Original article

Prevalence and Correlates of Microalbuminuria among Type 2 Diabetes Patients at Muhimbili National Hospital, Dar es Salaam, Tanzania

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Abstract

Background
Regular screening for microalbuminuria among type 2 diabetes patients is less common in most low-income countries while it is an early marker of diabetic nephropathy and cardiovascular complications.

Objective
This study aims to assess the need for regular screening for microalbuminuria among type 2 diabetes patients.

Methodology
 with cross-sectional approach, 124 diabetic patients were recruited at Muhimbili National Hospital, in Tanzania; their age, gender, body mass index, fasting blood sugar levels (by Accu Chek Active Glucometer), random urine albumin levels (by Microalbumin 2-1 Combo Test Strips), and the duration of diabetes were recorded.

Results
The study indicated that 62.1% of the participants were microalbuminuric while 2.4% were macroalbuminuric. The risk of microalbuminuria was 4.55 higher in patients aged 60-69 years (95% CI: 1.32-16.51), and 17.4 times higher in patients aged 70 and above (95% CI: 1.49-202.86) compared to individuals aged below 50 years. Patients with high blood sugar level had a risk of 8.09 times higher compared to those with normal blood sugar (CI: 2.53-25.86). Also, the odds were 7.89 higher in patients who lived with diabetes for 10-14 years compared to those lived with the disease less than 5 years (95% CI:1.33-45.59).

Conclusion

The odds of microalbuminuria increased significantly as the patient gets older, with high blood sugar, and the duration of diabetes. Health policies need to establish programs that enhance care at the diabetic clinic through regular screening for microalbuminuria to reduce the risk of developing kidney and cardiovascular complications.

Introduction

The world and Sub-Saharan Africa, in particular, are experiencing a high increase of non-communicable diseases which will continue to lead as the cause of mortality and morbidity until 2030.[1] Currently, type 2 diabetes mellitus is already on top of reported non-communicable diseases and the main cause of chronic illness and deaths worldwide, and it is causing premature deaths, especially in low-income countries. For instance, in 2013, the majority of deaths caused by diabetes worldwide were among people under the age of 60 years, and the sub-Saharan Africa region accounted for 75% of these deaths.[2] The data from the International Diabetes Federation in 2009 shows that more than 371 million people globally had diabetes, and this number is predicted to increase to over 550 million by 2030, with a large number living in low-and middle-income countries.[3] For instance, in 2006, the Tanzania Diabetes Association (TDA) estimated that there were more than 400,000 people with diabetes.[4]

Diabetes mellitus, defined as persistent hyperglycemia, reflects derangements in carbohydrates, fats, and protein metabolism which itself is a consequence of insulin deficiency, insulin resistance, or both.[5] Type 2 diabetes mellitus (T2DM) is common among middle-aged and older people, although it can occur at any age.[6] It is mostly associated with insulin resistance and impacts the main organs involved in the carbohydrates and lipids metabolism. T2DM induces glucose production in the liver and overproduction of free fatty acids by fat cells and also impedes glucose uptake in both liver and skeletal muscle.[7] Insulin deficiency occurs following the gradual failure of beta-cells which produce an insufficient amount of insulin.[8] Most of the people with T2DM live with it for a long time unknowingly as the disease remains asymptomatic until the individual shows signs of diabetes complications. The excess of blood

glucose, as it takes years to appear or be recognized, silently, destroys the body.[6] The metabolic derangements of long duration, progressively affect the integrity of body cells and sometimes lead to the permanent loss of function for some organs of the body. The first to be affected is the vascular system due to high blood glucose levels and other abnormal metabolites present in the blood which induce endothelial dysfunction. The dysfunctional endothelium is at the heart of developing diabetes complications.[9] These complications mainly include cardiovascular diseases, diabetic neuropathy, amputations, renal failure, and blindness.[3]

The majority of the causes of morbidity and mortality among diabetic patients result from microalbuminuria because of its association with cardiovascular diseases, proliferative retinopathy, peripheral neuropathy, and renal impairments, which, when not controlled, lead to end-stage renal disease (ESRD).[10] Many people with T2DM will show microalbuminuria at the time of diabetes diagnosis.[11] Studies indicated that up to 30% of people newly diagnosed with T2DM have an abnormal amount of albumin protein in the urine, an indication that they may have overt proteinuria even at diagnosis.[12]

Several studies indicated microalbuminuria as the first sign of diabetic nephropathy. It develops in the very early stages of diabetes mellitus even when the glomerular filtration rate (GFR) is still normal.[13] This stage is very critical in the management of diabetes as studies have shown that when microalbuminuria is detected early, it is easily addressed to prevent the future development of overt diabetic nephropathy.[12,14]

Microalbuminuria does not have symptoms in the earliest stages. Therefore, it is essential to screen for it among T2DM patients to offer optimal protective therapy against renal failure and cardiovascular events.[15,16] However, the screening is not common in Sub-Saharan Africa even though diabetes is already a serious health challenge in the region.[17] This study intended to assess the need for regular screening for microalbuminuria among type 2 diabetes patients by determining its magnitude and its correlates among those attending the outpatient clinic at Muhimbili National Hospital in Tanzania.

Methods

Study design, setting, and population
The study used a cross-sectional design. Data were collected from December 2014 to January 2015

among outpatients diagnosed with T2DM that attended the diabetes clinic of Muhimbili National Hospital (MNH), the largest hospital in Tanzania located in Dar es Salaam city. The clinic receives T2DM patients twice a week, about 60 patients a day. Patients see a doctor for follow-up once in three to five months, the attendance pattern can change depending on the status of the disease.

Sample size and sampling procedure
The study involved 124 participants calculated using the formula designed for cross-sectional studies. As a reference, we used the prevalence of microalbuminuria among type 2 diabetes patients found by a study done at Kilimanjaro Christian Medical Centre (KCMC) in Tanzania (29%).[18] A convenient sampling procedure was used to collect data; participants were recruited based on their scheduled visits to the diabetes clinic. The procedure was appropriate to collect data within the limited time of 2 months and to abide by the working plan of twice a week of the diabetes outpatient clinic of MNH. Around 500 patients attended the clinic during the two months of data collection among whom we recruited the study participants based on predefined inclusion criteria. We only included T2DM patients who did not have any of the known conditions associated with microalbuminuria, including proteinuria, renal diseases, acute illness, hematuria, hepatic and heart-related diseases, polyuria, urinary tract infection, and hypertension. Also, we included patients who accepted to sign the consent to participate in the study.

We identified 146 potential participants among those who attended the clinic during the period of data collection using the patient's clinical sheets available at the outpatients' diabetes clinic of the hospital. Each potential candidate who consented to participate in the study provided a urine specimen which was screened using dipstick strips with 11 parameters. Only individuals whose specimens tested negative for urinary tract infection (leukocytes, nitrites), proteinuria, and glycosuria were included in the study. In total, we selected 124 participants after the screening.

Ethical considerations
We got the ethical clearance from the Muhimbili University of Health and Allied Sciences (MUHAS) ethical review board and requested permission from the MNH administration. We explained the purpose and the importance of the study to the patients before enrolment. Participants got hard copies of the consent form written in Swahili, which is the local language, to read and ask questions about

whatever they could not understand. The consented participants signed the consent form showing their willingness to participate in the study.

Data collection
Basic information
We used a structured form for each participant to record information on age, sex, and the duration of diabetes. We recorded the without shoe height and weight of each participant for BMI calculation. We calculated BMI by taking the weight of an individual in kilograms divided by the square of his/her height in meters. We classified patients' weight as the normal weight for BMI of 18.5-24.9kg/m^2, overweight for BMI between 25-29.9 kg/m^2, and obese for BMI of 30 kg/m^2 and above.

Laboratory procedures
Capillary fasting blood glucose was tested using Accu-Chek Active Glucometer measuring blood glucose into mmol/L. A mean value of 7.2 mmol/L of blood sugar was considered normal while the value above 7.2 mmol/L was considered as high.[19] Urine samples were tested for microalbuminuria using Microalbumin 2-1 combo strips (CLIA waived, Inc. 2-1 Creatinine/Microalbumin Rapid Test Strips) as per the manufacturer's instructions. The obtained results of albumin and creatinine were used to calculate the albumin/ creatinine ratio (ACR). The microalbuminuria was defined as a value of albumin to creatinine ratio ranging from 30-300mg/g while the value above 300mg/g was considered macroalbuminuria.[20]

Data analysis
We classified participants according to their baseline characteristics that are age, gender, BMI, blood sugar levels, and the duration of diabetes. Then, we cross-tabulated the participants' characteristics with the ratios of albuminuria (the outcome variable) in three levels (normal, micro, macro) to observe its prevalence patterns. The chi-square test was used to assess whether there was a significant association between the albuminuria levels by the baseline characteristics. Finally, we conducted the logistic regression analysis test with a 95% level of statistical significance to determine the factors associated with microalbuminuria among the baseline characteristics. Age and duration of diabetes were used as continuous variables while gender, BMI, and blood sugar levels were used as categorical variables.

Results

Baseline characteristics of the study participants by gender

Table 1 presents the baseline characteristics by gender for the 124 T2DM patients that participated in

the study. Among the participants, 75 (60.5%) were females and 49 (39.5%) males. The majority (65.4%) were below the age of 60, with a quarter being below the age of 50 (40.3%). Three-quarters of the participants had high blood sugar

levels among which female participants had the highest percentage (45.2%) compared to male participants (29.8%).

Table 1. Baseline characteristics of study participants by gender

Variable	Categories	Frequency N=124 n (%)	Females 75 (60.5%)	Males 49 (39.5%)
Age (in years)	≤ 49	31(25.0)	16(12.9)	15(12.1)
	50-59	50(40.3)	30(24.3)	20(16.1)
	60-69	34(27.4)	23(18.5)	11(8.9)
	≥70	9(7.3)	6 (4.8)	3(2.4)
Blood sugar	Normal(≤7.2 mmol/L)	31(25.0)	19(15.3)	12(9.7)
	High (≥7.3 mmol/L)	93(75.0)	56(45.2)	37(29.8)
BMI	Normal weight	43(34.7)	20(16.1)	23 (18.5)
	Overweight	49(39.5)	26(21)	23(18.5)
	Obesity	32 (25.8)	29(23.4)	3(2.4)
Duration of diabetes (in years)	≤ 4	48(38.7)	29(23.4)	19(15.3)
	5-9	39(31.5)	22(17.7)	17(13.7)
	10-14	23(18.5)	16(12.9)	7(5.6)
	≥15	14(11.3)	8 (6.5)	6 (4.8)

Concerning the body mass index, 39.5% were overweight whereas 25.8% were obese. Also, the body mass index was higher in females than in males. The majority (70.2%) of the patients had diabetes for less than ten years among which 38.7% had diabetes for five years or less.

The prevalence of albuminuria

Table 2 presents the prevalence of albuminuria in levels cross-

tabulated with the patients' baseline characteristics, and the chi-square test of association between the two. The data shows that 35.5% of the participants had a normal level of urine albumin. Seventy-seven of the participants (equivalent to 62.1%) had microalbuminuria while 3(2.4%) of them had macroalbuminuria. Most patients in the 50s and 60s had microalbuminuria with a combined

percentage of 46.8 for the two groups.

Table 2. The prevalence of albuminuria by the characteristics of the study participants

| Variable | Category | Frequency N= 124 | Urine albumin levels | | | P-value |
			Normal-albuminuria 44 (35.5%)	Micro-albuminuria 77 (62.1%)	Macro-albuminuria 3 (2.4%)	
Gender	Females	75	27 (21.8)	47 (37.9)	1 (0.8)	0.585
	Males	49	17 (13.7)	30 (24.2)	2 (1.6)	
Age	≤ 49	31	16 (12.9)	15 (12.1)	0 (0)	0.001*
	50-59	50	20 (16.1)	29 (23.4)	1 (0.8)	
	60-69	34	5 (4.1)	29 (23.4)	0 (0)	
	≥ 70	9	3 (2.4)	4 (3.2)	2 (1.6)	
Blood sugar	Normal	31	20 (21.0)	11 (8.9)	0 (0)	
	High	93	24 (19.4)	66 (53.2)	3 (2.4)	0.000*
	Normal	43	14 (11.3)	28 (22.6)	1 (0.8)	0.944
BMI	Overweight	49	15 (12.1)	33 (26.6)	1 (0.8)	
	Obese	32	15 (12.1)	16 (12.9)	1 (0.8)	
Duration of diabetes (in years)	≤ 4	48	26 (21.0)	22 (17.7)	0 (0)	
	5-9	39	13 (10.5)	26 (21.0)	0 (0)	0.000*
	10-14	23	4 (3.2)	18 (14.5)	1 (0.8)	
	≥15	14	1 (0.8)	11 (8.9)	2(1.6)	

* Significant at 0.05 level

Likewise, the prevalence of microalbuminuria in patients with high blood sugar was relatively high, comprising 53.2% of all the samples tested. The distribution of albumin levels was significantly associated with the age, blood sugar levels and the duration of diabetes (P<0.001). However, there was no statistically significant difference in the distribution of the albumin levels by gender and BMI categories.

Correlates of microalbuminuria

Table 3 presents the results of the logistic regression analysis of the association between microalbuminuria and the selected predictors. The results indicate an increased risk of microalbuminuria as the age of the patient increased. Patients aged between 60-69 years had 4.66 times the risks of microalbuminuria compared to patients aged below 50 years (95% CI: 1.32-16.51), and the risk increased 17.4 times in patients aged

70 years and above (95% CI: 1.49-202.87). Similarly, the risk for microalbuminuria increased with the duration an individual lived with diabetes. Patients who lived with diabetes for 10-14 years had 7.89 times risks of developing microalbuminuria compared to those who lived with the disease less than 5 years (95% CI: 1.37-45.59); patients with high blood sugar had 8.09 times risks of microalbuminuria compared to those with normal blood sugar (95% CI: 2.53-25.86).

Table 3. Results of the logistic regression analysis of the association between microalbuminuria and the selected predictors

Univariate model				Multivariable model		
	Odds ratio	95% CI	P- value	Odds ratio	95% CI	P value
Age (in years)						
≤ 49	1	-	-	1	-	-
50-59	3.03	1.17-7.83	0.022*	1.99	0.66-6.00	0.222
60-69	4.45	1.53-12.97	0.006*	4.66	1.32-16.51	0.017*
≥70	32.45	3.80-277.1	0.001*	17.4	1.49-202.87	0.023*
Duration of diabetes (in years)						
≤ 4	1	-	-	1	-	-
5-9	2.08	0.89- 4.85	0.089	2.31	0.81-6.64	0.119
10-14	12.67	2.65-60.46	0.001*	7.89	1.37-45.59	0.021*
≥ 15	7.33	1.47-36.66	0.015*	2.46	0.34-17.87	0.374
BMI						
Normal weight	1	-	-	1	-	-
Overweight	0.96	0.42-2.20	0.923	1.07	0.38-3.01	0.899
Obese	1.84	0.69-4.90	0.223	0.46	0.10-2.09	0.315
Blood sugar						
Normal	1	-	-	1	-	-
High	10.73	3.92-19.41	0.000*	8.09	2.53-25.86	0.000*
Gender						
Female	1	-	-	1	-	-
Males	1.53	0.72-3.26	0.264	1.17	0.43-3.22	0.753

* Significant at 95% confidence interval

However, there was no statistically significant association between the prevalence of microalbuminuria and the body max index of the patients, nor was it associated with gender.

Discussion

This study assessed the magnitude of microalbuminuria among type 2 diabetes patients and analyzed its correlates to inform the diabetes clinics of the need for regular microalbuminuria screening. Results indicated that the prevalence of

microalbuminuria among type 2 diabetes outpatients at MNH was 62.1%. Our finding is close to that observed in earlier studies conducted in developing countries similar to Tanzania.[10,21] However, this prevalence is higher compared to what was found 10 years earlier in the same hospital.[22] Several reasons could explain the difference, among which is the ten years-time lapse. It is reasonable that in ten years many things could have happened including an increased number of patients, delayed diagnosis among others. The other reason may be the different methods used in the detection of microalbuminuria. The mentioned study used 24 hours excretion rate whereas ours used an albumin to creatinine ratio. The 24 hours urine albumin excretion rate is considered the gold standard method. However,

due to the challenges of imperfect adherence of the patient to the protocol, the method is not suitable to be used in epidemiological research and clinical settings. Therefore, the albumin to creatinine ratio in a random spot urine sample has been the recommended method as it is easy, rapid, and accurate.[19]

The study did not indicate the association between obesity and microalbuminuria, contrary to what was reported in other studies where obesity was found to be a risk factor for microalbuminuria in type 2 diabetes patients.[9] The lack of association could not be attributed to the size of the sample of 124 patients, as the referenced study used a much smaller sample of 60. Rather, the reason could be the differences in populations, as in our study, T2DM patients had the disease for a relatively shorter period (mean duration of seven years), whereas, in the referenced studies, patients had had the disease for a much more extended period. Equally important, is the fact that in a case-control study done to evaluate the association between obesity and microalbuminuria among non-diabetic patients, a strong association between obesity and microalbuminuria was reported. The same study indicated that microalbuminuria was highly prevalent among obese subjects compared to the controls.[23] It

seems that this difference may be related to factors other than diabetes which may be linked to obesity and causing microalbuminuria.

The results of the present study also show that the association between microalbuminuria and gender was not statistically significant, which is similar to what was reported.[24] Nevertheless, Malir Cantt, in Pakistan found that microalbuminuria was correlated with female sex,[25] while a study conducted in the Indian population reported a statistically significant correlation between microalbuminuria and male sex.[24] Based on these results we can assume that these variations in the results may be attributed to differences in lifestyle, which could have exposed men and women differently in the different societies involved.

The study shows a significant association of microalbuminuria with age. This finding is similar to the study conducted at a diabetic clinic in King Abdulaziz university hospital, Saudi Arabia.[26] but contrary to what reported in the study conducted at Al-Husain Hospital, Iraq.[21] These conflicting findings may be due to other confounding factors than the age of subjects, such as dyslipidemia, undiagnosed hypertension among others.

Microalbuminuria is considered to be a meaningful early sign of diabetic nephropathy, which by itself is one of the severe complications of diabetes mellitus.[27] Microalbuminuria develops after 5-10 years from diabetes onset.[28] Consequently, we hypothesized that the degree of microalbuminuria would increase as the number of years an individual lived with diabetes would increase. The findings from this study supported our hypothesis as they indicated that the risk of microalbuminuria increased with the number of years an individual lived with diabetes, which agreed with other related studies.[29] However, some studies, like the one conducted by Ibrahim et al., reported no association between the duration of diabetes and the prevalence of microalbuminuria.[21] This difference may be due to other factors such as poor control of blood sugar and being elderly especially considering that T2DM is common in older people. Another factor to take into account is the delayed diagnosis of diabetes given that its signs appear at an advanced stage.

Last, the study investigated the relationship between microalbuminuria and blood glucose levels. The data show that T2DM patients with high blood glucose levels have an increased risk of microalbuminuria compared to T2DM patients with normal blood

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glucose, just as it was reported elsewhere.[30] The patients with high blood glucose levels indicate a high prevalence of microalbuminuria due to that the high blood glucose level increases pressure in the kidney, which leads to the development of microalbuminuria.

Limitations

The first limitation is that the study did not account for some potential confounders like dyslipidemia, HIV, and hypertension. Consequently, the findings should be interpreted considering this limitation. Secondly, it was not possible to determine the exact date on which a patient developed diabetes. Therefore, the data presented on the duration of diabetes was based on the date a patient was diagnosed and pronounced to have diabetes. The third limitation is that the study was conducted at one hospital, and for a limited period, meaning that if it could have been extended much longer and recruiting patients from various hospitals, probably the findings could have been different. However, we remain confident that the findings of this study are valuable to inform health providers and policymakers on the improvement of care given to patients with diabetes.

Conclusions and Recommendations

Microalbuminuria is high among patients with T2DM. The most vulnerable patients are those aged between 50 years and 60 years, and those with high glucose levels. The risk for microalbuminuria increases with age and with the duration of diabetes. Gender and BMI are not significantly associated with microalbuminuria. The study recommends diabetes clinics to conduct regular screening for microalbuminuria in T2DM patients to inform clinical decisions to prevent the risk of developing kidney diseases. Screening should be done at diagnosis and repeated regularly on an annual basis, and proper control of blood glucose should be emphasized to reduce the risk of microalbuminuria and kidney damage.

This study was cross-sectional, and the findings are interpreted to the design and the associated limitations and advantages. We recommend further studies to use the findings to design a longitudinal study involving more extended population coverage.

Conflicts of Interest

No conflicts of interest are associated with this study

Authors' Contributions

EK conceived the idea, and designed the study methodology. She carried out the literature review, data collection, and wrote the first draft. DU worked on data analysis and critically revised the manuscript. TM supervised all research activities. All authors read and revised the manuscript and agreed on the final version before submission.

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