Prevalence of Macroalbuminuria and Associated Risk Factors Among Diabetic Patients in Moshi, Northern Tanzania

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Research Article

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Abstract

Background: Diabetic nephropathy (DN) is a leading cause of end-stage renal disease (ESRD) globally. Macroalbuminuria signals a critical stage in DN progression, often associated with poor glycemic control. However, data from sub-Saharan Africa remain limited. This study aimed to assess the prevalence and associated risk factors of macroalbuminuria among patients with type 2 diabetes mellitus (T2DM) in Northern Tanzania.
Methods: A descriptive cross-sectional study was conducted at the Kilimanjaro Christian Medical Centre among 119 T2DM patients. Macroalbuminuria was defined as proteinuria ≥ +1 on Multistix® dipstick. Clinical and biochemical data were collected and analyzed using logistic regression.
Results: The prevalence of macroalbuminuria was 16.8%. Bivariate analysis showed significant associations with male sex, longer diabetes duration, elevated creatinine and cholesterol, and high systolic blood pressure. However, no variable remained statistically significant in multivariate analysis.
Conclusion: Macroalbuminuria is common in this population. Routine dipstick testing may help identify high-risk patients early and prevent progression to ESRD in resource-limited settings.

Introduction

Diabetic nephropathy is a significant health and economic burden across the world as its prevalence is increasing rapidly among diabetic patients and usually occurs within 10 to 15 years since onset of diabetes.[1]

The prevalence and incidence rate of diabetic nephropathy is increasing rapidly in parallel to a rapid growing pace of diabetes, without radical improvements in prevention and treatment of diabetes, its prevalence will continue to increase[1]

Diabetic nephropathy (DN) usually begins as micro albuminuria followed by macroalbuminuria (persistent proteinuria > 300mg/day) and eventually leading to ESRD, it is currently considered as the single commonest indication for renal replacement therapy worldwide.[2]

Studies in the Western world have shown that diabetic patients with micro albuminuria have increased risk of progression to overt proteinuria, and approximately 20% usually develop ESRD after 20 years[3], however very little is known about its prevalence in Africa and SSA is no exception.

DN, Its epidemiology has been studied to a large extent in microalbuminuria than in macroalbuminuria, in contrast to diabetic Patients with microalbuminuria, macroalbuminuric patients may progress to ESRD within a very short period of time, due to increasingly poor glycemic control and other commonly related risk factors. However recently, several clinical studies have reported that intensive intervention including inhibition of the renin-angiotensin system could induce a reduction in macroalbuminuria and improve renal prognosis.[4]

Since most of our clinics in sub-Saharan Africa, we do miss patients who are at microalbuminuric stage due to unavailability of highly sensitive methods of detecting protein in this stage, early identification during the macroalbuminuric stage is essential by doing dipstick test. Dipstick testing is one of the easiest methods of detecting protein in urine and it is easily available in most diabetic clinics, and once protein is detected in urine prompt interventions should be taken to protect this patients from progressing to ESRD. However data on the prevalence of macroalbuminuria in patients with diabetes and its associated risk factors are scarce in most low-resource sub-Saharan African settings including our Centre.

So the purpose of present study was to determine the prevalence and its related risk factors of macroalbuminuria in patients with diabetes and provide a gap for further interventional studies aiming at reducing macroalbuminuria, and hence improving renal prognosis in patients with diabetes in Northern Tanzania.

Methods

This cross sectional descriptive study was conducted at the diabetic clinic of Kilimanjaro Christian Medical Centre (KCMC), All Type 2 diabetic patients aged 18 years and above who attended diabetic clinic during the study period were enrolled, patients with urinary tract infections, decompensated heart failure, severe hypertension or generalized body swelling were excluded, A total of 119 eligible patients provided informed consent and were included in the study, macroalbuminuria was defined as proteinuria ≥ + 1.

Multireagent Urine dipstick (Multistix®) which detects clinical albuminuria when the albumin in urine is greater than + 1 which is equivalent to 500mg of protein per day was used. Structured questionnaire was used by principal investigator as a tool to collect information from the participants which included social demographic characteristics of the study participants, family history, duration of diabetes, blood pressure and weight measurements.

Blood pressure measurements was taken from each patient after 5minutes rest in the clinic, Patients were categorized as hypertensive if they were on antihypertensive treatment, or if their systolic blood pressure was ≥ 140mm Hg and/or diastolic blood pressure was ≥ 90 mm Hg

Weight was measured using a calibrated SECA weighing scale without participants wearing shoes and recorded to the nearest 0.5 kg. Height was measured using height measuring rod and written to the nearest 0.5 cm. BMI classifications followed WHO guidelines: normal (18.5–24.9 kg/m²), overweight (25.0–29.9 kg/m²), and obese (≥ 30 kg/m²), overweight if it was 25 kg/m2 to 29.9 kg/m2, and obesity if it was equal or greater than 30 kg/m2

Glycosylated hemoglobin was analysed by spectrophotometric technique using COBAS INTERGRAL400PLUS Plus serial NO 397672, red blood cells were hemolysed in order to expose hemoglobin, thereafter glucose which bound to hemoglobin was analysed for HbA1c.

A single-spot morning urine specimen was collected in a clean dry disposable container, a reagent (Multistix®) was then dipped, a color matching greater than 1 + against color chart on bottle label indicated clinically significant proteinuria.

Results

Macroalbuminuria in relation to socio demographic and clinical characteristics. Of those presented with macroalbuminuria, male were significantly 3.8 times more likely to have macroalbuminuria (OR = 3.8; p = 0.008). Patients aged 60 years and above were 0.4 times more likely to have macroalbuminuria (OR = 0.4, P = 0.070), though the difference was not statistically significant. Patients with duration of diabetes of more than 10years were significantly 0.3 times more likely to have macroalbuminuria (OR = 0.3; P = 0.035) while patients having eGFR stage 3–5 were significantly 4.7 times more likely to have macroalbuminuria, patients who were Overweight/obese were 1.5 more likely to have macroalbuminuria (OR = 1.5; p = 0.487) though the difference was statistically insignificant. Those found to have elevated systolic blood pressure were significantly 6 times more likely to have macroalbuminuria (OR = 6; p = 0.001). Patients who were using ACEI/ARB’s were 0.6 times less likely to have macroalbuminuria (OR = 0.6; p = 0.293) (Table 1).

Table 1
Relationship between macroalbuminuria and demographic and clinical characteristics.

Variable	Total	Macro-albuminuria		OR (95% CI)	p-value
		Present	Absent		
		No. (%)	No. (%)		
Sex:					
Male	49	13 (26.5)	36 (73.5)		
Female	70	6 (8.6)	64 (91.4)	3.8 (1.3–11.0)	0.008
Age (years):					
Younger than 60	54	5 (9.2)	49 (90.8)		
60 and older	65	14 (21.5)	51 (78.5)	0.4 (0.1–1.1)	0.070
Duration of DM (years):					
Up to 10	64	6 (9.4)	58 (90.6)		
More than 10	55	13 (23.6)	42 (76.4)	0.3 (0.1-1.0)	0.035
Body Mass Index (kg/m^2)					
Underweight-normal	30	6 (20.0)	24 (80.0)	1.0	
Overweight/obese	89	13(14.6)	76(85.4)	1.5(0.5–4.3)	0.487
Stage of renal failure (GFR stage):					
Stage 3–5	25	9 (36.0)	16 (64.0)		
Stage 1–2	51	10 (10.6)	84 (89.4)	4.7 (1.6–13.5)	0.002
Systolic blood pressure (mmHg):					
Elevated (≥ 140 mmHg)	46	14 (30.4)	32 (69.6)		
Normal (< 140 mmHg)	73	5 (6.8)	68 (93.2)	6.0 (2.0–18.0)	0.001
Diastolic blood pressure (mmHg):					
Elevated (≥ 90 mmHg)	30	5 (16.7)	25 (83.3)		
Normal (< 90 mmHg)	89	14 (15.7)	75 (84.3)	1.1 (0.4–3.3)	0.904
Use of ACEI/ARB's					
Use	57	7(12.3)	50(87.7)		
*Fisher's exact test;					

Variable	Total	Macro-albuminuria		OR (95% CI)	p-value
		Present	Absent		
		No. (%)	No. (%)		
Not use	62	12(19.4)	50(80.6)	0.6(0.2–1.6)	0.293
*Fisher's exact test;					

Biochemical factors associated with macroalbuminuria

Patients with macroalbuminuria were 3.2 times significantly more likely to have high cholesterol level (OR = 3.2 CI = 1.1–9.2; P = 0.022), likewise they were 6 times significantly more likely to have high serum creatinine (OR = 6.0 CI = 2.0–18.0; p = 0.001). (Table 2)

Table 2
Relationship between biochemical factors and macroalbuminuria.

Variable	Total	Presence/absence of macro-albuminuria		OR (95% CI)	p-value
		Present	Absent		
		No. (%)	No. (%)		
Glycosylated haemoglobin:					
Elevated	106	17 (16.0)	89 (84.0)		
Normal	13	2 (15.4)	11 (84.6)	1.1(0.2–5.2)	1.000*
Total cholesterol level:					
High	53	13 (24.5)	40 (75.5)		
Normal	66	6 (9.1)	60 (90.9)	3.2 (1.1–9.2)	0.022
Serum creatinine level:					
High	46	14 (30.4)	32 (69.6)		
Normal	73	5 (6.8)	68 (93.2)	6.0 (2.0–18.0)	0.001

Multiple Regression Analysis of using macroalbuminuria as the dependent variable

Table 3 shows adjusted OR for sex, duration of diabetes, stage of renal failure, serum creatinine level and systolic blood pressure of which none of them were significantly associated with macro proteinuria.

Table 3
Multiple regression analysis using macroalbuminuria as the dependent variable.

Variable	COR (95% CI)	AOR (95% CI)	p-value
Sex:			
Male	3.8 (1.3–11.0)	2.8 (0.9–9.3)	0.082
Female	1.0	1.0	
Duration of diabetes (years):			
More than 10	3.0 (1.0-8.5)	2.3 (0.7–7.4)	0.161
Up to 10	1.0	1.0	
Stage of renal failure:			
Stage 3–5	4.7 (1.7–13.5)	2.2 (0.6–7.7)	0.223
Stage 1–2	1.0	1.0	
Creatinine:			
Elevated	6.0 (2.0–18.0)	2.5 (0.6–9.5)	0.187
Normal	1.0	1.0	
Systolic blood pressure (mmHg).			
≥140	2.7 (0.9-8.0)	2.3 (0.7–7.5)	0.167
<140	1.0	1.0	

Discussion

In this study, prevalence of macroalbuminuria obtained was 16.8% with mean duration of 10.5years. Various studies have reported lower and higher prevalence compared to that obtained in the present study. Studies across Asian countries and Europe showed marked variation in prevalence.[5,7, 8, 11]. As well as studies done across Africa including sub-Saharan Africa.[12,15]

These differences in prevalence between the present study and other studies can be attributed by factors such as differences in populations/ethnic variations, methods used for urine collection and for proteinuria assessment (dipstick vs. quantitative methods), study design and definition of macro proteinuria (i.e. cut off values).

However other factors which can contribute to this high observed prevalence could be due to high prevalence of hypertensive patients and good number of patients with poor diabetes control obtained, as the two are known to cause glomerular damage and cause them to leak protein into urine.

The present study showed significant correlation between longer duration of diabetes and macroalbuminuria, similar findings were reported in some other prior studies [7, 8] This can be attributed by observed poorly glycemic control among participants in this study, usually excess glucose combine with free amino acids with later formation of advanced glycosylation end products which contribute to glomerular damage and micro vascular complications and hence proteinuria.

Also in the present study, macroalbuminuria was strongly associated with elevated systolic blood pressure, some studies have reported similar findings [5,7,9]. This could be explained by the fact that most of study population in the present study were elderly who are prone to isolated systolic blood pressure attributed by diminished arterial compliance due to old age, However Bruno et al reported diastolic blood pressure to be strongly associated with macroalbuminuria[6].. This observed variation could be due to his study population being younger compared to the present study and hence low risk of having isolated systolic blood pressure. it is of interest that Mohan et al in Southern India didn't find any correlation between hypertension and macroalbuminuria,[8] this can be explained by small number of patients with macroalbuminuria who were found in his study.

In the present study, male sex was found to be significantly associated with macroalbuminuria, this could be explained by the fact that women had increased awareness in health seeking behavior than men, this could be the factor preventing them from ending up with diabetes complications, Similar findings was reported by Yeung et al in 2006 9 and Nakhjavan in Iran.[11] In Iran male participants were older than female which could explain this significant association since old age is a risk factor for proteinuria, however Farhat in Egypt found female sex to be strongly associated with macroalbuminuria.

Since poorly controlled glycaemia has been reported to be closely associated with macroalbuminuria,[7,8,13,14] in the present study no significant association has been observed between macroalbuminuria and glycosylated hemoglobin, this discrepancy could be explained by the smaller sample size recruited in this study which could lead to lack of power of association, prior studies also reported that in the presence of renal insufficiency usually true value of glycosylated hemoglobin is underestimated and hence lack of its threshold effect to make an association[16], in this present study most of the study participants had an element of renal insufficiency, however those studies which showed an association, those studies excluded participants with renal insufficiency.

Furthermore, elevated serum creatinine was significantly associated with macroalbuminuria, this could be explained by the fact that longer duration of diabetes and poor glycemic control observed among participants could be the reason leading to elevated serum creatinine simply because, chronic hyperglycemia plays key role in diabetic nephropathy progression with poor renal outcome if persisiting, this is in accordance with results obtained by Zakerkish in Iran and Mohan in India.[8, 10]

Moreover, elevated serum cholesterol was also significantly associated with macroalbuminuria, this was to be expected in this study as nearly more than half of study participants were either obese or overweight which promotes insulin resistance and may lead to lipolysis with fatty deposition which ultimately causing damage to the renal glomeruli, thereby increasing permeability of the glomerular filtration barrier [17] earlier studies have reported that lipid reduction using statins decrease proteinuria in diabetic patients.[19] However Nakhjavani in Iran found lower HDL-C to be strongly associated with macro proteinuria.[18]

Conclusion

This is one among few studies on prevalence of macroalbuminuria among Type 2 Diabetes in Sub-Saharan Africa using Dipstick to measure protein in urine. The overall prevalence of macroalbuminuria at our diabetic clinic in Northern Tanzania was 16.8%. Male sex, duration of diabetes, systolic blood pressure, serum cholesterol, serum creatinine seemed to be associated with macroalbuminuria.

Renal insufficiency is highly prevalent among adult diabetic outpatients attending our clinic but is usually undiagnosed.

Recommendation

A large population based studies should be done to confirm these findings and to look for genetic association in the wake of development of diabetic nephropathy in our communities.

Limitation of study

This was a hospital-based study which could have introduced a referral bias and generalizability of which may limit the generalizability of the findings.

Declarations

Ethics approval and consent to participate

Ethical clearance to conduct this study was obtained from the Kilimanjaro Christian Medical University College Ethics Committee. The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment.

Consent for publication

Not applicable as no individual patient data (images, videos, or personal details) are published in this article.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

SM conceptualized the study, collected and analyzed data, and drafted the manuscript. KK contributed to study design, literature review, and manuscript editing. HA supervised data analysis and contributed to manuscript revision. All authors read and approved the final manuscript.

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