Adjustments of medication dosages in patients with renal impairment in Botswana; findings and implications to improve patient care

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ABSTRACT
Background and aims: Medication dosage adjustments for renally impaired patients have not been studied in Botswana. This study was conducted to determine prescribing practices among patients with renal impairment in medical wards to improve future patient care. *Methods:* We conducted a retrospective study involving medical charts of patients admitted at a tertiary level hospital in Gaborone Botswana. Study participants included all patients admitted between August and October 2016 who were hospitalized for ≥24 hours. "Drug prescribing in renal failure: dosing guidelines for adults and children." was used to determine extent of dosage adjustments. A logistic regression model was used to assess which patient factors were associated with inappropriate dosage adjustment. *Results:* Twenty nine percent (233/804) of patients had renal impairment. Of these, 184 patients with renal impairment were included in the final analysis. There were 1143 prescription entries, of which 20.5% (n=234) required dosage adjustment for renal function but only 45.7% (n=107) were adjusted correctly. Of note, 112 patients were prescribed at least one drug that required dosage adjustment and only 30.4% (n=34) patients had all of their medications appropriately adjusted. Patient factors associated with inappropriate dosage adjustment included a higher number of medicines being prescribed. Mortality among patients with renal impairment was independently associated with higher scores of Charlson comorbidity index and hospital stay duration of 1-7 days. *Conclusion:* The renal function status of patients was not sufficiently taken into account when prescribing medicines especially in patients with severely impaired kidney function in Botswana. Continuous medical education needs to be encouraged to address this, which is being implemented. We will be following this up in future studies.

Key words: Medicine dosage adjustment, renal impairment, Mortality, Charlson index, Botswana

1. INTRODUCTION

Elimination of most medicines and their active metabolites is dependent on renal filtration, secretion and re-absorption [1]. In renal impairment, the clearance of medicines eliminated primarily by the kidney is decreased, and dosage adjustment should be considered when medicines are prescribed to patients with impaired renal function [2]. Over and above this, most medicines and their active metabolites have the potential to induce nephrotoxicity, or worsen renal impairment [3]. This is the case for instance for certain medicines for patients with human immune-deficiency virus (HIV), which is very prevalent in Botswana and across sub-Saharan Africa [4, 5]. For instance, at one stage, nearly 50% of the women in Botswana aged 30 to 34 years had HIV [5], and an appreciable proportion of hospitalized patients in Botswana are HIV positive [6]. HIV is itself an independent risk factor for kidney disease [7].

Studies have reported that 20-67% of prescriptions for patients with impaired renal function contain errors [8, 9]. There are many causes for these prescribing errors, which include prescribers' poor knowledge of medications requiring dosage adjustment, the presence of renal impairment being overlooked by prescribers, underestimation of potential adverse events of medicines, and the lack of evidence-based data to guide prescribers on precautions and dosage adjustments [10, 11]. Drug-related problems can result in an increase in morbidity and mortality, as well as an increase in the cost of healthcare [12].

There is currently no data on the extent of application of any medication adjustment guidelines among renally impaired patients in Botswana. This is a concern especially among patients with HIV in Botswana. Consequently, this study was conducted to assess the patterns of medication dose adjustments among patients with renal impairment admitted to a tertiary hospital and its clinical outcomes in Botswana. As a result, provide guidance for the future care of these patients in this and other hospitals in Botswana as well as wider

2. METHODOLOGY

2.1 STUDY SITE

Princess Marina Hospital (PMH) was chosen for this initial investigation as it is the leading tertiary hospital in Botswana training future physicians. It is also the leading hospital for treating patients with HIV in Botswana, and also treats ambulatory care patients from Gaborone and across the Southern part of Botswana with non-communicable diseases (NCDs) such as chronic kidney diseases, hypertension and diabetes [13]. There are two medical wards in the hospital, male and female medical wards, with bed capacities of 30 patients in each and a monthly admission rate ranging from 125-150 patients per ward. Consequently, if there are concerns with renally impaired patients in this setting, these are likely to be echoed throughout Botswana. A similar situation may also exist in other African countries with high rates of both HIV and NCDs such as diabetes [14-16].

2.2 STUDY DESIGN AND POPULATION

This was a descriptive retrospective cross-sectional study conducted during August to October 2016. All patients admitted to the male and female medical wards and aged 14 years and above were included in the study. The medical charts of eligible patients were reviewed for the level of creatinine at admission or during the course of inpatient treatment during the study period to understand their renal impairment status. Renal impairment constituted four groups of patients; - firstly those with documented chronic kidney disease with evidence of at least two elevated serum creatinine three months apart, secondly patients with end stage renal disease (ESRD) on renal replacement therapy in the form of haemodialysis or peritoneal dialysis. The third group consisted of patients admitted either without baseline serum creatinine or with some results of serum creatinine in the integrated patient management system (IPMS). Those patients without previous serum creatinine had their estimated baseline serum creatinine back-calculated using the MDRD (Modification of Diet in Renal Disease) equation with an estimated GFR (glomerular filtration rate) of 75ml/min/1.73m^2 in a similar way to previous studies [17]. Patients with previous several creatinine results had the minimum serum creatinine available within the past 12 months considered as baseline similar to a previous study [18]. For both categories in the third group, obtained

values were compared to values of serum creatinine at admission to establish whether these patients had evidence of renal impairment according to KIDGO criteria for AKI [19]. The fourth group comprised patients who were admitted with serum creatinine within the normal laboratory hospital range but developed renal impairment over the course of hospital admission.

Exclusion criteria included admission of less than 24 hours either due to discharge or death, patients admitted for a day procedure such as gastroscopy, and patients whose renal function tests were either not undertaken or not traceable.

2.3 SAMPLE SIZE CALCULATION AND TOTAL NUMBER OF PATIENTS

Based on the prevalence of inappropriate medication adjustment in patients with renal impairment was reported to be 73.5% reported by Sweileh et al [11], the sample size was calculated using allowable error (d) in estimating a prevalence of 10%.

The following formula was used for calculating the adequate sample size in prevalence study [20]; $N=(Z_{\alpha/2}{}^2 pq)/d^2$

Where N is the sample size, Z is the statistic corresponding to level of confidence, p is expected prevalence, and d is precision (corresponding to effect size) [20-22].

Based on a prevalence 73.5% and allowable error in estimating a prevalence of 10% where:
p = 0.735
q = 1-p = 0.265
d = allowable error = 10% of p= 0.1*0.735=0.0735
= probability of type I error
= 0.05 (2-sided) = $Z_{\alpha/2} = Z_{0.025}$=1.96
$N = ((1.96)^2(0.735)\ (0.265))/(0.0735)^2 = 138.50 \approx 139$.

Consequently, the minimum required sample size was 139 patients. Given the duration of the study, we ended up with 184 patients in the final analysis as shown below.

During the study period, a total of 856 patients were admitted in the medical wards, 50.1% (n=429) males and 49.9% (n=427) females. Of these patients, 6% (n=52) had no record of renal functions from admission on the Integrated Patient Management System (IPMS). From the remaining 804 patients, 29% (n=233) had renal impairment, either on admission or they developed it during their hospital stay. Of the 233 patients with renal impairment, 49 were excluded from the final analysis due to either their folders not being traced, discharged/died within 24 hours, or they were admitted as lodgers. Hence, 184 patients were included in the final analysis, 54.3% (n=100) males and 45.7% (n= 84) females (Figure 1), higher than our sample size calculation.

Insert Figure 1

2.4 DATA COLLECTION

The hospital Integrated Patient Management System (IPMS) was used to retrieve the total admissions into the male and female medical wards of Princess Marina Hospital from August to October 2016. The electronic medical record system (Meditech©) of each patient was searched using the unique patient number on admission assigned to each patient (PA number). The information retrieved was entered into an excel sheet. The following information was retrieved from the Electronic Medical Record (EMR) and folders of each patient: age, gender, serum creatinine on admission and their highest serum creatinine level while admitted which on computation resulted in the eGFR meeting the study definition of renal impairment described below. These variables were subsequently entered into an electronic calculator for Modification of Diet in Renal Disease (MDRD) approved by NKF-KDQOI clinical practice guidelines to obtain the estimated glomerular filtration rate (eGFR) [23]. The documented HIV serostatus of the patients were also retrieved from either the EMR or patient folders. The uptake of HIV testing is typically

high in the hospital as patients with unknown HIV status usually consent to be tested at the time of admission.

The definition and classification of renal impairment differs among different information sources [5]. However, drug dosing guidelines are typically derived from studies performed in patients with stable, chronic renal insufficiency and the recommendations are extrapolated to seriously ill patients with acutely decreased renal function [24]. For the purpose of this study to evaluate appropriateness of drug dosing adjustment, renal impairment was defined as estimated GFR corresponding with CKD 3 or worse (<60 mL/min/1.73 m^2) [25]. The Charlson comorbidity index (CCI) was used to assess risk for both the inappropriateness of medication adjustment as well as outcome at discharge. CCI for each individual patient was computed using an online calculator [26]. For the purpose of this study, CCI was categorized as low (0-1), intermediate (2-3), high (4-5) and very high (≥6) similar to other studies [27, 28].

Patients with eGFR values of <60 mL/min/1.73m^2 had their medical records folders retrieved from the medical records department. For all patients, detailed clinical data was collected using a structured Excel data sheet. Medications administered and dosage adjustments were recorded from day 2 of admission, or the date from which the first renal function test results were available, or from the date renal impairment developed in the scenario a patient was admitted with normal renal function and subsequently developed renal impairment during their hospital stay. For those patients identified with renal impairment, an audit was performed to assess if dosages of medications administered were adjusted appropriately according to standard formulae. Medication dosages recorded were correlated for dosages recommended according to their eGFR using Drug Prescribing in Renal Failure: Dosing Guidelines for Adults and Children 5th edition [24]. This source was preferred because it has a section for medication adjustment in patients on continuous renal replacement therapy (CRRT) which was the case for some patients in this study. To ensure validity of findings of appropriateness of medications adjustment, data was checked and verified by two reviewers (the first two authors).

Polypharmacy has a range of definitions that refer to different medication regimens without any standard definition [29]. For the purpose of this study, polypharmacy is defined as prescription containing four or more medications [30].

2.5 MEDICATION WORK FLOW IN THE HOSPITAL

For the purpose of this study, medications used for assessing the appropriateness of adjustments were those administered as appearing in the patients' treatment charts. Medication work flow in the hospital begins with doctors prescribing medications and writing them in patients' treatment charts. The majority of prescribed medications are available in the ward; consequently, nurses administer these as prescribed by the doctors. Pharmacists are not involved during the ward rounds to verify whether the medications have been appropriately adjusted in patients with comorbid conditions such as renal impairment or hepatic failure. Pharmacists can be involved whenever drugs listed as a special order category are prescribed and the files sent to Pharmacy for medication issuing.

2.6 DATA MANAGEMENT AND STATISTICAL ANALYSIS

Statistical Package for Social Sciences (SPSS) version 24.0 was used for analysis. Descriptive statistics was performed for social-demographic parameters and clinical characteristics and expressed in frequencies and percentages for categorical variables. For numerical variables, the median with interquartile range (IQR) and the mean (SD) were used as appropriate. Bivariate and multivariate logistic regression analyses were used to assess which patient factors were associated with inappropriate dosage adjustment. Due to the problem of collinearity, some variables were removed from multivariate model. A p-value of < 0.05 was considered statistically significant.

2.7 ETHICAL CLEARANCE

Ethical clearance to conduct this study was obtained from University of Botswana Office of Research and Development, Ministry of Health, Research and Development Division, and the Princess Marina Hospital Research and Ethics Committee.

Overall, we followed the STROBE checklist in the design and reporting of our findings (https://www.strobe-statement.org/fileadmin/Strobe/uploads/checklists/STROBE_checklist_v4_cross-sectional.pdf).

3. RESULTS

3.1 Sociodemographic and clinical characteristics of study participants

Table 1 describes the background and clinical characteristics of the patients enrolled in this study. The median age of patients was 53.0 years with an interquartile range (IQR) of 25-75 years. Male patients accounted for 54.3% of the patients. In terms of comorbidities, 71.2% (n=131) had comorbid conditions such as hypertension, diabetes and congestive cardiac failure. Hypertension and diabetes mellitus were present in 92/184 (50.0%) and 43/184 (23.4%) respectively. The HIV status was unknown in 14.7% (n=27), with 38.0% (n=70) being HIV negative and 47.3% (n=87) being HIV positive. On the other hand, among the enrolled patients, 33/184 (17.9%) were known to have end stage renal disease (ESRD) on continuous renal replacement therapy (CRRT).

Insert Table 1

The mean creatinine in μmol/L was 462.8 with a range of 45-2702. Using the MDRD Study equation the mean eGFR ± SD was 29.3 mL/min/1.73m^2 ± 24.7 mL/min/1.73m^2. When patients were classified according to the corresponding KDIGO classification for CKD, 96.2% (n=177) of the patients had renal impairment stage III or worse (Table 1). Seven (7) patients were admitted with eGFR of >60 mL/min/1.73m^2 but developed renal impairment during the course of admission.

Of the 184 patients, 61.9% (n=112) were prescribed at least one medicine that required dosage adjustment for the level of renal impairment. The median number of medications prescribed to patients with renal impairment was 6 (range= 0-13). The median (range) of the number of medicines than needed dosage adjustment was 1 (range= 0-6). The overall mortality rate or patients admitted with renal impairment was 23.9% (n=44); whereas HIV positive patients with renal impairment had a mortality of 28.7%,

3.2 Appropriateness of dosage adjustment in renal impaired patients

For the 184 patients with renal impairment there were 1143 prescription entries, of which 20.5% (n=234) required dosage adjustment for renal function. Out of the 234 entries, 54.3% (n= 127) were not appropriately dose adjusted.

Among 112 patients that had prescriptions that needed dosage adjustment, 41.1% (n=46) of patients had none of their medications adjusted and only 30.4% (n=34) had all their medications appropriately adjusted. Over a quarter of patients, 28.6% (n=32), had some of their medications appropriately adjusted.

3.3 Factors affecting dosage adjustment

In the logistic regression model, gender, age of patient, history of diabetes mellitus, hypertension, comorbidities and severity of renal impairment had no association with medication dosing errors. The number of medicines needing renal adjustment that were prescribed did have a significant association. The higher the number of medicines prescribed, specifically 3 or more, the more likely that appropriate dosage adjustments would not be made (Adjusted OR= 13.78 (2.47, 76.74) p-value= 0.003) (Table 2).

Insert Table 2

3.4 Patients outcomes and associated factors

Bivariate analysis was performed to assess if HIV status, comorbidities, extent of dosage adjustment, length of hospital stay and the degree of renal impairment have any association with the eventual outcome of either death or discharge of the 184 patients with renal impairment. All the variables except length of stay and the Charlson comorbidity index had no relationship with the eventual outcome. Mortality was noted to be significantly higher within the first 7 days of admission in patients with renal

impairment at 33.8% (25/74). Similarly, higher Charlson comorbidity index scores were significantly associated with mortality (Table 3).

Insert Table 3

Multivariate analysis revealed the following factors to be independently associated with a higher mortality rate;- high and very high Charlson comorbidity index and having part of the medications not adjusted. On the other hand, prolonged hospital stay of ≥15 days or more was associated with less likelihood of mortality among patients with renal impairment (Table 4)

Insert Table 4

3.5 Subgroup analysis of appropriateness of dosage adjustment among ESRD patients on dialysis
Multivariate analysis involving 33 ESRD patients who were on dialysis revealed no association between studied variables (age, gender, HIV status, hospital stay duration, number of drugs needing dosage adjustment and Charlson comorbidity index score) and appropriateness of medication dosage adjustment (Table 5)

Insert Table 5

4. DISCUSSION

This study found the prevalence of renal impairment among patients admitted in the medical wards at this leading hospital in Botswana at 29%, which was appreciably higher than previously reported in the same setting in 2014 where the prevalence of renal impairment was found to be 16.3% [31]. The possible explanation for this discrepancy in prevalence rates are differences in methodology with this being retrospective and including both patients with renal impairment on admission and those who developed renal impairment while admitted. This is in contrast to the previous study that only included patients with renal impairment at admission. In a regional study from South Africa conducted in Groote Schuur Hospital general medical wards, the authors found renal impairment in 32% of medical admissions [32]. However, an eGFR of <50 mL/min/1.73m^2 was used in their study to define renal impairment compared to eGFR <60 mL/min/1.73m^2 in this study. The prevalence of renal impairment amongst inpatients elsewhere in sub-Saharan Africa ranged from 9% to 55% [9, 33]. Consequently, our prevalence rate appears similar to those found elsewhere in sub-Saharan Africa.

The mean age of patients admitted with renal impairment in this study was 54.6 years, which falls within the range of 42-63 years found in other similar studies [9, 11, 32]. The mean eGFR of the population group studied in our study was 29.3 ml/min/1.73 m^2. This was almost identical to a study from Northern Ethiopia with a mean eGFR of 28.84 mL/min/1.73m^2 [33]. However, in comparison to studies that used the Cockcroft Gault equation to calculate creatinine clearance (CrCl) it was much lower, with those studies finding mean CrCl ranging from 36-39.6 for their study populations [9, 11]. This difference could possibly be due to the different equations used [34]. In some studies, the MDRD study equation has been reported to be more accurate than the Cockcroft–Gault equation [35, 36], and has been shown to provide unbiased and reasonably accurate estimates across a wide range of subgroups when eGFR is less than 60 ml/min per 1.73 m^2 [37].

In this study, it was found that male patients seemed to be more prone to renal impairment than female patients though this was not statistically significant; with 55% of the total patients with renal impairment being male. This is in line with other published studies [9, 33, 38, 39]. This difference in susceptibility to renal impairment based on gender could be attributed to the fact that, on average, women have a lower muscle mass that may result in a lower serum creatinine and, thus, higher eGFR than men [40]. Whereas, it would have been plausible to compare body mass index (BMI) between male and female gender to verify this, this was not possible in this situation due to study design being retrospective and patients' charts missing either weight or height information which are required for BMI calculations.

The median number of medicines prescribed to patients with renal impairment was six. The higher number of medications prescribed in our study may partly be explained by the fact that 68/112 (60.7%) of patients with medications required dosage adjustments were HIV positive; with an expected increased pill burden. Polypharmacy in patients with renal impairment has been found across many similar studies [9, 32], and it is well established that the incidence of adverse drug events is much higher in patients with renal insufficiency [1, 2, 41].

Out of the 1143 prescription entries, 20.5% required dosage adjustment. This is similar to Decloedt et al who found 19% of the prescription entries requiring dosage adjustment [32]. However, the rates seen are half of those found in other studies where 39-42% of the prescriptions required dosage adjustment [33, 42]. Our study also showed that 54.3% of the drug prescriptions were not appropriately adjusted. Comparing this to higher income countries, in an Australian hospital the dosages were found to be inappropriately high in 42.2 % of inpatients [43] and 34% of inpatients in a French Hospital [44]. In more resource limited settings, similar to ours, the findings are comparable with between 51 and 54.5% of medicines being inappropriately adjusted [9, 38].

When assessing patients' factors that were associated with inappropriate dosage adjustment, we found that the higher the number of medicines prescribed, specifically 3 or more, the less likely that appropriate drug adjustments would be made. Severity of renal impairment was though not associated with increased likelihood of medication dosage errors. Previous studies suggested predictors of medication dosing errors, i.e. severe-to-end stages of chronic kidney disease and/or renal impairment, the presence of comorbidities such as hypertension, and a higher number of prescribed medicines [39, 45]. We did not find a significant association between the presence of comorbidity and medication dosing errors. This finding is similar to a study conducted in Ethiopia [9].

On the other hand, the mortality rate of patients admitted with renal impairment was 23.9%. The highest mortality rate was within the first 7 days of admission, i.e., 33.8%. This may be due to patients presenting very late with renal impairment, or presenting with illnesses with multisystem involvement. Even though it was not shown to be statistically significant, HIV positive patients with renal impairment had a mortality rate of 28.7%, which was higher than the overall mortality rate found in this study of 23.9%. This again may not be unsurprising, and will be the subject of future research projects. Patients with higher, very high Charlson comorbidity index and those with part of medications not adjusted were though significantly more likely to die, which agree with previous studies [46, 47].

Lastly, subgroup analysis involving patients on dialysis showed no significant association between medication adjustment errors and studied variables including age, gender, number of drugs requiring adjustment and Charlson comorbidity index scores. This contrast with previous findings which found higher rates of dosing errors among patients on dialysis [48, 49]. The possible reason for a lack of association in our study is that the sample size for this subgroup analysis was quite small and it may not have been powered to detect any association. We will be looking at this further in future studies.

Study limitations

Despite interesting findings elicited in this study, we are aware of several limitations with this study. Firstly, in the absence of a concise definition of renal impairment in the literature, we used an eGFR of <60 mL/min/1.73m^2 which corresponds to CKD stage 3. Some studies have used this exact definition; however, we are aware of other studies that have used absolute serum creatinine values or lower cut offs of eGFR. Secondly, most dosing guidelines use stable GFR; some of patients in this study had AKI making their serum creatinine/GFR unstable. Consequently, there is a need for future studies to focus on dosing adjustment specifically for patients with stable GFR. Thirdly, prescriber factors, such as, level of training and years of experience were not captured, which could be a major confounder. We are also aware that we did not estimate the sample size; consequently, the relatively small sample size might have resulted in a lack of power to determine the association to some variables. However this being the first study on this topic in Botswana, we believe that our findings will motivate future studies with larger sample sizes to enhance more understanding and improve future care. Furthermore, we used the MDRD equation to calculate GFR in this study. This equation has not been validated in this setting; likewise, this study is limited in the fact that we did not extract data on whether dosing adjustment was undertaken

using other equations such as CKD-EPI or Cockcroft-Gault equations although these tend to produce variable GFR estimations especially for CKD 2-3 and CKD 4-5. Lastly, this study was conducted retrospectively so as not to influence prescribing habits. Retrospective data collection may be hampered by missing and incomplete data, as in our study where 49 patients were excluded. Likewise, retrospective studies are bound to the problem of difficulties of estimating and measuring the effects of confounders. Never-the-less, we believe our findings are of interest which we will be taking further in future studies.

5. Conclusions and recommendations

We established that one in five prescriptions to patients with renal impairment in this leading hospital in Botswana required dosage adjustment, of which less than half were appropriately adjusted. The patient factor that we established in our setting to be related to inappropriate dosage adjustment was a higher number of prescribed medications. Higher scores of Charlson comorbidity index and hospital stay of 1 to 7 days were independent predictors of mortality among patients with renal impairment. Continuous medical education and access to aides for clinicians to improve their prescribing needs to be emphasized. The collaboration of clinicians with pharmacy personnel is paramount in this regard with potentially Drugs and Therapeutic Committees playing an active educational role. We will be following this up in the future.

We hope the findings of our study will be of interest to other African countries facing similar issues with high rates of both infectious and non-infectious diseases including patients with HIV as they struggle to manage patients effectively.

Disclosure of interest

We declare to have no conflicts of interests. All authors have approved the final version of the manuscript to be submitted

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Figure 1: Flowchart of reviewed medical patients

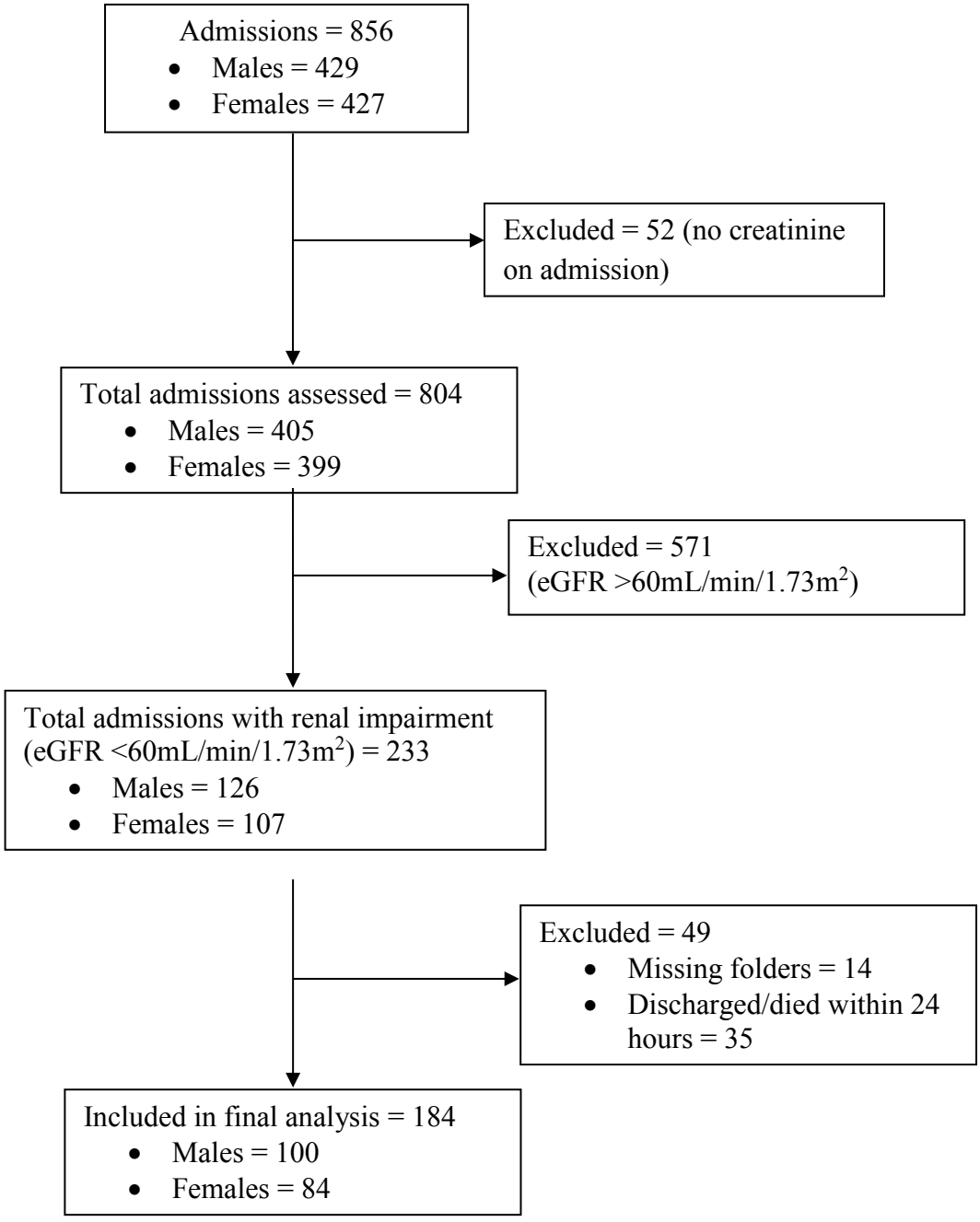

Table 1: Background and clinical characteristics of patients who were either admitted with renal impairment or developed renal impairment during the course of admission (N=184)

Variables	Frequency	Percentage
Gender		
Male	100	54.3%
Female	84	45.7%
Age in years; Median (IQR)	53 (25-75)	
14-29	14	7.6%
30-39	31	16.8%
40-49	36	19.6%
50-59	26	14.1%
60-69	36	19.6%
70 & above	41	22.3%
Creatinine in umol/l; Mean (Range)	462.8 (45-2702)	
Estimated GFR (ml/min/1.73m^2); Mean (SD)	29.3 (24.7)	
Stage 1 (≥ 90)*	3	1.6%
Stage 2 (60-89)*	4	2.2%
Stage 3 (30-59)	73	39.7%
Stage 4 (15-29)	41	22.3%
Stage 5 (< 15)	63	34.2%
Patients requiring at least one drug dose adjustment		
Yes	112	61.9%
No	72	39.1%
Number of medications prescribed; Median (Range)	6 (0-13)	
No of drugs that need renal adjustment; Median (Range)	1 (0-6)	
Comorbid conditions		
Yes	131	71.2%
No	53	28.8%
Diabetes		
Yes	43	23.4%
No	141	76.6%
Hypertension		
Yes	92	50%
No	92	50%
Charlson's comorbidity index		
Low (0-1)	9	5.7%
Intermediate (2-3)	23	14.6%
High (4-5)	28	17.7%
Very high (≥6)	98	62.0%
HIV status		
Negative	70	38.0%
Positive	87	47.3%
Unknown	27	14.7%
Number of medicines for HIV positive patients on antiretroviral therapy (mean)	8.7	
Number of medicines for HIV positive patients not on antiretroviral therapy (mean)	6.2	

*7 patients were admitted with normal renal functions but subsequently deteriorated over the course of hospital admission

Table 2: Factors associated with inappropriate dose adjustment in patients with renal impairment who needed dose adjustment (N=112)

Variables	Inappropriately adjusted	Appropriately adjusted	Adjusted OR (95% CI)	p-value
Gender				
Male	42 (68.9%)	19 (31.1%)	Reference	0.31
Female	36 (70.6%)	15 (29.4%)	1.89(0.55, 6.34)	
Age in years				
14-39	20 (74.1%)	7 (25.9%)	Reference	
40-49	16 (64.0%)	9 (36.0%)	0.59(0.13, 2.79)	0.51
50-59	14 (70.0%)	6 (30.0%)	1.35(0.18, 10.03)	0.77
60-69	14 (66.7%)	7 (33.3%)	1.69(0.23, 12.39)	0.60
70 or more	14 (73.7%)	5 (26.3%)	1.15(0.11, 12.40)	0.91
HIV status				
Negative	20 (29.0%)	49 (71.0%)	Reference	
Positive	53 (60.9%)	34 (39.1%)	1.41(0.07, 28.49)	0.82
Unknown	5 (18.5%)	22 (81.5%)		
Hospital stay in days				
1-7	24 (32.9%)	49 (67.1%)	Reference	
8-14	26 (43.3%)	34 (56.7%)	0.93(0.22, 4.01)	0.93
≥15	28 (56.0%)	22 (44.0%)	0.47(0.11, 2.09)	0.32
Comorbid conditions				
Yes	51 (68.9%)	23 (31.1%)	0.77(0.17, 3.47)	0.73
No	27 (71.1%)	11 (28.9%)	Reference	
Diabetes				
Yes	16 (37.2%)	27 (62.8%)	1.28(0.17, 9.60)	0.81
No	63 (44.7%)	78 (55.3%)	Reference	
Hypertension				
Yes	37 (40.2%)	55 (59.8%)	1.30(0.26, 6.62)	0.75
No	41 (45.1%)	50 (54.9%)		
Charlson's comorbidity index				
Low (0-1)	0 (0.0%)	8 (100.0%)	-	
Intermediate (2-3)	7 (30.4%)	16 (69.6%)	0.63(0.03, 13.82)	0.77
High (4-5)	9 (32.1%)	19 (67.9%)	1.02(0.07-14.88)	0.99
Very high (≥6)	57 (58.2%)	41 (41.8%)	Reference	
Number of drugs needing renal adjustment				
1	28 (54.9%)	23 (45.1%)	Reference	
2	18 (66.7%)	9 (33.3%)	1.34 (0.37, 4.83)	0.65
3 or more	32 (94.1%)	2 (5.9%)	13.78 (2.47, 76.74)	**0.003**
Classification of renal impairment				
Stage 3 (eGFR 30-59mL/min/1.73m^2)	17 (56.7%)	13 (43.3%)	Reference	
Stage 4 (eGFR 15-29mL/min/1.73m^2)	24 (75.0%)	8 (25.0%)	1.22(0.26, 5.74)	0.80
Stage 5 (eGFR <15mL/min/1.73m^2)	37 (74.0%)	13 (26.0%)	1.49(0.35, 6.46)	0.59

Table 3: Bivariate analysis of different factors versus outcome of admission for all patients with renal impairment

Variables	Died	Discharged	p-value
HIV status			
Negative	11 (6.0%)	59 (32.1%)	0.12
Positive	25 (13.6%)	62 (33.7%)	
Unknown	8 (4.3%)	19 (10.3%)	
Charlson's comorbidity index			
Low (0-1)	0 (0%)	9 (5.7%)	**0.026**
Intermediate (2-3)	1 (0.6%)	22 (13.9%)	
High (4-5)	8 (5.1%)	20 (12.7%)	
Very high (>5)	28 (17.7%)	70 (44.3)	
Dosage adjustment			
None adjustable drugs appropriately adjusted	10 (5.4%)	36 (19.6%)	0.24
Part of the adjustable drugs dose adjusted	12 (6.5%)	20 (10.9%)	
All adjustable drugs appropriately adjusted	6 (3.3%)	28 (15.2%)	
None of the drug needs adjustment of dose	16 (8.7%)	56 (30.4%)	
Hospital stay in days			
1-7	25 (13.6%)	49 (26.6%)	**0.02**
8-14	11 (6.0%)	40 (21.7%)	
≥15	8 (4.3%)	51 (27.7%)	
Severity of renal impairment			
Stage 3 (eGFR 30-59mL/min/1.73m^2)	17 (9.2%)	63 (32.1%)	0.72
Stage 4 (eGFR 15-29mL/min/1.73m^2)	10 (5.4%)	31 (17.4%)	
Stage 5 (eGFR <15mL/min/1.73m^2)	17 (9.2%)	46 (26.6%)	

Table 4: Multivariate analysis of different factors versus death of patients with renal impairment

Variables	Adjusted OR (95% CI)	p-value
HIV status		
Negative	Reference	
Positive	0.79 (0.17, 3.64)	0.76
Unknown	empty	
Charlson's comorbidity index		
Low-Intermediate(0-3)	Reference	
High(4-5)	12.68(1.37,117.14)	**0.025**
Very high(>6)	15.85(1.33, 188.78)	**0.029**
Dosage adjustment		
None adjustable drugs appropriately adjusted	Reference	
Part of the adjustable drugs dose adjusted	3.42(1.06, 11.003)	**0.039**
All adjustable drugs appropriately adjusted	1.03 (0.25, 4.24)	0.97
None of the drug needs adjustment of dose	1.51 (0.46, 5.03)	0.49
Hospital stay in days		
1-7	Reference	
8-14	0.41 (0.15, 1.11)	0.08
≥15	0.25 (0.09, 0.71)	**0.009**
Severity of renal impairment		
Stage 3 (eGFR 30-59mL/min/1.73m^2)	Reference	
Stage 4 (eGFR 15-29mL/min/1.73m^2)	0.50 (0.15, 1.66)	0.26
Stage 5 (eGFR <15mL/min/1.73m^2)	0.80(0.29-2.21)	0.67

Table 5: Subgroup analysis of factors associated with inappropriate dose adjustment among ESRD patients on dialysis (N=33)

Variables	Inappropriately adjusted	Appropriately adjusted	Adjusted OR (95% CI)	p-value
Gender				
Male	8	7	Reference	0.975
Female	8	10	1.05(0.05, 20.27)	
Age in years				
14-49	7	7	Reference	
50 or more	9	10	0.83(0.02, 37.56)	0.922
HIV status				
Negative	6	9		
Positive	10	6	Omitted*	-
Unknown	0	2		
Hospital stay in days	4	6		
1-7	6	3	Omitted*	-
8-14	6	8		
≥15				
Comorbid conditions	0	1	Omitted*	-
No	16	16		
Yes				
Diabetes				
Yes	5	3	2.06(0.05, 83.52)	0.701
No	11	14	Reference	
Hypertension				
Yes	14	12	17.71(0.44,	0.13
No	2	5	718.18)	
Charlson's comorbidity index	4	9	Reference	
Low-High(1-5)	12	6	4.37(0.20, 94.76)	0.35
Very high(>5)				
Number of drugs needing renal adjustment	9	3	Reference	
1	3	4	0.08 (0.002, 2.83)	0.17
2	4	1	0.22(0.002, 17.88)	0.50
3 or more				

*Omitted due to collinearity