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Prevalence, associated factors and clinical outcomes of acute kidney injury among elderly patients admitted at Princess Marina Hospital, Gaborone, Botswana.

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Abstract

Background: Acute Kidney Injury (AKI) is a major problem worldwide as it is associated with high morbidity and mortality. The picture is likely to be worse in the geriatric population of developing countries due to associated comorbid conditions. This study describes the prevalence, associated factors and clinical outcomes of Acute Kidney Injury among elderly patients admitted at Princess Marina Hospital (PMH), Gaborone, Botswana.

Methods: A retrospective cross-sectional study involved elderly patients admitted to the medical wards of Princess Marina Hospital in Gaborone, Botswana from 1st March 2017 to 28th February 2018. The medical charts of participants admitted in the study period were screened to identify and include all the participants meeting the inclusion criteria. Frequencies were used to describe demographic, clinical characteristics and outcomes of study participants. Bivariate and multivariate logistic regression analysis was used to evaluate the factors associated with AKI. A p-value of < 0.05 was considered statistically significant.

Results: Almost a third, 261/871 (29.96%) of admitted elderly patients had AKI. Final analysis involved 613 retrieved records (242 records of AKI and 371 records without AKI). The mean age of participants was 66.98 (11.86) years. The male gender comprised 58.1% of the participants. The factors independently associated with AKI were hypertension, heart and liver failure, sepsis, use of nephrotoxic drugs, polypharmacy and hypotension. About a fifth of patients, 50/242 (20.7%) with AKI, either recovered to normal or baseline serum creatinine before discharge. Over a third of participants did not recover to normal/ baseline serum creatinine at discharge; they comprised 96/242 (39.7%). Similarly, over a third of elderly patients with AKI, 96/242 (39.7%) died. Serum potassium was significantly associated with AKI non-recovery to normal or baseline serum creatinine. Age over 80 years, chronic lung disease, heart failure and higher creatinine level at AKI diagnosis were independently associated with high all-cause mortality.

Conclusions: The prevalence of AKI among elderly patients admitted to medical wards of a referral hospital in Botswana is high and AKI is associated with a high all-cause mortality. The commonest risk factors independently associated with AKI among elderly participants were hypertension, heart failure, liver failure, sepsis, polypharmacy, use of nephrotoxic drugs and hypotension. Serum potassium was significantly associated with AKI non-recovery. The old age of more than 80 years old, chronic lung disease and worse serum creatinine at AKI diagnosis were associated with mortality whereas having heart failure conferred a better chance of survival. There is a need to conduct a prospective multicenter observational study in Botswana to obtain findings that will help generalizability while at the same time establishing long-term outcomes of patients discharged with impaired renal functions

Key-words: Acute kidney injury, Prevalence, Sepsis, Nephrotoxic drugs, Elderly, Mortality, Serum Potassium, Botswana

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Introduction:

Acute kidney injury (AKI) is a common disorder worldwide occurring in more than 13 million people every year, 85% of whom live in developing countries (Lameire et al., 2013). Acute kidney injury (AKI) is a challenging problem in Africa because of the burden of diseases including Human Immunodeficiency Virus [HIV], diarrheal disease, malaria, and nephrotoxic drugs (Naicker et al., 2008). Late presentation of patients to healthcare facilities, and lack of resources to support patients with established AKI in many countries also play a part in associated poor outcomes (Naicker et al., 2008; Jaryal et al., 2021).

Older people have many risk factors for developing acute kidney injury as compared to other age groups (Abdel-Kader & Palevsky., 2009). The ageing kidney is one of the factors that increase the risk of developing acute kidney injury. The kidney undergoes a number of important age-dependent changes. Renal mass decreases with ageing reaching appropriately 75-80% of young adulthood weight by the age of 80 to 90 years (Abdel-Kader & Palevsky., 2009). At age 70 years the kidneys have lost between 30-50% of their cortical glomeruli due to ischaemic changes and a significant number of the remaining glomeruli manifest some degree of sclerosis (Abdel-Kader & Palevsky., 2009).

The elderly population are also prone to comorbidities such as hypertension, diabetes and arthritis. These comorbidities are risk factors for acute kidney injury both as complications and due to the medications used (Lautrette et al., 2012). Because of the ageing kidney and the predisposition to various comorbidities, the elderly population are more likely to develop AKI as compared to their younger counterparts (Del Giudice et al., 2012).

Acute kidney injury is associated with an extremely high mortality rate ranging from 37% to 60% (Garzotto et al., 2014), with higher rates being reported in critical care settings as compared to non-critical care settings (US Renal Data System., 2009). In a study by Li Q et al on outcomes of renal function in elderly patients with acute kidney injury, the 90-day mortality rate was 33.6% and out of those that survived (433/652), 73.0% recovered to their baseline estimated glomerular filtration rate (Li et al., 2017). Another study showed that the mortality rate of AKI was 6.2% in the young patient group, 10.3% in patients aged 65 to 80 and 19.6% in patients older than 80 years (Ge et al., 2016).

Several studies looking at the outcome of AKI have attributed the following factors to the increase in mortality;-age, gender, comorbidities, hyponatremia, hyperphosphatemia, acidosis, dialysis requirement, anaemia, duration of oliguria, septicemia and neuropsychiatric manifestations (Vachiat et al., 2013; Coca et al., 2012; Arogundade et al., 2007).

There is a dearth of documentation on the prevalence and associated factors for kidney diseases in Botswana. A published study on risk factors for chronic kidney disease (CKD) in the same setting revealed that HIV positivity, diabetes mellitus and hypertension were significant contributors to CKD (Rwegerera et al., 2017). The published study in Botswana differs from this study as it was cross-sectional on CKD while this study is retrospective in design on AKI. On the other hand, the previous study included participants above 18 years, whereas this index study was on participants aged 50 years and above. There are no studies documenting the prevalence of AKI among the elderly in Botswana. Given the fact that AKI incidence among the elderly is on the increase globally (Del Giudice et al., 2012); it is imperative to have supportive local data to guide the prevention and management of AKI among the elderly; hence, reducing associated morbidity and mortality. This study was conducted to determine the prevalence, associated factors and clinical outcomes of AKI among elderly patients in a tertiary hospital in Botswana.

Methodology

Study design and setting

A retrospective cross-sectional study was carried out involving medical records of elderly patients admitted to the medical wards of Princess Marina Hospital (the main referral hospital in Gaborone, Botswana) from 1st March 2017 to 28th February 2018.

Study population

Elderly patients aged 50 years or above formed the study population. Age 50 years is increasingly used as a lower threshold by African gerontologists (WHO., 2000), who argue that life expectancy at birth in Sub-Saharan Africa (SSA) is typically ten or more years lower than in developed regions and that biomarkers of ageing and the social construction of age are set at a younger age (Kinsella & Phillips., 2005; Ferreira & Kowal., 2006). Likewise, WHO estimated that in 2016, life expectancy in Botswana was 64 and 68 years for males and females respectively (WHO., 2016) The WHO MDS study used the lower cut-off of 50 years for all indicator categories (Ferreira & Kowal., 2006) and for the same reasons outlined; this study adopted age 50 years as lower cut-off age definition for the elderly. The inclusion criteria for this study were all medical records of patients aged 50 years and above who were admitted during the study period. Files of participants with incomplete records to ascertain whether they had AKI were excluded. Files of participants with a confirmed diagnosis of end stage renal disease (ESRD) were also excluded.

Sample size and sampling

We searched for the medical records of elderly participants who were admitted in medical wards from 1st March 2017 to 28th February 2018 and included every participant meeting the inclusion criteria. There was no sample size calculation. Given, the design of the study, we did not perform systematic random sampling.

Data collection

Data were retrieved from participants' charts, which were kept in the medical records of Princess Marina Hospital. Data extracted included socio-demographic characteristics such as age and gender and established risk factors for AKI, past medical history such as HIV status, Diabetes Mellitus and Hypertension. HIV positive status was documented if there was either evidence of laboratory investigation or participants were on antiretroviral therapy. Diabetes mellitus status was according to documentation and/or being on antidiabetic medications; this also applied to hypertension status. Possibility of associated factors such as sepsis and nephrotoxins were ascertained based on study definitions of the two conditions. Drug history information was also obtained from participant information sheets. In order to be more precise, modifiable and non-modifiable associated factors namely diabetes mellitus, hypertension, heart failure, liver failure, chronic lung disease, underlying renal insufficiency, confirmed malignancy, HIV infection, chronic gastrointestinal disease, sepsis, use of nephrotoxins, polypharmacy, nephrotoxic procedures, anaemia and hypotension as discussed by Mehta et al., 2015 were included. Acute kidney injury (AKI) was diagnosed whenever any of the following criteria was met; - (a) an increase of at least 0.3 mg/dl (26.5umol/l) of creatinine when the creatinine baseline was known (Sawhney et al., 2017). (b) a reduction of at least 25% of the eGFR, or increase of at least 50% of the baseline creatinine for people with known chronic kidney disease (Fouda et al., 2016 & Bellomo et al., 2004).

The estimated GFR (e GFR) was calculated using modification of diet in renal disease (MDRD) equation that is found online at https://www.mdcalc.com/mdrd-gfr-equation. Community acquired AKI was defined as acute kidney injury that is present on admission (Kaufman et al., 1991). Hospital acquired AKI was defined as a change of serum creatinine or eGFR that meets definition of AKI; provided changes occurred while a participant is admitted in the ward. AKI severity was categorized according to Kidney Disease Improving Global Outcomes (KIDGO., 2012) as follows; Stage 1: 1.5-1.9 times baseline OR ≥ 0.3mg/dl (≥26.5 umol/l) of creatinine increase; Stage 2: 2.0-2.9 times baseline of serum creatinine; Stage 3: 3.0 times baseline OR increase in serum creatinine≥4.0mg/dl (≥353.6 umol/l) OR initiation of renal replacement therapy. Sepsis was defined

according to an increase in the Sequential (Sepsis-related) Organ Failure Assessment (SOFA) score of 2 or more (Singer et al., 2016). To assess for this life-threatening organ dysfunction quick SOFA score [(systolic hypotension (≤ 100mmHg), tachypnea (≥ 22/min) or altered mentation) (Seymour et al., 2016) was used or actual documented sepsis was used as the risk factor for AKI.

Participants' vital signs of either discharge alive or death were documented. For the purpose of this study, participants' outcomes were grouped into any of the following categories; - (a) Complete recovery of the AKI to normal or to baseline without dialysis (b) Complete recovery of the AKI to normal or to baseline after dialysis. (c) Non-recovery of the AKI to normalcy or to baseline even after dialysis on discharge (d) All-cause mortality (death due to any cause in the elderly with AKI).

Statistical data analysis

The Statistical Package for Social Sciences (SPSS) version 20 computer software was used for data entry, cleaning and analysis. Frequencies were used to describe demographic, clinical characteristics and outcomes of study participants. The distribution of continuous variables was checked in order to determine the appropriate summary statistics. Odds ratios were used to test associations between participants with and without AKI. Bivariate and multivariate logistic regression analysis were used for evaluating the factors associated with AKI, recovery and mortality. Only significant variables in the bivariate logistic regression were computed in the multivariate regression model.

Ethical considerations

Ethical clearance to conduct this study was obtained from the University of Botswana Institutional Review Board (UBR/RES/IRB/GRAD/052), Ministry of Health Botswana (HPDME: 13/18/1) and Princess Marina Hospital (PMH 5/79 {457-2-2018}) Institutional Review Boards. A waiver of consent was granted due to the retrospective nature of the study. During data collection, participants' identifiers were removed from all data collected for this study.

Results

Overall, there were 2486 participants admitted to medical wards of PMH during the study period as per information from Integrated Patient Management System (IPMS). Out of those 2486, 1051 met the inclusion criteria for this study (≥ 50 years old). From the 1051 elderly participants admitted during the study period; 180 participants were excluded because of being either known to have ESRD or without results of serum creatinine in the IPMS, hence remaining with 871 patient charts. From IPMS search, 261 participants had AKI (261/871; 29.96%). Out of 261 participants with AKI, 242 charts were found at medical records whereas out of 610 participants without AKI, 371 charts were found at medical records. Hence, a total of 613 elderly participants' charts were used in subsequent comparison analysis **(Figure 1).**

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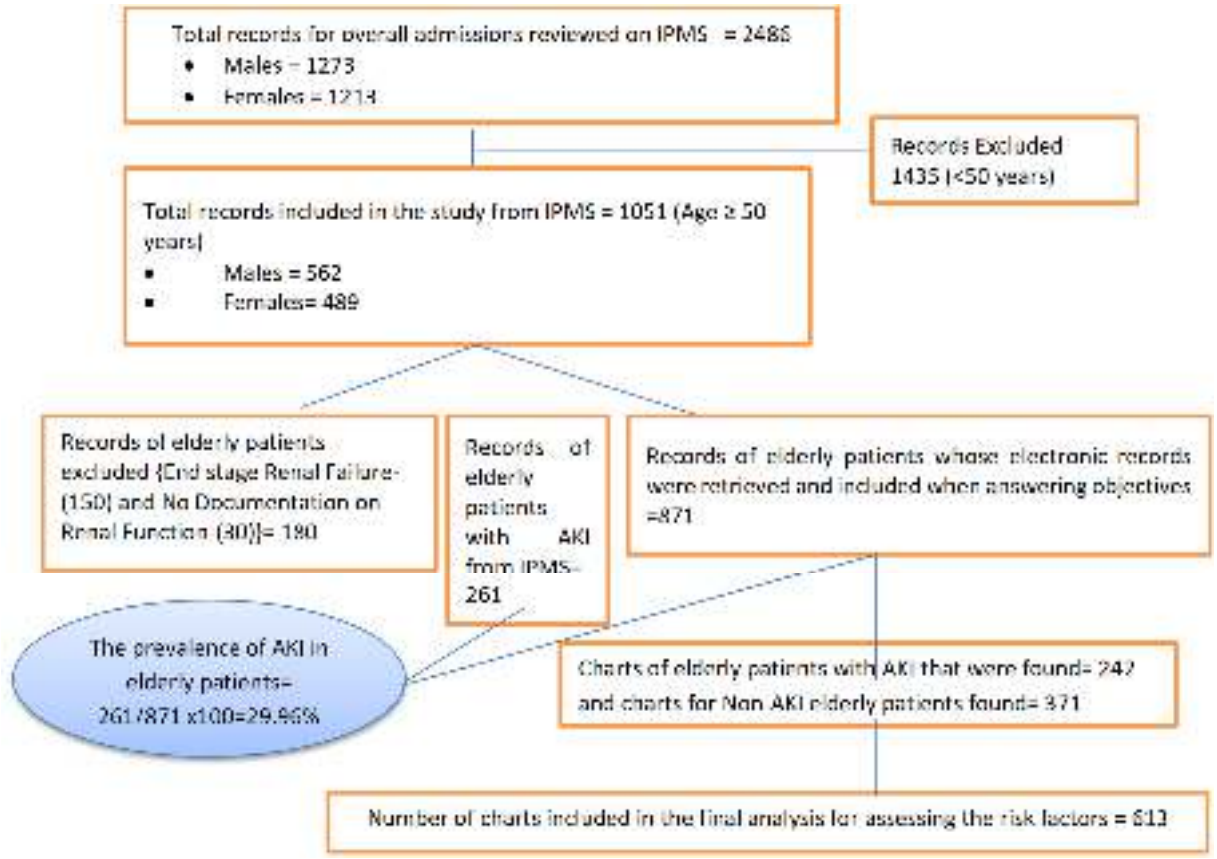

Figure 1: Flowchart of reviewed records of patients admitted in medical wards during the study period

Mean age (standard deviation) of elderly participant enrolled in the study was 66.98±11.86 with age range of 50-98 years. Males comprised 58.1% of study participants. Over a quarter (26.6%) of the elderly patients enrolled in the study were HIV positive. Community acquired AKI was the most common presentation (89.3%). On the other hand, half of the patients (50.8%) belonging to stage 1 AKI. Hypertension, diabetes mellitus, heart failure and chronic lung disease were the most common underlying comorbidities among study participants constituting 55.6%, 19.8%, 19.2% and 19.1% respectively. **(Table 1).**

Table 1: Socio-demographic and clinical characteristics of study participants enrolled in the study (N= 613)

Demographics and clinical profiles	Frequency (%)
Age in years (Mean± SD)	66.98± 11.86
50-64	279 (45.5)
65-79	229 (37.4)
≥80	105 (17.1)
Total	613 (100)
Gender	
Male	356 (58.1)
Female	257 (41.9)
Total	613 (100)
HIV status	
Positive	163 (26.6)
Negative	360 (58.7)
Unknown	90 (14.7)
Total	613 (100)
Type of AKI	
Community- acquired	216 (89.3)
Hospital-acquired	26 (10.7)
Total	242 (100)
AKI Stage	

Stage 1	123 (50.8)
Stage 2	42 (17.40
Stage 3	77 (31.8)
Total	242 (100)
Diabetes mellitus	
Yes	121 (19.8)
No	490 (80.2)
Total*	611 (100)
Hypertension	
Yes	341 (55.6)
No	270 (44.0)
Total*	611 (100)
Heart failure	
Yes	118 (19.2)
No	495 (80.8)
Total	613 (100)
Liver failure	
Yes	26 (4.2)
No	587 (95.8)
Total	613 (100)
Chronic lung disease	
Yes	117 (19.1)
No	496 (80.9)
Total	613 (100)
Confirmed Malignancy	
Yes	33 (5.4)
No	580 (94.6)
Total	613 (100)
Chronic Gastrointestinal Disease	
Yes	14 (2.30)
No	599 (97.7)
Total	613 (100)

*Missing information for some patients making total of participants less than 613

Among the modifiable risk factors for AKI; anaemia, polypharmacy, and nephrotoxic drugs, were seen in 60.2%, 55% and 54.5% of recruited participants respectively. On the other hand; sepsis, hypotension and diarrhea and/or vomiting, were present in 24.1%, 23.4% and 19.1% of patients respectively. **(Table 2).**

Table 2: Modifiable risk factors for AKI among enrolled participants (N=613)

Risk factor	Frequency, n (%)
Sepsis	
Yes	148 (24.1)
No	465 (75.9)
Total	613 (100)
Use of Nephrotoxic drugs	
Yes	334 (54.5)
No	278 (45.4)
Total	613 (100)
Polypharmacy (≥5 prescription drugs)	
Yes	337 (55.0)
No	276 (45.0)
Total	613 (100)
Nephrotoxic Procedure e.g. Contrasted CT or Angiography	

Yes	38 (6.2)
No	574 (93.8)
Total	613 (100)
Use of traditional medicines	
Yes	7 (1.1)
No	606 (98.9)
Total	613 (100)
Vomiting and/or Diarrhea	
Yes	117 (19.1)
No	496 (80.9)
Total	613 (100)
Anaemia (Hb < 12 for both men and women)	
Yes	363 (60.2)
No	240 (39.8)
Total	613 (100)
Hypotension	
Yes	143 (23.4)
No	469 (76.6)
Total	613 (100)
Others**	
Yes	163 (26.6)
No	450 (73.4)
Total	613 (100)

**Obstructive Uropathy, Previously treated with Tenofovir based regimen, Systemic lupus erythromatosus

Bivariate regression analysis revealed the following factors to be significantly associated with AKI; Age more than 80 years, diabetes mellitus, hypertension, heart failure, liver failure - sepsis, use of nephrotoxic drugs, history of vomiting and/or diarrhea and hypotension. **(Table 3).**

Table 3: Bivariate regression analysis of factors associated with AKI

Variable	AKI, n (%)	Non-AKI, n (%)	P-value	OR	95%CI
Age (Mean± SD, Range)	69 (12)	66 (12)			
50-64	99(35.5)	180(64.5)			
65-79	93(40.6)	136(59.4)	0.236	0.804	0.561-1.153
≥80	50(47.6)	55(52.4)	**0.030**	1.652	1.049-2.604
Gender					
Male	126(35.4)	230(64.6)	0.789	0.666	0.48-0.924
Female	116(45.9)	141(54.9)			
Diabetes mellitus					
Yes	59 (48.8)	62 (51.2)	**0.022**	1.596	1.069-2.383
No	183 (37.3)	307 (62.7)			
Hypertension					
Yes	153 (44.9)	188(55.1)	**0.003**	1.657	1.191-2.304
No	89 (33.0)	181 (67.0)			
Heart failure					
Yes	64 (54.2)	54 (45.8)	**<0.001**	2.111	1.406-3.168
No	178 (36.0)	317 (64.0)			
Liver failure					
Yes	20 (76.9)	6 (23.1)	**<0.001**	5.480	2.168-13.855
No	222 (37.8)	365 (62.2)			
Chronic lung disease	42 (35.9)	75 (64.1)	0.379	0.829	0.546-1.259
Yes	200 (40.3)	296 (59.7)			
No					

Confirmed malignancy Yes No	 12 (36.4) 230 (39.7)	 21 (63.6) 350 (60.3)	 0.707	 0.870	 0.336-3.542
Anaemia Yes No	 164 (45.2) 78 (32.5)	 199 (54.8) 162 (67.5)	 1.712	 0.002	 0.166-6.185
HIV status Negative Positive Unknown	 148(41.1) 74(45.4) 20(22.2)	 212(58.9) 89(54.6) 70(77.8)	 0.358 **0.001**	 0.84 2.443	 0.578-1.219 1.425-4.191
Chronic Gastrointestinal Disease Yes No	 5 (71.4) 237 (39.1)	 9 (64.3) 362 (60.4)	 0.771	 0.849	 0.166-6.185
Sepsis Yes No	 81 (54.7) 161 (34.6)	 67 (45.3) 304 (65.4)	 **<0.001**	 2.283	 1.237-3.680
Use of Nephrotoxins Yes No	 153 (45.8) 88 (31.7)	 181 (54.20 190 (68.3)	 **0.037**	 1.402	 1.020-1.926
Polypharmacy (≥5 drugs) Yes No	 88 (26.1) 154 (55.8)	 249 (73.9) 122 (44.2	 **<0.001**	 0.280	 0.468-0.725
Nephrotoxic Procedure e.g Contrasted CT or Angiography Yes No	 10(26.1) 232(55.8)	 28(73.9) 32(44.2)	 0.09	 0.526	 0.251-1.105
Use of traditional medicine Yes No	 5(71.4) 237(39.1)	 2(28.6) 369(60.9)	 0.106	 3.892	 0.749-20.226
Vomiting and/or Diarrhea Yes No	 78 (66.7) 164 (33.1)	 39 (33.3) 332 (66.9)	 **0.002**	 1.712	 1.383-4.535
Hypotension Yes No	75(52.4) 167(35.6)	68(47.6) 302(64.4)	<0.001	1.995	1.366-2.913
Others[**] Yes No	 34(20.9) 208(46.2)	 129(79.1) 242(53.8)	 <0.001	 0.307	 0.201-0.467

[**]Obstructive Uropathy, previously treated with Tenofovir based regimen, Systemic lupus erythromatosus

Multivariate logistic regression revealed the following factors to be independently associated with AKI in this study; - hypertension, heart failure, liver failure, sepsis, use of nephrotoxic drugs, polypharmacy, vomiting and/diarrhea and hypotension. (**Table 4).** It was observed that only 50/242 (20.7%) of participants with AKI had either recovered to normal or baseline serum creatinine. Over a third of participants did not recover to normal/ baseline serum creatinine at discharge; they

comprised 96/242 (39.7%). A high all-cause mortality rate of 96/242 (39.7%) was also observed among elderly participants with AKI **(Table 5).**

Table 4: Multivariate regression of factors associated with AKI

Variable	P-value	Adjusted OR	95%CI
Diabetes mellitus			
Yes	0.055	1.646	0.990-2.737
No			
Hypertension			
Yes	**0.001**	2.079	1.338-3.228
No			
Heart failure			
Yes	**<0.001**	3.531	2.067-6.032
No			
Liver failure			
Yes	**0.043**	3.326	1.038-10.655
No			
HIV status			
Negative			
Positive	0.164	0.719	0.451-1.145
Unknown	0.004	2.551	1.346-4.832
Sepsis			
Yes	**0.001**	2.168	1.361-3.455
No			
Use of Nephrotoxins			
Yes			
No	**0.037**	1.577	1.028-2.418
Polypharmacy (≥5 drugs)			
Yes			
No	**<0.001**	0.133	0.083-0.214
Vomiting and/or Diarrhea			
Yes			
No	**<0.001**	2.652	1.598-4.401
Hypotension			
Yes	**0.031**	1.694	1.049-2.736
No			
Others**			
Yes	<0.001	0.377	0.228-0.625
No			

**Obstructive Uropathy, previously treated with Tenofovir based regimen, Systemic lupus erythromatosus

Table 5: Clinical outcomes of study participants (N= 242)

Clinical outcome	Frequency (%)
Complete Recovery to normal or to baseline without dialysis (at discharge)	50 (20.7)
Complete Recovery to normal or to baseline with dialysis (at discharge)	0 (0.0)
Non- Recovery to normal or to baseline (at discharge)	96 (39.7)
Mortality (From whatever cause)	96 (39.7)
Total	242 (100)

Several socio-demographic, clinical characteristics and both modifiable and non-modifiable risk factors were assessed in bivariate analysis against recovery status of AKI among study participants. Participants with diabetes mellitus (DM) were less likely to recover to normal/baseline as compared to those without DM (22.5% versus 38.7%); however the association was not statistically significant (p-value= 0.070). Participants with underlying renal insufficiency (CKD) who presented with AKI were more likely not to recover to their baseline compared to those without underlying CKD (80.0% versus 63.5%); however this was not significant (p-value= 0.157). Severity of AKI and whether AKI was community or hospital acquired did not predict renal recovery. The rest of risk factors were also not associated with recovery status among the study participants **(Table 6).**

Table 6: Factors associated with recovery status of AKI

Variable	AKI- recovered (%)	AKI- not recovered (%)	P-value	Crude OR	95%CI
Age (Mean± SD)	69.1±10.6	65.7±10.8	0.072	0.971	0.940-1.003
Age 50-64 65-79 ≥80	 17 (26.6) 25 (39.1) 8 (44.4)	 47 (73.4) 39 (60.9) 10 (55.6)	 0.151 0.681	 2.212 1.248	 0.749-6.530 0.434-3.590
Gender Male Female	 25(33.3) 25 (35.2)	 50 (66.7) 46 (65.8)	 0.811	 0.920	 0.464-1.823
Diabetes mellitus Yes No	 9 (22.5) 41 (38.7)	 31 (77.5) 65 (61.3)	 0.070	 0.460	 0.199-1.065
Hypertension Yes No	 37 (36.6) 13 (28.9)	 64 (63.4) 32 (71.1)	 0.364	 1.423	 0.665-3.047
Heart failure Yes No	 15 (31.3) 35 (35.7)	 33 (68.8) 63 (64.3)	 0.594	 0.818	 0.392-1.710
Liver failure Yes No	 5 (50) 45 (33.1)	 5 (50) 91 (66.9)	 0.285	 2.022	 0.557-7.346
Chronic lung disease Yes No	 6 (33.3) 44 (34.4)	 12 (66.7) 84 (65.6)	 0.931	 0.955	 0.335-2.716
Underlying renal insufficiency (CKD) Yes No	 4 (20.0) 46 (36.5)	 16 (80.0) 80 (63.5)	 0.157	 0.435	 0.137-1.379
Confirmed malignancy Yes No	 3 (42.9) 47 (33.8)	 4 (57.1) 92 (66.2)	 0.625	 1.468	 0.315-6.832
Anaemia Yes	 28 (31.8)	 60 (68.2)	 0.447		

No	22 (37.9)	36 (62.1)		0.764	0.381-1.530
HIV status Positive Negative Unknown	 17 (37.8) 30 (32.3) 3 (37.5)	 28 (62.2) 63 (67.7) 5 (62.5)	 0.522 0.988	 1.275 1.012	 0.606-2.681 0.214-4.782
Sepsis Yes No	 16 (41.0) 34 (31.8)	 23 (59.0) 73 (68.2)	 0.299	 1.494	 0.701-3.183
Use of Nephrotoxic drugs Yes No	 28 (30.1) 22 (41.5)	 65 (69.9) 31 (58.5)	 0.164	 0.607	 0.300-1.227
Polypharmacy (≥5 prescription drugs) Yes No	 16 (28.6) 34 (37.8)	 40 (71.4) 56 (62.2)	 0.256	 0.659	 0.321-1.353
Use of traditional medicines Yes No	 1 (50) 49 (34)	 1 (50) 95 (66)	 0.642	 1.939	 0.119-31.665
Vomiting and/or Diarrhea Yes No	 14 (34.1) 36 (34.3)	 27 (65.9) 69 (65.7)	 0.987	 0.994	 0.464-2.127
AKI Stage Stage 1 Stage 2 Stage 3	 28 (35.0) 8 (32.0) 14 (34.1)	 52 (65.0) 17 (68.0) 27 (65.9)	 0.783 0.926	 1.144 1.038	 0.439-2.982 0.470-2.293
Type of AKI Community- acquired Hospital-acquired	 42 (32.8) 8 (44.4)	 86 (67.2) 10 (55.6)	 0.334	 0.610	 0.225-1.660

Patients without AKI recovery had higher median serum creatinine compared to those who had AKI recovery to normal or baseline. However the difference was not statistically significant (p-value= 0.066). Analysis of laboratory parameters for association with recovery status showed that only serum potassium was associated with AKI recovery status (p-value= 0.018) **(Table 7).**

Table 7: Association between laboratory parameters and recovery status of AKI

Variable	AKI-recovered	AKI-not recovered	P-value	OR	95%CI
Serum creatinine at AKI diagnosis (Median,IQR)	143(109-619)	170(131-1086)	**0.066**	1.002	1.000-1.004
Serum urea in mmol/l (Median,IQR)	13.7(9.5-42.8)	18.6(10.1-65.6)	0.208	1.017	0.991-1.044

White blood Count(WBC) in 10^9/l (Median,IQR)	9.6(5.63-31.86)	9.92(7.04-21.11)	0.528	0.996	0.986-1.007
Haemoglobin (Hb) in g/dl (Median,IQR)	11.1±3.3	10.6±3.1	0.386	0.953	0.854-1.063
Platelet Count in x10^3 /ul (Median,IQR)	220(148-719)	235.5(146-518.5)	0.690	1.000	0.997-1.002
ALT in umol/l (Median,IQR)	24(14-137)	22(13-218)	0.995	1.000	0.996-1.004
AST in umol/l (Median,IQR)	43(28-270)	34.5(20.55-359)	0.616	0.999	0.997-1.002
GGT in umol/l(Median,IQR)	58.5(30-478)	58.5(29-420)	0.214	0.998	0.995-1.001
ALP in umol/l (Median,IQR)	105(61.5-307)	107.5(73-331)	0.789	0.999	0.994-1.005
Albumin in g/dl (Median,IQR)	29.25(22.5-47)	30.4(24.2-47.5)	0.463	1.015	0.975-1.056
Serum Sodium in m/l (Median,IQR)	133.9±26.7	131.6±6.9	0.462	0.992	0.971-1.013
Serum Potassium in mEq/l (Median,IQR)	4.6(4-6.9)	6.9(3.6-6.01)	**0.018**	1.539	1.076-2.199

Bivariate analysis revealed that; old age of ≥ 80 years [p-value < 0.001], chronic lung disease [p-value= 0.012], sepsis [p-value= 0.006] and presenting with diarrhea/vomiting [p-value= 0.002] were associated with significant higher mortality. On the other hand; hypertension [p-value= 0.018] and heart failure [p-value= 0.006] predicted survivor among patients with AKI. Other studied variables including gender, presence of Diabetes mellitus, HIV status, underlying CKD and severity of AKI did not predict mortality in bivariate analysis **(Table 8).**

Table 8: Socio-demographic and clinical predictors of mortality among patients with AKI

Variable	Survivors (%)	Non-survivors (Died) (%)	P-value	OR	95%CI
Age					
50-64	64 (65.6)	35 (35.4)			
65-79	64 (68.8)	29 (31.2)	**0.001**	3.251	1.599-6.608
≥80	18 (36.0)	32 (64.0)	**<0.001**	3.923	1.900-8.103
Gender					
Male	75 (57.5)	51 (40.5)	0.789	1.073	0.708-1.978
Female	71 (61.2)	45 (38.8)			
Diabetes mellitus					
Yes	40 (67.8)	19 (32.2)	0.179	0.654	0.352-1.215
No	106 (56.3)	77 (43.7)			
Hypertension					
Yes	101 (66.0)	52 (34.0)	**0.018**	0.527	0.309-0.898
No	45 (50.6)	44 (49.4)			
Heart failure					
Yes	48 (75.0)	16 (25.0)	**0.006**	0.408	0.216-0.773
No	98 (55.1)	80 (44.9)			
Liver failure					
Yes	10 (50.0)	10 (50.0)	0.327	1.581	0.632-3.957
No	136 (61.3)	86 (38.7)			

Chronic lung disease					
Yes	18 (40.5)	24 (59.5)	**0.012**	2.370	1.206-4.660
No	128 (63.0)	72 (37.0)			
Underlying renal insufficiency (CKD)					
Yes	20 (58.8)	14 (41.2)			
No	126 (60.6)	82 (39.4)	0.846	1.076	0.515-2.249
Confirmed malignancy					
Yes	7 (58.3)	5 (41.7)	0.885	1.091	0.336-3.542
No	139 (60.4)	91 (39.6)			
Anaemia					
Yes	88 (53.7)	76 (46.3)	0.988	1.014	0.166-6.185
No	58 (74.4)	20 (25.6)			
HIV status					
Positive	45 (60.8)	39 (39.2)			
Negative	93 (62.8)	55 (37.2)	0.769	1.090	0.614-1.934
Unknown	8 (40.0)	12 (60.0)	0.101	0.430	0.157-1.178
Chronic Gastrointestinal Disease					
Yes	3 (60.0)	2 (40.0)	0.988	1.014	0.166-6.185
No	143 (60.3)	94 (39.7)			
Sepsis					
Yes	39 (48.1)	42 (51.9)	**0.006**	2.134	1.237-3.680
No	105 (65.2)	56 (34.8)			
Use of Nephrotoxins					
Yes	93 (60.4)	61 (39.6)	0.980	0.993	0.582-1.696
No	53 (60.2)	35 (39.8)			
Polypharmacy (≥5 prescription drugs)					
Yes	56 (63.6)	32 (36.4)			
No	90 (58.4)	64 (41.6)	0.427	0.804	0.468-1.379
Vomiting and/or Diarrhea					
Yes	41 (52.6)	37 (47.4)	**0.002**	2.505	1.383-4.535
No	102 (62.2)	62 (37.8)			
AKI Stage					
Stage 1	80 (65.0)	43 (35.0)			
Stage 2	25 (59.5)	17 (40.5)	0.521	0.790	0.385-1.622
Stage 3	41 (53.2)	36 (46.8)	0.098	0.612	0.342-1.095
Type of AKI					
Community-acquired	128 (59.3	88 (40.7)			
Hospital-acquired	18 (59.2)	8 (30.8)	0.329	1.547	0.644-3.714

Non-survivors were more likely to have low serum albumin as compared to survivors; however, the association was not statistically significant. Of all the studied laboratory parameters, only higher serum urea [p-value= 0.002] and serum creatinine [p-value= 0.012] predicted mortality in bivariate analysis (**Table 9).**

Table 9: Association between laboratory parameters and mortality in patients with AKI

Variable	Survivors (%)	Non-survivors (%)	P-value	OR	95%CI
Serum creatinine (umol/l) at AKI diagnosis (Median,IQR)	154(118-252)	190(132-393.5)	**0.012**	0.999	0.998-1.000
Serum urea at AKI diagnosis in mmol/l (Median,IQR)	14.9(9.5-24.6)	20.95(12-34.6)	**0.002**	0.975	0.959-0.991
White blood Count(WBC) in 10^9/l (Median,IQR)	9.05(6.44-13.68)	10.79(7.20-17.21)	0.731	1.002	0.990-1.014
Haemoglobin (Hb) in g/dl (Mean± SD)	10.8±3.2	10.0±3.2	0.055	1.084	0.998-1.176
Platelet Count in x10^3 /ul (Median,IQR)	234 (104.5-328)	231.5(184.61-326.5)	0.259	1.001	0.999-1.003
ALT in umol/l (Median,IQR)	24(15.1-49.7)	21(13-36)	0.098	0.998	0.995-1.000
AST in umol/l (Median,IQR)	46(27.15-88.7)	31.5(20-58)	0.148	0.999	0.997-1.000
GGT in umol/l(Mean± SD)	71(31.5-149)	49(27-117)	0.312	0.999	0.997-1.001
ALP in umol/l (Median,IQR)	110.5(73-182)	104(71-145)	0.090	0.997	0.994-1.000
Albumin in g/dl (Median,IQR)	32.8(26-39.2)	27.2(21.1-32)	0.066	1.028	0.998-1.058
Serum Sodium in m/l (Mean± SD)	132.3±16.5	133.4±18.0	0.658	0.996	0.981-1.012
Serum Potassium in mEq/l (Median,IQR)	4.7(3.7-5.8)	14.9(9.5-24.6)	0.346	0.968	0.904-1.036

Stepwise technique was used to select variables that fit the final model. The following variables; - hypertension, sepsis, vomiting and/or diarrhea and serum urea at AKI diagnosis though significant in bivariate analysis were not a fit; hence they were left out in the final model. Multivariate regression analysis revealed that old age of 80 years or more, presence of heart failure, presence of chronic lung disease and serum creatinine level at AKI diagnosis were the only factors independently associated with mortality **(Table 10).**

Table 10: Multivariate logistic regression for factors associated with mortality among AKI patients

Variable	Survivors (%)	Non-survivors (Died) (%)	P-value	Adjusted OR	95%CI
Age					
50-64	64 (65.6)	35 (35.4)			
65-79	64 (68.8)	29 (31.2)	0.996	1.003	0.394-2.553
≥80	18 (36.0)	32 (64.0)	**<0.001**	0.090	0.024-0.341
Heart failure					
Yes	48 (75.0)	16 (25.0)	**0.021**	0.294	0.104-0.828
No	98 (55.1)	80 (44.9)			
Chronic lung disease					
Yes	18 (40.5)	24 (59.5)	**0.038**	2.997	1.063-8.448
No	128 (63.0)	72 (37.0)			

Serum creatinine at AKI diagnosis (Median± IQR)	154(118-252)	190(132-393.5)	**<0.001**	0.994	0.992-0.997
Albumin in g/dl (Median± IQR)	32.8(26-39.2)	27.2(21.1-32)	0.146	1.026	0.991-1.063

Discussion

The prevalence of AKI among elderly patients in medical wards of Princess Marina Hospital in Botswana was found to be 29.96%. The mean age of participants with AKI in this study was 66.98 years. Our findings are similar to findings of a study done in India where the prevalence of AKI in elderly was found to be 29.4% (Arora et al., 1993). On the other hand, the prevalence of AKI in this study was lower than the one in an old study in a Chinese geriatric unit where the prevalence was 42.2% (Kafetz & Hodkinson., 1982). Several factors including differences in study design, duration of the study, variations of risks for AKI and the age range used in this study could have attributed to the discrepancy observed.

This study revealed that the very elderly participants (> 80 years old) were significantly associated with AKI in bivariate analysis. This is most likely due to high burden of contributing other comorbid conditions. Advanced age has been shown to be associated with AKI in previous studies (Ge et al., 2016; Wen et al., 2013; Chao et al., 2015). Male gender comprised majority of participants with AKI in our study. This compares to studies done elsewhere (Xue et al., 2006; Bucuvic et al., 2011). The predominance of male gender in AKI is not surprising because males have several predispositions including hormonal (Park et al., 2004; Neugarten et al., 2018) and likewise female gender has been shown to be protective against AKI associated ischemic-reperfusion injury as compared to male gender (Hutchens et al., 2008; Hutchens et al., 2012).

Previous studies have shown HIV positivity to be associated with increased prevalence of AKI. This may be attributed to multiple HIV-associated and non-HIV associated comorbidities (Venter et al., 2018; Gameiro et al., 2018). Given the high National prevalence of HIV in Botswana (Kandala et al., 2014), it is not surprising that over a quarter of participants (26.6%) were HIV-infected. History of unknown HIV status was associated with less likelihood of having AKI; whereas it appears difficult to explain this finding, it is possible from clinical experience of working in the hospital that majority of these patients were stable admitted for elective procedures like colonoscopy, upper endoscopy and pacemaker insertion.

Hypertension was the leading associated chronic illness (55.6 %) among elderly participants in this study, followed by diabetes mellitus (19.8%) and heart failure (19.2%). Hypertension and heart failure were significantly associated with AKI; these factors have been found to be associated with AKI in previous studies (Gameiro et al., 2018; Hwang et al., 2017; Kayatas et al., 2014; Jönsson et al., 2014).

Sepsis, use of nephrotoxic drugs, vomiting and/or diarrhoea, anaemia and hypotension were most common modifiable risk factors present in 24.1%, 54.5%, 55.0%, 19.1%, 60.2% and 23.4% of elderly participants respectively. All these factors were independently associated with AKI when comparing to participants without AKI in this study; this is similar to other previous studies (Han et al., 2015; Sreenivasan et al., 2018; Chao et al., 2015b; Bradshaw et al., 2018).

Malignancy is among the most common contributors of AKI with associated prolonged hospital stay and increased costs (Christiansen et al., 2011). However, this was not the case in our study where only 5% of patients with AKI had confirmed malignancy. The most likely explanation for a relatively low frequency of malignancy among patients in this study is that; once confirmed with malignancy, such patients are moved to oncology ward; hence very few patients with malignant conditions were admitted in medical wards in this study.

Furthermore, this study revealed that only 1 in 5 of participants with AKI recovered to normal or baseline at discharge. Of note, none of the participants placed on hemodialysis recovered to normal/baseline. Possible explanation is that these participants (ones placed on haemodialysis and did not recover to normal/baseline) might have had pre-existing chronic kidney disease. It was

observed that, 39.7% of patients died in this study; a worrying trend given that majority of patients with AKI did not require dialysis and had less severe AKI, it does suggest however, that patients might have died due to other comorbid conditions, which were highly predominant among study participants. The high all-cause mortality among patients with AKI seen in this study compares to several other global studies on AKI that found mortality to range from 31% to 86% (Tang et al., 2017; Effa et al., 2015; Martensson et al., 2010; Pedersen et al., 2017; Olowu et al., 2016).

Several factors including;- old age, severity of AKI, presence of hypertension, serum creatinine level, presence of anaemia, malignancy have been shown to predict AKI recovery in other studies (Pajewski et al., 2018; Yao et al., 2018). On the contrary, in this study demographic and clinical variables were not significantly associated with AKI recovery. Patients who did not recover renal function appeared to have higher serum creatinine, however the association was not statistically significant (p-value= 0.066). On the other hand, these study findings are similar to a study that did not find an association between laboratory parameters and AKI recovery (Nie et al., 2017). This study showed that, only high serum potassium was significantly associated with non-AKI recovery.

Previous studies have consistently shown several factors to be associated with mortality among patients with AKI. Factors include; - old age, severe AKI stage, serum albumin, leukocytosis, thrombocytopenia, heart failure, malignancy and sepsis (Nie et al., 2017; Xue et al., 2006; Singh et al., 2019; Abdelsalam et al., 2018; Osman et al., 2017). This study revealed that old age above 80 years, chronic lung disease and higher serum creatinine levels at AKI diagnosis were the only factors significantly associated with higher mortality. Other laboratory parameters including white blood cell count, platelet and serum urea and potassium were not significantly associated with mortality. Serum potassium level was not associated with mortality in this study. This findings contrasts evidence from previous studies that showed serum potassium to be a predictor of mortality among AKI patients (Cheungpasitporn., 2017; Park et al., 2017). The lack of association between AKI severity and mortality in this study may partly be due to high prevalence of pre-existing other serious comorbid conditions contributing to high all-cause mortality among this study population.

Heart failure was significantly less likely to be associated with mortality in this study, which is in contrast to other studies (Nie et al., 2017; Sezer et al., 2006; Samimagham et al., 2011). It is possible that patients with heart failure in this study responded well to anti-failure medications and were discharged compared to other chronic conditions. There is a need to conduct more studies establish the reason for this unexpected finding.

This study had few limitations that were associated with the fact that it was a retrospective study; hence not possible to obtain missing information in some participants. The study has strength in terms of reporting outcomes. There was no follow up to elicit long-term outcomes of participants given the design of the study. Some participants discharged with impaired renal functions, might have converted to normal or baseline like in previous studies (Pajewski et al., 2018). On the other hand, it was not possible to determine whether some participants presenting with AKI had pre-existing chronic kidney disease that might have explained higher rates of non-recovery and mortality. The difference in the definitions of elderly between this study and other studies also limit comparability because even though the mean age is 66.98 years, the entry age was slightly lower for this study. This is the first study on the prevalence and factors associated with AKI in the local context. Future prospective studies on this area in Botswana will help to enhance more understanding and enable evidence-based interventions.

Conclusion

The prevalence of AKI among elderly participants admitted in medical wards of a referral hospital in a developing country in Africa (Botswana) is high at 29.96% and there is a high all-cause mortality among admitted participants with AKI. The commonest risk factors independently associated with AKI among elderly participants were hypertension, heart failure, liver failure, sepsis, polypharmacy, use of nephrotoxic drugs and hypotension. Serum potassium was significantly associated with AKI non-recovery. Old age more than 80 years old, chronic lung disease and worse serum creatinine at AKI diagnosis were associated with mortality whereas having heart failure conferred better chance

of survival. There is a need to carry out prospective observation multi-centric study across Botswana to help in understanding of local risk factors among patients with AKI. Studies should also involve follow-up component to elicit both short and long-term outcomes of patients with acute kidney injury.

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