Original Article

The Prevalence of Chronic Kidney Disease and Associated Factors Among Patients Admitted at Princess Marina Hospital, Gaborone, Botswana

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Abstract

Background: Chronic kidney disease (CKD) has become a major public health problem worldwide. Due to the asymptomatic nature of CKD during earlier stages, patients tend to present late, missing opportunities for prevention. **Aims:** This study was conducted to determine the prevalence and assess the risk factors associated with CKD in patients admitted at Princes Marina Hospital. Settings and Design: Hospital inpatient setting. Subjects and Methods: A case-matched comparison study was done involving 86 cases and 86 matches by gender and age (± 5 years) from March 21, 2014, to May 31, 2014. Statistical Analysis Used: SPSS software version 20 (SPSS Inc. Chicago Illinois) was used for data entry, cleaning, and analysis. Frequency, percentage, mean, and standard deviation were used to describe the data. Chi-squared test and odds ratio (OR) with 95% confidence interval (CI) were employed to analyze the associations of categorical variables. Logistic regression analysis was done to control for possible confounding variables. A $P < 0.05$ was considered statistically significant. **Results:** In the study period, CKD prevalence was 74/550 (13.5%), and 23/99 (23.2%) of mortality occurred in patients with CKD. Over half of the 86 cases of CKD (53.5%) were not aware of their CKD status and were diagnosed during the index admission. Hypertension (HTN), diabetes mellitus, and HIV-positive status were significantly associated ($P < 0.05$) with CKD in the bivariate analysis, while HTN (adjusted OR [AOR] [95% CI]: 11.28 [4.56, 27.89]) and HIV-positive status (AOR [95% CI]: 8.68 [3.58, 20.99]) remained significant predictors of CKD in the multivariate analysis. CKD within the HIV-positive patients was significantly associated with duration of <3 years since HIV diagnosis and lower CD4 levels ($P < 0.05$). **Conclusions:** Significant admissions and mortality in medical wards are attributed to renal impairment. There is an urgent need to establish follow-up programs in high-risk populations (hypertensives, diabetes, and HIV) which aims to identify patients at early stages of CKD, and devise prevention mechanisms to reduce burden in terms of cost, morbidity, and mortality.

Keywords: *Botswana, chronic kidney disease, risk factors*

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Introduction

Chronic kidney disease (CKD) is increasingly recognized as a major public health problem worldwide.[1] Due to the asymptomatic nature of this disease, CKD is not frequently detected until its late stages, resulting in lost opportunities for prevention. Progression to end-stage renal disease or other adverse outcomes could be prevented or delayed through early detection and treatment of CKD.[2,3] Epidemiology of patients with CKD and subsequent end-stage kidney disease in Sub-Saharan Africa (SSA) differs from developed countries. In SSA, CKD mainly affects young, reproductive adults between 20 and 50 years who are economically productive.[4] With the poverty and debt burden increasing in most of the SSA coupled with late presentation, absent or poor distribution of renal replacement therapy (RRT) and its associated high cost, identifying risk factors for CKD and ultimately determining screening and prevention strategies may help reduce the cost burden and improve morbidity and mortality.[4]

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The kidney disease outcomes quality initiative (K/DOQI) of the National Kidney Foundation developed a practice guideline in 2002. CKD is defined as either kidney damage or glomerular filtration rate (GFR) below 60 ml/min/1.73 m2 for three or more months with or without evidence of kidney damage, irrespective of the cause.[5] According to data from National Health and Nutritional Examination Survey, <10% of patients with CKD Stage 3 (GFR between 30 and 59 ml/min/1.73 m2) knew of their diagnosis. In addition, only 45% of patients with CKD Stage 4 (GFR between 15 and 29 ml/min/1.73 m2) had been told of the condition, underlining the difficulty with diagnosis even in developed countries.[6]

According to a study done in Kinshasa, Democratic Republic of Congo, where CKD was defined as either loss of kidney function (estimated GFR <60 ml/min/1.73 m2) or kidney damage (proteinuria), the prevalence of all stages of CKD by K/DOQI was 12.4%. Of people studied, 8% had CKD Stage 3 or below.[7]

Furthermore, in a large cross-sectional community study done in Beijing, China, the prevalence of CKD was found to be 13.0%.[8]

Evidence from several studies revealed hypertension (HTN) and diabetes to be the two major causes of kidney disease worldwide.[7,9] Older age followed by HTN were found to be the strongest predictors of lower estimated GFR in another study conducted in the United States of America.[10] Other studies have implicated HIV disease as a risk factor for CKD.[11] Lower CD4 levels, older age, and tenofovir use were significantly associated with increased incidence of CKD in HIV-positive patients.[11] In a study conducted in China, older age, history of cardiovascular disease, diabetes mellitus (DM), and HTN status were found to be associated with CKD.[8] In the same study, when adjustment was made, age, rural residence, history of cardiovascular disease, and HTN of >10 years were the only factors independently associated with CKD.[8]

The cost associated with the treatment of end-stage renal disease is enormous, especially in developing countries like Botswana where the health system is overburdened with communicable diseases such as HIV/AIDS and tuberculosis.[12] There has been no study done in Botswana to assess the burden of CKD in the hospital medical admissions and the factors associated with CKD. Botswana is one of the countries with a huge burden of HIV, and it is worth exploring the risk factors associated with CKD including determining the impact of HIV infection as one of the risk factors.

This study was conducted to determine the prevalence of CKD and to assess the associated risk factors for CKD in patients admitted at Princess Marina Hospital.

Subjects and Methods

Princess Marina Hospital is a referral and teaching hospital located in Gaborone, the capital city of Botswana. The Department of Medicine provides both out- and in-patient services to adult medical patients. Male and female medical wards have a total bed capacity of 88 with an average of 250-300 new patient admissions monthly.

A case-matched study was conducted from March 21, 2014, to May 31, 2014, on patients admitted to the medical wards who comprised a source population to obtain the cases. The matches were selected from the wards with nonmedical conditions (orthopedics and surgical wards) regardless of whether they were admitted for elective or nonelective procedures. Cases and matches were compared by gender and age (±5 years). Enrollment of cases involved two steps; all patients admitted in medical wards during the study periods had their charts examined, and serum creatinine results on the day of admission were obtained from the Integrated Patients Management System (IPMS). Serum creatinine obtained was used to compute estimated GFR by using the Modification of Diet in Renal Disease equation formula.

GFR (ml/min/1.73 m2) = 1.86 × (Scr)1.154× (Age)0.203 × (0.742 if female) × 1.210 if black.[13]

The CKD case definition for this study included all patients with estimated GFR <60 ml/min/1.73 m^2[5,7,8] (which equates to CKD Stages 3, 4, 5), who had no evidence of factors that can cause acute kidney injury (AKI). Patients without a history of prior kidney disease in the previous 3 months were categorized to have CKD only if there was radiological evidence of CKD such as small and/or hyperechoic kidneys, loss of corticomedullary differentiation.[14]

Each time, investigators identified a case in medical ward, they would go to nonmedical wards and look at the list of patients and identify all the names of patients matching by age and gender provided that the matches had estimated GFR of ≥60 ml/min/1.73 m^2; this was followed by a lottery to identify a particular match. The process was repeated in situations where identified matches did not consent.

Sample size calculation was done by Epi-Info 3.5.3 (CDC). To calculate sample size, we used HTN as a risk factor, the estimate prevalence of HTN is available in the Botswana's STEPS survey.[15] The assumptions utilized a 95% confidence level of detecting a difference, 80% power, and the rate of HTN among controls and cases according to STEPS survey estimated to be 33.1% and 55.3%, respectively. A total of 86 cases and 86 matches were required considering the above assumptions.

For the purpose of this study, HTN was defined as the average of three blood pressure measurements of >140/90 mmHg. The definition was according to the Joint National Committee 8. The data extraction form was used to obtain information from patients or their next of kin. Other information was obtained from patients' charts and IPMS.

For both cases and matches, the following data were collected: Age, gender, highest level of education, occupation, place of residence, smoking, alcohol use, and family history of CKD. Patients with CKD were also interrogated as to whether or not they knew the diagnosis at index admission. Risk factors for CKD included a history of chronic conditions such as HIV, HTN, and DM. For HIV-positive patients on highly active antiretroviral therapy (HAART), the duration of treatment, as well as the current and previous regimens, was elicited.

Laboratory assays

HIV-positive patients either on HAART or not on HAART with unknown CD4 count within past 3 months had their blood collected by venipunctures to test for CD4. Patients who had CD4 results in the previous 3 months were not subjected to another CD4 count testing. Patients whose HIV serostatus was unknown were counseled by the principal investigator or by other doctors involved in the study for the HIV test to be performed and those found to be HIV positive were offered treatment according to the national guidelines. All patients were screened for DM to rule out undiagnosed cases; this was done by means of fasting blood glucose.

Statistical analysis

SPSS software version 20 (SPSS Inc. Chicago Illinois) was used for data entry, cleaning, and analysis. Frequency, percentage, mean, and standard deviation were used to describe the data. Chi-squared test and odds ratio (OR) with 95% confidence interval (CI) were employed to analyze the associations of categorical variables. Logistic regression analysis was done to control for possible confounding variables. A $P < 0.05$ was considered statistically significant.

Ethical consideration

Ethical clearance to conduct the study was obtained from the University of Botswana Ethics Committee and the Institutional Review Board and Ethics Committee at Princess Marina Hospital. Permission to do the study was also obtained from the Ministry of Health Botswana Research Office.

Results

During the study period, 569 patients were admitted to the medical wards of Princess Marina Hospital. The number of patients with CKD (defined as estimated GFR of <60 ml/min/1.73 m2, Stages 3, 4, and 5) admitted during the study period regardless of their recruitment status was 93/569 (16.3%). On the other hand, 19/93 (20.4%) of patients admitted with CKD were already receiving RRT, making prevalence of CKD excluding known patients to be 74/550 (13.5%). Eighty-six out of 93 patients were included in the final analysis because two did not consent and the remaining five patients were either discharged or died before recruitment. Of the 550 admissions, 9 (1.6%) patients were diagnosed with AKI. Overall mortality in medical wards during the study period was 99/569 (17.4%) with 62/99 (62.6%) of deaths being male patients and 37/99 (37.4%) being females. Twenty-three, 23/99 (23.2%) of deaths during the study period occurred in patients with renal impairment.

All aspects of sociodemographic characteristics between cases and matches were appropriately comparable [Table 1].

Over half of our patients, 46/86 (53.5%) were not aware of their CKD status and were diagnosed during the index admission. Of those admitted with CKD, 65/86 (75.6%) were patients in end-stage renal disease (including 19 patients already on hemodialysis at recruitment), whereas

Table 1: Sociodemographic characteristic distribution of study participants

Characteristics	Cases (*n*=86) (%)	Controls (*n*=86) (%)	*P**
Gender			
Male	50 (58.1)	50 (58.1)	1.0
Female	36 (41.9)	36 (41.9)	
Age in years			
19-35	22 (25.6)	22 (25.6)	0.98
36-50	24 (27.9)	25 (29.1)	
51-65	21 (24.4)	22 (25.6)	
66+	19 (22.1)	17 (19.8)	
Mean (SD)	49.3 (17.2)	48.8 (17.3)	
Education			
No formal school	14 (16.3)	19 (22.1)	0.12
Less than primary school	11 (12.8)	10 (11.6)	
Primary school complete	26 (30.2)	14 (16.3)	
Secondary school complete	25 (29.1)	24 (27.9)	
College/university complete	10 (11.6)	19 (22.1)	
Employment status			
Government employee	14 (16.3)	14 (16.3)	0.85
Nongovernment employee	23 (26.7)	28 (32.6)	
Unemployed (able to work)	18 (20.9)	17 (19.8)	
Unemployed (unable to work)	31 (36.0)	27 (31.4)	
Residence			
Urban	45 (52.3)	35 (40.7)	0.16
Rural	41 (47.7)	51 (59.3)	

*P<0.05. SD=Standard deviation

21/86 (24.4%) were either in CKD Stage 3 or Stage 4. Bivariate analysis showed that the factors significantly associated with CKD were being HIV positive, history of HTN and DM ($P < 0.05$); whereas the history of smoking or alcohol use were not associated with CKD [Table 2]. Further analysis by backward conditional logistic regression for medical conditions associated with CKD only retained HIV positivity (adjusted OR [AOR] [95% CI]: 8.68 [3.58, 20.99]) and the history of HTN (AOR [95% CI]: 11.28 [4.56, 27.89]) as significant predictors; DM was no longer significant [Table 3].

Trend analysis of factors associated with CKD showed that being hypertensive regardless of duration was still a significant factor for CKD. For HIV-positive patients, CKD was significantly associated with the duration of <3 years since HIV diagnosis [Table 4].

Analysis to compare urban and rural CKD patients regarding traditional (HTN and DM) versus nontraditional causes of CKD (HIV and other unknown

Table 2: Medical characteristic distribution of study participants

Characteristics	Cases (*n*=86) (%)	Controls (*n*=86) (%)	*P**
History of smoking			
Yes	21 (24.4)	32 (37.2)	0.09
No	65 (75.6)	54 (62.8)	
History of alcohol use			
Yes	53 (61.6)	48 (55.8)	0.53
No	33 (38.4)	38 (44.2)	
HIV serostatus			
Positive	48 (55.8)	22 (25.6)	0.00
Negative	38 (44.2)	64 (74.4)	
History of HTN			
Yes	58 (67.4)	18 (20.9)	0.00
No	28 (32.6)	68 (79.1)	
History of DM			
Yes	22 (25.6)	5 (5.8)	0.00
No	64 (74.4)	81 (94.2)	

*$P<0.05$. HTN=Hypertension; DM=Diabetes mellitus

Table 3: Logistic regression analysis of factors associated with chronic kidney disease

Characteristics	Number of cases (*n*=86)	Number of controls (*n*=86)	OR (95% CI)	
			Step 1	Step 6
Gender				
Male	50	50	1.00	
Female	36	36	0.67 (0.28-1.58)	
Age in years				
19-35	22	22	1.00	
36-50	24	25	0.67 (0.22-1.97)	
51-65	21	22	0.56 (0.14-2.15)	
66+	19	17	0.81 (0.19-3.39)	
Residence				
Urban	45	35	1.00	
Rural	41	51	0.64 (0.26-1.55)	
History of smoking				
Yes	21	32	0.62 (0.23-1.68)	
No	65	54	1.00	
History of alcohol use				
Yes	53	48	1.55 (0.64-3.75)	
No	33	38	1.00	
HIV serostatus				
Positive	48	22	8.65 (3.41-21.94)	8.68 (3.58-20.99)
Negative	38	64	1.00	1.00
History of HTN				
Yes	58	18	12.61 (4.62-34.40)	11.28 (4.56-27.89)
No	28	68	1.00	1.00
History of DM				
Yes	22	5	3.42 (0.91-12.79)	2.95 (0.86-10.14)
No	64	81	1.00	1.00

HTN=Hypertension; CI=Confidence interval; OR=Odds ratio; DM=Diabetes mellitus

causes) revealed that overall there were 58/86 (67.4%) CKD cases related with HTN/DM, among them 24/58 (41.4%) were also HIV positive [Table 5]. Results can further be summarized as that there was more proportion of urban, younger age category and HIV positive cases in the CKD due to other causes group (nontraditional causes) than the CKD secondary to HTN or DM [Table 5].

The analysis comparing the CKD stages with the degree of immunosuppression in HIV-positive cases demonstrated that higher CD4 count was significantly associated with better estimated GFR ($P < 0.001$). Analysis to compare CKD patients who are HIV positive based on being on antiretroviral medications (ARVs) versus not being on ARVs yielded no significant difference ($P = 1.00$).

Table 4: Trend analysis of the significant factors associated with chronic kidney disease

Characteristics	*n*=86		Crude OR (95% CI)	Chi-square for linear trend (*P*)
	Cases	Controls		
Duration since HIV diagnosis				
Negative	38	64	1.00	3.47 (0.06)
3 years and less	30	6	8.42 (3.21-22.08)	
More than 3 years	18	16	1.89 (0.86-4.15)	
Duration of HTN				
Normotensive	28	68	1.00	31.34 (0.00)
0-5 years	24	7	8.32 (3.22-21.53)	
More than 5 years	34	11	7.50 (3.34-16.87)	

HTN=Hypertension; CI=Confidence interval; OR=Odds ratio

Table 5: Distribution of chronic kidney disease due to hypertension or diabetes mellitus versus chronic kidney disease due to others causes

Variables	CKD due to HTN or DM (%)	CKD other causes (%)	*P*
Residence			
Urban	25 (43.1)	20 (71.4)	0.025[a]
Rural	33 (56.9)	8 (28.6)	
Age in years			
19-35	11 (19.0)	11 (39.3)	0.001[a]
36-50	12 (20.7)	12 (42.9)	
51+	35 (60.3)	5 (17.9)	
HIV serostatus			
Positive	24 (41.4)	24 (85.7)	<0.001[b]
Negative	34 (58.6)	4 (14.3)	

[a]Chi-square test; [b]Fisher's exact test. CKD=Chronic kidney disease; DM=Diabetes mellitus; HTN=Hypertension

Analysis of HIV-positive patients based on the duration of ARVs revealed that patients on ARV treatment over 3 years duration were significantly less likely to have CKD compared to counterparts on ARV treatment <3 years ($P = 0.007$).

Discussion

CKD was found in 16.3% of all patients in medical ward admitted for different reasons. This is a higher rate compared to studies from the Democratic Republic of Congo and China.[7,8] This may partly be due to our center being a referral hospital where patients with complications requiring RRT are also admitted. It is noteworthy that over 50% of admitted patients with CKD were not aware of their CKD status. This implies that a significant burden of CKD in the community remains undiagnosed and explains why patients present at the end-stage with increased chance of undesired outcomes. The higher percentage can also partly be explained by the fact that Princess Marina Hospital is one of the two public hospitals in the country offering RRT services, hence receiving more referrals from primary and district hospitals.

The study revealed that an HIV positive result is associated with CKD as found in a previous study.[11] HTN was also found to be associated with CKD as found in the previous studies.[7,9,10]

DM is a significant condition associated with CKD in other studies. In our studies, its significance as a risk factor for CKD was seen in bivariate analysis but lost on multivariate logistic regression analysis. This may partly be explained by the small number of DM patients recruited in our study. The possibility of missing undiagnosed cases of DM patients was reduced as both cases and matches were screened with fasting blood glucose.

Analysis of CKD patients on ARVs versus those not on ARVs showed a similar CKD rate without any statistically significant difference. This might rule out at least in this study that CKD was not attributed to complications of ARVs. Indeed, CKD could be attributed to the direct effect of HIV on the renal system as CKD was associated with lower CD4 count and more recent diagnosis. CKD could also be related to standard risk factors as in HIV-negative populations. When analyzing the HIV-positive CKD patients on ARVs, the proportion with CKD was significantly higher on the antiretroviral treatment of <3 years duration compared to those more than 3 years duration. It is likely that ARVs treated HIV-associated CKD and patients got better in later years.

Furthermore, when we analyzed the severity of CKD in a subset of HIV-positive patients, we found a significant

correlation between severe immunosuppression (low CD4) and severe CKD (lower GFR). These results compare to findings obtained elsewhere.[12,13]

Our study showed the prevalence of 1.6% for AKI; this is lower compared to the previous studies. The possible explanations include; first, difficult to rule out AKI in patients without baseline creatinine values. Second, we might have missed some hemodynamically unstable patients with AKI who were admitted directly from the emergency department to the Intensive Care Unit for RRT. Third, some of the patients with CKD might have presented acutely; this was difficult to ascertain as the most patients did not have a trend of serum creatinine values.

Several studies across the world have shown that recurrent heat exposure with physical exertion and inadequate hydration, especially in rural areas can lead to CKD that is distinct from that caused by traditional causes (DM, HTN, or glomerulonephritis).[16-18] Our findings appear opposite to those found globally as younger patients with nontraditional causes of CKD were found more in urban than rural areas. This could possibly be explained by the fact that both rural and urban Botswana are equally exposed to extreme temperatures during summer, making its effect becoming difficult to assess in this study. A large community survey may have to be conducted comparing urban and rural Botswana to elicit the effect of heat stress.

CKD was found to be a major burden on the hospital medical admission with late patient presentation and contributed to higher mortality. HIV/HTN/DM comorbidity is widely seen, and it suggests the need to have collaborative approaches in the HIV and chronic disease (HTN/DM/CKD) clinics.

Conclusion

Health-care workers in HTN, diabetic, and HIV care facilities need to pay more attention with regards to patient counseling on CKD and regular assessment for renal function. There is an urgent need to establish follow-up programs in high-risk populations (hypertensives, diabetics, and patients with HIV) with an aim to identify patients at early stages of CKD, and put in place prevention mechanisms so as to help to reduce the burden in terms of cost, morbidity, and mortality.

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Conflicts of interest

There are no conflicts of interest.

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