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Research Article

Chronic Kidney Disease among Hypertensive Patients Attending a National Referral Hospital in Uganda

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Abstract

Background: Hypertension is the most common cause of cardiovascular disease in the world and the leading risk factor for heart failure, stroke and kidney failure, which characteristically occur, in a much younger population in sub-Saharan Africa. Uganda has a high burden of hypertension in both urban and rural areas. The purpose of this study was to determine the prevalence of Chronic Kidney Disease (CKD) and associated factors among hypertensive patients attending an urban hospital in Uganda.

Methods: This was a cross sectional study among patients aged ≥18years. Data was collected on the demographic characteristics, clinical signs and laboratory tests (full blood count, creatinine, HIV status). Abdominal ultrasound scan was done on all patients to assess kidney size. Data was analyzed using STATA 12.

Results: Out of 431 patients screened 360 completed the study, mean age 52 years (±SD), 300 (83.3%) were females. Majority 346 (96.1%) were known hypertensive patients for more than 6 months. The prevalence of CKD was 17.2%. The factors that were independently associated with CKD included; Smoking [Odds Ratio 5.47 (OR) 95% Confidence Interval (CI) (1.07 - 27.8), p=0.04], pedal edema [OR 3.93 95%CI (1.15 - 13.45) p=0.03], Hemoglobin < 11.5g/dl [OR 3.97 95% CI (1.61 - 9.83), p=0.003], and proteinuria OR 4.68 95%CI (2.22 - 9.90), p<0.001.

Conclusions: The prevalence of CKD among hypertensive patients attending Mulago Hospital is high and associated with smoking, proteinuria and anemia. Therefore, there is a need to screen for CKD among hypertensive patients especially those presenting with anemia or proteinuria as well as those with a history of smoking.

Keywords: Chronic Kidney Disease; Hypertension; Uganda

Abbreviations:

CKD	:	Chronic Kidney Disease
HAART	:	Highly Active Antiretroviral Treatment
HIV	:	Human Immunosuppressive Virus
MDRD	:	Modification of Diet in Renal Disease
GFR	:	Glomerular filtration rate
ESRD	:	End Stage Renal Disease

Background

Non-Communicable Diseases (NCDs) are on the rise in the world especially in the developing countries and are becoming of public health importance alongside infectious diseases [1] Hypertension is currently the most common Cause Of Cardiovascular Disease (CVD) in the world and is a major factor contributing to high mortality is Sub-Saharan Africa (SSA). It has been suggested that CVD and hypertension are increasing rapidly in SSA [2]. The prevalence of hypertension in the developing world is estimated to be comparable to that found in the developed countries [3]. With limited resources in SSA, the increase in hypertension prevalence is expected to be of grave consequence. In a recent study, system-

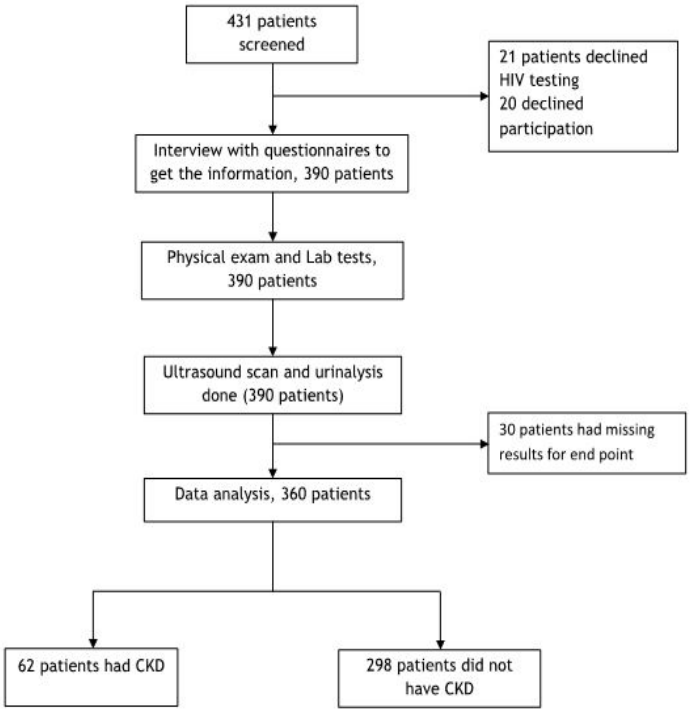
atic review [4], the prevalence of hypertension in Africa ranged from 9.3% to 44%, with a suboptimal levels of awareness, treatment and control.

Chronic Kidney Disease (CKD) is becoming a major health problem worldwide especially among patients with hypertension. The prevalence of CKD among hypertensive patients is greatly varied across studies and countries. In a study done among 3534 hypertensive patients in Italy attending specialized clinics, 42% of them had significantly low GFR and Albumin Creatinine Ratio (ACR)of 2.5 mg/mmol in men and 3.5 mg/mmol in women [5]. Another study done among hospitalized hypertensive patients in Atlanta found the prevalence of chronic kidney disease to be 11.8 % [6].

In Nigeria, a study done in a teaching hospital among hypertensive patients revealed a prevalence of 23.1% and in some areas in Burkina Faso it has been found to be 36% [7]. There have been several renal related deaths occurring because of hypertension and or diabetes type II [8,9] There is growing burden of renal disease in Uganda and most of these patients present with complications like End Stage Renal Disease (ESRD) which is very expensive to treat [10]. CKD and hypertension usually co-exist and consequently result in poor quality of life, causing significant morbidity and mortality [11]. CKD may co-exist with hypertension as the same mechanism that causes atherosclerosis may cause CKD. In the presence of poorly-controlled hypertension, patients quickly progress to End Stage Renal Failure and may require renal replacement therapy [12]. Patients with CKD are more likely to die of CVD earlier than its complications and also have increased non-CVD mortality [13]. Prevention of CKD involves blood pressure control, diabetes control, diet, exercise and screening high risk patients with early interventions [14]. Early screening using GFR and ACR (Albumin: Creatinine ratio) may help to identify patients with CKD early enough so that progression to End Stage Renal Disease (ESRD) is delayed or reversed. The purpose of this study therefore was to determine the prevalence of chronic kidney disease and the associated factors among patients attending a hypertension clinic in Uganda.

Methods

This was a cross sectional study done between November 2011 and March 2012. Participants from the hypertension clinic in Mulago Hospital Outpatient department aged ≥ 18 years were included in the study after providing informed consent. Patients who were too sick to communicate or cooperate with the study investigators and those who did not consent for HIV testing were excluded (Figure 1).



Chronic Kidney Disease (CKD) was defined as participants who had eGFR of less than 60ml/min/1.73m2 using both Modification of Diet in Renal Disease (MDRD) and CKG formulae for at least three months plus kidney size less than 9cm on ultrasound. Patients aged 18 years and above were invited to participate in the study on the basis of every 4th patient after a first random pick until the required sample size was achieved. Patients were being enrolled once and assigned numbers to avoid multiple recruitment. We required 2 creatinine readings at least three months apart. Participants who did not have a creatinine recorded at least three months old were called back after three months for another creatinine. Patients who were found with CKD were called up and referred to the nephrologists for further management and those without CKD were called up, informed and educated about avoiding CKD. Patients were also informed about their HIV results and those found positive were referred to HIV clinic within and around the hospital for further management.

Data Collection

Participants that were eligible provided informed consent and were counseled for HIV testing then blood pressure was measured in a quiet room with the patient seated using the left arm and they were interviewed to obtain social, demographic, lifestyle and clinical characteristics including age, sex, marital status, level of

education, diet, alcohol, smoking, use of herbal medication, family history of diabetes mellitus, hypertension and renal disease, drugs and duration of hypertension. Physical examination was done to assess for edema, pallor of mucous membranes, and a repeat BP was done and an average was recorded. Participants enrolled into the study had 10 mls of their blood drawn under aseptic conditions into EDTA bottle and a plain red top in divisions of 4mls each and the remaining 2 mls put in a grey top to measure Serum creatinine and urea using the Mulago Hospital Chemistry machine model Cobis e 601 manufactured by Roche, full blood count using an automated CBC machine, HIV serology using determine strips and Unigold, and blood sugar measured in the chemistry machine model Cobis e 601 manufactured by Roche. A mid stream urine sample was obtained from the participants for a dipstick urinalysis to measure proteinuria and all these results were recorded.

A qualified sonographer assessed kidney size and echogenicity with assistance of a radiologist. We chose to consider a length less than 9.0 cm basing on a study done by Werner et al which shows the variation in kidney size using CT scan of the kidneys to be 10.0 with a standard deviation of +/- 1 cm and thus as we were using ultrasound we took the lower limit to be 9.0cm and thus everyone with kidney length less than 9.0 was considered to have small kidneys [15]. Patients who did not have an old creatinine were asked to return after 3 months to repeat their renal functions to obtain a second creatinine.

Statistical Analysis

Data was entered using EPIDATA version 3.1 and exported to STATA version 12 for analysis. We used proportions for categorical data; univariate and multivariate analysis was done to determine factors that were associated with CKD. Factors with P-values less than 0.05 were statistically significant.

Ethical Considerations

Institutional approval was sought from the School of Medicine Research and Ethics committee; Makerere University College of Health Sciences. Written informed consent was obtained from all the study participants prior to study procedures.

Results

We included 360 patients in the study, mean age 56 ± 14 years, 224 (62.2%) of patients were between the ages of 41 - 65 years. Majority of these patients were female 300 (83.3%), 239 (66.4%) had a family history of hypertension, 114 (31.7%) had family history of Diabetes Mellitus and very few 21 (5.8%) had a family history of renal disease. All the patients were known hypertensive with the majority 346 (96.1%) of them having known their hypertensive status for more than 6 months. Few of them 10 (2.8%) had history of smoking, 90 (25%) of patients were staying with a smoker, and 70 (19.4%) had history of alcohol consumption. A sizable number of participants 190 (52.8%) were taking part in some form of exercise. Less than a third (23.9 %) had a systolic blood pressure less than 140 mmHg, and 39.2% had a diastolic blood pressure less than 90mmHg. Overall 66 (18.3%) had a blood pressure of less than 140/90mmHg. A tenth of participants, 28 (10.3%) were HIV positive (Table 1).

Characteristic	CKD, n =62	Total, n = 360
Age		
18 - 40 years	15 (24.2)	45 (12.5)
41 - 65 years	26 (41.9)	224 (62.2)
66 - 100 years	21 (33.9)	91 (25.3)
Sex (Female)	38(61.3)	300(83.3)
Family history of renal disease	5(8.1)	21(5.8)
Family history of Diabetes	24(38.7)	114(31.7)
Family history of hypertension	37(59.7)	239(66.4)
Smoking	6(9.7)	10(2.8)
Alcohol use	12(19.4)	70(19.4)
Exercise	39(62.9)	170(47.2)
Addition of raw salt in food	53(85.5)	319(88.6)
Presence of oedema	15(24.2)	24(6.7)
BMI		
Under weight	9 (14.5)	33 (9.2)
Normal	32 (51.6)	143(39.9)
Overweight	12 (19.4)	103 (28.8)
Obese	8 (12.9)	57 (15.9)
Morbid obesity	1 (1.6)	22 (6.2)
Waist circumference*	26 (41.9)	210 (58.3)
Normal	36 (58.1)	150 (41.7)
Abnormal	26 (41.9)	210 (58.3)
Blood Pressure ≥ 140/90 mmHg	49(79.0)	294(81.7)
Blood sugar >7 mmol/l	7 (11.2)	43 (11.9)
Hemoglobin <11.5 g/dl	24(38.7)	42(17.7)
HIV Positive	11(17.7)	29(8.1)
Urine protein		
Less than 30	32(51.6)	65(18.1)
30 or more	30(48.4)	295(81.9)

CKD: Chronic Kidney Disease, **BMI:** Body Mass Index, **HIV:** Human immunodeficiency virus, *Abnormal waist circumference (Men >102cm, Women >88cm)

Table 1: Characteristics of hypertensive patients attending Mulago Hospital, Kampala, Uganda.

Of the 360 participants included in our analysis, 62 (17.2%) had Chronic Kidney Disease. On bivariate analysis, the factors that were associated with chronic kidney disease included: age 40 years and below (p=0.003); male sex (p<0.001), active smoking

and passive smoking, p=002 and p=0.007 respectively, hemoglobin less than 11.5 g/dl (p<0.001), HIV (p=0.003) and proteinuria (p<0.001) (Table 2).

Variable	Crude OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Age > 40 years	0.35 (0.18 - 0.70)	0.003	0.81 (0.31 - 2.11)	0.67
Gender - male	4.60 (2.48 - 8.53)	<0.001	1.93 (0.83 - 4.50)	0.13
Smoker	7.88 (2.15 - 28.81)	0.002	5.47 (1.07 - 27.8)	0.04
Passive smoking	2.22 (1.24 - 3.96)	0.007	1.49 (0.71 - 3.12)	0.29
Exercise	0.46 (0.26 - 0.81)	0.007	0.84 (0.43 - 1.65)	0.62
Pedal edema	10.25 (4.24 - 24.76)	<0.001	3.93 (1.15 - 13.45)	0.029
Abnormal BMI	0.56 (0.32 - 0.98)	0.041	0.96 (0.45 - 2.08)	0.92
Abnormal waist circ	0.45 (0.26 - 0.78)	0.005	0.67 (0.30 - 1.49)	0.34
Hemoglobin <11.5	9.69 (4.70 - 20.0)	<0.001	3.97 (1.61 - 9.83)	0.003
HIV positive	3.35 (1.50 - 7.52)	0.003	1.66 (0.57 - 4.76)	0.35
Proteinuria	8.57 (4.63 - 15.85)	<0.001	4.68 (2.22 - 9.90)	<0.001

OR: Odds Ratio, **CI:** Confidence interval, **CKD:** Chronic Kidney Disease, **BMI:** Body Mass Index, **HIV:** Human Immunodeficiency Virus, *Abnormal waist circumference (Men >102cm, Women >88cm)

Table 2: Multivariate analysis for factors associated with chronic kidney disease among hypertensive patients attending Mulago hospital, Kampala, Uganda. (N=360).

On multivariate analysis patients who smoked were 5 times more likely to have CKD [Odds Ratio 5.47 (OR) 95% Confidence Interval (CI) (1.07 - 27.8), p=0.04], four time more likely for those with pedal edema [OR 3.93 95%CI (1.15 - 13.45) p=0.03] patients with a hemoglobin of less than 11.5 g/dl were 4 times more likely to have CKD [OR 3.97 95% CI (1.61 - 9.83), p=0.003] and those who had proteinuria on dipstick were more likely to have CKD [OR 4.68 95%CI (2.22 - 9.90), p<0.001] (Table 2).

Discussion

Prevalence of CKD Among Hypertensive Patients

From this study, the prevalence of CKD was 17.2%, about 2 out of 10 patients had CKD which is close to what was found in Nigeria, where 23.1% of hypertensive patients attending a teaching hospital had decreased renal function [16]. However, a higher prevalence has been found in other areas of West Africa. In Burkina Faso it was found to be 36 % [7] and in Ghana, the prevalence was found to be 46.9% [17]. This high prevalence in these studies could be attributed to the fact that only one value of GFR was used and therefore a likelihood of including patients with acute kidney injury. This study done in Burkina Faso included patients that had a blood pressure >160/95mmHg and it was noted that majority (69%) of patients had CVD complications. All these can explain a high proportion of CKD. A study done in Italy found the prevalence of CKD patients with hypertension to be as high as 42% [5] and a study done Nwankwo et al revealed that 45.5% of patients admitted with hypertension in Maiduguri, Nigeria had impaired renal function [18].

Persistence of the low GFR constitutes a diagnosis of CKD so it is possible that in these studies CKD was over estimated given the fact that acute renal failure is more common than chronic renal failure. To prevent over diagnosing CKD, we used two values of creatinine that were three months apart. A patient was considered to have CKD if the GFR as calculated from two values of creatinine at least 3 months apart was below 60 ml/min/1.73m2 (stage 3 and above) using both Cockroft-Gault and MDRD Formulae or the patients who had one reading of GFR as calculated using both the CKG and Modified MDRD formulae and a kidney length less than 9.0 cm.

Factors Associated with Chronic Kidney Disease

In the bivariate model, we found age less than 40 years and male gender were associated with CKD. This finding is contrary to studies done elsewhere that found advancing age to be significantly associated with CKD and its progression [19]. The study done in Ghana [17] found no association between age or gender with kidney disease despite having comparable demographics to our study. Unemployment was found to be significantly associated with CKD in our study with a p-value of 0.037. This is can be equivalent to the social economic status, which was found in a study done in the United Kingdom to be associated with CKD [6]. HIV infection was also found to be associated with CKD in our study with a p-value of 0.023, however this was not significant in the multivariate analysis, this may be due to the fact that patient who declined HIV testing were excluded and the prevalence then was low. HIV has also been found to be significantly associated with CKD especially with among patients with CD4 less than 200 cells/ml [20]. HAART was not found to be significantly associated with CKD in our study, but studies done in Thailand show that Truvada is associated with CKD. Very few patients were on Truvada and PI based regimen in our study even though over 57% of HIV positive patients were on HAART.

Obesity was not found to be associated with CKD in our patients as has been demonstrated in some studies however, our

findings are in agreement with a Nigerian study that also found that obesity was not associated with CKD [21]. Still in this model active and passive smoking were found to be associated with CKD. Tobacco smoke has been found to be associated with CKD and its progression especially in hypertensive and diabetic patients [22]. In our study, we found that use of herbal medication was not significantly associated with CKD. However a study done in Taiwan showed an association between herbal medication use and CKD [23]. This may also be explained by the fact that the way we measured for herbal medication use was inadequate. In multivariate model, we found smoking to be a risk for CKD as those who smoked were 5 times more likely to get disease(p=0.004). This is similar to the studies elsewhere which have shown tobacco smoking to be a significant risk factor for CKD and its progression especially among hypertensive and diabetic patients [22]. In ours study we also found Hemoglobin level < 11.5g/dl (anemia) to be significantly associated with CKD (p=0.03). We also found urine protein of 30mg/dl and more to be significantly associated with CKD (p<0.001). This finding was having also been found in hypertensives in Italy by Leoncino et al as about 10% of participants with hypertension had concomitant proteinuria and low GFR. (Leoncino, et al. Journal of hypertension 2010)

The study limitations included were mainly financial and the fact that some of the patients failed to turn up for a repeat creatinine within a period of 3 months and thus we could not measure for end point (CKD) and we excluded them from the analysis.

Conclusion and Recommendations

The prevalence of CKD among patients with hypertension was 17.2%, which is huge given the limitations of managing CKD in a low limited setting. The factors that were independently associated with CKD include smoking, having pedal edema, hemoglobin <11g/dl, and proteinuria. Routine screening should be done among the hypertensive patients in the clinic since it takes simple tests to diagnose CKD. Patients in the clinic should always be educated about life style modification and be counseled against smoking as it has showed to be a significant factor for CKD. In resource limited setting and busy clinics, frequent screening may be mainly in patients who have proteinuria ≥30mg/dl, Haemoglobin level ≤ 11.5g/dl and smoking exposure. Further studies should be done to assess the causal relationship between smoking and CKD as well as determining the things we can do to prevent progression of disease.

Competing Interests: None

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