Factors Associated with Microalbuminuria amongst Older Patients with Hypertension Attending a Geriatric Clinic in Nigeria

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Abstract

Background: Microalbuminuria has been shown to be a predictor of both renal and cardiovascular outcomes which has assumed public health importance in Nigeria. Early Detection allows for interventions to limit the progression of renal disease with a subsequent reduction in overt complication and by implication, a reduction in the overall cost of health care especially in a resource-constrained environment.

Methods: A cross-sectional study using systematic random sampling was conducted to determine the prevalence of microalbuminuria among hypertensive older persons aged 60 years and above attending a Geriatric Centre.

Results: The mean age of participants was 70.9 ± 7.1 years. The point prevalence of microalbuminuria was 63.5% with increasing positivity with age. The population with microalbuminuria demonstrated a higher mean SBP compared with those with negative microalbuminuria. They also had longer duration of diseases with a lowe eGFR.

Conclusion: The point prevalence of microalbuminuria is high among hypertensive Geriatric population especially among those with other known cardiovascular risk factors. There is a need to incorporate screening for microalbuminuria which may be an indicator for the presence of other cardiovascular risk and end-organ damage in the study area.

Keywords: Hypertension, Microalbuminuria, Geriatrics, Chronic kidney disease, Low middle income country

Introduction

Microalbuminuria is defined as an abnormal increase in albumin excretion rate within a specific range of 30–299 mg of albumin/g of creatinine [1]. The presence of persistent microalbuminuria is a marker of increased vascular permeability associated with a variety of cardiovascular risk factors. The pathophysiology of microalbuminuria in hypertension is not fully understood, Rosa et al [2] in a review article postulated two possible mechanisms; In subjects with mild hypertension, the haemodynamic load appears to be the main determinant of Albumin excretion ratio because the elevated blood pressure increases the glomerular ultrafiltration of albumin while in those with severe hypertension and hypertensive complications, albuminuria may be a consequence of a systemic microvascular disturbance which involves the glomeruli. It is most important to perform a screening test on any patient at risk for microalbuminuria in whom knowledge of the test will provide information on cardiovascular and renal risk stratification and may have therapeutic implications including identifying those that require intensive risk modification [2,3]. The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure recognized microalbuminuria as a cardiovascular risk factor and recommends testing for microalbuminuria annually among hypertensive patients [4].

The prevalence of microalbuminuria increases with age although the risk factors for microalbuminuria in the elderly are less well defined than in younger adults in whom hypertension and diabetes mellitus seem to be a major risk factor for microalbuminuria [5]. The prevalence of microalbuminuria in Nigerian patients with hypertension range between 32.3% and has been reported to be as high as 58% in patients with diabetes mellitus in Southern Nigeria [6,7].

Screening for microalbuminuria is cheap and can be easily performed on the spot in the clinic for risk assessment of hypertensive patients for optimizing blood pressure therapy with a resultant reduction of cardiovascular disease risk of patients [8]. A randomized controlled study - Prevention of REnal and Vascular ENdstage Disease Intervention Trial (PREVEND IT) to study the effect of albuminuria lowering in patients with microalbuminuria, found that Fosinopril reduced albuminuria by 26% ($p<0.001$) and was associated with a 40% reduction in the primary endpoint (a composite of mortality and hospitalization for non-fatal MI or myocardial ischaemia, heart failure, peripheral vascular disease, or cerebrovascular accident). Overall, the body of evidence indicates that microalbuminuria is an important marker of target organ involvement in hypertension and can identify those hypertensive patients who are likely to have target organ injury especially in those with multiple cardiovascular risks [2]. Early identification of cardiovascular risks in patients by detection of microalbuminuria would allow for the provision of disease-modifying drugs like antihypertensive that provide the Renin-Angiotensin-Aldosterone System. Blockage to limit morbidity from cardiovascular disease, slow the progression of the disease and overall reduce the cost of health care [3, 9].

In addition to being a predictor of cardiovascular risk, Urinary albumin is a marker/predictor of the progression of chronic kidney disease [5]. Hypertensive nephrosclerosis is one of the major indications for renal replacement therapy accounting for up to 42% in Ibadan Nigeria. The limitation of progression of the disease with early intervention is important to limit the overall cost to healthcare especially in a country like the study site where sustaining Chronic Renal Replacement Therapy is difficult for most patients [10].

The Urine Albumin: Creatinine Ratio (UACR), is recommended for quantification of albumin in urine because it is a direct and quantitative measurement of albumin and creatinine in a random urine sample and calculating the ratio improves the sensitivity of the test such that the result is not and is not confounded by a dilute or concentrated urine sample [3]. Transient albuminuria may occur as a result of a temporary increase in glomerular capillary permeability such as in decompensated heart failure, vigorous exercise, fever, urinary tract infection, postural changes, or sleep apnea [3].

Hypertension is a common medical condition in older patients in Nigeria with a prevalence of 62.2% reported by Raji et al [11]. It accounts

for a high percentage of cardiovascular morbidity and mortality. Even though screening for microalbuminuria is advised by some guidelines, it is not routinely done in the Study Centre where overt proteinuria (Urine Albumin: Creatinine >300 mg/d) is more commonly assessed meaning patients are missed in the early stages of renal impairment with no intervention to limit disease progression.

The study set out to determine the prevalence of microalbuminuria in older patients being managed for hypertension in the Geriatric Centre of University College Hospital Ibadan and to identify factors associated with it in the study population. The study would bridge the gap of paucity of study in older people in the study area and possibly serve as a basis of local policy formulation for screening. The patients would be offered risk factor modifications as required.

Methods

Study Site

This study was conducted at the Chief Tony Anenih Geriatric Centre (CTAGC) of the University College Hospital, Ibadan. Ibadan is the capital of Oyo state, situated in the South-Western region of Nigeria, West Africa.

Study Population

The study was a cross-sectional study (Part of a preliminary study). Consenting patients attending the Geriatric clinic and being managed for hypertension were recruited by systematic random sampling.

Study Procedure

Informed consent was obtained from all patients. Information regarding the demographic data was obtained and anthropometric parameters were taken. The BMI was calculated as weight (kg) divided by height (m^2). The average blood pressure on the clinic day and readings in the preceding two visits within the 9 months was recorded.

The procedure for the sterile collection of midstream urine was explained to the participants. About 10mls of urine was collected in a sterile universal bottle. Urinalysis was done using DUS 10® urinalysis strip. Patients who meet the exclusion criteria were removed from the study and the next eligible participant was recruited.

Urinary Microalbumin was calculated using the Microalbumin-Creatinine ratio determined by albustick measured using CYBOW 2AC® Lot number 180223. If the ratio was <30mg/g the patient is classified as negative for microalbuminuria, ratios between 30-299 mg/g would be indicative of microalbuminuria and above 300mg/g macroalbuminuria.

Estimated glomerular filtration rate (eGFR) was derived using Cockcroft-Gault formula:

$$eGFR = (140 - age\ [years]) / serum\ creatinine\ (^{*}mol/L)\ X\ 0.85\ (if\ female)$$

Statistical Analysis

Categorical variables were represented in proportions, and numeric variables in mean, median and standard deviation. Statistical analysis was done using SPSS Windows version 12.0.

Ethical Considerations

Permission for the study was granted by the Chairman Medical Advisory Committee of the University College Hospital Ibadan and the Director of the Chief Tony Anenih Geriatric Centre. Informed consent was obtained from all the participants and data confidentiality was ensured.

Results

A total of 189 patients with hypertension were included in the study. The mean age of respondents was 70.89 ± 7.1 with a female to male ratio of 3:1. More than a third of participants had co-existing diabetes mellitus. The point prevalence of Microalbuminuria in this study was 63.5%.

The positivity of microalbuminuria increased with age in the study and was almost equally distributed among both genders. Among the participants, 58% were on Calcium Channel Blockers(CCB) , 38.6% were on Angiotensin Receptor Blocker (ARB) and Angiotensin Converting Enzyme inhibitor (ACEI) ,Overall, the pharmacotherapy prescribed to patients with microalbuminuria was in the following order: CCB > Diuretics > ACE inhibitors and ARBs as shown in Table 1.

The median duration of hypertension and diabetes mellitus was higher in participants with microalbuminuria compared to those with negative microalbuminuria. Participants with microalbuminuria likewise had a higher mean Systolic Blood Pressure (SBP) and lower eGFR compared with those with negative microalbuminuria as shown in Table 2.

Table 1. Descriptive pattern of microalbuminuria in participants (categorical variables).

	Negative ALB n (%)	Positive ALB n (%)	Total = 189 N (%)
Age groups (years)			
60-69	37(41.6)	52(58.4)	89 (100.0)
70-79	24(34.3)	46(65.7)	70 (100.0)
≥ 80	8(25.9)	22(73.3)	30 (100.0)
Gender			
Male	19(38.8)	30(61.2)	49 (100.0)
Female	50(35.7)	90(64.3)	140 (100.0)
BMI (Kg/m^2)			
Underweight	1(25.0)	3(75.0)	4 (100.0)
Normal	16 (43.2)	21(56.8)	37 (100.0)
Overweight	21(30.9)	47(69.1)	68 (100.0)
Obese	31(38.7)	49 (61.3)	80 (100.0)
Morbidities			
HTN only	46(35.7)	83(64.3)	129 (100.0)
HTN +DM	23(38.3)	37(61.7)	60 (100.0)
Medications			
CCB	43(39.4)	66(60.6)	109 (100.0)
ARB/ACEI	25(34.2)	48 (65.8)	73 (100.0)
OHA	20(38.5)	32(61.5)	52 (100.0)
Diuretics	30(34.9)	56(65.1)	86 (100.0)
Statins	9(33.3)	18(66.7)	27 (100.0)

*HTN - Hypertension, DM - Diabetes Mellitus, CCB - Calcium Channel Blockers, OHA - Oral Hypoglycemic Agent, ARB - Angiotensin Receptor Blocker, ACEI - Angiotensin Converting Enzyme inhibitor.

Table 2. Descriptive pattern microalbuminuria and clinical parameters in numeric form.

N = 189	Negative ALB	Positive ALB
Median Duration of DM (years)	3 (2-6)	5 (1-11)
Median Duration of Hypertension(years)	5 (3-12)	7 (4-15)
MSB(mmHg)	141 ± 14.4	144 ± 18.2
MDB (mmHg)	82.6 ± 7.0	78.8 ± 12.5
eGFR (ml/min per 1.73m^2)	78.9 ± 25.4	73.8 ± 49.1
Mean LDL	121.0 ± 34.7	126.0 ± 41.0
Mean Triglyceride	103.6 ± 37.6	107.5 ± 39.2
Mean HDL	54.7 ± 14.1	60.0 ± 30.1
Mean Total Cholesterol	193.6 ± 39.3	199.7 ± 50.0

*DM-Diabetes mellitus, LDL - Low Density Lipoproteins, HDL - High Density Lipoprotein, MSB - Mean Systolic Blood pressure, MDB - Mean Diastolic Blood pressure, eGFR - Estimated Glomerular Filtration Rate.

Discussion

This study set out to describe the prevalence and pattern of microalbuminuria amongst Geriatric patients being managed for hypertension. High point prevalence of microalbuminuria was found among the participants (63.5%). This is higher compared to most studies done in hypertensive populations in Nigeria where the prevalence of 32.3% and 22% respectively [6,12]. The wide disparity in prevalence reported in those studies and the current one may be due to the older population in the current study: the mean ages in the above studies were 49.7 and 58 years respectively which is lower than the mean age of 70.89 ± 7.1 in the current study and Increasing age has been reported to be a risk factor for microalbuminuria [5]. In addition to cardiovascular risk factors like hypertension and diabetes mellitus, microalbuminuria in the older population is affected by factors such as social deprivation, poor oral hygiene, periodontitis, higher rates of exposure to nephrotoxic agents and atherosclerosis [5]. These factors were not considered in the current study and may contribute to the high prevalence. Fernando et al [13] in Spain and Habbal et al [14] in Morocco both multicenter studies, however, they reported a high microalbuminuria prevalence of 62.5% and 67.8% respectively similar to this study. The study population in the Moroccan study were patients attending cardiology clinic who possibly had end-organ damage, and demonstrated a higher prevalence of microalbuminuria than the general population in that study; could this also be said of the population of elderly patients in this study Centre which offers secondary and tertiary care to the older population. The study in Spain also recruited participants with uncontrolled hypertension with likely end-organ damage similarly accounting for the high prevalence of microalbuminuria. It was furthermore, substantially higher than found in studies on unselected persons in the general population.

The patients with microalbuminuria had a longer duration of diseases (hypertension and diabetes mellitus) and were likely to have coexisting diabetes mellitus and a higher mean systolic blood pressure: Even though the mean of systolic and diastolic blood pressure were within the therapeutic range of <150 mmHg systolic and 90 mmHg (diastolic). The findings show that microalbuminuria could occur even with adequate blood pressure control. Catena et al [15] in Italy also reported that higher Urinary Albumin Creatinine Ratio was associated with significant and progressively higher SBP and DBP even though the group with negative albuminuria had higher diastolic blood pressure in this study.

In the current study, the eGFR was higher in patients who were negative for urinary microalbuminuria. Increasing Urinary Albumin Creatinine Ratio is reported to be associated with lower glomerular filtration [15]. A low eGFR and microalbuminuria are synergistic cardiovascular mortality risk factors and age-stratified analyses showed that eGFR and microalbuminuria were particularly strong risk factors for persons over 70 years old [5]. The patients who had positive microalbuminuria in this study also had a higher level of total cholesterol and triglyceride likewise tend towards the extreme of weight categories which are known predictors of cardiovascular risk; though the HDL is higher in this group of patients. These findings suggest an overall increased cardiovascular risk in those with positive microalbuminuria. Similar to this study, Catena et al [15] in Italy also reported that microalbuminuria was significantly associated with higher HDL-cholesterol.

The use of ACE-I and ARBs is recommended for patients with microalbuminuria and has been shown to reverse microalbuminuria [4,9]. Similar to findings in this study, ACEI and ARBS were not one of the top antihypertensives in a study by Fernando et al [13] who also reported a high microalbuminuria prevalence; the top medications in that study were calcium channel blockers (48%), diuretics (38.8%), beta-blockers (21.8%), alpha-blockers (13.6%), and other hypertensive drugs (3.8%). Akande-Sholabi et al [16] also reported underutilization of ACEI and ARBs in the same Clinic as this study: Most patients in that study were receiving calcium channel blockers (33.8%), followed by diuretics (45.5%), angiotensin receptor blockers (23.4%) and angiotensin-converting enzyme inhibitors (10.8%). The high prevalence of microalbuminuria found in this study may be a pointer to the under-prescription of ARBs/ACEI due to not testing for albuminuria routinely in the patients to allow for intervention. Contrary to expectation, a higher proportion of people with microalbuminuria were on ARBs compared to those who were negative in this study. A possible explanation is that the duration of use of those medications was not explored and patients were possibly newly introduced to the medication.

Conclusion

There is a high prevalence of microalbuminuria amongst the study population with prevalence increasing with age, rising lipid profile values and systolic blood pressure. Patients with microalbuminuria also had a lower eGFR. The study demonstrates a high global cardiovascular risk among those with microalbuminuria, there is a need to incorporate screening for microalbuminuria in patients attending the clinic. The high prevalence could be a pointer to the importance of screening for other end-organ damage in patients with hypertension attending the clinic.

Recommendations

A study to determine the presence of microalbuminuria with other end-organ damage may be a cheaper way to identify high-risk patients who require further evaluation for end-organ damage in a resource-constrained environment.

Authors' Contributions

The Conceptualization and initial draft of the manuscript was written by EO, LA, and OO. K.O did statistical analysis. All authors revised and modified the manuscript. All authors read and approved the manuscript.

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