

Comorbidities, Intradialytic Complications and Prescription Pattern among Patients with Chronic Kidney Disease on Maintenance Dialysis at Tertiary Hospital in Tanzania: A Descriptive Cross-Sectional Study

Rajabu H. Mnkugwe^{1*}, Shalifu Faraji¹, Jacqueline Shoo², Peter Kunambi¹, Kelvin Mwageni¹,
Dinna Gabriel¹, Irene Godlove¹, Joseph J. Madaha¹, Mohamed A. Khalfan¹, Tosi
Mwakyandile¹, Sabina Mugusi¹, Philip Sasi¹

¹Department of Clinical Pharmacology, School of Biomedical Sciences, Campus College of Medicine, Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania

²Renal Unit, Muhimbili National Hospital, Dar es Salaam, Tanzania

***Corresponding author:**

Dr. Rajabu H. Mnkugwe
Muhimbili University of Health and Allied Sciences
P. O. Box 65001,
Dar es Salaam, Tanzania
Email: rajabuhussein06@gmail.com

Abstract**Background**

Chronic kidney disease (CKD) is a major public health challenge and a widely prevalent non-communicable disease in both the developed and developing world. Patients with CKD on maintenance dialysis have been shown to present with different comorbidities and hemodialysis-associated complications that make them at risk of multiple drug prescriptions. We investigated comorbidities, hemodialysis-associated complications, and prescription patterns among patients with CKD on maintenance dialysis at a tertiary hospital in Tanzania.

Methods

This was a retrospective cross-sectional study conducted among 180 patients who attended maintenance dialysis service at the Muhimbili National Hospital dialysis unit from 01 January to 30 June 2022. A structured questionnaire was used to collect both sociodemographic and clinical data from the dialysis unit database. Prescription pattern was assessed by arranging medications to their first level of an anatomical main group according to the Anatomical Therapeutic Chemical (ATC) classification system.

Results

A total of 180 patients with CKD on maintenance dialysis were included in this study. The median age of study participants was 52 years (range 23-80 years), with male predominance (75.0%). The most common comorbidities were hypertension (35.2%), anaemia (21.6%), coronary artery disease (21.6%) and diabetes mellitus (12.7%). The major hemodialysis-associated complications observed include fatigue (34.5%), nausea and vomiting (17.9%), and headache (16.0%). Based on the Anatomical Therapeutic Chemical (ATC) classification system, drugs for the cardiovascular system were the most prescribed class of drugs (50.1%) followed by drugs for digestive and metabolic disorders (25.1%) and drugs for blood and blood forming organs (21.2%).

Conclusions

The majority of patients with CKD on maintenance dialysis have comorbidities and present with intradialytic complications. The prevalent comorbidities and complications observed in the study were hypertension and anaemia, and fatigue, nausea, vomiting, and headache, respectively. These findings underscore the critical need for comprehensive management of such patients, with a focus on cardiovascular health, as cardiovascular drugs were the most frequently prescribed.

Keywords: *Chronic Kidney Disease, Hemodialysis-associated complications, Prescription pattern, Dialysis, Tanzania.*

Introduction

Chronic kidney Disease (CKD) is a major public health challenge and a widely prevalent non-communicable disease in both developed and developing world (1-3). CKD remains one among the commonest reasons for hospitalization and clinic visit (4,5). CKD is reported to contribute nearly 850,000 deaths worldwide annually (6,7). The burden of CKD is high in Sub-Saharan Africa (SSA) due to the increase in unhealthy lifestyles, changes in the built environment, and rapid urbanization (1). The reported increase in these risk factors has led to an increase in number of individuals affected with CKD globally. In addition, limited resources and advanced treatment options such as Renal Replacement Therapy (RRT) keeps the African continent highly prevalent to end-stage renal disease (ESRD) (8). In Tanzania, a 7% prevalence of CKD has been reported in a community setting with a significantly higher prevalence in urban setting (15%) as compared to rural setting (2%) (8). A study conducted at the emergency medical department (EMD) and nephrology unit of Muhimbili National Hospital (MNH) (a tertiary hospital) in 2018 reported renal failure in 8.8% of screened patients (266 out of 3013). Of the 266 patients with renal failure, 195 (73.3%) had CKD and 41.7% had indications for dialysis (9).

The current most common causes of CKD include advanced age, hypertension, Human Immunodeficiency virus (HIV) and diabetes mellitus (DM) (7). ESRD is a serious complication of CKD and it requires RRT in the form of hemodialysis, peritoneal dialysis or renal transplantation as the mainstay of treatment (10). Of recent, in Tanzania, hemodialysis services have become more available and the number of patients with ESRD receiving hemodialysis as the mainstay supportive treatment has significantly increased (8). Renal transplantation as a definitive management of ESRD is also available but it is expensive and therefore, the service is limited to a few patients who can afford. Dialysis removes waste and excess water by transfer of uremic solutes from blood to an extracorporeal fluid (dialysate) by diffusion across a semi-permeable membrane (11). Previous studies have shown that solute removal via hemodialysis is relatively efficient and is usually done intermittently – typically three times per week. Peritoneal dialysis has been shown to be an alternative supportive treatment for patients with ESRD to hemodialysis but requires about 12–24 hours every day (11).

Patients with CKD on maintenance dialysis have been reported to present with various comorbidities (12,13). Some of these comorbidities such as hypertension and diabetes mellitus (DM) are also the independent risk factors of CKD (7). Hypertension, painful conditions (musculoskeletal pain such as arthralgia, osteoarthritis and carpal tunnel syndrome), anemia, ischaemic heart disease (IHD), DM, thyroid disorders and infections have

been reported as the most common comorbidities (14,15). Additionally, patients with CKD on maintenance dialysis are faced with different complications while on dialysis (16,17). Hypotension is the most common acute complication (18,19). Other complications include arrhythmias, nausea and vomiting, muscle cramps, headache, chest pain, back pain, fever, and chills (18). These complications can be either acute or chronic and are therefore managed differently according to their presentation. In addition, the complications can be recurrent and may be persistent in some patients interfering with well-being, and often needing clinician's consultation and prescription. Both comorbidities and hemodialysis-associated complications may necessitate a prescription (11), and because CKD patients are prone to multiple comorbidities with several consultations to different physicians resulting in multiple prescriptions, the likelihood of an individual patient being on many concomitant medications is high. Indeed, polypharmacy has been reported among patients with CKD (13). In CKD patients, preservation of residual renal function is of paramount importance, but at the same time, some medications that the patient may be using can cause further deterioration of the remaining kidney function (20) and some may interact negatively with each other. Additionally, in view of the critical role of the kidney in drug clearance, patients with CKD are at higher risk of experiencing drug-related complications that may be associated with increased hospital stays, visits and health care costs (21,22). Hence, drug therapy in patients with CKD needs optimal dosages, and careful review and monitoring of all prescribed medications in order to avoid toxicity and disease severity (23) and thus improved treatment outcome and quality of life among patients with CKD. These strategies call for regular tracking of prescriptions patterns in this population.

Despite the reported increase in the burden of CKD globally, studies to assess comorbidities, hemodialysis complications and prescription pattern among patients with CKD on maintenance dialysis are scarce in developing countries including Tanzania. This may be partly because renal replacement therapy is relatively new in these countries. The present study reports on commodities, hemodialysis complications and prescription pattern among patients with CKD on intermittent hemodialysis.

Methods

Study Area

This study was conducted at the dialysis unit of the Muhimbili National Hospital (MNH), the National referral hospital located in the Eastern Zone of Tanzania in the capital city of Dar es Salaam. MNH receives referral patients from both public and private hospitals from all over the country. Patients with kidney failure/CKD are attended at the nephrology unit through

emergency department (EMD) or out-patient department (OPD) clinics. The nephrology unit runs a weekly outpatient clinic every Wednesday for CKD patients with approximately 50 patients who are at different kidney disease stages being attended per day. By June 2022, the units had about 300 to 350 patients who were on maintenance dialysis. Staffing of the clinic and dialysis unit includes a team of five consultant physicians, two resident physicians/nephrology fellows, three registrars, fifteen nurses, and four nursing assistants. The unit has about 52 hemodialysis machines and carries dialysis as part of both inpatient and outpatient care with an average of 100 dialysis sessions per day. For most patients, dialysis is done three times a week and a few have two sessions of dialysis per week and each session is four hours.

Study design and population

This was a retrospective cross-sectional study conducted between 1st January and 30th June 2022 among 180 adult patients with CKD on maintenance hemodialysis. The study included adult patients with CKD aged 18 years and above on maintenance hemodialysis at Muhimbili Dialysis Unit receiving care during the study period. Patients with incomplete information and duplicate medical records were excluded from the study.

Data collection tool and procedures

A study specific data extraction checklist was used to collect information for each participant from the Muhimbili Dialysis Unit medical records system. The data checklist was designed to capture both sociodemographic and clinical information including age, sex, drug prescribed, associated comorbidities and complications associated with dialysis.

Information on prescribed drugs and specific patient's comorbidities were obtained from the system's database and filled into the checklist. Thereafter, each prescribed medication was arranged to its first level of an anatomical main group according to Anatomical Therapeutic Chemical (ATC) classification system (24).

Thereafter, these patients' clinical conditions and disease were classified by using the International Classification of Disease version 11 (ICD 11) (25). Hypertension was defined as a blood pressure of ≥ 140 mmHg systolic blood pressure and/or ≥ 90 mmHg diastolic blood pressure and/or current or history of using antihypertensive drugs and/or diagnosed with hypertension. We defined intradialytic hypertension as an increase in blood pressure during or immediately after hemodialysis. Diabetes mellitus was defined as a current or history of diagnosis of diabetes mellitus and/or current or history of using antidiabetic drugs. Anaemia was defined as haemoglobin concentration of < 11 g/dL. Other associated comorbidities such as coronary artery diseases, infections, blindness and liver diseases were also recorded from

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patient's medical records. Similarly, hemodialysis-associated complications were also obtained from the database and filled into the checklist. Assessed complications included but not limited to intradialytic hypertension, hypotension, nausea and vomiting, muscle cramps, headache, chest pain, back pain, fever, and chills. These complications were recorded into the database by the attending clinicians after the hemodialysis session ends.

Data management and statistical analysis

The collected data were entered into IBM SPSS Statistics for Windows, version 28.0 (SPSS, IBM Corporation, Armonk, NY, USA) for analysis. Descriptive statistics were used to summarize the data. Continuous variables were presented as mean $\pm$ standard deviation (SD) or median (IQR) depending on the normality of data, while categorical variables were presented as frequency and percentages.

Results**Sociodemographic and clinical characteristics**

A total of 180 out of 221 screened patients were enrolled into the study (Figure 1). The median age of studied population was 52 years (range 23-80 years) and most patients were aged between 50 and 69 years. Males accounted for the majority of study participants (75.0%). Most of the patients were attending three sessions of dialysis per week (57.2%). Table 1 summarizes the sociodemographic and clinical characteristics of study participants.

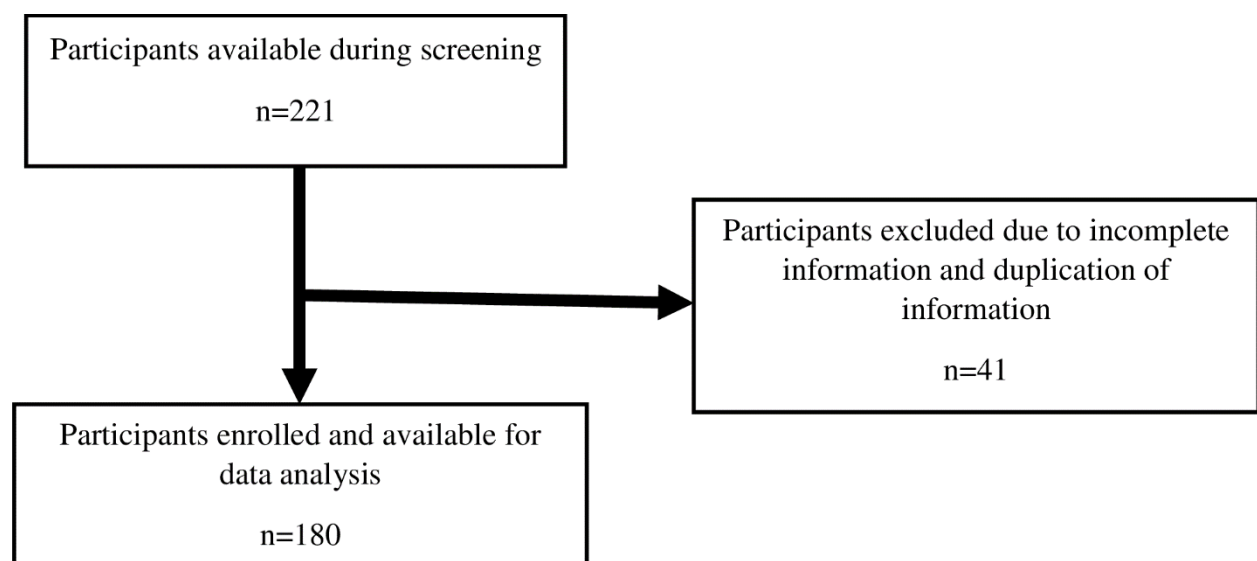


Figure 1. Study flow chart

Table 1: Sociodemographic and clinical characteristics

Variable	Category	Frequency (n)	Percentage (%)
Age	18-49	80	44.4
	50-69	89	49.4
	>70	11	6.2
	Median (IQR)		52 (40 – 63)
Sex	Male	135	75
	Female	45	25
Number of dialysis session per week	Two	77	42.8
	Three	103	57.2

Drugs prescription pattern

Based on the ATC classification system, drugs acting on the cardiovascular system were the most prescribed (50.1%), followed by alimentary tract and metabolism (25.9%) and blood and blood forming organs (21.2%) (Table 2).

Table 2: Drugs prescription pattern based on the ATC classification system

ATC class	Frequency (n)	Percentage (%)
Cardiovascular system	360	50.1
Blood and blood forming organs	152	21.2
Alimentary tract and metabolism	186	25.9
Nervous system	10	1.4
Anti-infective for systemic use	7	1.0
Genito-urinary system sex hormones	2	0.3
Antineoplastic and immunomodulating agents	1	0.1

Among drugs acting on the cardiovascular system, calcium channel blockers were commonly prescribed (47.2%) followed by antihypertensive drugs (31.7%) and beta blocking agents (9.7%). For alimentary and metabolism, vitamins were highly prescribed (66.7%) followed by drugs used in diabetes (26.3%) and Drugs for acid related disorders (5.4%) (Table 3).

Table 3: Class of drug prescribed

Drug class	Frequency (n)	Percentage (%)
Cardiovascular system		
Antihypertensives	114	31.7
Agents acting on the renin-angiotensin system	11	3.1
Beta blocking agents	35	9.7
Calcium channel blockers	170	47.2
Diuretics	27	7.5
Lipid modifying agents	3	0.8
Blood and Blood Forming Organs		
Antianemic preparations (such as Iron, vitamin B12, folic acid preparations and erythropoietin)	152	100.0
Alimentary Tract and Metabolism		
Drugs used in diabetes	49	26.3
Vitamins	124	66.7
Drugs for acid related disorders	10	5.4
Stomatological preparations	1	0.5
Antidiarrheals, intestinal anti-inflammatory/anti-infective agents	2	1.1
Anti-infective for Systemic Use		
Antivirals for systemic use	1	14.3
Antimycobacterial	4	57.1
Antibacterial for systemic use	2	28.6
Nervous System		
Analgesics	10	100.0
Genito Urinary System and Sex Hormones		
Urological	2	100.0
Antineoplastic and Immunomodulating Agents		
Antineoplastic agents	1	100.0

Based on individual drugs, nifedipine (13.9%), amlodipine (10.1%), hydralazine (13.7%), carvedilol (2.7%) and furosemide (3.3%) and alpha-2 agonist clonidine (1%) were mostly prescribed cardiovascular drugs while calcitriol 15.5%), insulin (4.2%), and vitamin B-complex (2.24%) were the common prescribed drugs that acts on alimentary canal and metabolism. Drugs acting on blood and blood forming organs included erythropoietin (4.21%), ferrous

sulphate (4.8%) and folic acid (12.2%). Figure 2 presents the most common drugs prescribed among study participants.

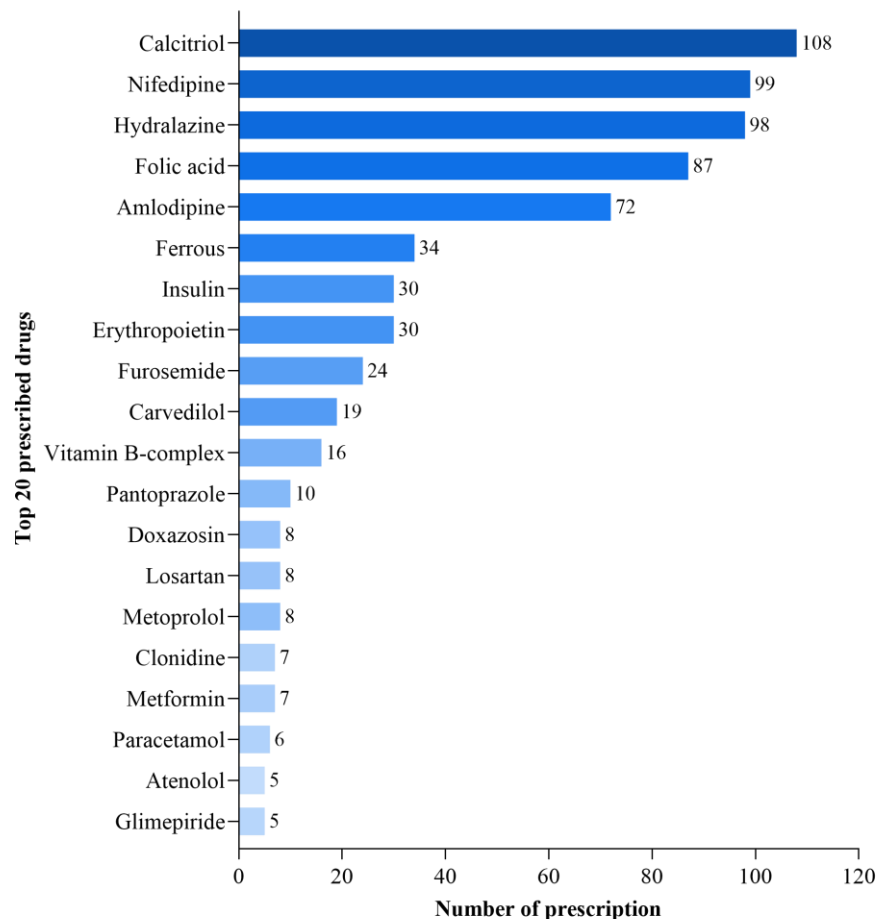


Figure 2. Top 20 most prescribed drugs among patients with CKD on maintenance hemodialysis

Comorbidities among patients with CKD on maintenance dialysis

Most frequent observed comorbidities among study participants were hypertension (35.2%), followed by coronary arterial disease (21.6%) and anemia (21.6%). CKD patients with Diabetes mellitus accounts about (12.7%) and urinary tract infections (2.2%) (Figure 3).

Complications during dialysis

In this study, fatigue was the most commonly reported intra-dialytic complication followed by nausea and vomiting and headache. Other complications observed were muscle cramps, chest pain fever, itching and hypotension (Figure 4).

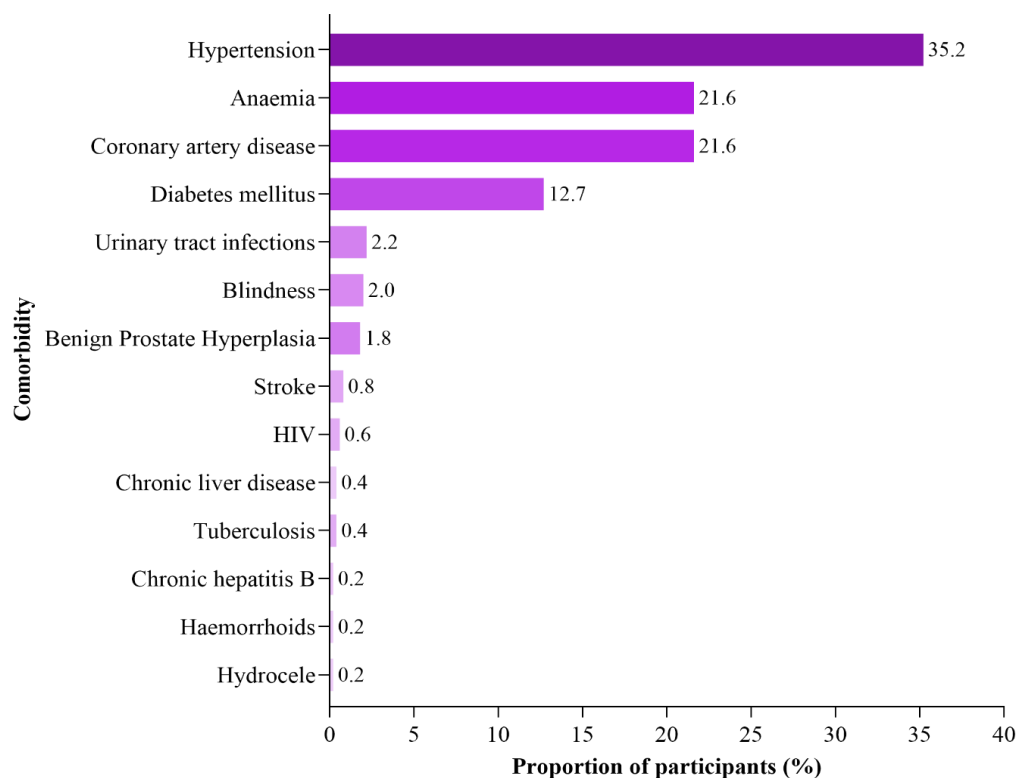


Figure 3. The common comorbidities among patients with CKD on maintenance hemodialysis

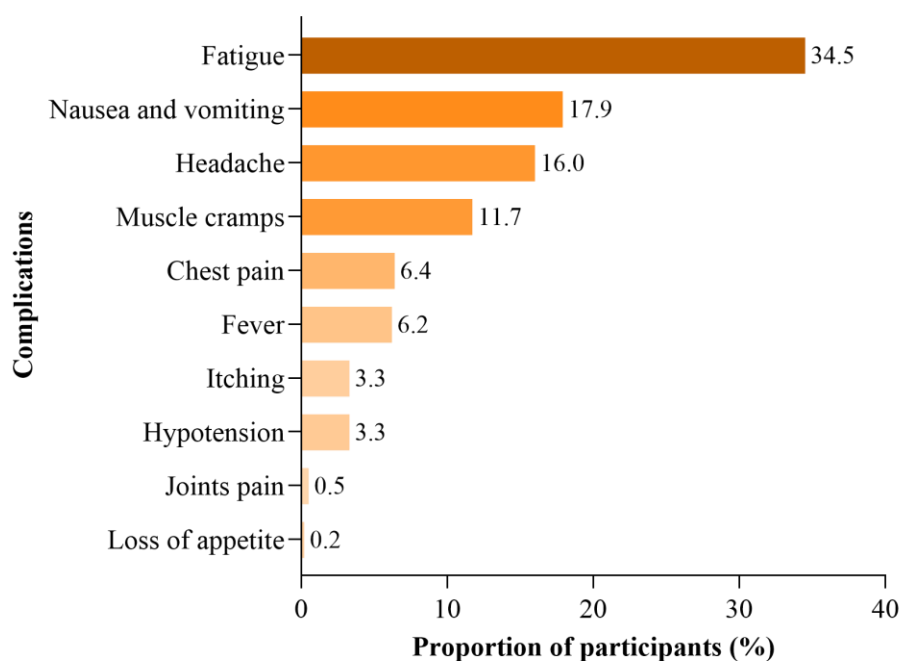


Figure 4. The common intradialytic complications among patients with CKD on maintenance dialysis

Discussion

This study was aimed at investigating the comorbidities, hemodialysis complications and pattern of drugs prescription among patients with CKD on maintenance dialysis attending a tertiary hospital in Tanzania. Prescription pattern was assessed by arranging prescribed drugs to its first level of an anatomical main group according to the Anatomical Therapeutic Chemical (ATC) classification system (24). Our major findings indicate that (i) drugs acting on cardiovascular (50.1%) and alimentary canal and metabolism (25.9%) were the most prescribed drugs, (ii) calcium channel blockers, antihypertensive and beta blocking agents were the commonly prescribed cardiovascular drugs while vitamins and drugs for acid related disorders were commonly prescribed drugs acting on alimentary canal and metabolism. Based on individual drugs, calcitriol (15.5%) nifedipine (13.9%) and hydralazine (13.7%) were the most prescribed. Hypertension, coronary arterial diseases and anaemia were the commonly observed comorbidities while fatigue, nausea and vomiting and headache were the commonly observed hemodialysis complications.

In our study, drugs acting on the cardiovascular system and alimentary canal and metabolism accounted for the highest percentage of prescriptions. Similar findings have been reported in previous studies where drugs acting on cardiovascular system were highly prescribed (6,26-28). Despite the similarity in findings, the percentage differences from the current study to other studies may be due to variations in the sample size and study population, comorbidities, and differences in prescribing patterns among physicians. It has been reported previously that drug prescriptions in patients with CKD may vary with physician's perspective, disease conditions, and population (11). In Tanzania, a drug formulary book to guide prescription among patients with kidney failure has been recently been launched. However, it is not routinely available in the clinics. Therefore, physicians are prescribing using their experience and some are adopting guidelines developed by National Kidney Foundation (NKF)'s Kidney Disease Improving Global Outcome (KDIGO) (29), Advance Care Planning (ACP) in CKD (30), Canadian Society of Nephrology (CSN) (31), and National Institute for Health and Clinical Experience (NICE) (32), which have been prepared for use in the setting of the developed world.

Among cardiovascular drugs, calcium channel blockers (CCB) were the most commonly prescribed drugs in the present study, followed by antihypertensive drugs and beta-blocking agents. Similar findings have been reported by Kamath L *et al.*, where CCB and antihypertensive drugs were commonly prescribed among patients with CKD attending Krishna Rajendra Hospital, Mysore India (6). Our findings are in disagreement with finding from Ahlawat R *et al.*, and Article O *et al.*, who reported that diuretics were the most commonly prescribed

drugs among Indians with CKD on maintenance dialysis (26,33). The observed difference may be due to the study populations whereby our study may have recruited more anuric patients. Among the cardiovascular agents in this study, the most frequently prescribed drugs were nifedipine and hydralazine, followed by amlodipine, furosemide and carvedilol. Almost a similar pattern has been reported in a study conducted by Pothen C *et al.*, in India (7). With regards to drugs acting on the alimentary canal and metabolism, calcitriol was the most commonly prescribed drug in our study, similar to what was reported in previous studies (6,26). Calcitriol, which is active vitamin D is used commonly in CKD patients for treatment and prevention of metabolic bone diseases because they cannot produce active vitamin D. Drugs acting on blood and blood-forming organs, folic acid was the most frequently prescribed, followed by ferrous sulphate and erythropoietin. Similar prescription pattern was reported previously by Kamath L *et al.*, and Ahlawat R *et al.*, (6,26). In this study, erythropoietin prescriptions were fewer compared to iron and folic acid this may be because it is expensive and may not be affordable to most patients. In the African setting, a study conducted among adult patients with CKD in Lagos, Nigeria showed a similar profile of prescribed medications to include furosemide heparin, lisinopril, oral calcium carbonate, α -calcidiol, erythropoietin, intravenous iron sucrose, amlodipine, hydrochlorothiazide folic acid and oral ferrous sulfate (34). Oral hypoglycemic agents like glimepiride was infrequently prescribed compared to insulin and this is because most patients with CKD stage 5 are shifted from oral hypoglycemic drugs to insulin to avoid hypoglycemia and other metabolic complications (35).

Monitoring of drug prescription among patients with CKD remains crucial because of several reasons; (i) CKD can significantly affect the pharmacokinetics and pharmacodynamics of many drugs and therefore, impaired kidney function can alter drug metabolism and clearance, leading to either poor therapeutic efficacy or potential drug toxicities. Monitoring prescription patterns allows clinicians to adjust drug dosages based on the patient's characteristics including renal function to ensure optimal therapeutic outcomes, (ii) preventing drug-related complications by closely monitoring prescription patterns, where clinicians can identify and avoid potentially harmful drug interactions that could worsen the patient's condition, (iii) managing comorbidities, and (iv) promoting medication adherence. Therefore, Clinicians play a critical role in ensuring safe and effective pharmacological management among patients with CKD as a vulnerable population.

Our results on prescription pattern go hand in hand with observed comorbidities in the studied population, and this is similar to previous studies. In the present study, the most frequently observed comorbidities among CKD patients were hypertension, coronary arterial disease,

anemia, and diabetes mellitus. Among the complications of CKD, cardiovascular complications appear to be prevalent and also are the major causes of death and it is not surprising that the drugs for such complications being the highest prescribed. Similar findings have been reported by a study conducted by Pothen C *et al.*, where most common comorbidities were hypertension, anemia, diabetes mellitus, and coronary artery disease (7). In other studies conducted by MacRae C *et al.*, and Al-Ramahi R *et al.*, a comparable pattern of comorbidities were reported where hypertension coronary artery disease and diabetes mellitus were the commonest (15,21). In Africa, a study conducted in Cameroon reported a similar pattern of comorbidities among patients with CKD including hypertension, diabetes mellitus. HIV, Hepatitis B, hyperuricemia, obesity, previous cardiovascular events, malnutrition and anaemia to be the commonest comorbidities associated with CKD patients (36). The observed and reported predominance of hypertension as the most commonly occurring comorbidity may be explained by the fact that the renin-angiotensin system is affected in CKD patients, which plays a role in controlling blood pressure (26).

In our study, fatigue was the most common observed intradialytic complication, followed by nausea and vomiting and headache. Other complications observed included muscle cramps chest pain, fever, itching, and hypotension. A similar profile of intradialytic complications has been reported previously by Raja SM *et al.*, and Ali M *et al.*, where hypotension, nausea and vomiting, hypertension, muscle cramps, and headache were reported (18,37). In sub Saharan Africa, a study conducted in Eritrea reported a similar pattern of intradialytic complications including hypotension nausea and vomiting, hypertension, muscle cramps and headache, back pain, chest pain, fever, chills and itching (37). Despite a similar profile of intradialytic complications between our study and previous studies, the observed difference in individual complication prevalence may be attributed to differences in the types of dialysis, comorbidities, dialysis sessions attended and age of the patients.

Despite the fact that the present study indicates that the prescription pattern is similar to previous studies conducted locally and in other settings and aligns with the observed comorbidities, this study did not investigate whether the prescription given were appropriate or not. This stands as a limitation to our study. However, the study provides current data regarding prescription pattern in relation to comorbidities among patients with CKD. Furthermore, the present study highlights the need for closely monitoring of prescription to this special population where administered drugs can further harm the patient.

Conclusion

Majority of patients with CKD on maintenance dialysis have comorbidities and presents with intradialytic complications. The prevalent comorbidities observed in the study were hypertension and anaemia while intradialytic complications observed were fatigue, nausea, vomiting, and headache. Drugs acting in the cardiovascular system were the most frequently prescribed among patients with CKD on maintenance hemodialysis.

Declarations**Ethics considerations**

Ethical clearance to conduct this study was granted by the Muhimbili University of Health and Allied Sciences Institutional Review Board (IRB) (Ref No. DA.282/298/01L/51) and further permission to conduct the study was obtained from the Muhimbili National Hospital IRB and the Dialysis Unit (Ref No. MNH/CRTCU/Perm/2023/211). Written informed consent was obtained from each participant after going through the study consent information sheet with the participant and addressing all the participant's questions and concerns. Study participants' identifier information such as names were not documented for anonymity and confidentiality.

Authors' contributions

RHM and SHF participated in the study design and protocol development; RHM, SHF and JGS data collection; RHM, SHF, JGS, PK, KM, DG, IG, JM, MAK, TM, SM and PS formal data analysis and interpretation; RHM wrote the original draft; RHM, SHF, JGS, PK, KM, DG, IG, JM, MAK, TM, SM and PS review and editing of the manuscript; all authors have read and approved the final version of the manuscript.

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Conflict of interest

The authors declare no conflict of interest

Data availability

All relevant data presented in this work are contained within the manuscript.

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