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Chronic kidney disease in patients admitted to the medical ward of Mbarara Regional Referral Hospital in southwestern Uganda: Prevalence and associated factors

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ABSTRACT

Background: In tropical Africa, although chronic kidney disease (CKD) is common, there are few data about its' prevalence among patients admitted to a general medical ward. **Aim:** We proposed to determine the prevalence of CKD among patients admitted to a general medical ward in Uganda. **Methods**: We conducted a cross sectional study consecutively enrolling adults admitted to the medical ward of Mbarara Regional Referral Hospital over three months. We collected socio-demographic and clinical data including presenting symptoms, history of diabetes, hypertension, and use of nephrotoxic medication. Consenting patients provided spot morning urine specimen for measurement of urine albumin and we also drew patients' blood for measurement of markers of renal function, complete blood count, hepatitis B surface antigen, and HIV. We also performed renal sonography for all included patients. We defined CKD as a glomerular filtration rate (eGFR) less than 60ml/min/1.73m². We used logistic regression to assess for factors associated with CKD. **Results:** Of the 372 patients enrolled, 57 (15.3%) had CKD. Body swelling (OR=2.79, 95% CI 1.53-5.07; p=0.001), active urine sediment (OR=3.13, 95% CI 1.64-6.41; p=0.016), microalbuminuria (OR=1.92, 95% CI 1.07-3.43; p=0.028), history of hypertension (OR=3.65, 95% CI 1.69-7.90; p=0.001), and high blood pressure (OR=3.34, 95% CI 1.33-8.40; p=0.010) were independently associated with CKD. **Conclusion:** Chronic kidney disease is common with hypertension as the etiology and associated with body swelling, active urine sediment and microalbuminuria among patients admitted to a general medical ward in southwestern Uganda. Screening for CKD of patients at risk should be prioritized in general medical wards.

Key words: Chronic kidney disease, epidemiology, nephrotoxicity, poor resource setting, Uganda

INTRODUCTION

The prevalence of impaired kidney function was estimated to range between 10% and 20% of the adult population in most countries worldwide.[1] Data from United States suggest that for every patient with end stage renal disease (ESRD), there are more than 200 with overt CKD (stage 3 or 4) and almost 5000 with covert disease (stage 1 or 2).[2] Analysis from the third national health and nutrition examination survey (NHANESIII) done on a representative sample of the United States (US) population showed that the prevalence rate of CKD was high.[2] Estimates from 1999 to 2004 were higher (13.1%) than those in 1988 to 1994 (10.0%).[2]

Studies from China suggest that between 12.1%[3] and 13%[4] of the population have evidence of CKD and kidney damage markers. The profound impact of CKD on chronic diseases and cardiovascular morbidity makes it especially important in the context of global disease, specifically in developing countries that have a mounting incidence of CKD-associated risk factors.[1,5]

In Africa, studies on CKD are scarce. Since little is known about CKD among people living with HIV/AIDS in Sub-Saharan Africa, the prevalence was assessed in Burundi using the modified diet in renal disease (MDRD) formula and was found to be 45.7%.[6] According to the National Kidney Foundation (NKF), 30.2% was classified as stage 1, 13.5% as stage 2 and 2% as stage 3 and none classified as stage 4 or 5.[6] In a cross-sectional study done in Democratic Republic of Congo (DRC) among residents in 10 of the 35 health zones of Kinshasa, the prevalence of CKD according to kidney disease outcome quality initiative (K/DOQI) guidelines (2002) was 12.4% (95% CI, 11.0-15.1%) while 2% had stage 1, 2.4% had stage 2, 7.8% had stage 3 and 0.2% had stage 5.[7] In Uganda, the prevalence of CKD among patients attending the hypertension clinic of Mulago national referral hospital was found to be 17.2%.[8]

In Mbarara, a prior study estimated the prevalence of renal disease among patients attending the HIV clinic of Mbarara University Teaching Hospital and found the prevalence of CKD to be around 12% among these patients.[9] Therefore, this study aimed to determine the prevalence of CKD among patients admitted to the medical ward of Mbarara Regional Referral Hospital (MRRH) and some of the associated factors.

METHODOLOGY

This was a cross sectional study conducted between over February and May 2013, on patients admitted to the medical ward of Mbarara Regional Referral Hospital (MRRH), Southwestern Uganda. At MRRH, patients with medical conditions are initially resuscitated in the emergency room where patients could stay overnight after admission before admission to the ward. Initial diagnoses are made by medical residents and then reviewed by faculty physicians. The facilities available at MRRH have been previously described.[10]

Using the Kish and Leslie formula,[11] we enrolled 457 patients during our study which took place from 7th February 2013 up to 16th May 2013.We consecutively included consenting adult patients aged 18 years or more and excluded those with features of acute kidney injury such as vomiting, diarrhea, and/or low blood pressure.

Per day, we enrolled a maximum of ten patients to allow ourselves time to perform kidney scans and to draw blood samples. The enrollment of patients and the scanning of the kidneys took place on afternoons of Sundays, Tuesdays and Thursdays of every week during the study period.

Data collection

We gave patients urine containers to collect about 15ml of early morning urine for measurement of albuminuria and urine microscopy for sediment. Also, we drew approximately 8ml of blood for measurement of renal function test (serum creatinine& potassium), random blood sugar using handheld device (one touch), complete blood count, hepatitis B surface antigen, albumin and electrolytes (serum sodium & chloride) using machine HUMALYTE (Human GesellschaftfürBiochemica und Diagnostica, Gemany). All laboratory tests were performed on Mondays, Wednesdays and Fridays at the Mbarara University Clinical Research Laboratory, which participates in external quality assurance programs by the National Health Laboratory Service (Johannesburg, South Africa).

An identification number was given to all patients who fulfilled the inclusion criteria. A standardized pre-tested questionnaire was then administered to them. We collected socio-demographic information: age and gender. Risk assessment data included family history of kidney disease, history of recent nephrotoxic medication use (and the duration) such as non steroidal anti-inflammatory drugs (NSAIDs); history of diabetes, hypertension and HIV status. Data on the symptoms of kidney disease was obtained: history of dysuria, haematuria, and body swelling with its duration.

Non-invasive measurements

Weight and height are measured using the weighing scale machine Seca. Height was measured to the nearest 0.1 cm after removal of shoes. Weight was measured to the nearest kilogram after removal of shoes and heavy clothing. The BMI was calculated as weight in kilograms divided by the square of height in metres. Blood pressures were measured using a mercury sphygmomanometer with small (<21 cm) and normal (22–32 cm) cuff sizes on the left arm at the level of the heart while the patient was seated. When the blood pressure was found to be above 140/90mmHg, we repeated the measurement on three consecutive days during hospitalization to confirm hypertension.

Kidney size measurements were performed using a standardized protocol by a single operator who completed a sonography training course at the department of Radiology, Makerere University college of health sciences. At the conclusion of the training, the operator performed paired measurements on volunteer participants daily to assure adequate image quality and calculate intra-observer reliability. All ultrasound measurements were performed with a Sonosite M-Turbo (Sonosite, Inc., Bothell, WA). We collected measurements of kidney sizes and echogenicity for all patients with supervision by a senior sonographer of the department of radiology at MRRH.

Screening process

The screening process consisted of estimating the GFR from serum creatinine using the MDRD formula and microalbuminuria from Urine Albumin Creatinine Ratio (UACR) formula. A urine dipstick was done to look for protein and blood; and, microscopy for cellular casts and red blood cells. Patients who were unable to give morning spot urine and those on whom we were unable to draw off blood were excluded.

Urine albumin creatinine ratio

We measured urine albumin using the chemical analyzer machine (Human Gesellschaft fur Biochemica und Diagnostica, Germany) by the Bromocresol-Green method (BCG-method) which is a standard photometric colorimetric test for urine albumin. We determined urine creatinine concentration using the Jaffé rate reaction method which is a standard photometric colorimetric test for kinetic measurement of creatinine. Spot urine ACR ratio was calculated for all subjects by dividing the

urine albumin (mg/dL) by urine creatinine (g/dL).

Ethical considerations

Study procedures were reviewed and approved by the institutional review committee of Mbarara University of Science and Technology(MUST-IRC). All participants gave written informed consent. Patients found to have CKD stage 4 or 5 were referred to an in house renal physician for management. Those with CKD stage 1, 2 or 3, patients were prescribed angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) and discharge through the renal clinic.

Statistical analysis

Data were summarized into tables using percentages, mean (standard deviation [SD], median and interquartile range [IQR]). Data were also represented graphically using flow-chart and histogram. We used unadjusted and multivariate logistic regression models to determine association between the some known risk factors and CKD. Results were considered statistically significant if a p value of less than 0.05 was obtained. All statistical analyses were conducted with Stata Version 12 (Statacorp, College Station, Texas).

RESULTS

During the study period, 457 patients were screened. We excluded 59 patients (11 diarrhea and vomiting, 17 only diarrhea, 7 only vomiting, 24 declined consent). We analyzed data of 372 patients after excluding 26 patients who did not complete (2 death, 14 no urine, 3 blood sample hemolyzed, and 7 withdrew consent) (figure 1).

When classified according to the National Kidney Foundation (NKF) definition of CKD, 213 had renal impairment which represents a prevalence of 57.3%. 71 (19.1%) were found to have CKD stage 1; 85 (22.8%) had CKD stage 2; 29 patients (7.8%) had CKD stage 3 of whom 19 (5.1%) were in stage 3A and 10 (2.7%) in stage 3B. 11 patients (3.0%) were in stage 4 and 17 (4.6%) were in stage 5 or end stage renal disease (ESRD) (table 2).

Prevalence of chronic kidney disease

Of the remaining 372 patients, 57 (15.3%, 95% CI 11.6%-19.0%) had eGFR of less than 60ml/min/1.73m². When eGFR was tabulated against urine albumin creatinine ratio (UACR), 18 (4.8%) had CKD with microalbuminuria whereas 138 (37.1%) patients had normoalbuminuria and no CKD (table 2).

Factors associated with chronic kidney disease

In the univariate logistic analysis (table 3), body swelling, history of hypertension, current high blood pressure, diabetes mellitus, microalbuminuria and active urine sediment were factors associated with CKD in patients admitted to our general medical ward during our study. However, in the multivariate model, body swelling, hypertension either history or current high blood pressure, active urine sediment and microalbuminuria remained independently associated with CKD.

DISCUSSION

Our study finding of a high prevalence of CKD among patients admitted to a general medical ward in a resource poor setting is similar to that documented in previous study[9] where CKD is a major public health problem. This prevalence is estimated using only eGFR<60ml/min/1.73m². If we exclude all patients without microalbuminuria having eGFR>60ml/min.1.73m², the prevalence goes up to 57.3%. This figure is higher than the one found by Johann among people living with HIV/AIDS in Burundi (45.7%).[7] This might be explained by the fact that our patients were not in good general condition. That is why we used only eGFR<60ml/min/1.73m² to estimate the prevalence as with this eGFR, 50% of

the function of the kidney is already affected.[12] Our finding is at the upper limit of the one seen in industrialized countries which in our setting implies a multifactorial effect resulting from an increase number of patients with hypertension, diabetes mellitus and HIV/AIDS. In fact, this study was done in only three months and we diagnosed 30 new patients with hypertension and 54 with hyperglycemia.

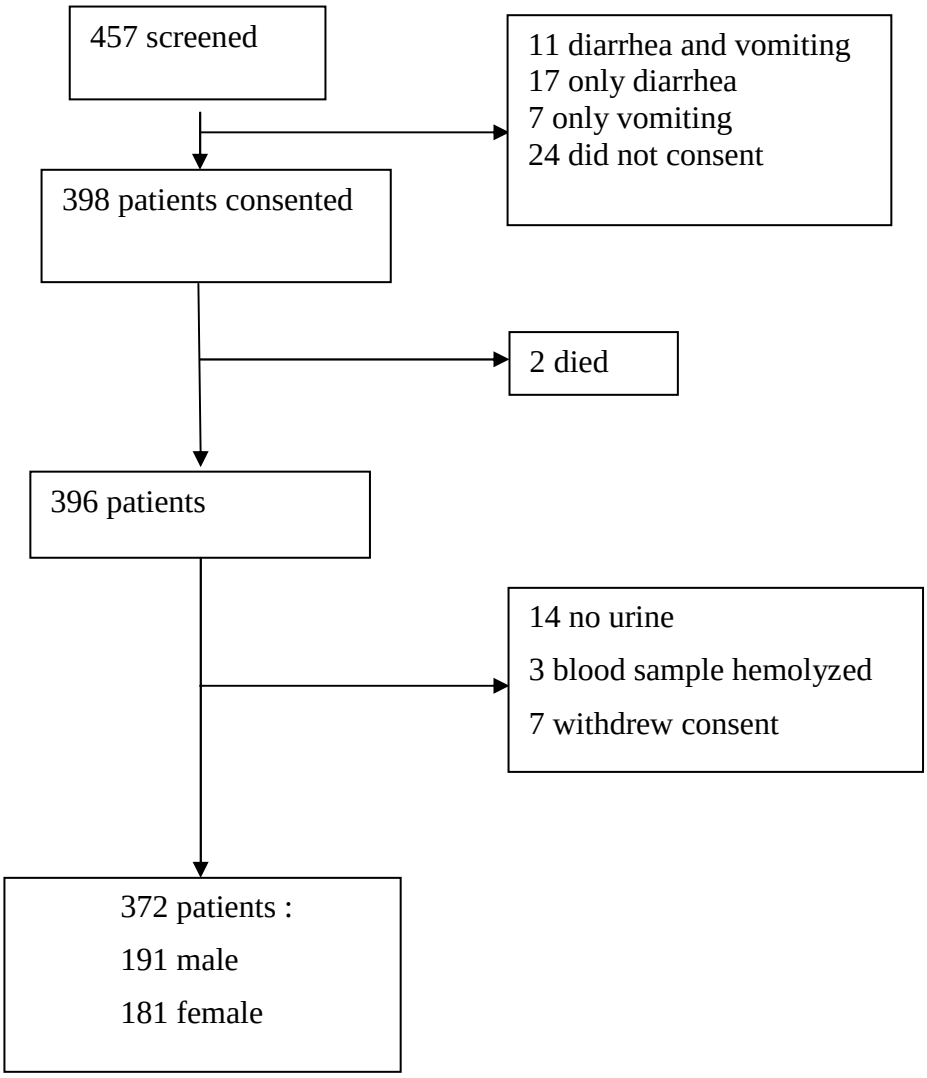

Figure 1: Flowchart of patients' recruitment

Table 1: Baseline characteristics of study participants

Baseline characteristics	**N=372**
a. Socio-demographic	
Age (years); median (IQR)	39 (28-52.5)
Gender; Male n (%)	191 (51.3%)
b. Clinical	
Dysuria; n (%)	140 (37.6%)
Haematuria; n (%)	24 (6.5%)
Body swelling; n (%)	157 (42.2%)
Duration of body swelling(months); median (IQR)	3 (1-12)
Family history of renal disease; n (%)	31 (8.3%)
Known hypertensive; n (%)	35 (9.4%)
Known diabetic; n (%)	21 (5.7%)
Smoking; n (%)	127 (34.1%)
NSAIDs use; n (%)	90 (24.2%)
HIV positive; n (%)	126 (33.9%)
BMI≥30kg/m²; median (IQR)	32.3 (30.7-33.6)
SBP/DBP (mmHg); median (IQR)	110(100-120)/70(60-80)
Diagnosed hypertensive; n (%)	30 (8.1%)
c. Laboratory	
eGFR (ml/min/1.73m²); median (IQR)	89 (72-106)
Fasting blood sugar (mmol/l); median (IQR)	6.1 (5.2-6.8)
Diagnosed diabetic; n (%)	54 (14.5%)
UACR 30-299mg/g; median (IQR)	48.6 (35.6-75.9)
UACR ≥ 300mg/g; mean±SD	506±191.7
Active urine sediment; n (%)	60 (16.1%)
Electrolytes abnormalities; n (%)	207 (55.6%)
HBsAg positivity; n (%)	11 (3.0%)
Hemoglobin (<11mg/dL); n (%)	190 (51.4%)

IQR= interquartile range; HBsAg: hepatitis B surface antigen; UACR: urine albumin to creatinine ratio; eGFR: estimated glomerular filtration rate

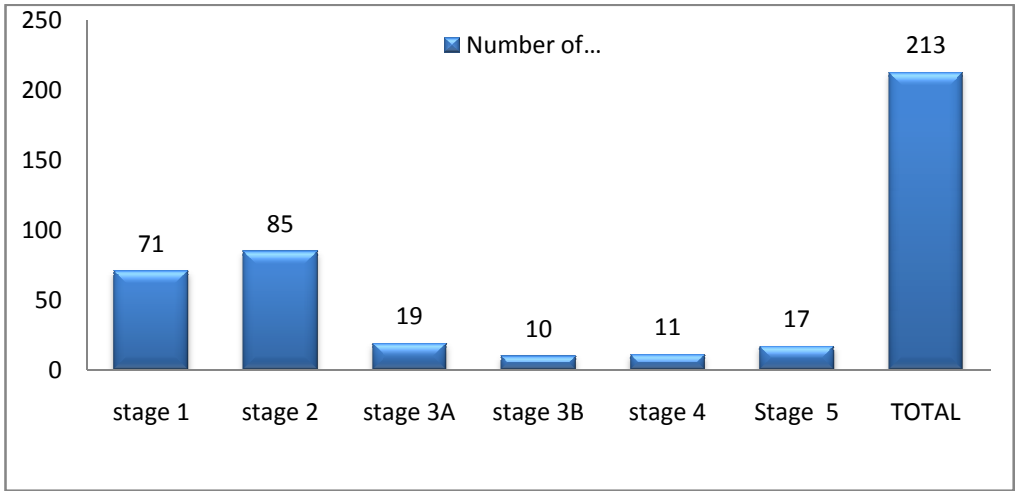

Figure 2: Stratification of patients with CKD according to the National Kidney Foundation

Table 2: Distribution of patients according to estimated glomerular filtration rate (eGFR) and Urine albumin-creatinine ratio (UACR)

UACR(mg/g) **GFR(ml/min/1.73m²)**	**< 30**	**>30**	**TOTAL**
< 60	39	18	57
>60	138	177	315
TOTAL	177	195	372

Table 3: Factors associated with CKD among patients admitted on medical ward of MbararaRegional Referral Hospital

Variables	**CKD**	**No CKD**	**OR**	**95% CI**	***P*-value**
Age >65years	10	31	1.87	0.84-4.16	0.1201
Female	32	149	1.43	0.81-2.52	0.2199
Body swelling	**37**	**120**	**3.01**	**1.65-5.49**	**0.0002**
FHRD	8	23	2.07	0.87-4.92	0.0910
Known HTN	**13**	**22**	**3.93**	**1.82-8.51**	**0.0002**
Known DM	2	19	0.57	0.13-2.51	0.4482
NSAIDs use	11	79	0.71	0.35-1.45	0.3490
HIV positive	15	111	0.59	0.31-1.14	0.1128
BMI≥30kg/m²	33.16±1.55	32.57±0.57	1.38	0.35-5.54	0.6451
Systolic BP(≥140mmHg)	**160.00±5.00**	**149.40±2.55**	**4.53**	**2.19-9.38**	**0.0000**
Diastolic BP(≥90mmHg)	**106.11±3.01**	**95±1.25**	**2.92**	**1.52-5.62**	**0.0008**
High FBG (≥7.0mmol/l)	**10.47±1.41**	**10.76±0.84**	**2.09**	**1.11-3.94**	**0.0197**
Elevated BP	**13**	**17**	**5.18**	**2.30-11.66**	**0.0000**
UACR 30-299 mg/g	**69.04±5.75**	**63.05±3.58**	**2.19**	**1.19-4.04**	**0.0095**
Active urine sediment	**51**	**63**	**6.09**	**2.81-13.40**	**0.0011**
Electrolytes abnormalities	49	158	1.90	1.60-6.43	0.0866
HBsAg positivity	3	8	2.13	0.55-8.32	0.2647

FHRD: family history of renal disease; FBS: fasting blood glucose; HBsAg: hepatitis B surface antigen, BMI: body mass index; OR: odds ratio; HBP: High blood pressure.

Table 4: Independent factors of CKD among patients admitted on medical ward of Mbarara Regional Referral Hospital

Variable	**AjustedOdds Rat (AOR)**	**95% CI**	**P value**
Body swelling	2.79	1.53-5.07	0.001
Known hypertension	3.65	1.69-7.90	0.001
Elevated blood pressure	3.34	1.33-8.40	0.010
Active urine sediment	3.13	1.64-6.41	0.016
Systolic BP (≥140mmHg)	3.28	1.36-7.92	0.008
UACR 30-299mg/g	1.92	1.07-3.43	0.028

HTN: hypertension; UACR: urine albumin to creatinine ratio.

Patients in stages 1; 2 and 3A (33.3%) need a proper follow up through renal clinic and be given drugs such ACEi or ARB to slow the progression to end stage renal disease (ESRD). The reason why patients present in ESRD is mainly because of lack of information and also the absence of screening of patients with known risk factors for CKD. The figures of our study are higher than the ones found in HIV/AIDS patients in Burundi where 30.2% of the 45.7% were in stage 1 of CKD and no patient was in stage either 4 or 5.[12] In Kinshasa, DRC, 12.2% were in stages 1 to 3 and only 0.2% of people enrolled was in stage 5.[7]

High blood pressure has been recognized in many studies as a risk factor for CKD.[3, 7, 13, 14] In our study, patients known to have hypertension and those who were newly diagnosed to be hypertensive were all showing a correlation with CKD. For those known hypertensive patients, the odds ratio was 3.93 and for the newly diagnosed hypertensive patients, the odds ratio was 5.18. This implies that hypertensive patients of our study are 4 to 5 times at risk of developing CKD. The odds of developing CKD are slightly lower in the group of patients known to have hypertension and are already on medications compared to those who are newly diagnosed with hypertension. Also, as hypertension is asymptomatic, many patients live with it undiagnosed and may present with complications such as renal involvement.

Worldwide, diabetes mellitus is recognized as one of the leading causes of CKD. Studies done in USA,[2] China,[14] Nigeria[13] and DRC[7] found a correlation between diabetes mellitus and CKD respectively. Our patients with diabetes mellitus were 2 times likely to develop CKD than the non-diabetic patients. This is explained by the fact that these patients were diagnosed while having already complications, one of them being diabetic nephropathy.

For patients who were known diabetic, we did not find any correlation between diabetes and CKD. It is possible that patients who are known to have diabetes had already been on medication and thus less likely to have CKD when compared to the newly diagnosed diabetics. Glycosylated haemoglobin (HbA1c) would have been ideal.

Chronic use of NSAIDs had been associated with CKD as demonstrated by Johann in Burundi.[6] In our study, this correlation was not found partly because our patients denied the use of NSAIDs. For those who were using these drugs, they took them for less than a week. The odds ratio was 0.71.

Human Immuno-deficiency Virus can lead to end stage renal disease (ESRD) through HIV associated nephropathy (HIVAN) especially in patients with low CD4 and not yet started on ARVs. This information was not recorded in our study as patients did not have their document with them to help us record the CD4 count and know which regimen they were on. We did not perform any biopsy. However in South Africa, HIVAN was found in 86% of microalbuminuric patients who underwent renal biopsy.[15]

CKD was associated with microalbuminuria. This is a known indicator for CKD. Hence, any patient with microalbuminuria should be screened for CKD and should have their UACR repeated after three months. A sub analysis done within patients with UACR ≥ 30mg/g revealed an association with high fasting blood sugar, hypertension, systolic and diastolic hypertension. After adjusting these factors, only high fasting blood sugar and systolic hypertension were independently associated with CKD. A recent study using data of an observational cohort showed that isolated microalbuminuria (that is, microalbuminuria in the absence of a cardiovascular disease (CVD) history, hypertension and diabetes) is associated with an increased risk for

incident cardiovascular events and mortality, incident hypertension and/or diabetes mellitus.[16]

CONCLUSION

The prevalence of CKD among adult patients admitted to a general medical ward of Mbarara Regional Referral Hospital was high (15.3%) and the majority of patients with CKD were in stages 1 and 2 using the NKF classification. Body swelling, history of hypertension, current high blood pressure, active urine sediment and microalbuminuria were independent factors related to the presence of CKD. These data are among the first to demonstrate a high prevalence of CKD among adult patients admitted to a general medical ward of a resource poor setting. This signals an important need to further explore the early screening for CKD in general medical wards.

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