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Prevalence and Predictors of Renal Dysfunction among Adult Hypertensive Patients Attending Medical Clinic in North-western Tanzania: A Cross Sectional Study

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Abstract

Background

Hypertension is a known risk factor for the development of renal dysfunction. With the increasing burden of hypertension in developing countries, especially due to lifestyle modifications, we expect a rise in the development of renal dysfunction. The prevalence, pattern and predictors of renal dysfunction among hypertensive patients in sub-Saharan Africa have not been well described.

Methods

An analytical cross-sectional study was conducted at Bugando Medical Centre (BMC) outpatient clinic from February 2013 to April 2013. The primary end point was renal dysfunction defined as an estimated glomerular filtration rate (eGFR) < 90ml/min/1.73m2 (calculated using the Cockroft-Gault equation) and/or the presence of albuminuria.

Results

The population consisted of more females than males (54.7% vs. 45.3%). The majority of the population came from urban areas. The prevalence of renal dysfunction was found to be 53.9%. Older age, female gender, obesity, high systolic blood pressure and type of antihypertensive medications were found to be strong predictors of renal dysfunction.

Conclusion

Renal dysfunction was highly prevalent in this population of non-diabetic hypertensive outpatients in North-western Tanzania. This highlights the critical and underappreciated need to monitor renal function in hypertensive patients in sub-Saharan Africa given the increasing high burden of hypertension in the region.

Keywords: Hypertension, Renal dysfunction, Proteinuria, Microalbuminuria, albuminuria, Chronic Kidney Disease, Tanzania

Background

Hypertension (HTN) is a growing public health challenge worldwide. Overall, 26.4% of the worldwide adult population were estimated to have HTN in the year 2000 and 29.2% are projected to have this condition by 2025 [1]. It is also becoming widely reported in both rural and urban settings in sub-Saharan Africa [2]. It has been identified as one of the commonest cause of morbidity and mortality in this region [2].

Hypertension is the second most common cause of renal dysfunction, behind diabetes mellitus, and has been shown to produce clinical proteinuria and reduction in renal function in 5-15% of patients [3–5]. Previous studies have shown that the presence of proteinuria, whether occult or overt, is associated with increased cardiovascular morbidity and mortality [6,7]. It is a known risk factor for the development of renal dysfunction, especially in the black population [8,9].

Renal dysfunction is caused primarily by chronic high blood pressure over many years [10–12]. The rate of end stage renal disease attributed to hypertension has grown by 8.7% since the year 2000 [13]. Hypertensive nephrosclerosis is reportedly the second most common cause of end stage renal disease in white people (23%) and is the leading cause of end stage renal disease in black people (46%) [14,15]. Despite the documented increased prevalence of HTN in developing countries, very few studies have been done to determine the prevalence of renal insufficiency in this population. This study aimed at determining the prevalence and predictors of renal dysfunction among adult hypertensive patients attending medical clinic in North Western Tanzania.

Materials and methods

Study design and setting

This study was an analytical cross-sectional study conducted at the medical outpatient clinic at Bugando Medical Centre (BMC) in North-western Tanzania. BMC is a university teaching hospital with a bed capacity of about 900 and is one of the four consultant hospitals in the country. It serves 8 regions, including Mwanza, Geita, Shinyanga, Simiyu, Tabora, Kagera, Kigoma, and Mara, covering a population of about 16 million people. The medical outpatient clinic is conducted 3 days per week (Tuesday, Wednesday and Friday) with an average of 50 to 60 hypertensive patients per day.

Inclusion and exclusion criteria

Hypertensive patients aged 18 years and above attending the medical outpatient clinic at BMC and who provided informed consent were enrolled for the study. Diabetic patients, critically ill and HIV-infected patients were excluded from the study.

Sample size and sampling procedure

The sample size was calculated using the Kish and Leslie formula, using prevalence in previous studies of 37.5%, accuracy of 5% to give the study a power of 80%. The minimum sample size obtained was 360 hypertensive adults. Recruitment was done serially until the predetermined sample size was reached.

Data collection

All adult known hypertensive patients meeting the above inclusion criteria during the study period were invited to participate in the study. Consent forms were given to the

study participants with an explanation of the aims of the study by the study investigator. The enrollment was done after obtaining written informed consent. Study participants were interviewed using a standardized data collection tool, which included a medical history and physical examination. Body weight was recorded in kilograms to the nearest 0.5 kg. Height in centimeters was recorded to the nearest 0.5 cm using a rigid measure against a vertical wall. Blood pressure was recorded using a mercury sphygmomanometer. A hypertensive patient was defined as anyone on antihypertensive medications or, as defined by American Heart Association (AHA), anyone with an average of two blood pressure readings with one minute interval of 140/90 mmHg or higher and measured to the nearest 2 mmHg [16]. Measurements were performed while the patient was seated comfortably with the back supported, legs uncrossed, and upper arm bared.

Laboratory procedures

For each patient, a venopuncture was done to obtain a blood sample to assess serum creatinine level (using COBUS automated chemistry analyzer). The creatinine clearance was then calculated using the Cockroft-Gault equation. Each patient was also given a sterile container to collect a urine sample and a dipstick urinalysis was done within five minutes of sample collection using urine dipstick Multistix (Bayer, Germany). Any patient with a urine dipstick negative for protein underwent further testing of urine for microalbuminuria (using Micral-TestB immunoassay (Boehringer-Mannheim, Germany). Albuminuria was reported as negative, 1+ (30mg/dl), 2+ (100 mg/dl), 3+ (300mg/dl), or 4+ (1000mg/dl). Negative value to 1+ was classified as normal to mildly increased albuminuria, 1+ to 3+ (>30mg/dl) as severely increased albuminuria and 3+ to 4+ as nephrotic range proteinuria [17]. All

patients with abnormal creatinine clearance and/or albuminuria were classified as having renal dysfunction and were categorized according to the Kidney Disease Outcomes Quality Initiative (KDOQI) CKD staging system [18]. Blood samples were obtained for determination of glucose levels (random blood sugars) using finger stick method. Patients with glucose levels higher than 7.0 mmol/l or 126 in mg/dl were excluded from the study

Data processing and analysis

Data was entered into Microsoft Excel. Double data entry was performed for all data and cleaning was done using MS Excel software. Data analysis was performed using STATA 11. The primary end point of this study was renal dysfunction defined by an estimated glomerular filtration rate (eGFR) < 90ml/min/1.73m2 (calculated using the Cockroft-Gault equation) and/or the presence of albuminuria. Descriptive statistics were computed by determining the median and interquartile range for continuous variables and the proportion for categorical variables. Medians and proportions were compared using the Wilcoxon rank sum test and chi-square or Fisher's exact test respectively. A p-value of less than 0.05 was considered significant. Predictors were evaluated by univariate and multivariate analysis. Any predictor with a p-value less than 0.20 by univariate analysis was evaluated by multivariate analysis using logistic regression. For predictors, odds ratios were determined with 95% confidence intervals.

Ethical consideration

All participants were recruited after obtaining written informed consent with signing or thumbprint of the consent forms. Patients were assured that their refusal to consent or withdrawal from the study would not alter or jeopardize their access to medical

care. Clearance was obtained from the Catholic University of Health and Allied Sciences (CUHAS)/BMC joint ethical committee and the respective departments prior to commencement of data collection. All results were made available to clinicians and were recorded in the patient's medical records.

Results

Characteristics of study participants

A total of 400 patients attended the clinic during the study period. Out of these, 35 were diabetic and 5 were HIV positive and thus excluded in the study. Therefore, 360 patients fulfilled the inclusion criteria and were enrolled for the study. The population consisted of more females than males (54.7% versus 45.3%). The median age of study participants was 52 [43 –61.5] years. A majority of the population (53.9%) came from urban areas. Most patients (31.9%) had a university or college education, though a large proportion of the patients (28.3%) were unemployed (Table 1).

Baseline clinical characteristics

Of the 360 participants, a majority of them had a BMI of < 30 Kg/M^2, more than half of them had suffered from hypertension for less than 5 years, and more than two thirds had good hypertensive control defined as average blood pressure of less than 140/90 mmHg in three recent blood pressure measurements during the last three clinic visits. Most of the patients were on a regimen containing an angiotensin II converting enzyme inhibitor or angiotensin II receptor blockers (75.3%) (Table2).

Prevalence of renal dysfunction

Of the 360 patients attending hypertensive clinic at BMC, 53.9% had renal dysfunction (KDOQI stage 1 to 5), while approximately one third of the patients (30.6%) had creatinine clearance of less than 90ml/min/1.72m^2 (KDOQI stage 2 and above). None of the patients had KDOQI stage 4 or 5 disease (creatinine clearance of < 30). Among 132 patients with proteinuric renal dysfunction 84, 35 and 13 patients were in KDOQI stage 1, 2 and 3 respectively. 250 patients (69.4%) had a creatinine clearance of ≥90, which is KDOQI stage 0 and 1, with 84 patients (23.3%) with albuminuria, which falls into stage 1 with the remaining 166 patients (46.1%) without albuminuria (KDOQI stage 0). The median creatinine clearance was 88.78 ml/min/BSA as summarized in table 3.

Predictors of renal dysfunction

The median age among patients with renal dysfunction was found to be 59 years (IQR 35-68), as compared with 46.5 (IQR 38-59) in patients without renal dysfunction (OR for each increasing year of age = 1.08 [1.06-1.10], p< 0.001) (Table 4). Obesity was also associated with a higher risk (OR = 7.70 [2.65 -22.31], p <0.001). Renal dysfunction was found to affect more women, 58.4% with renal dysfunction versus 41.6% without renal dysfunction (OR = 1.93[1.10-3.38], p=0.02). High systolic blood pressure significantly predicted occurrence of renal dysfunction (OR 1.02 [1.00-1.04], P=0.04). The use of medications other than ACE-inhibitors or angiotensin receptor blockers was also associated with a higher incidence of renal dysfunction (OR 6.84 [3.68 –12.71], p value <0.001).

Discussion

In this study, we report a high prevalence (53.9%) of renal dysfunction among hypertensive outpatients. Obesity, increasing age, female gender, high systolic blood pressure and the use of anti hypertensives other than ACE-inhibitors or angiotensin converting enzyme inhibitors were all significantly associated with renal dysfunction in this cohort.

The estimated GFR in this study was calculated using Cockroft Gault equation. None of the equations for estimation of GFR have been validated to be used in black population. Only one study has been done in South Africa comparing the two equations (CG and MDRD); this study showed that MDRD without the ethnicity factor performed better that CG equation [19]. A study done in Asia found that CKD prevalence, sex ratios, and KDIGO composite risk groupings varied widely depending on the equation used [20]. A study by Msango et al among HIV infected patients that was conducted in the same study setting as our study found no difference when MDRD equation was compared with CG equation [21]. Recent reports however have shown that the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation provides more accurate GFR estimates, lower CKD prevalence estimates, and better risk predictions [22].

The prevalence obtained in our study is higher compared to the previous studies done in Africa [23]. It is also higher than that observed in studies done outside Africa [24,25]. Participants for our study were enrolled from an outpatient medical department. The observed prevalence was lower than one found in diabetic patients from the same setting (BMC), which found a renal dysfunction prevalence of 89.8% [26]. A total of 132 patients (36.7%) had proteinuric renal dysfunction and 62

patients (17.2%) had non-proteinuric renal dysfunction. This is similar to a study done in Uganda which found the prevalence of albuminuria of 39.5% [27].

In this study, the diagnosis of renal dysfunction was made based on both the creatinine clearance and the presence of albuminuria as per the KDOQI classification [18]. Different studies have used different definitions of renal dysfunction/insufficiency. Some studies have used only one criteria (i.e. microalbuminuria) to diagnose renal dysfunction [7,27], while others set their cut off point for the creatinine clearance at <60 ml/min [25]. In our study, we did not find any patient with KDOQI stage 4 or 5. This may be explained by the fact that the study surveyed an outpatient population, often in the initial stages of renal dysfunction as compared to inpatients with more advanced renal disease.

Obesity has been shown to be associated with glomerular hyperfiltration and increased GFR increasing the risk of renal damage [28–30]. Previous reports show that obesity magnifies the effect of hypertension and proteinuria [31]. In our study, we found that renal dysfunction was significantly associated with obesity. Our finding is similar to other studies which found significant association between obesity and renal dysfunction among hypertensive patients [25]. Weight loss in these patients has been shown to reduce glomerular hyperfiltration, which may help to prevent the development of overt nephropathy [32].

The renoprotective role of ACE inhibitors or angiotensin receptor blockers has been well established [33]. They have been shown to reduce proteinuria in both hypertensive patients and normotensive diabetic patients [24,34,35], thereby slowing nephropathy progression [36]. In our study, the use of ACE-inhibitors or angiotensin converting enzyme inhibitors was significantly protective against the development of

renal insufficiency. This finding is similar to a study which found a significant difference in the occurrence of renal dysfunction between those hypertensive patients on ACE-inhibitors and those not on ACE-inhibitors [37]. The effect of ACE-inhibitors on reducing renal events has been shown to be independent of blood pressure control [37].

In our study, high SBP was significantly associated with renal insufficiency. Other studies have found that hypertension, and more so SBP, predicts development of renal insufficiency and end stage renal disease [38]. Even in diabetic patients, SBP predicted greater progression of nephropathy [39]. One other study concluded that even relatively modest increases in blood pressure remains an independent risk factor for renal insufficiency [11]. A previous study showed that people with higher than normal blood pressure (SBP 130-139 mmHg or DBP 85-89 mmHg) were twice as likely to have albuminuria compared to people with optimal BP (SBP<120 and DBP 80 mmHg). It also showed that lowering the systolic blood pressure by 20 mmHg decreases the risk of developing ESRD by two-thirds [40].

Our study had several limitations. It was a single centre, clinic-based study and therefore, the results may not be generalizable to the general population. The sample size for the study was relatively small. In addition, renal biopsy, which is the gold standard in diagnosing hypertensive nephropathy, was not done in these patients. This study was also done in a Schistosomiasis endemic setting; however screening for Schistosomiasis and hepatitis C, both of which could cause renal dysfunction, was not done in these patients. APOL 1 risk allele which has been shown to increase the risk of CKD in blacks [41] was not tested in this cohort. However, other more

common causes of renal insufficiency, such as diabetes and HIV, were screened and excluded as possible confounders.

Conclusion

The prevalence of renal dysfunction was high in this cohort of clinically stable hypertensive outpatients. More than 50% of study participants had renal dysfunction, out of whom 5% had eGFR<60 mL/min. Older age, female gender, obesity, systolic blood pressure and the use of non-ACE inhibitors and ARB antihypertensive medications were found to be strong predictors of developing renal dysfunction in this study population. Our findings highlight the need for regular nephropathy screening among hypertensive patients to prevent progression to end stage renal disease.

Competing interest

The authors have no conflict of interest to declare.

Authors' Contributions

AS, SK, RK designed the study. AS, SK, RK enrolled the patients and collected the samples. AS, DWG, SK, RK, BCM analyzed the data. AS, DWG, SK, RK, BCM wrote the manuscript which was revised and approved by all coauthors

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Table 1: Socio-demographic characteristics of patients presenting to Hypertension Clinic at BMC in Mwanza, Tanzania February-April 2013 (n=360)

CHARACTERISTICS		NUMBER (%) or MEDIAN [IQR]
Gender		
	Male	163 (45.3%)
	Female	197 (54.7%)
Residency		
	Urban	194 (53.9%)
	Rural	166 (46.1%)
Age (Years)		52 [43 –61.5]
Education		
	Not formally educated	86 (23.9%)
	Primary	65 (18.1%)
	Secondary	94 (26.1%)
	University/college	115 (31.9%)
Occupation		
	Unemployed	102 (28.3%)
	Peasants	86 (23.9 %)
	Employed	90 (25%)
	Petty traders	82 (22.8%)

IQR: interquartile range

Table 2: Clinical characteristics of Patients attending Hypertensive Clinic at BMC in Mwanza, Tanzania February-April 2013 (n=360)

CHARACTERISTICS	NUMBER (%) / MEDIAN [IQR]
Body Mass Index	26.09 [24.3 –27.5]
Obese (≥ 30)	35 (9.7%)
Overweight (25-29.99)	202 (56.1%)
Normal (18.5-24.99)	123 (34.2%)
Underweight (<18.5)	0 (0%)
Duration of Hypertension (years)	5 [2-10]
0 to 5	198 (55%)
6 to 10	88 (24.4%)
11 to 20	49 (13.6%)
≥21	25 (6.9%)
Hypertension control	
Good	273 (75.8%)
Poor	87 (24.2%)
Antihypertensive medications	
ACE-I and/or ARB	271 (75.3%)
Others (non ACE-I)	89 (24.7%)
Smoking	
Smokers	5 (1.4%)
Non- smokers	355 (98.6%)
Quantity of alcohol (units/week)	14 [10 –14]
Alcohol use	25 (6.5%)
Systolic blood pressure (mmHg)	130 [122.5- 150]
Diastolic blood pressure (mmHg)	80 [80 –90]
Random blood sugar (mmol/l)	6.3 [5.4 –7.4]

**ACE-I: Angiotensin converting enzyme inhibitor; ARB: Angiotensin receptor blocker; IQR: Interquartile range*

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Table 3: Primary Renal Outcomes of Patients Attending the Hypertensive Clinic at BMC (n=360)

OUTCOME		N (%) OR MEDIAN [IQR]
Proteinuria/microalbuminuria		132 (36.7%)
Creatinine clearance		88.78 [88.4 –107.2]
KDOQI classification		
Stage 0	CrCL > 90 with risk of renal damage	166 (46.1%)
Stage 1	CrCL> 90 with renal damage	84 (23.3%)
Stage 2	CrCL 60 –89 with renal damage	96 (26.7%)
Stage 3	CrCL 30 -59 with renal damage	14 (3.9%)
Stage 4	CrCL 15- 29 with renal damage	0 (0%)
Stage 5	CrCL < 15 with renal damage	0 (0%)
Any renal dysfunction (KDOQI stage 1-5)		194 (53.9%)

**IQR: Interquartile range; KDOQI: Kidney Disease Outcomes Quality Initiative*

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Table 4: Multivariate Analysis of Predictors of Renal Dysfunction among Patients Attending the Hypertensive Clinic at BMC, Mwanza Tanzania February-April 2013

VARIABLE	ADJUSTED ODDS RATIO [95% CI]	P-value
Age	1.07 (1.04-1.10)	<0.001
Female gender	1.93 (1.10-3.38)	0.02
Obese	4.34 (1.30-14.40)	0.02
SBP	1.02 (1.00-1.04)	0.04
DBP	1.02 (0.99-1.05)	0.14
Other anti HTN	4.14 (2.04-8.39)	<0.001
Education		
Primary	0.82 (0.35-1.86)	0.63
Secondary	1.20 (0.49-2.91)	0.68
University	2.18 (0.79-6.03)	1.13
Occupation		
Peasants	0.95 (0.42-2.14)	0.91
Employed	0.39 (0.13-1.01)	0.05
Business	0.79 (0.32-1.94)	0.61

**CI: confidence interval; DBP: Diastolic blood pressure; HTN: Hypertension; SBP: Systolic blood pressure*