher in the diabetic group than the control group ( $p < 0.05$ ). There was a linear increase with positive and significant association between GHbA1c control and MA development as the control worsens. According to disease duration (DOD), MA increased linearly as DOD elongated but the difference was insignificant. Female gender has higher but insignificant MA compared to the male gender. GHbA1c control has a direct effect on MA while disease duration effect may be pronounced as the time prolonged. BMI, gender, urea and FBG have no significant effect on ACR.

**Keywords:** Microalbuminuria, GHbA1c,**Introduction**

Diabetes is a major worldwide health problem with the leading cause of morbidity and mortality being its long-term vascular complications. For the development of these complications, hyperglycaemia has been shown to be a necessary but not sufficient condition. Diabetic nephropathy (DN) is defined as albuminuria (albumin excretion rate  $> 300$  mg/24 h) with a decline in renal function in a patient with known diabetes and in the absence of urinary tract infection or any other renal disease (Gross *et al.*, 2005). Diabetic nephropathy as one of the late systemic complications is increasing steeply along with diabetes epidemic. This is associated with increase premature mortality, ESRD, renal replacement therapy, cardiovascular diseases and escalating health care costs.

Early detection of DN is required so importantly to prevent or slow evolution of ESRD. Microalbuminuria (MA) as a biomarker plays an important role in the early detection of diabetic nephropathy (DN). Early detection of diabetic nephropathy is therefore important in order to prevent or slow the progression of patients to end stage renal disease. For the early detection of diabetic nephropathy, biomarkers predictive of the onset of DN play an important role and the best-known biomarker for DN is microalbuminuria testing. Microalbuminuria (MA) is an early marker of nephropathy (Son *et al.*, 2015). Therefore, early detection and appropriate interventions in asymptomatic individuals may

help in preventing deterioration in renal function and progression to diabetic nephropathy and end stage renal disease (Okpere *et al.*, 2012).

### Materials and Method

Fasting blood samples (10 hours) were collected in ethylene diamine tetra acetic acid EDTA (for glycated haemoglobin), fluoride oxalate (for glucose) and plain (for urea and creatinine) containers. Urine samples were collected randomly in sterile containers and used for urinalysis and microalbumin analysis. All pre-analytical errors were avoided, and proper sample transportation was ensured.

Eighty-four type 2 diabetic patients (18-80 years) with (ACR of 30-300 mg/g) and without microalbuminuria (ACR of less than 30 mg/g) attending Aminu Kano Teaching Hospital, Kano, Murtala Muhammad Specialist Hospital and Muhammad Abdullahi Wase Specialist Hospital were included in this study. The control group were eighty-four (84) (age and gender- matched) apparently healthy individuals from the blood donor clinic. Patients excluded include hypertensive type 2 diabetic patients, type 2 diabetic patients with other complications likely to affect the renal integrity like smoking, fever, vigorous exercise, urinary tract infection, and drugs. Patients with diabetic macroalbuminuria and cardiovascular disease were also excluded. Ethical approval was obtained from the ethical committee of Aminu Kano Teaching Hospital Kano before the commencement of sampling. Likewise ethical approval was collected from the Health and Research Ethical Committee of Kano State Ministry of Health. Selected patients were duly informed about the research and consent form signed willingly. A structured interviewer questionnaire was administered to obtain necessary information on the subject's blood pressure, age and anthropometric variables such as height, weight and history of DM.

### Statistical Analysis

The results were expressed as mean  $\pm$  SD. Statistical analysis was performed using statistical package for social science (SPSS) version 25.0 (SPSS Inc. Chicago, IL, U.S.A.). The independent t-test was used to compare variables between the case and control groups

since the variables were normally distributed. Chi square was used to check for relationships. Multiple regression analysis was used to check for relationships. Significant level was set at  $p < 0.05$ .

### Results

A total of one hundred and sixty-four 168 participants were recruited in this study. Eighty-four (84) type 2 diabetic patients and eighty-two (84) apparently healthy controls. Comparison of the mean values between the two groups was done using independent t-test. There was a statistically significant difference in the mean values of height, weight BMI and age between the two groups. This is shown in table 1.

Comparison of the mean values of some clinical parameters between the diabetic patients and controls was done using independent t-test. There were higher values of measured biochemical parameters in patients than in controls and were all statistically significant ( $p = 0.05$ ) in all the comparison including FBG, urea, creatinine and HbA1c. This is shown in table 2

Among the diabetic group, frequency of normal albuminuria was 65 (77.4%) while that of microalbuminuria was presented as 19 (22.6 %). Likewise, among the control groups frequencies of 78 (92.9%) and 6 (7.1%) were observed respectively for normal albuminuria and microalbuminuria. The prevalence is shown in table 3.

Diabetic patients were classified according to glycaemic control status. Patients with poor glycaemic control  $>7.0\%$  have the highest prevalence 58(69.0%) followed by those with 6.5-7.0% that are 12(14.3%) and lastly those with  $<6.5\%$  that are 14(16.7%).

Also, categorization according to albuminuria level was done among the groups. Diabetic patients with glycaemic status of  $>7.0\%$  have the highest number of M-ALB 13 and N-ALB 45 followed by glycaemic status of 6.5-7.0% with M-ALB 2 an N-ALB 10 and lastly, is the glycemic status of  $<6.5\%$  with M-ALB 3 an N-ALB 5. Chi- square test (0.528) was used to check for relationship and a p- value of 0.002 that indicate a significant relationship was obtained.

The diabetic patients were grouped according to duration of DM into three groups. Those <5 years have the highest frequency 41 (48.8%) followed by 5-10 years with 30 (35.7%) and lastly is the > 10 years with 13(15.5%). Diabetic patients under the >5 years have the highest number of M-ALB 11 and N-ALB 30 followed by 5-10 years with M-ALB 6 and N-ALB 24 and lastly are the > 10 years with M-ALB 2 and N-ALB 11. Chi square (0.922) was used to check for relationship and a p- value of 0.631 that indicated no significant relationship was obtained.

Among the eighty -four participants of the study group, female gender accounted for 57 (67.9%) while the male gender accounted for 27(32.1%). Also, the female gender shows higher M-ALB 13 and N-ALB 44 when compared with the Male gender having M-ALB 6 and N-ALB 21. This is shown in table 6.

Table 7 presented the proportional contribution of BMI, duration of diabetes, FBG, urea, creatinine and HbA1c as influential factors for

the development and progression of microalbuminuria. This was done using multiple regression analysis taking ACR as dependent variable while BMI, duration of diabetes, FBG, urea and creatinine were independent variable. Based on the analysis HbA1c (p=0.035) and creatinine (p=0.046) were found to be significantly related to ACR. BMI (p=0.658), urea(p=0.365) and FBG(p=0.382) were found not significantly related to ACR.

Table 8 presented the mean values for the comparison of creatinine, urea, HbA1c, DDT and FBG between the normoalbuminuric and macroalbuminuric categories. No statistical difference and significance was found in urea (p=0.525), FBG (p=0.058), HbA1c (p=0.965), BMI (p=0.657) and DD (p=0.438) between the N-ALB and M-ALB of the diabetic group. However, a statistical significance was found when creatinine (p=0.027) was compared among the N-ALB and M-ALB of the diabetic group. Independent t-test was used to obtain the statistical data.

**Table 1: Comparison of Anthropometric Parameters (Mean±SD) between Diabetic Patients and Controls**

Parameters	Test Group (n=84)	Control Group (n=84)	P-value
Age(Years)	44.05±12.08	36.04±9.11	0.000
Height(cm)	160.89±4.984	163.27±4.195	0.001
Weight(Kg)	64.60±13.73	61.02±5.48	0.028
BMI(Kg/m <sup>2</sup> )	25.00±5.20	22.66±1.75	0.000

BMI=Body mass index n=number of subjects t-test p<0.05

**Table 2: Comparison of Biochemical Parameters between Diabetic Patients and Controls**

Parameters	Diabetic Group (n=84)	Control Group (n=84)	P-value
FBG(mmol /L)	11.63±6.00	4.27±0.69	0.000
Serum Urea (mmol /L)	10.04±7.58	4.30±1.13	0.000
ACR(mg/g)	27.21±17.94	15.21±8.08	0.000
HbA1C (%)	8.47±2.23	4.59±0.49	0.000
Creatinine(µmol/L)	66.27±36.07	50.89±10.01	0.000

HbA1C= Glycated haemoglobin FBG= Fasting blood glucose n= number of subjects ACR= albumin creatinine ratio p 0.05

**Table 3: Frequency Distribution of Microalbuminuria in patients with type 2 DM**

Albuminuria Level	Test (n=84)	95% CI	Control (n=84)	95% CI
N-ALB <30 mg/g	65 (77.4%)	67.9-85.7	78(92.9)	86.9-97.6
M-ALB 30 – 300 mg/g	19 (22.6%)	14.3-32.1	6(7.1)	2.4-13.1

N-ALB=normoalbuminuria, M-ALB= microalbuminuria, n= number of subjects, CI= confidence interval.

**Table 4 Prevalence of Microalbuminuria among Diabetic Patients in Relation to Glycemic Control**

HbA1c Level	Frequency	N-ALB (n=65)	M-ALB (n=19)
<6.5%	14(16.7%)	10(15%)	4(21%)
6.5-7.0%	12 (14.3%)	10(15%)	2(10%)
>7.0%	58 (69.0%)	45(70%)	13(68%)

$\chi^2 = 0.528$  df=2 p=0.002

HbA1c= Glycated haemoglobin N-ALB= Normoalbuminuria M-ALB= Microalbuminuria

**Table 5: Prevalence of Microalbuminuria among Diabetic Patients in Relation to Duration of DM**

Duration of DM	Frequency	N-ALB (mg/g) (n=65)	M-ALB (mg/g) (n=19)
<5years	41(48.8%)	30(46%)	11(37%)
5-10years	30(35.7%)	24(37%)	6(25%)
10years	13(15.5%)	11(17%)	2(18%)

N-ALB: Normoalbuminuria M-ALB: Microalbuminuria n=no of subjects

**Table 6: Prevalence of Microalbuminuria among Diabetic patients in Relation to Gender**

Gender	Frequency	N-ALB (mg/g) (n=65)	M-ALB (mg/g) (n=19)
Male	27(32.1%)	21	6
Female	57(67.9%)	44	13

$\chi^2 = 0.004$ , df=1 p=0.593 n= number of subjects

**Table 7: Relationship between BMI, Duration of Diabetes, FBG, Urea, Creatinine, HbA1c and ACR**

Dependent Variable	Independent Variable	$\beta$	P- value
ACR	BMI(Kg/m <sup>2</sup> )	-0.052	0.658
	FBG (mmol/L)	-0.108	0.382
	Urea (mmol/L)	-0.158	0.365
	Creatinine (mmol/L)	0.342	0.046
	HbA1c %	0.025	0.035

BMI= body mass index, FBG= fasting blood glucose, HbA1c= Glycated haemoglobin

**Table 8: Comparison of Mean Values of Parameters among Normoalbuminuric and Microalbuminuric Diabetic Patients**

Parameter	N-ALB	M=ALB	P value
Creatinine(mmol/L)	61.49±11.51	82.31±71.96	0.027
BMI(Kg/m <sup>2</sup> )	24.86±6.05	25.44±4.87	0.657
FBG (mmol/L)	12.24±6.18	9.56±4.93	0.058
HbA1c (%)	8.48±2.18	8.45±2.47	0.965
DOD(Years)	6.49±6.05	5.39±5.15	0.438
Urea(mmol/L)	3.79±1.34	4.26±3.11	0.525

BMI=body mass index FBG=fasting blood glucose HbA1c= glycated haemoglobin DOD=duration of disease N-ALB=normoalbuminuria M-ALB= microalbuminuria

**Discussion**

Diabetic nephropathy is one of the complications of diabetes mellitus of public importance. Early detection of diabetic nephropathy is of paramount importance in order to provide appropriate therapy that prevent or slows the evolution towards end stage renal disease. In early detection of diabetic nephropathy, biomarkers play an important role and the best known is microalbuminuria testing. Microalbuminuria (MA) is an early marker of nephropathy (Son *et al.*, 2015). Therefore, early detection and appropriate interventions in asymptomatic individuals may help in preventing deterioration in renal function progression to diabetic nephropathy and end stage renal disease (Okpere *et al.*, 2012a).

In the current study, the prevalence of microalbuminuria was 22.6% (ACR 30-300 mg/g), and 77.4% normoalbuminuria (ACR < 30 mg/ g) among type 2 diabetic patients in Kano State, Nigeria. This implies that 2 diabetic patients have or

may develop diabetic nephropathy (DN) in every 10 diabetic patients in the current study. In Africa, MA has been estimated to be twice the prevalence in the general population among persons with DM (Perkins *et al.*, 2000). And approximately half the patients with MA will progress to overt proteinuria over the next decade (Perkins *et al.*, 2003).

The 22.6% prevalence reported in this study agrees with the finding reported among diabetic patients in Jigawa, Kaduna (Zaria) and Sokoto States by Ahmad *et al.* (2019a), Ahmad *et al.* (2014) and Bunza *et al.* (2014) where a prevalence of 20%, 23% and 22% were reported respectively as well as the 20% reported by Sheikh (2009) in Pakistan. A likely reason for the similarity may be the method of testing urinary albumin assessment. Immunoturbidometric method which is considered to be the method of choice employed by the current and reported studies.

Some prevalence higher than the current study were reported. Ogbu *et al.* (2009) and Udenze *et al.* (2013) in a research carried out in Enugu State and Lagos University Teaching Hospital respectively reported prevalence range of 49.2% and prevalence of 58%, 50% and 38 % were reported respectively by Ufuoma *et al.* (2016) in medical outpatient department of central hospital, Warri. Unuigbe *et al.* (2001) in Benin and Orluwene *et al.* (2008) in Port Harcourt. Halliru *et al.* (2016) reported a higher prevalence of 34% in Gumel, Jigawa State. Also, higher prevalence of 71.8% by Buch *et al.* (2012a) in an Indian population, 44.6 % by Molefe- Baikai *et al.* (2018a) in Botswana population, 37% by Chowta *et al.* (2009) in an Indian population and 27.2 % by Meisinger (2008a) were also reported. Ejuoghanran *et al.* (2009) reported a prevalence of 76.23% in Southern Nigeria. Elsewhere, Jatou *et al.* (2022) reported a prevalence of 9.8% in Saudi Arabia, and a prevalence of 30.3% was document by Hode *et al.* (2023) in Cotonou, Benin Republic.

Factors such as differences in population, definition of MA, method of urine collection and testing of MA have been attributed to the variations in the prevalence of MA. The current study recruited only non-hypertensive type 2 diabetic patients whereas in some other studies both type 1 and type 2 diabetic patients as well as those with hypertension were recruited. This population characteristic difference may likely be the cause of the disparity. Microalbuminuria was defined by the current study as ACR >30-300 mg/g and normoalbuminuria as ACR < 30 mg/g. Socio-economic disparity and disparities in access to health care among the different population studied would have also contributed.

Most importantly among the factors that may have contributed to the disparity is the method of testing albuminuria. Most of the studies used semi-quantitative micral test for assessing urinary albumin. This method has been reported to be less specific (Lutalle *et al.*, 2007a) compared to the immunoturbidimetric method employed by the current study. Immunoturbidimetric method has been considered to be a method of choice for urinary albumin estimation. Several studies have demonstrated numerous demographic and clinical variables

such as gender, age, long duration of DM and poor glycemic control to be predictors of microalbuminuria among diabetic patients.

In the current study, diabetic patients were categorized according to gender, duration of DM and glycemic control and the results obtained for the prevalence of MA were found to be considerably different. Based on glycaemic control, a prevalence of 16.7%, 14.3% and 69.0% for the patients that fall in the <6.5%, 6.5-7.0% and >7.0% category respectively. There is increase in the number of M-ALB as glycaemic control worsens and therefore an increase in the risk of MA. The association between MA and poor glycaemic control reported by the current study may be due to lack of availability and accessibility of diagnostic tools affecting Sub-Saharan Africa with Nigeria inclusive. It was reviewed that lack of amenities were pointed out to be associated with nephrology (Swanepoel *et al.*, 2013). Also, according to the current study, there was a simultaneous linear increase between the glycaemic status and MA as glycemic control deteriorates. This finding agrees with the finding of Ahmad *et al.* (2019b)

Therefore, the current study revealed that poor glycemic control which was demonstrated by HbA1c testing is directly linked to the occurrence of MA in type 2 diabetic patients. Higher and significant mean values of HbA1c and more M-ALB were seen in the study group with poor glycemic control when compared with the rest of the categories and likewise with the controls too. There was a strong and significant association between the glycaemic control and development of MA according to the current study. This is alarming and shows the clinical importance of HbA1c testing among diabetic patients to check for glycaemic control. Poor glycaemic control is a good risk factor to MA development and progression and finally to ESRD whereas good glycaemic control will stop or slow the development of MA and subsequent renal disease progression. The study Ghosh *et al.* (2012) shows a significant relationship between glycaemic control and MA showing an agreement with the current findings. Reports in contrast to the present study show no significant relationship between the glycaemic control and MA (Lutale *et al.*, 2007b; Molefe-Baikai *et al.*,

2018b; Martin *et al.*, 2019). The difference may be as a result of difference in definition of microalbuminuria, categorization of glycaemic control and method used in analyzing HbA1c.

On categorizing based on disease duration, a prevalence of 48.8%, 35.7% and 15.5% for the patients that fall in the <5 years, 5-10 years and >10 years category respectively. There was a simultaneous linear decrease in M-ALB as disease duration elongates. Duration of DM has significant contribution to the development of microalbuminuria due to prolonged exposure to hyperglycemia induced advanced glycosylation and accumulation of end products. However, the present study found no statistically significant association between disease duration and ACR. This is agreement with some findings (Alfehaid, 2017; Abougambou and Abougambou, 2013a). Possible explanation to the current finding may be the fact that only few people had longer duration of diabetes (15.5%) in the study. Also, older patients may likely be symptomatic due to multiple DM complications and therefore adhere more to antidiabetic medications with the latter likely to improve glycemic control and then cause regression of MA. However, Iwalokan *et al.* (2006) in Lagos, Lutalle *et al.* (2007c) in Tanzania and Ahmad *et al.* (2019c) in Jigawa are in contrast with the current finding. Findings reported by Meisinger *et al.* (2008b), Sheikh (2009) and Buch *et al.* (2012b) revealed an association between duration and MA. ADA (2018) reported that the duration of diabetes is a strong predictor of complications associated to diabetes. Dating the onset of DM is by self-reporting which is subjected to recall by the person and therefore results in difficulty in dating the onset of DM. This may have resulted in this conflicting factor.

Regarding differences in the gender of the patients recruited in this study, a prevalence of 32.1% and 67.9% was reported for male and female gender respectively. The finding of this study reported a prevalence higher in the female gender than in the male gender. Also, no significant association between gender and development of microalbuminuria was reported by the current study. Studies reported by Varghese *et al.* (2001), Abougambou and Abougambou (2013b), Molefe-Bakai, (2018c)

and Ahmad *et al.* (2019d) also show no statistical difference in the prevalence and association among gender. Okpere *et al.* (2012b) and Martin *et al.* (2019) reported a contrasting finding.

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**Citation:** Suleiman, J.I., Babale, N.S., Ahmad, M.B., Idris, Y.M., Adamu, F. Prevalence of Microalbuminuria and Associated Risk Factors Among Type 2 Diabetic Patients Attending Some Selected Hospitals in Kano State, Nigeria. *Sokoto Journal of Medical Laboratory Science*; **10**(1): 73–80. <https://dx.doi.org/10.4314/sokjmls.v10i1.8>

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