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Prevalence and Correlates of Chronic Kidney Disease in Patients with hypertension in Rural Malawi

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Abstract

Background The prevalence of chronic kidney disease (CKD) in patients with hypertension is very high in Africa. We investigated the prevalence and correlates of CKD in patients with hypertension attending longitudinal care in rural Malawi, where currently no data on prevalence of CKD in patients with hypertension exists. Methods We retrospectively reviewed medical records of all hypertensive patients who were screened for CKD between January 2018 and April 2019. Screening was done using serum creatinine and CKD epidemiology formula was used to estimate the glomerular filtration rate (eGFR). We used Kidney Disease: Improving Global Outcomes definitions of renal insufficiency and CKD. Logistic regression analysis was used to identify correlates of CKD. Results During the study duration, 1197 patients with hypertension were screened for CKD. The mean creatinine and eGFR was 0.90 mg/dl (Confidence Interval (CI) 0.85-0.94 mg/dl) and 84.1 ml/min/1.73m2 (CI 82.7-85.4 ml/min/1.73m2) respectively. About half of the patients had a normal eGFR (48.3%, n=578) and 36.3% (n=435) had mildly decreased eGFR. The prevalence of renal insufficiency was 15.4% (CI 13.4-17.5, 184/1197) and the prevalence of CKD was 7.1% (CI 5.7-8.7%). By eGFR category in the CKD patients, 41.2% (n=35), 31.8% (n=27), 24.7% (n=21) and 2.3% (n=2) had CKD stage 3a, 3b, 4 and 5 respectively. CKD was strongly associated with age and diabetes. Conclusions We found moderately high renal insufficiency and CKD in this cohort. We propose investing in screening for CKD in patients with hypertension in other clinics in Malawi.

Background

Globally, the prevalence of hypertension is high, affecting over 31% of adults (1). Low-and-middle-income countries, especially African countries, are severely affected with over 75% of patients with hypertension living in these countries (1,2). In Africa alone, hypertension affect over 30% of adults(3), and is the most common cause of chronic kidney disease (CKD) (4).

CKD is a growing public health problem in Africa with recent increases in CKD incidence, prevalence and mortality (5). Whilst 15% of the general population have CKD, this is higher in patients with hypertension, with a recent systematic review reporting a prevalence of 36% (4). Additionally, the burden of CKD in patients with hypertension varies widely. For example, studies in Cameroon and one study in Ghana reported about 50% prevalence of CKD in patients with hypertension (6,7), but a study in Uganda and another study in Ghana report lower prevalence, at 38.5% and 13% respectively (8).

The management of CKD and its complications is expensive, and most African countries cannot afford to manage the complications of CKD, particularly end stage renal disease (9,10). Additionally, these countries are struggling with a high burden of communicable diseases and maternal and child health conditions, with some of these diseases such as HIV also increasing the risk of CKD (11). Dialysis and renal replacement therapy is not affordable and feasible for all the patients that need these services in African countries (10,12). However, screening for CKD, which is feasible and affordable, provides an opportunity for early detection and management of CKD in Africa.

Screening for CKD, especially in high risk groups like patients with hypertension, has many advantages. Screening allows for early detection as CKD may be asymptomatic in early stages. This enables early interventions to reduce progression of CKD and may help improve the quality of life and extend life expectancy in these patients (11). Additionally, screening saves patient and health care costs as it is cheaper than managing complications of CKD (9,13). Far more importantly, screening helps to improve awareness of CKD, as many patients in Africa are not aware that they have CKD (14). All of these advantages can be achieved by using relatively cheap screening tests such as urinary albumin and/or serum creatinine, which have been shown to be effective and feasible in many African countries (15).

Situated in southern Africa, Malawi currently faces an increase in non-communicable diseases (NCDs), in addition to an existing burden of HIV (16). Up to 16% of adults aged 18 years and above have hypertension (17). Although screening for CKD is included in the National NCD Action Plan for Prevention and management of NCDs in Malawi, most facilities, especially district and rural health facilities, have minimal capacity to screen for CKD (18–20). Currently, limited data exists on the prevalence of CKD patients with hypertension, especially in rural Malawi where over 84% of the population resides (21). The majority of studies on CKD were done in the context of HIV and are all from urban facilities(22–25).

We present a study on the prevalence and correlates of CKD in hypertensive patients aged 18 years and above attending Integrated Chronic Care Clinics in Neno District, Malawi. This study is relevant because 1) It estimates the prevalence of undiagnosed CKD in a

cohort of patients with hypertension, a key high risk group in Malawi; 2) It investigates CKD in rural Malawi, where despite the majority of Malawians living in rural areas, no data exists on CKD; and 3) It measures context specific correlates of CKD.

Methods

Setting

This is a cross-sectional study conducted between January 2018 and April 2019 in Neno District, Malawi. We retrospectively reviewed medical records of all patients with hypertension screened for CKD in Integrated Chronic Care Clinics.

Neno District is a remote and rural south-western district of Malawi with an estimated population of 138,000 in 2018 (21).Within the Neno District's 14 health facilities (2 hospitals and 12 primary health facilities), the Ministry of Health (MOH) in collaboration with a non-governmental organization called Partners In Health has been providing integrated HIV-NCD care since 2015 (26). In the Integrated Chronic Care Clinic, a team of mid-level providers, nurses, and other support staff provide longitudinal care to patients with HIV, hypertension, diabetes, epilepsy, chronic obstructive respiratory disease, mental illnesses, and other chronic NCDs. By April 2019, over 7850 HIV and 3400 NCD patients, of which 2184 were patients with hypertension, were receiving care in this clinic (Partners In Health internal data). The Integrated Chronic Care model has been described elsewhere (26,27).

Hypertension Enrolment, CKD Screening and Laboratory Measurements

In the Integrated Chronic Care clinics, patients were referred for treatment for hypertension from several places: inpatient wards, outpatient clinics, and community screening events (28). Patients were enrolled in the clinic for treatment for hypertension either if they were currently on hypertension treatment or based on a systolic blood pressure ≥ 160 mmHg and/or diastolic blood pressure ≥110 mmHg , procedures initiated in Neno District in order to capture the highest risk patients first and avoid early overcrowding of the Integrated Chronic Care Clinics.

Beginning January 2018, Neno District introduced annual routine screening for CKD in patients with hypertension in the Integrated Chronic Care Clinics using two point of care chemistry analyzers. For eligible hypertensive patients, at least one milliliter of venous blood was collected in heparinized bottles by clinic nurses using aseptic techniques for the measurement of plasma creatinine (mg/dl). In order to provide immediate results and expedite patient care, the samples were analysed immediately in the clinic using an I-Stat analyzer and chem8+ cartridges (Abbot, USA). The analysis was done by support staff working in the clinic with support from a laboratory technician who provided a one day training followed by longitudinal mentorship at least once every 3 months.

In the event an I-Stat analyzer was malfunctioning or not available in the clinic, the samples were transported to one of the two hospitals in Neno for same day analysis on I-Stat analyzers located in the laboratories. Towards the end of 2018, the MOH purchased a new chemistry analyzer, Mindray BS 120 chemistry analyzer, that was used when I-Stat cartridges were in short supply.

Based on the initial serum creatinine, an estimated glomerular filtration rate (eGFR) was calculated. If the patients had renal insufficiency on their initial test, creatinine was checked again after at-least 3 months in order to confirm the diagnosis of CKD. Follow up was facilitated by reminders to clinic staff, using community health workers to inform patients to come to the clinic for follow up testing, and, if necessary, home visits were conducted by the clinical team to identify and escort patients to nearest clinic for CKD screening.

Inclusion and Exclusion Criteria of the Study

We retrospectively reviewed the electronic medical record (EMR) of patients with hypertension. All patients' clinical information was recorded in the MOH standardized patient chart, and the data was also duplicated in the EMR. All hypertensive patients aged 18 years and above who were screened for CKD were included in the study. We excluded hypertensive patients with an existing diagnosis of CKD.

Clinical Measurements and Outcomes

CKD was the main outcome and was defined based on Kidney Disease: Improving Global Outcomes (KDIGO) definition: an estimated eGFR of less than 60ml/min/1.73m^2 persistent for at least 3 months (29). EGFR of less than 60ml/min/1.73m^2 on one occasion only was defined as renal insufficiency. In addition, we categorized eGFR in all patients based on KDIGO categories of eGFR.

We derived an eGFR from plasma creatinine using CKD Epidemiology formula without the factor of race. The CKD Epidemiology formula without race was chosen as it has been shown to better predict eGFR in Malawians than CKD epidemiology formula with black as a race factor or other formulas of predicting eGFR (30).

We extracted several other variables from the patients' charts based on data that was routinely collected during clinical encounters and variables that have been shown to be associated with CKD in other studies. Therefore, we extracted the following independent for each patient with hypertension:

Demographic variables: Age (years), gender (male or female)

Clinical history of hypertension: Years since diagnosis of hypertension and duration of enrolment in the clinic (less than one year, 1-2 years, more than 2 years), and most recent systolic and diastolic blood pressures (mmHg)

Risk factors of hypertension: Body mass index (BMI) (kg/m^2), BMI over 25, BMI categories (<18.5, ≥18.5-<25, ≥25-<30, ≥30), proteinuria (negative and trace were coded as protein <1+, protein 1+, 2+ and 3+ were coded as protein ≥1+)

Comorbidities (yes or no): Patients with concurrent diabetes and/or HIV.

We planned to include variables that are representative of the hypertensive population. Therefore we opted to exclude from the final analysis any variable that had more than 90% of the participants' data missing. This included history of smoking and alcohol and the following complications: stroke, cardiovascular disease, peripheral vascular disease and neuropathy. All included data were collected during routine clinical encounters, and protocols for their measurement is explained elsewhere (27).

Data Management and Statistical Analysis

All data used in this study were initially extracted from the EMR to Microsoft Excel version 2013. Data cleaning and analysis was performed using Stata 15 (Stata Corp, Texas). Descriptive statistics were used to describe the data. Depending on normality, mean and standard deviation were used for continuous variables and median and Interquartile range (IQR) were used non-normally distributed data. Depending on normality and type of variables, Chi^2, t-test , Mann Whitney U test were used to explore the relationship between the independent variables and patients CKD.

We performed logistic regression analysis to determine correlates of CKD. Initially, we performed single predictor models to identify significant correlates of CKD. We then performed multivariable logistic regression using identified significant factors from the single predictor models. Statistical significance was defined at a p value <0.05 at 95% confidence interval.

Ethics Approval and Consent to Participate

All data were collected as part of routine patient care and analysed retrospectively. As a result, we did not obtain informed consent from patients. Access to data was given only to investigators and data were kept securely. The study received ethical clearance from Malawi National Health Sciences Research Committee protocol number 1216.

Results

Baseline Characteristics of the Participants

Between January 2018 and April 2019, 1197 out of 2184 (54.8%) patients with hypertension were screened for CKD (Figure 1). Seventy nine percent (n=942) were females and the median age was 61 years (IQR 51-70 years). About half of the patients had had

been diagnosed and enrolled in Integrated Chronic Care Clinic for more than 2 years. The median body mass index (BMI) was 22.9 kg/m^2 (IQR 20.3-26.6 kg/m^2) and only 5% (n=46) had proteinuria >=1+. 5.3% (n=63) and 10.9% (n=112) had diabetes and HIV as comorbidities of hypertension respectively (Table 1).

Figure 1. Screening Results for Patients with Hypertension

Table 1. Characteristics of Patients with Hypertension Screened for CKD

Among all hypertensive patients that were screened for CKD, the mean creatinine was 0.90 mg/dl (Confidence Interval (CI) 0.85-0.94 mg/dl) and the mean eGFR was 84.1 ml/min/1.73m^2 (CI 82.7-85.4 ml/min/1.73$m^{2)}$. About half of the patients had a normal eGFR (48.3%, n=578) and 36.3 % (n=435) had mildly decreased eGFR (Table 2).The prevalence of renal insufficiency was 15.4% (CI 13.4-17.5, 184/1197).

Among the 184 hypertensive patients with renal insufficiency, 126 patients were successfully re-tested after a minimum of 3 months (Figure 1). Of these, 85 had persistent eGFR < 60 ml/min/1.73m^2, hence the prevalence of CKD in this study was 7.1% (CI 5.7-8.7 %). By eGFR category in the CKD patients, 41.2% (n=35), 31.8% (n=27), 24.7 % (n=21) and 2.3% (n=2) had CKD stage 3a, 3b, 4 and 5 respectively.

Table 2: Distribution of eGFR in all patients screened for renal insufficiency and CKD

After univariate logistic regression model, increasing age (unadjusted odds ratio (OR) 1.06, CI 1.04-1.08, p<0.001), higher systolic blood pressure (unadjusted OR 1.01, CI 1.004 -1.02, p<0.001) and concurrent diagnosis of diabetes (unadjusted OR 2.32, CI 1.10-4.88, p=0.03) were all associated with CKD (Table 3). In multivariable logistic regression, older age (adjusted OR 1.06, CI 1.04-1.08, p<0.001) and a history of diabetes (adjusted OR 2.63, CI 1.21-5.69, p=0.01 were strongly associated with CKD. Most recent systolic blood pressure was weakly associated with CKD (adjusted OR 1.01 CI 1.00- 1.02, p=0.048)

Table 3 Univariate Analysis of Correlates of CKD

Table 4 Multivariable analysis of Correlates of CKD

Discussion

As far as we know, this is the first study to investigate CKD among patients with hypertension attending longitudinal care in rural Malawi. Approximately half of the patients with hypertension tested had abnormal eGFR, and at-least 15% of the patients had evidence of renal insufficiency. This demonstrates the clinical importance of routine screening for CKD in hypertension clinics. Most patients with renal insufficiency benefitted from follow up after three months for confirmation of CKD. The screening and dissemination of their results may also have helped with raising the awareness of CKD.

The confirmation of CKD by KDIGO guidelines requires re-testing after at least 3 months, and in rural impoverished settings, more effort was needed to find these patients for repeat testing. This challenge has been reported in a previous study that used KDIGO guidelines (31). Despite our efforts to track the patients, we were not able to re-test all patients with renal insufficiency; 126 out of 184 (68%) patients with hypertension were reached and re-tested. It was impossible to track other patients; some had died or transferred outside the district, and others could not be located for testing within our study period. Therefore, we may have underestimated the prevalence of CKD. Other programs implementing screening for CKD should consider how to strengthen the ways used to track patients in this study, which also has benefits for patient care beyond screening, or try other strategies that can be used to effectively track patients for confirmation of CKD.

We found a lower prevalence of CKD in patients with hypertension in comparison to most studies published in Africa (13,32). The prevalence may have been underestimated since we could not find all the patients who needed a repeat test. Additionally, we had used KDIGO guidelines, and therefore some people had an initially low eGFR which normalized after repeat testing.

Additionally, most of the patients in this study are females, which reflects health service utilization in Malawi, where more females utilize services than men. After controlling for multiple factors, only older age and diabetes were strongly associated with CKD in patients with hypertension, and this has also been shown in other studies in Africa (8,33)

There are many clinical and research implications from these results. First, we concluded that all patients with hypertension should be screened for CKD, and Neno District continues to gradually screen all patients and plans to repeat CKD screening annually. Additionally, Neno District has created 2 Advanced NCD Clinics where patients with CKD stage 4 and 5 are routinely managed alongside patients with other severe chronic NCDs. Beyond Neno, hypertension clinics need to invest in CKD screening for early detection and management of kidney disease. Additionally, more research needs to be generated, particularly in urban areas, to compare with the results from this study.

There are a few key limitations in this study. We used only eGFR only to define patients with CKD, and we were unable to measure albumin-creatinine ratio or other measures of CKD as defined by KDIGO guidelines. The study is also a facility based audit and was conducted in a rural area. As a result, the study may not be generalizable to populations outside Neno District. We also investigated CKD in patients with hypertension aged 18 years and above thereby excluding all patients less than 18 years old. In addition, to be enrolled for hypertension treatment in clinics in Neno, patients have blood pressures ≥160/110, so the results are not generalizable to patients with Stage I hypertension. Finally, we measured prevalence and not incidence of CKD, therefore we could not differentiate the temporal sequence of hypertension and CKD.

Conclusions

The study found moderately high prevalence of renal insufficiency and CKD in a rural cohort of hypertension patients, 15.4% and 7.1% respectively. Additionally, CKD was significantly associated with older age and a history of diabetes. We advocate for investing in CKD screening among patients with hypertension attending longitudinal care in order to optimize early diagnosis and management in this population.

List Of Abbreviations

CI confidence interval

CKD Chronic kidney disease

NCD Non-communicable disease

EGFR Estimated glomerular filtration rate

KDIGO Kidney Disease: Improving Global Outcomes

BMI Body mass index

IQR interquartile range

MOH Ministry of Health

EMR Electronic medical record

OR Odds ratio

Declarations

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Availability of data and materials

The data and materials used for this study belongs to the Ministry of Health in Neno District therefore cannot be shared publicly. However, the data and materials can be shared upon reasonable request to the corresponding author.

Authors' contributions

CK, LN, EN, GCT and EBW conceptualized the study. LT, RK, CK and GCT performed data curation. CK performed data cleaning and analysis. CK wrote the first draft. All authors provided feedback and approved the final manuscript for publication.

Ethics approval and consent to participate

All data were collected as part of routine patient care and was analysed retrospectively. As a result, we did not obtain informed consent from patients. Access to data was given only to investigators and data were kept securely. The study received ethical clearance from Malawi National Health Sciences Research Committee protocol number 1216.

Consent for publication

Not applicable

Competing interests

The authors declare no competing interests

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Tables

Table 1. Characteristics of patients with hypertension screened for CKD

	Total hypertension patients	No CKD	CKD
Total number of patients screened (%)	1197	1112 (92.9)	85 (7.1)
Median age(IQR)-years *	61 (51-70)	60 (50-69)	70 (62-78)
Female gender (%)	942 (78.7)	878(79.0)	64(75.3)
Years since diagnosis of hypertension (%)			
Less than 1	290 (24.3)	275 (24.7)	15 (17.6)
1-2	274 (22.9)	252 (22.7)	22 (25.9)
Over 2	632 (52.8)	584 (52.6)	48(56.5)
Duration in clinic (%)-years			
Less than 1	291(24.3)	276 (24.8)	15 (17.6)
1-2	276 (23.1)	254 (22.9)	22 (25.9)
Over 2	630 (52.6)	582 (52.3)	48 (56.5)
Median most recent systolic blood pressure(IQR)-mmHg*	135 (123-148)	135 (123-148)	140.5 (124.5-157)
Median most recent diastolic blood pressure(IQR)-mmHg	84 (76.5-93)	84 (77-93)	83 (73-92)
Risk factors			
Median BMI (IQR)-kg/m2	22.9 (20.3-26.6)	22.8 (20.3-26.5)	23.7 (20.3-27.4)
BMI over 25 (median, IQR)-kg/m2	29.1(27.3-32.9)	27.8 (26.0-31.6)	29.3 (27.3-33.2)
BMI category (%)-kg/m2			
<18.5	115 (9.7)	105 (9.5)	10 (11.9)
18.5-<25	684 (57.4)	641(57.9)	43 (51.2)
25-<30	270 (22.7)	245 (22.1)	25 (29.8)
30 and above	122 (10.2)	116 (10.5)	6 (7.1)
Proteinuria			
Protein <1+	946 (95.4)	883 (95.5)	63 (94.0)
Protein >=1	46 (4.6)	42 (4.5)	4 (6.0)
Diabetes*			
No	1134 (94.7)	1058 (95.1)	76 (89.4)
Yes	63 (5.3)	54 (4.9)	9 (10.6)
HIV			
Negative	916 (89.1)	845 (88.6)	71 (95.9)
Positive	112 (10.9)	109 (11.4)	3 (4.1)

CKD Chronic Kidney Disease

% Percentage

Sd Standard deviation

IQR interquartile range

BMI Body mass index

*significant differences between CKD patients and patients without CKD

Table 2 Estimated GFR stages in all patients with hypertension screened for chronic kidney disease

Stages of eGFR	eGFR (ml/min/1.73m2)	N (%)
Normal EGFR	≥ 90	578 (48.3)
G2 (Mildly decreased)	60-89	435 (36.3)
G3a (Mildly to Moderately decreased)	45-59	85 (7.1)
G3b (Moderately to severely decreased)	30-44	57 (4.8)
G4 (Severely decreased)	15-29	33 (2.8)
G5 (Kidney failure)	<15	9 (0.7)
Total		**1197 (100)**

eGFR Estimated GFR

CKD Chronic kidney disease

Table 3. Univariate Logistic Regression of Correlates of CKD

Independent Variable	Odds ratio (CI)	P value
Age (years)	1.06 (1.04-1.08)	<0.001*
Gender		
Female	ref	ref
Male	1.23 (0.74-2.06)	0.43
Years since diagnosis		
<1 year	ref	
1-2 years	1.60 (0.81-3.15)	0.17
Over 2 years	1.51 (0.83-2.73)	0.19
Diagnosis duration		
<1 year	ref	
1-2 years	1.59 (0.81 -3.14)	0.19
Over 2 years	1.52 (0.83 -2.76)	0.17
Most recent systolic blood pressure	1.01 (1.004 -1.02)	<0.001*
Most recent diastolic blood pressure	0.99 (0.98-1.01)	0.60
BMI	1.02 (0.99 -1.06)	0.40
Overweight or obesity	1.01 (0.93-1.09)	0.82
BMI category		
<18.5	1.42 (0.69-2.91)	0.34
18.5-<25	Ref	Ref
25-<30	1.52 (0.91-2.5)	0.11
30 and above	0.77 (0.32 -0.85)	0.56
Proteinuria		
Less than 1+	Ref	
1+ and above	1.33 (0.46-3.80)	0.59
Diabetes diagnosis		
No	Ref	
Yes	2.32 (1.10-4.88)	0.03*
HIV diagnosis		
Negative	Ref	
Positive	0.33 (0.10-1.06)	0.06

*significant associations

Table 4 Multivariable analysis of Correlates of CKD

Independent Variable	Adjusted Odds ratio (CI)	P value
Age (years)	1.06 (1.04-1.08)	<0.001
Most recent systolic blood pressure	1.01 (1.00- 1.02)	0.048
Diabetes diagnosis		
No	Ref	
Yes	2.63 (1.21- 5.69)	0.01

CKD Chronic kidney disease

Figures

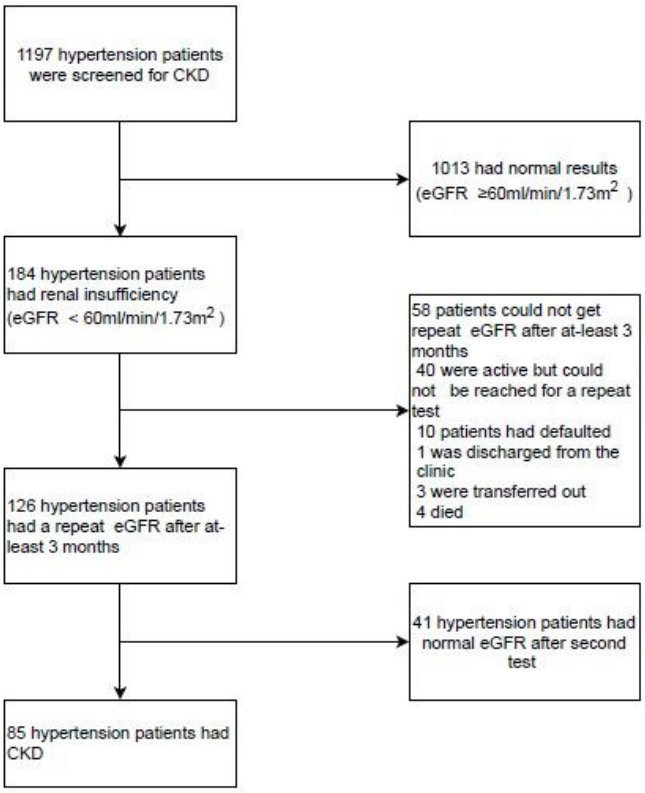


Figure 1

Screening Results for Patients with Hypertension CKD Chronic kidney disease eGFR Estimated glomerular filtration rate