MEDICATION ERRORS AMONG PATIENTS ADMITTED WITH CARDIOVASCULAR DISORDERS AT THE CRITICAL CARE UNIT OF KENYATTA NATIONAL HOSPITAL

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A dissertation submitted in partial fulfilment of the requirements for the award of the Degree of Master of Pharmacy in Clinical Pharmacy, School of Pharmacy, University of Nairobi.

Department of Pharmaceutics and Pharmacy Practice

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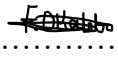
2. Signature……  ……Date…17th November, 2021…

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DEDICATION

I dedicate this write up to my parents, Mr. and Mrs. Ngovi for their support and prayers in my academic journey. I also dedicate this dissertation to my husband, son and siblings for their prayers and support.

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ACRONYMS AND ABBREVIATIONS

ACS:	Acute Coronary Syndrome
ACEI:	Angiotensin-Converting Enzyme Inhibitors
ADE:	Adverse Drug Event
ADHF:	Acute Decompensated Heart Failure
ADR:	Adverse Drug Reaction
AKI:	Acute Kidney Injury
ARB:	Angiotensin II Receptor Blockers
ARDS:	Acute Respiratory Disease Syndrome
ASHP:	American Society of Hospital pharmacist
CCB:	Calcium Channel Blockers
CCU:	Critical Care Unit
CHF:	Congestive Heart failure
CKD:	Chronic Kidney Disease
CVA:	Cerebrovascular Accident
CVD:	Cardiovascular Disorder
CVS:	Cardiovascular System
DCM:	Dilated Cardiomyopathy
DKA:	Diabetic Ketoacidosis
DM:	Diabetes Mellitus
DVT:	Deep Venous Thrombosis
HIV:	Human immunodeficiency virus
HTN:	Hypertension

IE:	Infective Endocarditis
KNH/UON-ERC:	Kenyatta National Hospital /University of Nairobi Ethics and Research Committee
KNH:	Kenyatta National Hospital
MCCU:	Medical Critical Care Unit
MI:	Myocardial infarction
MICU:	Medical Intensive Care Unit
NCCC MERP:	National Coordinating Council for Medication Errors and Reporting Programme
PCNE:	Pharmaceutical Care Network Europe
pDDI:	Potential Drug-Drug Interaction
PE:	Pulmonary Embolism
PTE:	Pulmonary thromboembolism
RHD:	Rheumatic Heart Disease
RVD:	Retroviral Disease
STEMI:	ST-Elevation Myocardial Infarction
SVT:	Supraventricular Tachycardia

OPERATIONAL DEFINITIONS

Adverse drug reaction: considers if the patient has a medical condition as a result of an adverse drug reaction

Cardiovascular disorder: Refers to conditions that affect the function of the heart, or its structures

Drug interactions: considers if the patient has a medical condition as a result of drug-drug or drug-food interactions. These interactions vary in their significance.

Drug use without indication: considers if a patient is taking a drug that has no valid indication

Failure to receive drugs: considers if a patient had a medical condition that is a result of not receiving a drug. This may be due to poor administration technique, poor adherence, sub-standard drug, missed doses, non-availability of prescribed drugs or inability to afford the medication

Improper drug selection: this considers if the patient has a medical condition, but a wrong drug is being taken. It considers if the most suitable drug has been chosen for treating the patient's condition.

Overdosage: considers if too much amount of correct drug is being taken. It also incorporates the period of treatment.

Sub-therapeutic dose: considers if the amount of drug being taken is insufficient for treatment of the targeted condition.

Untreated indication: any untreated condition the patient has and could benefit from drug therapy. However, it is important to separate an indication from an adverse drug effect. For example, diarrhoea may be due to the use of antibiotics.

ABSTRACT

Background: Drugs used to treat cardiovascular disorders are associated with the highest rates of medication errors. Patients in the cardiovascular critical care unit (CCCU) are inherently predisposed to high mortality and morbidity rates owing to complex management approaches and deranged physiological parameters. Studies on medication errors in the cardiovascular critical care unit are few, particularly in resource-limited settings.

Broad Objective: To identify and classify medication errors and the risk factors for such errors among patients with cardiovascular disorders at the CCCU.

Methods: A prospective cohort study was conducted. Patients' prescriptions at Kenyatta National Hospital (KNH) CCU wards were reviewed. Approval for this study was granted by the KNH/UoN Ethics Review Committee. Forty patients were selected through convenient sampling. A pre-designed questionnaire was used to extract on patient's sociodemographic and clinical characteristics from their files. Fischer's exact or Pearson's Chi-square tests established the association between the predictor variables and the medication errors. A regression analysis identified the independent predictors of medication errors at $P<0.05$.

Results: Most participants were female (n=22, 55.0%), unemployed (n=30, 75.0%) and admitted through the outpatient department (n=20, 50.0%). The mean age was 47.7 (S D: 15.4) years and the average duration of admission was 7.6 (S D: 3.9) days.

Ninety-seven prescriptions were reviewed from which 74 medication errors were identified. Most patients had at least one error (n=38, 95.0%). The main types of errors were potential drug-drug interactions (n=37, 92.5%) and drug choice problem error

(n=18, 45.0%). Patients with Acute kidney injury were 10.3 times more likely to have an adverse effect compared to those without (p=0.012). Additionally, being employed reduced the odds of an adverse event by 0.3 (p=0.006).

Conclusion: Critically ill patients with cardiovascular disease and acute kidney injury are at high risk of developing adverse drug events. Therefore, they require frequent medication reviews, dose adjustment and close monitoring by pharmacists.

CHAPTER ONE: INTRODUCTION

1.1 Background

According to World Health Organization (WHO), cardiovascular diseases are the leading cause of death across the globe, with a mortality rate of 17.7 million people in 2015 (1). Cardiovascular related deaths represent 31% of all global deaths, and most of the deaths (80%) are as a result of coronary heart diseases and stroke (1). It is estimated that more than 75% of these CVD-related deaths happen in middle-and-low income countries. Sub-Saharan Africa contributed to 5.5% of the CVD deaths, and the number is projected to rise in future (2). In Kenya, CVDs contribute to 25% of all hospital admissions and 6–8% of overall mortality, with about 13% of autopsies revealing the cause of death as a CVD (3). This makes CVD the second leading cause of death after maternal, perinatal and infectious diseases. This clinical picture is aggravated by the fact that cardiovascular medications are associated with the highest rate of medication errors (4,5).

The ADE Prevention Study Group established that the odds of serious ADEs with cardio-vascular medications was 2.4 times that of other classes of drugs (4). A study found that of 182 deaths due to cerebrovascular accidents, myocardial infarction and pneumonia, between 14 and 27% of deaths might have been preventable (6). For deaths attributed to MI, preventable deaths reflected errors in management, as opposed to diagnosis. The most common cause of preventable deaths was medication errors and toxicity (6). This illustrates the propensity of cardiovascular medications to cause medication errors in both inpatient and outpatient settings.

The United States National Coordinating Council for Medication Error Reporting and Prevention defines a medication error as *"any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing, order communication, product labelling, packaging, and nomenclature, compounding, dispensing, distribution, administration, education, monitoring, and use"* (7). This definition implies that medication errors can be prevented at different levels.

Medication errors contribute to 78% of serious medical errors in the critical care setting (8), and they also contribute to 2 in every 1000 deaths (9), making it a serious public health concern. Delivering a single drug to a hospitalized patient requires the execution of 80 -100 steps. The hospital-based medication use process is grouped into 5 broad steps: prescription, transcription, preparation, dispensing and administration (8). A medication error is an error that occurs at any of the above-mentioned steps, with or without accompanying adverse consequences. The majority of the errors happen at the administration stage, which accounts for 53% of all errors, followed by the prescribing stage (17%), then preparation (14%), and transcription (11%) (8). For instance, in the United States critical care setting, it is estimated that patients experience on average 1.7 medical errors per day, and all patients experience a life-threatening error in the course of their stay at the critical care units.

In Africa, a systematic review carried out in 2016 reported that approximately one in every twelve patient admissions were due to adverse drug events. Additionally, adverse

drug events accounted for 1.5 to 6.3% of adult admissions, but a lower rate in paediatric admissions at 0.6% (10) (8). A study done by Nassali et al. in 2016 in Kenyatta National Hospital determined that the prevalence of medication errors was 45% (11). Most of these errors were due to inappropriate duration of prescribing (71.2%).

The rate of medication errors among patients admitted to critical care is higher than that of those admitted in the general medical ward (12). Most medications in the critical care unit are administered intravenously, which requires the calculation of weight-based doses, dilution and infusion rates. This creates opportunities for error. Additionally, patients in the CCU receive more medications compared to patients in the general medical wards. In the CCU, patients also have a reduced physiological reserve, increasing their risk of being harmed by medications. Notably, most patients in the CCU are comatose and are therefore not able to identify the medical errors themselves (12). Furthermore, these patients receive complex drug therapies, frequent interventions and are likely to have other comorbidities (13).

Medication errors can be classified using different methods. The different methods are not mutually exclusive, and the method used depends on the setting and the objective of the classification. One approach is to classify the errors based on the stage in which it occurs in the medication process. These errors include prescribing, transcribing, dispensing, administration and monitoring errors. A different approach is based on describing the type of error, for example, wrong medication, wrong formulation, wrong route of administration, and wrong frequency. The errors could be based on whether they occur during clinical decision making, for example, rule-based or knowledge-based

mistake. They can also be based on whether they occur during the implementation stage, such as action-based errors, for example, memory-based errors or slips, for example, lapses. Medication errors can also be classified based on their level of severity (7).

Classification systems for the identification and categorization of medication errors include the Hepler & Strand, the National Coordinating Council for Medication Errors and Reporting Programme (NCC MERP) and the Pharmaceutical Care Network Europe (PCNE) (14). The Hepler and Strand classification is based on the understanding that drugs are administered to ameliorate a patient's standard of life. However, there is a possibility of outcomes that can cause a reduction in the quality of life. The Pharmaceutical Care Network Europe (PCNE) classification separates the problem from its cause and has four sections: problem, cause, intervention and outcome (15). The NCC MERP is the most commonly used classification, and it provides a standard categorization of medication errors, which are used in combination with systems analysis in recording and tracking medication errors (14).

Medication errors are a universal problem, and they contribute to a large proportion of patient harm. The burden of medication errors in Africa, and by extension Kenya, is unclear due to the lack of rigorous studies that comprehensively capture the errors (10).

1.2 Problem Statement

Medication errors are a notable cause of mortality and morbidity. Even though only 10% of the medical errors cause adverse drug events, these errors have significant repercussions on the health care providers, the patients and their families. The Institute of

Medicine (IOM) report indicates that 44,000 to 98,000 patients lose their lives annually due to medical errors (8). Approximately 19% of CCU medication errors are considered life-threatening, and 42% are considered clinically relevant with the patients requiring additional life-sustaining treatments (8). Medication errors also cause a societal and human burden, with some resulting in prolonged hospital stays, increased treatment costs and inability to recover to premorbid status (8). It is estimated that in the United States, medical errors cost more than 4 billion dollars per year, with hospital costs of approximately 3.5 billion dollars (16).

Medication errors come with substantial undesirable psychological impact. They erode the public, family and patients' confidence in the healthcare system (17,18). The effect of medication errors on health care providers is often not considered. There exists a professional and personal responsibility on health care providers, and expectations around these responsibilities carry a great burden and weight. Physicians suffer a barrage of emotions of doubt, loss of sleep, self-blame, anxiety, loss of confidence, embarrassment, guilt and remorse after making errors. They may also face the consequences such as suspension, criminal prosecution, probation and even termination of employment (19).

It seems logical to expect a high prevalence of medication errors in critical care units because it is a busy and stressful environment, and it is characterized by complexity and frequent pharmacotherapeutic interventions. The data on the prevalence of medication errors appears to vary widely between patient populations, clinical settings and between studies. Errors have been reported to occur in roughly 6% of all medical use occasions. Among the critically ill patients, the rate of errors ranges from approximately 1.2 to 947

errors for every 1000 patient CCU days, with a median of 106 errors for every 1000 CCU days (8).

A Kenyan study in 2016 on adherence to the principles of rational use of medications in Kenyatta National Hospital (KNH) determined the overall prevalence of irrational prescribing practice to be 95.6%. The prevalence of medication errors was 45%, with inappropriate duration (71.2%) being the most common error.

Despite the high prevalence of medication errors and their adverse outcomes, most of them are considered preventable with ordinary standards of care. Identifying the types of medication errors, their prevalence and risk factors play a critical role in planning for mitigation. Most institutions have no processes to capture the extent of medication errors and hence rely on voluntary reporting through a reactive model, which is triggered by the occurrence of an adverse patient outcome. Kenyatta National Hospital has a system for medication error reporting which relies on voluntary reporting. Proactively identifying the problem areas in the medication use process and identifying the high-risk population can promote the safe use of medicines in the critical care unit (20). The Pharmacy and Poisons Board (PPB), through the Ministry of Health, developed a pharmacovigilance system, which focuses on reporting adverse drug reactions (21). Recently, a medication reporting error form was also established.

There is a paucity of epidemiological data with regard to the type, prevalence and risk factors of medication errors in cardiovascular critical care in developing countries, including Kenya (22). This study has not been done in KNH, which one of the leading tertiary hospital in Kenya. Proactive determination of errors in the CCU for

cardiovascular patients will improve patients' safety by identifying patients at the highest risk and the most implicated medications. This information provides a basis upon which health care workers can be more vigilant in identifying and preventing medication errors. Besides filling in the literature gap on cardiovascular CCU practices in limited resources settings, findings from this study can assist the institution in tailoring its policies according to the gaps identified in the medication process.

1.3 Objectives

1.3.1 Main Objective

The study aimed to identify and classify medication errors occurring among cardiovascular patients admitted to the critical care unit at Kenyatta National Hospital. In addition, the prevalence and risk factors for selected errors were also identified.

1.3.2 Specific Objectives

The study was done among patients with CVS disorder admitted to the KNH critical care to:

1. Determine the prevalence of medication errors
2. Determine the types of medication errors
3. Identify the risk factors for medication errors

1.3.2 Research Questions

1. What is the prevalence of medication errors among patients with cardiovascular disorders admitted to the KNH critical care unit?

2. What types of medication errors occur among patients with cardiovascular disorders admitted to the KNH critical care unit?

3. What are the risk factors for selected medication errors among patients with cardiovascular disorders admitted to the KNH critical care unit?

1.4 Justification

Literature on medication errors in African hospitals, specifically the critical care unit, is scarce. Nonetheless, the few studies that have been done have reported high rates of medication errors, particularly the prescribing stages (10). Medication errors come with the burden of increased health care costs, exposing health providers to litigations, loss of trust in the healthcare systems, psychological harm to the healthcare providers, and increased morbidity and mortality. Therefore, there is a need for a study to quantify the errors, describe them, and determine the risk factors for medication-related errors. This information will provide a starting point for identifying the systematic weakness in the healthcare system and help in finding viable solutions to reduce the recurrence of similar errors in future.

This study will be of benefit to the healthcare workers and, by extension, the critical care unit patients. The study will help in the identification of high-risk drugs that are most prone to medication errors. Additionally, through the identification of risk factors, the healthcare workers will gain better knowledge in assessing the patient's risk category, hence highlighting the need to be more cautious when medicating them. Recommendations on the use of less risky drug alternatives will be made to assist the clinicians in making better clinical decisions.

The study identified knowledge gaps in the clinical practice that could be propagated the occurrence of medical errors. This will advise the institution on the areas that they need to train their staff on and sensitize them on the need to mitigate the recurrence of errors.

Additionally, the findings will inform policy making in the institution on the need to develop protocols that can systematically reduce medication errors.

The Joint Commission on Accreditation of Health Care Organization emphasizes the need for analysis of error reports to prevent future errors through implementing additional safety standards (23). This study will provide local data upon for the quality assurance personnel in KNH to reflect on the current practices and review them with the aim of enhancing the quality of care provided.

CHAPTER TWO: LITERATURE REVIEW

2.1 Classification of Medication Errors

There exist many systems of classifying drug-related problems, for example, the National Coordinating Council for Medication Errors and Reporting Programme (NCC MERP), which is the most commonly used system (14). This system was adopted on July 16th, 1996, when the Council realized the need for a standardized method of categorizing errors. The Council adopted the Medication Error Index, which classifies errors based on the severity of the outcome (24). The system also considers if a patient was harmed, and if yes, to what extent (24) (Table 1).

Table 1: NCC MERP classification of a medication error and risk assessment index (27)

Category	Description of category
No error	
A	Circumstances or events that have the capacity to cause error
Error, no harm	
B	An error occurred, but the medication did not reach the patient
C	An error occurred that reached the patient but did not cause patient harm
D	An error occurred that resulted in the need for increased patient monitoring but no patient harm
Error, harm	
E	An error occurred that resulted in the need for treatment or intervention and caused temporary patient harm
F	An error occurred that resulted in initial or prolonged hospitalization and caused temporary patient harm
G	An error occurred that resulted in permanent patient harm
H	An error occurred that resulted in a near-death event (e.g., anaphylaxis, cardiac arrest)
Error, death	
I	An error occurred that resulted in patient death

KEY: NCC MERP - National Coordinating Council on Medical Error Reporting and Prevention

Another classification system is the Hepler & Strand classification, which introduces several categories of drug-related problems. This method of classification does not

separate the problems and the causes (25). The Hepler & Strand classification classifies drug-related problems as an untreated indication, improper drug selection, over dosage, sub-therapeutic dose, failure to receive drugs, adverse drug reaction, drug use without indication, and drug interactions.

The Pharmaceutical Care Network Europe (PCNE) classification, which was developed in January 1999 during the PCNE working conference, differs from other classification methods in that it distinguishes the problems from the causes (15). The basic classification has six primary domains for problems, six primary domains for the causes and five primary domains for the interventions (Table 2). However, a more detailed version of PCNE classification consists of 21 groups of subdomains for problems, 33 groups of subdomains for causes, and 15 groups of subdomains for the principal domains (15).

Table 2: PCNE Classification scheme for drug-related problems V5.01 the basic classification (94)

	Code V4	Primary domains
Problems	P1	Adverse reaction(s) Patient suffers from an adverse drug event
	P2	Drug Choice Problem Patient gets or is going to get a wrong (or no drug) drug for his/her disease and/or condition
	P3	Dosing problem Patient gets more or less than the amount of drug he/she requires
	P4	Drug Use/Administration Problem Wrong or no drug taken/administered
	P5	Interactions There is a manifest or potential drug-drug or drug-food interaction
	P6	Other
Causes	C1	Drug/Dose Selection The cause of the DRP can be related to the selection of the drug and/or dosage schedule
	C2	Drug Use Process The cause of the DRP can be related to the way the patient uses the drug, in spite of proper dosage instructions (on the label)
	C3	Information The cause of the DRP can be related to a lack or misinterpretation of information
	C4	Patient/Psychological The cause of the DRP can be related to the personality of the patient.
	C5	(Pharmacy) Logistics The cause of the DRP can be related to the logistics of the prescribing or dispensing mechanism
	C6	Other
Interventions	I0	No intervention
	I2	At prescriber level
	I2	At patient (or carer) level
	I3	At drug level
	I4	Other

KEY: PCNE: Pharmaceutical Care Network Europe

Other less commonly used classification systems for drug-related problems include the American Society of Hospital Pharmacist (ASHP), the Hanlon approach, the Krska et al. system, and Granada Consensus (25). For purposes of this study, medication errors will be classified based on the PCNE Classification.

2.2 Global Prevalence of Medication Errors

Overall, there is a wide variation among reported cases of medication errors. This can be attributed to the differences in methods used to detect the errors and the difference in definitions of the same type of errors (12). In 2016, a systematic review of medication errors in critical care was carried out in the United States by MacFie et al. (26). Out of the 40 studies reviewed, there was significant variability in the incidences of medication errors reported. Medication errors were noted to be relatively common, being estimated at 1 to 96.5 per 100 patient days (26). In 2014, a study carried out in the United States identified medication errors as the single most common form of error in health care. This figure represented 19% of all adverse drug events and accounted for in excess of 7000 deaths annually (16).

In a 2014 study on the nature of medication errors in critical care units in Korea by Insook et al., it was noted that out of 534 prescriptions issued, 53.6% (286) had at least one error (27). A multi-method study carried out in Spain on drug knowledge gaps among nurses and medication errors, out of the 2634 medications administered in critical care, 316 potential errors were detected, which corresponds to the global medication errors index of 1.93% (9). This global medication error index was considered higher than that identified by other multi-centre Spanish studies (1.74%) (9).

An observational study carried out in a Canadian hospital detected an error rate of 38.0% in the critical care unit and 17.4% in the high dependency unit (28). In a similar study carried out in paediatric critical care units of two hospitals in Iran, 74.8% of the patients had at least one medication error (29). A study carried out in the United Kingdom by Ridley et al. for 4 weeks showed of all prescriptions prescribed within the study period, 85% were error-free, but 15% had at least one error, averaging at 2.2 erroneous prescriptions per patient (30). Most of the identified errors were minor and not harmful, but 19.6% were considered harmful and potentially life-threatening.

2.3 Prevalence of Medication Errors in Africa

In 2018, a systematic review on medication errors and adverse drug events in African hospitals was carried out by Alemayehu et al. Several studies drawn from 9 countries were analysed, with 33 of them focusing on medication errors. The commonest type of medication errors was prescribing errors, with a median prevalence of 57.4%. The main risk factors for medication errors were identified as environmental factors, for example, high workload, distractions, inadequate knowledge and fatigue (10).

A study carried out in Ethiopia in 2011 at Jimma University Specialized Hospital critical care unit found the prevalence of medication errors in the critical care unit was 52.5% (17). The most common prescription errors were wrong drug combinations (25.7%), wrong frequency (15.5%), and then wrong dose (15.1%). Additionally, errors related to antibiotic administration contributed to a majority of the medication errors (32.5%) (17). A similar study in Ethiopia carried out in Tikur Anbessa Specialized Hospital found the prevalence of medication errors was 40%. The most common errors included omission errors (42.9%), wrong combinations (28.1%), wrong abbreviations (13.4%), wrong dose

(8.4%), wrong frequency (5.0%) and wrong indications (2.2%) (22). A study carried out in two hospitals in Uganda in 2019 found the prevalence of medical errors was 53.2%, with overdosing leading to a prevalence of 42.9% (31). None of the two hospitals had in place a medication error reporting system, suggesting an under estimation of the stated prevalence.

2.4 Prevalence of Medication Errors in Kenya

Studies on medication errors, especially in the critical care units, in Kenya are lacking. A study carried out in Mbagathi District Hospital by Onsare et al. in 2019 reported the number of prescribing errors among paediatric patients admitted at the hospital with infectious diseases as 1298, with every prescription having at least one prescribing error. The errors included incomplete prescriptions (53.2%), dosing errors (25.3%), indication errors (10.9%) and documentation errors (10.6%) (32). Another study determining the prevalence and risk factors of medication discrepancies among elderly diabetic patients admitted at Kenyatta National Hospital found a prevalence of 63.2% (33). Additionally, a study carried out in Kisii Level 5 hospital in the paediatric critical care unit in 2013 revealed the prevalence of medication errors was 75.8% (14).

2.5 Common Types of Conditions Managed within the Critical Care Unit

The critical care unit admits patients in need of intensive medical care, monitoring and advanced life support. Among patients admitted to the CCU, the most common conditions include shock, traumatic brain injury, stroke, trauma, sepsis, post-operative care, heart failure, cancer-related intensive care, and respiratory failure (34). Most of the conditions are potentially recoverable diseases.

In a study on patterns of clinical outcomes and admission of patients admitted in MICU in an Ethiopian hospital, it was found that cardiovascular disease was the most common diagnosis, followed by respiratory and infectious diseases (36.1%, 17.9/5, 13.111% respectively) (35). The most common types of specific diagnosis are as shown in Table 3.

Table 3: Distribution of common specific admission diagnosis among patients admitted to Medical Critical Care Unit of a Referral Hospital, Ethiopia (September 2015 to April 2019) (38)

Specific Diagnosis	**n**
Myocardial infarction (MI)	96 (19%)
Congestive Heart failure (CHF)	56 (11.1%)
Acute respiratory disease syndrome (ARDS)	45 (8.9%)
Septic shock	37 (7.3%)
Diabetic keto Acidosis (DKA)	28 (5.6%)
Stroke	25 (5%)
Human immunodeficiency virus (HIV) infection	25 (5%)
Pneumonia	25 (5%)
Cardiogenic shock	20 (4%)
Pulmonary thromboembolism (PTE)	19 (3.7%)

In Kenya, a survey of critical Care unit setups carried out by Okech (36) found that cardiac illness contributed to 15% of CCU admissions, while cerebrovascular accidents contributed to 8%.

2.6 Most Commonly Used Drugs in the Critical Care Unit

Drugs mostly prescribed drugs in CCU have been summarized by a 2018 study done by Adhikari et al. on drug utilization pattern in a tertiary healthcare institution (37) (Table 4). Antimicrobials were the commonly utilized class of drugs.

Table 4: Most common category of drugs prescribed in Medical Critical Care Unit (40)

Category of drugs prescribed in ICU	% of drugs prescribed in ICU (n=8848 drugs)
Antimicrobials	19.80
Antiulcer drugs	6.00
Laxatives	3.30
Antiepileptic drugs	3.60
Analgesics	3.20
Inotropes	5.20
Antihypertensive	2.70
Bronchodilator	5.30
Diuretics	5.60
Vitamin minerals	4.60
Hormones	2.00
Others (Antiemetics, steroids, probiotics, Glycosides, hypnotics, anticoagulants etc.)	38.70

Ceftriaxone, metronidazole, penicillin and quinolones are the most common prescribed antimicrobials. They are indicated for septicaemia. Antipeptic ulcer drugs are used for prophylaxis of stress-induced ulcers, and they include omeprazole and esomeprazole. Atropine is used mainly for bradycardia and organophosphate poisoning, while adrenaline and dopamine are used for cardiac resuscitation.

2.7 Drugs with the Highest Risk of Medication Errors

Generally, in the CCU, vasoactive drugs, magnesium sulphate, potassium chloride, heparin, analgesic and sedatives have been identified as the drugs with the greatest risk of medication errors within the critical care setting (8). In terms of the classification of drugs, cardiovascular medications are the most implicated cause of adverse drug events (ADEs) and medical errors. A study done by the Prevention Study Group established that the odds of ADEs for CVS medications are 2.4 higher than other classes of drugs (4). Administering the wrong dose is among the common error in the cardiology services in several studies, but a study in the cardiology unit highlighted the wrong drug administration as the main error (4). Among the medical errors, 48.4% were attributed to digoxin or other antiarrhythmic agents.

2.8 Most Common Medication Errors among the Drugs in CVD

Some of the most prevalent cardiovascular disorders associated with medication errors are acute coronary syndrome (ACS), acute heart failure, and acute stroke. Among patient with ACS, the most prominent errors are dosing errors (failure to account for diminished renal functions), miscalculation of the patient’s weight (using the actual body weight

instead of the ideal body weight), and omission (failure to provide a recommended drug) (5). For instance, in one study of STEMI patients, there is a notable low prescribing rate of reperfusion therapy, clopidogrel, aspirin, beta-blockers, and angiotensin-converting enzyme inhibitors (5).

About 5 -12% of patients with STEMI have been reported to receive incorrect dosing of fibrinolytics. In the GUSTO-I trial, medication errors (incorrect dose or infusion duration) were reported in 13.5% of the patients using streptokinase and 11.5% of those using tissue plasminogen activator (38). Importantly, these medication errors were significantly associated with a high 30-day mortality rate for both drugs.

Anticoagulants are associated with 4% of preventable adverse drug events and about 10% of possible adverse drug events. Almost half of the STEMI patients (49%) being treated with fibrinolytics receive an excess dose of unfractionated heparin, leading to higher rates of bleeding and the need for transfusion (39). Similar findings have been reported with enoxaparin, where 29% of patients were under dosed, and 19% were overdosed (40).

The omission error for statins is quite common despite the known potential benefits in ACS and other conditions. However, simvastatin is known to cause rhabdomyolysis in doses greater than 20mg when co-administered with amiodarone and other cytochrome p450 inhibitors.

There is limited literature on the incidence of adverse clinical outcomes in heart failure, but generally, due to the limitation in kidney and liver functions, careful monitoring of drug serum concentrations and electrolytes levels is recommended. If possible, some

drugs can be withheld until the condition improves. Studies on stroke have reported a medication errors rate of 4 - 19%, leading to a three times increase in the hospital stay for the patients (40).

2.9 Research Gap

A study done by Kivuva et al. (41) assessed medication-related problems among critically ill neonates admitted at KNH. However, no study has been done in KNH on the prevalence of medication errors occurring among cardiovascular disease patients admitted in the critical care unit. This study aims to fill this gap.

2.10 Conceptual Framework

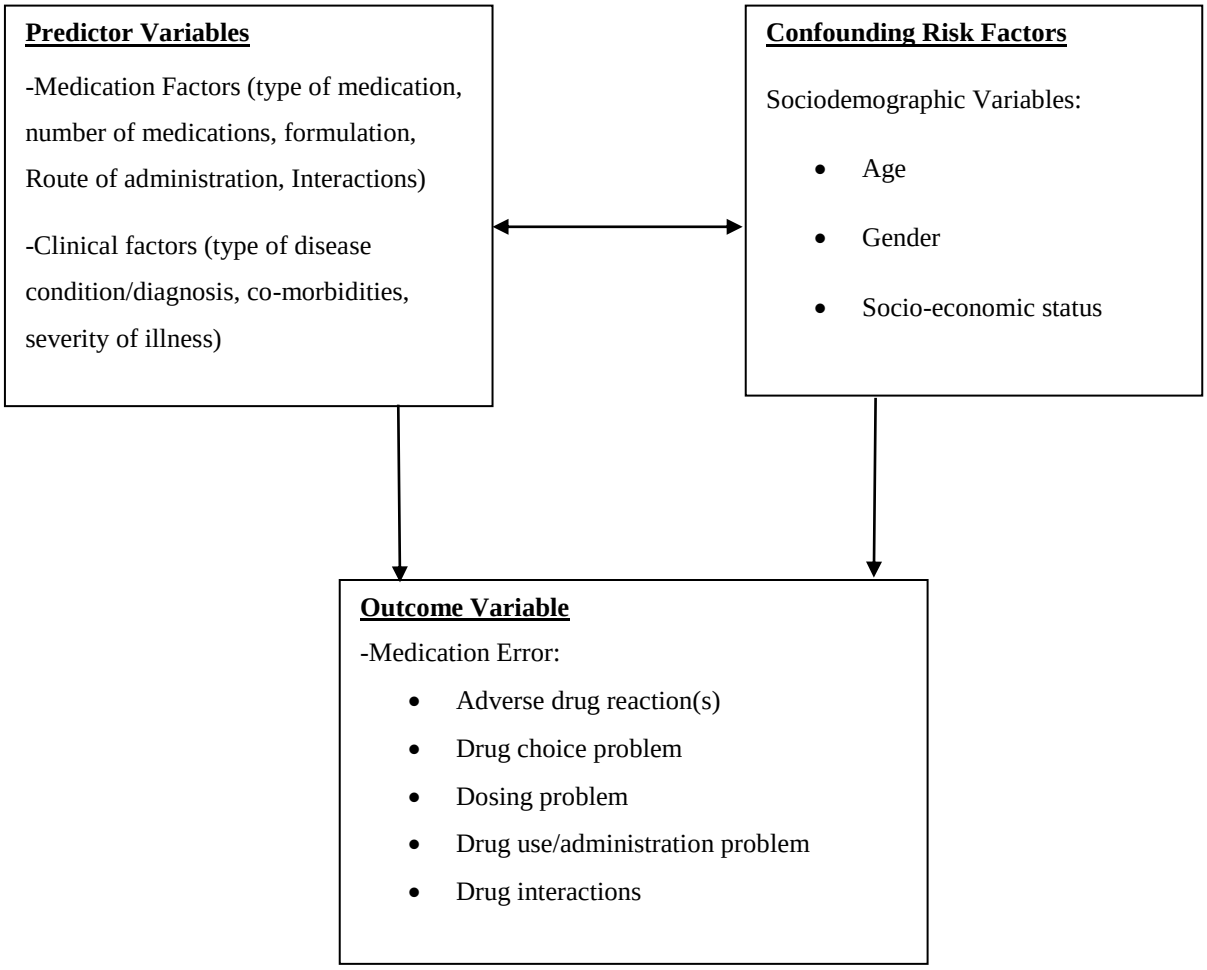

Figure 1: Conceptual framework of factors interacting to cause medication errors

The conceptual framework illustrates the interaction between different variables to cause medication errors. These interactions can result in either an increased or a decreased risk of the incident of medication errors. The key outcome variable will be medication errors. These should include ADRs, drug choice problem, dosing errors and drug administration errors.

Medication factors influencing the occurrence of medication errors include the number of medications per prescription, the route of administration, the type of medications, and the formulations. The higher the number of medications in a prescription, the higher the likelihood of medication errors. Drugs administered via intravenous route are more likely to cause medication errors due to weight-based dosing and the precision required in diluting the drugs and the administration. Additionally, some drugs are known as high-risk drugs in regards to medication errors, meaning they are more likely than others to cause medication errors when prescribed. In 2009, Eric et al. determined the risk associated with cardiovascular drugs at 24%-33%, sedatives or analgesics at 26%, anticoagulants at 11-20%, and anti-infective at 13% (42).

Clinical factors also play a role in the probability of occurrence of medication errors. These factors include the clinical status of the patient as predicted by the Glasgow Coma Scale (GCS) score. A severely sick patient is likely to experience medication errors due to the complexity of their management and a reduced pharmacological reserve (9). Additionally, comorbidities result in a higher risk for medication errors due to the increased need for pharmacological therapy. The most common comorbidities

experienced within the CCU setting include diabetes mellitus, heart failure, end-stage liver disease, chronic obstructive pulmonary, end-stage renal disease, and hypertension (43).

Other predictor variables include provider factors like exhaustion, level of knowledge, and level of experience. Environmental predictor factors such as a patient being admitted in the general ward versus the CCU, poor lighting, noise and inappropriate room temperature and ventilation, and disruptions by both staff and patients could affect the patient's outcomes. Organizational factors such as the working conditions such as lack of standardized procedures, inadequate resource, lack of protocols, and inadequate supervision of junior and new staff could lead to the occurrence of several medication errors. A poor patient-nurse ratio can also lead to medication errors due to fatigue (44).

The sociodemographic factors of a patient play an important role in the health status of a patient. Older patients are likely to have comorbidities, hence the increased need for pharmacological therapy, and by extension, the increased risk for medication factors. Other sociodemographic factors include the socioeconomic status of the patient which affects their ability to afford medication (45).

CHAPTER THREE: MATERIALS AND METHODS

3.1 Introduction

This chapter highlights the methodological details of the study. These include the research design, the location of the study, the target and the study population, the sample section, which explains the sample size calculation and the sampling procedure. Additionally, the chapter elaborates on the research instruments, how the researcher ensured validity and reliability, the data collection process and the data analysis. Lastly, the chapter provides a work plan and a budget for the study.

3.2 Research Design

The study design was a descriptive cohort study that was carried out over a period of three months. This study design was most appropriate as, during the course of treatment, medications were changed, and adverse outcomes took time to evolve. Additionally, this study design minimized the problem of missing records.

The study entailed a prospective review of treatment sheets and files of cardiovascular patients admitted at the Kenyatta National Hospital CCU for a period of three months. The patients were followed from the date of admission for ten days or to the date of discharge, whichever came first. This information was used to determine the overall incidence of medication errors and the associated risk factors.

3.3 Study Site

The study was carried out at Kenyatta National Hospital (KNH), which is the largest referral hospital in Kenya, serving both Central and East Africa. Kenyatta National Hospital caters for patients from all over the country. The hospital has a bed capacity of 2000, with one main critical care ward with a bed capacity of 21, and five subsidiary intensive care units (ICU).

The study focused on the medical CCUs located on the 7th and 8th floor of the hospital. Both of these CCUs were hived off from the main medical wards, Ward 7A and 8A, respectively, and they cater for the critically ill patients with conditions related to internal diseases. These two CCUs have a total bed capacity of nine. This study site was appropriate since critically ill patients with cardiovascular disorders are admitted to this unit unless it is not logistically possible, for instance, when the ward is full to capacity.

3.4 Target and study population

The target population of the study was all adult patients with a cardiovascular illness diagnosis, who were admitted to the critical care unit in KNH. The study population was adult patients with a cardiovascular illness diagnosis who were admitted to the CCU at KNH from June 2021 to September 2021.

3.5 Eligibility Criteria

3.5.1 Inclusion criteria

The inclusion criteria included:

1. Patients admitted at the KNH CCU from June 2021 to August 2021

2. Adults aged above 18 years
3. Patients with a cardiovascular disease diagnosis as outlined in Appendix B

3.5.2 Exclusion Criteria

The exclusion criteria included:

1. Patient files with incomplete clinical records
2. Patients under the age of 18 years
3. Patient without a diagnosis of a cardiovascular disease

3.6 Sample Size Determination

Since the study design was a descriptive cohort study, with the outcome of interest being a categorical variable (prevalence), the most appropriate formula for sample size calculation was the Cochran formula given in equation 1 (46):

Equation 1: Cochran formula for sample size computation

$$n = \frac{z^2 p(1-p)}{d^2}$$

Where:

n = the sample size,

Z = standard normal deviation at 95% confidence interval set at 1.96

P = incidence of medication errors

d = precision of the study, set at 5%.

A study carried out at medical wards in KNH found the prevalence of medication errors as 45%, while a study carried out at Kisii level 5 Hospital paediatric CCU estimated the

prevalence was 75.8% (11,14). For the purpose of this study, the prevalence was averaged from the two studies to obtain 60.4%. The calculated sample is 368 patients

Since the sample size was drawn from a small population, and a finite population correction was applied shown in equation 2.

Equation 2: Cochran's adjustment for a finite population

$$n = \frac{no}{1 + \frac{no}{N}}$$

Where:

N = population size (40)

n_o= calculated sample size (368)

n = adjusted sample size

N was obtained after anecdotal reports from the records department were obtained. The total number of patients admitted within the CCUs catering for internal medicine patients for a 3-month period, October 2020 to December 2020, was 178. The prevalence of cardiac illness and cerebrovascular accidents within CCU admissions in Kenya was found to be 23% (36). Therefore, an assumption was made that 23% of these admissions would be due to cardiovascular disorders.

The sample size was 40. To cater for unforeseen data losses, for instance, missing data in the files, a 10% adjustment of the sample size was done. Therefore, the adjusted sample size was 44 patients.

3.6.1 Sampling Method

Convenient sampling method was used because the study population was small since the bed capacity is 9 at the medical CCU wards. Secondly, CCU patients have unpredictable prognosis and a relatively short-time window at the ward. These factors made it difficult to obtain the sample size using other methods. Consequently, every adult patient admitted to the internal medical CCUs and meeting the inclusion criteria as outlined in appendix A was requested to be a participant until the desired sample size was obtained.

3.6.2 Participants Recruitment and Consenting Process

The principal researcher recruited the patients. The files of all newly admitted patients in the CCU were obtained in the morning from the nursing station. Patients with cardiovascular disorders were identified from the medical records. The principal researcher would approach the patient to assess their ability to communicate. However, most of the patient's in the ICU did not have the cognitive and physical capacity to provide informed consent; surrogate consent was obtained from the caregiver or the attending clinician. The participant or the surrogate were briefed about the study and taken through the consenting process. An explanation of the study, its possible harm, benefits and confidentiality was also given. Once verbal consent to participate was obtained, the participant (or the surrogate) was asked to sign the consent form (Appendix B). The principal investigator collected the relevant data from the patient's file. Data collection was done in the early morning or afternoon after ward rounds to avoid interruption of services. This data was entered into a predesigned questionnaire (Appendix B).

3.7 Research Instruments

The study used an eligibility checklist (Appendix A) to screen for eligible participants. Medical and medication-related information were abstracted from the treatment sheet using the data collection tool appendix B. This tool contains forms 1 to 4, each capturing different medication information. Form 1 captured information such as the age, weight, gender, reasons for admission, date of admission and discharge, diagnosis, and comorbidities. Form 2 captured the available laboratory monitoring parameters of the patient. Form 3 captured medication information including the drug class, indication, and appropriateness of the dosing. Form 4 captured information on the potential drug-drug interactions, while Form 5 captured information on adverse drug events. A checklist for the medication errors (Appendix C) was used to classify the errors using the PCNE classification.

3.8 Data Management

Data was collected daily from the patients' files by the principal investigator, coded and entered into Microsoft excel 2013 version until the desired study sample was achieved. Data collection was done in the afternoon after the principal investigator has attended ward rounds to avoid interruption of services. The data was also screened for accuracy and completeness by the principal investigator. The electronic data was protected using a password and is only accessible to the principal investigator. The stored data was backed up regularly in a location separate from the primary data. The hard copies of the data are stored in a lockable file cabinet only accessible to the researcher. The hard copies will be shredded and incinerated after storing them for a period of ten years.

3.9 Validity, Reliability and Quality Assurance

Internal validity was ensured by ensuring that the correct sampling method for the study was used, and by ensuring that a correctly calculated sample size for the study was used. Additionally, standardized recruitment of the participants eliminated selection bias.

The external validity was ensured by the use of a broad inclusion criterion and a narrow exclusion criterion, as highlighted in the criteria section, to increase the generalizability of the study findings. The correct estimation of sample size also ensured that the study is representative of the population. The target population was also clearly defined in terms of person, place and time.

Drug information was extracted from evidence-based guidelines. Information on possible drug-drug interactions was extracted from IBM Micromedex interaction checker, which is a validated tool.

The reliability was also ensured by pretesting the questionnaire by the principal investigator. Assuming that data entry into patients' files was accurate, the form should reliably collect similar data when repeated by a different researcher. The researcher used five questionnaires to enter data from the same patient to verify that the results were reproducible.

Quality assurance of the study was done by ensuring consistency in the recruitment of participants and the management of data. Daily checks on the filled tools was done by the researcher to ensure completeness and accuracy of the collected data.

3.10 Pre-Testing

The data collection tool was pretested on 10% of the actual sample size after the study approval by the Kenyatta National Hospital /University of Nairobi Ethics and Research Committee (KNH/UON-ERC). The data was collected by the principal investigator from the medical CCUs in KNH. The collected data was then assessed to ensure they contributed to the objectives of the study accurately. Errors in the data collection tool were noted and modifications were done.

3.11 Data Analysis Plan

The variables recorded included the sociodemographic data, diagnosis, comorbidities, laboratory results of the monitoring parameters, drugs prescribed, potential drug-drug interactions, and adverse drug events. The data was then coded and entered into Microsoft Excel 2016 Edition, where descriptive analysis was done.

Patients demographic data such as age, education level, employment status, and gender was analysed using frequency tables. Measures of central tendency such as the mean, median and standard deviation for some continuous variables such as age were analysed and displayed in the frequency table. Additionally, bar charts were used to describe the categorical variables such as diagnosis and the comorbidities. The patient's prescription was analysed for appropriateness against the Kenya National Guidelines for Cardiovascular Diseases.

These data were exported to STATA version 13.0 for further analysis. Fischer's exact or Pearson's Chi-square tests were used to assess the association between the independent variables such as comorbidities and sociodemographic factors and the dependent variable

(medication errors). A bivariate logistic analysis was used to assess the association between the patient's sociodemographic variable and the outcome variable. Analysis was done at a statistical significance level of 0.05. The results were presented as shown in chapter 4.

3.12 Ethical Considerations

Ethical approval was obtained from the Kenyatta National Hospital/University of Nairobi Ethics and Research Committee (KNH/UON-ERC P118/02/2021) in appendix E. The study was registered with the KNH Research and Program department (Appendix F). The forms that were approved by the KNH/UoN ERC were used to collect data. All patients or their surrogates were briefed about the study requested to participate willingly and without inducement. The informed consent was obtained before any data was collected from the patient or their files.

3.13 Confidentiality

Unique identification codes for the patient files, as opposed to their names or patient numbers, were used in the data collection forms. Additionally, all forms used to collect data were stored under lock and key, accessible to only the researcher. The electronic information was password protected and is accessible to only the researcher.

3.14 Dissemination Plan

A write up of the findings of the study will be deposited at the KNH research unit. The findings of the study will also be disseminated to the members of the CCU department through a CME. Further dissemination of the findings of the study will be done through

the publishing of the work in a journal, the University of Nairobi repository and presentation at conferences. Additionally, copies of the research project will be deposited in the library for access.

CHAPTER 4: RESULTS

4.0 Introduction

This chapter discusses the sociodemographic characteristics of the patients, their clinical profiles, the primary diagnosis, and comorbidities. It also highlights the medication errors, the potential drug-drug interactions, and their probable associations with the patient's profiles and the covariates of the predictor variables.

4.1.1 Recruitment of Participants

Forty-eight patients were identified for recruitment into the study. Two of the patients/care givers declined to participate in the study. Three other potential participants were below 18 years of age. Another three were excluded once their primary diagnosis was changed and they were transferred to other wards for appropriate management, as shown in the consort diagram (Figure 2)

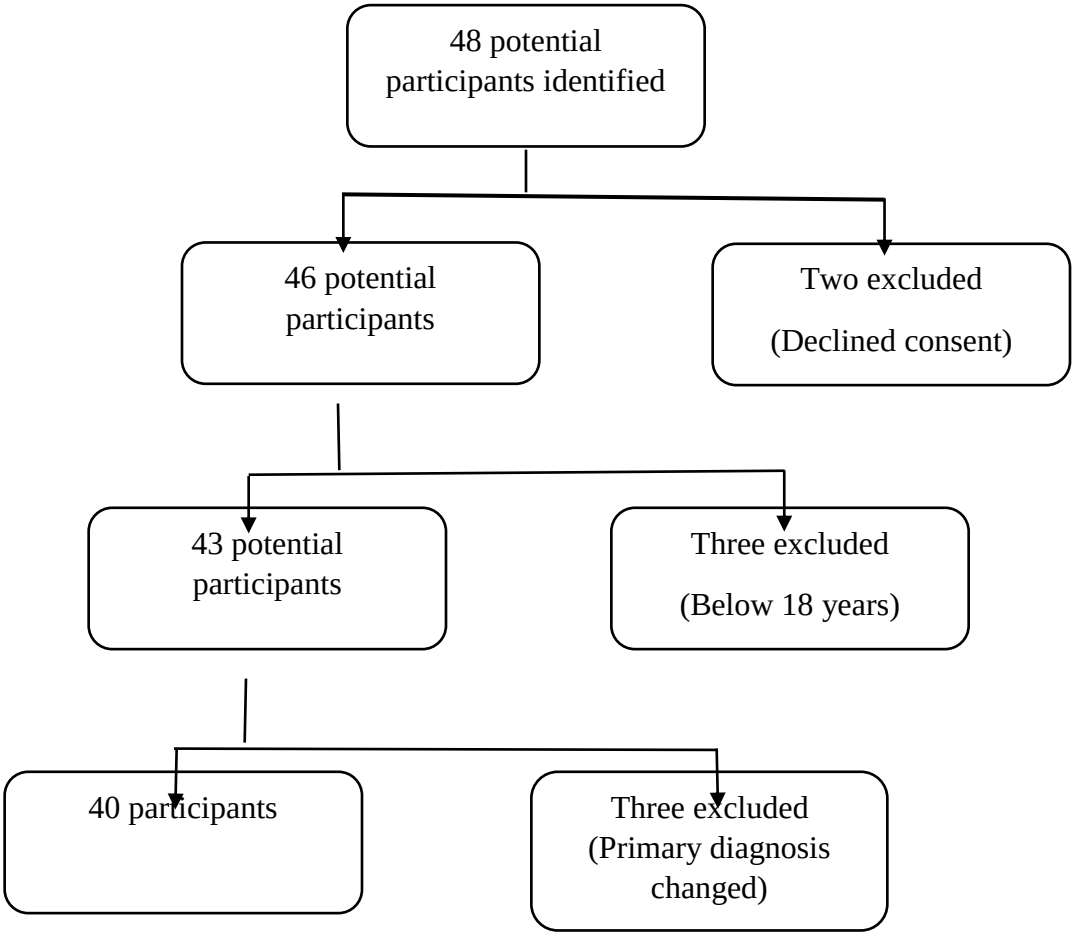

Figure 2: Consort diagram of participant recruitment and reasons for exclusion

4.1.2 Sociodemographic Characteristics of the Patients Admitted at the KNH Medical Critical Care Unit

Majority of the participants were female (n=22, 55.0%) and unemployed (n=30, 75.0%). Most admissions were done through the outpatient department (n=20, 50.0%) (Table 5).

Table 5: Sociodemographic/clinical characteristics of the participants

Variable	Frequency, n (%)
Sex	
Male	18 (45.0%)
Female	**22 (55.0%)**
Age (Years)	
18-32	8 (20.0%)
33-47	12 (30.0%)
48-62	12 (30.0%)
63-77	8 (20.0%)
Median (IQR)	48 (34.5, 61)
Mean ± SD	47.7 ± 15.4
Education Level	
Primary	15 (37.5%)
Secondary	18 (45.0%)
Tertiary	7 (17.5%)
Employment Status	
Unemployed	**30 (75.0%)**
Employed	10 (25.0%)
Admission	
From ward	17 (42.5%)
Through outpatient department	**20 (50.0%)**
Referral from other hospitals	3 (7.5%)
Length of stay in ICU (days)	
0 to 3	5 (12.8%)
4 to 7	18 (46.2%)
8 to 11	8 (20.5%)
11 to 15	8 (20.5%)
Median (IQR)	6 (5, 11)
Mean ± SD	7.6 ± 3.9

KEY: IQR – Interquartile range, SD – Standard deviation

4.2 Primary Cardiovascular Diagnoses Amongst Patients with Cardiovascular Disorders Admitted at KNH Medical Critical Care Unit

Eleven patients (27.5%) were admitted with hypertension (HTN), nine patients (22.5%) were admitted with hypertensive urgency, three patients (7.5%) had acute decompensated heart failure (ADHF) and three patients had a myocardial infarction (MI) (Figure 3).

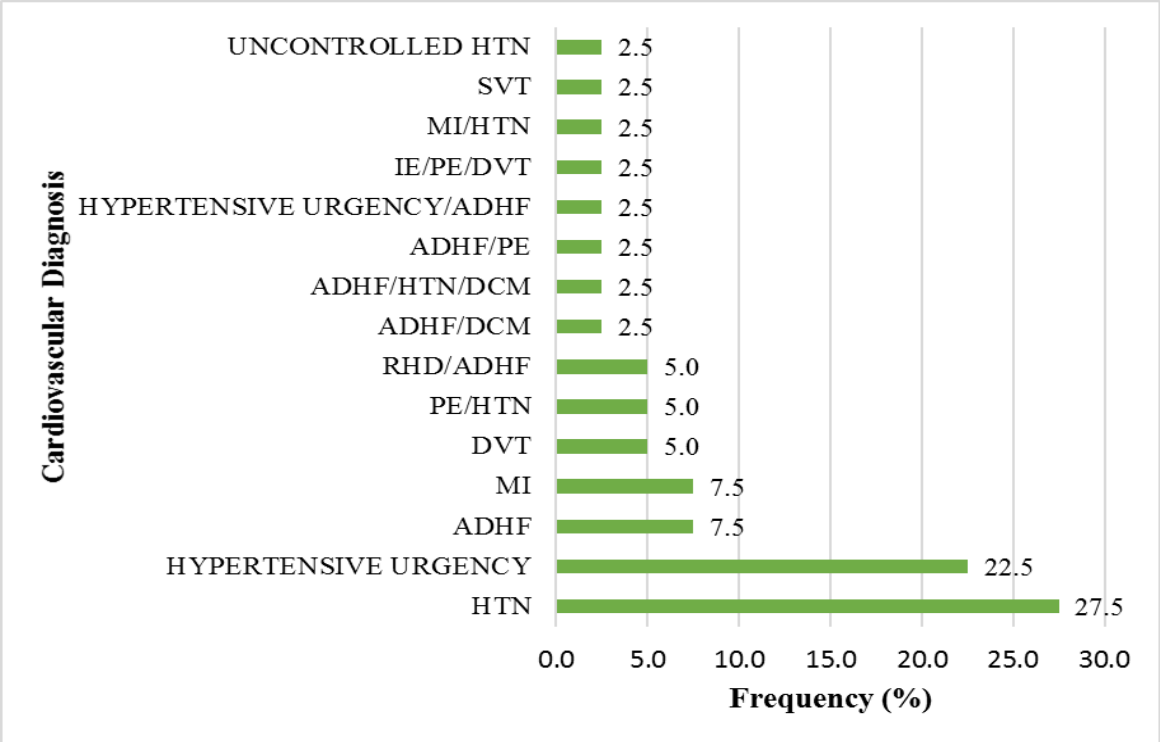

Figure 3: Cardiovascular diagnosis of participants admitted at KNH Medical Critical Care Unit

KEY: ADHF - Acute decompensated heart failure, DCM -Dilated cardiomyopathy, DVT – Deep venous thrombosis, HTN – Hypertension, IE- Infective endocarditis, MI – Myocardial infarction, PE – Pulmonary embolism, RHD – Rheumatic heart disease, SVT- Supraventricular tachycardia.

4.3 Comorbidities Amongst Patients with Cardiovascular Disorders Admitted at KNH Medical Critical Care Unit

Participants in this study had 74 comorbidities. Majority of the participants (n=18, 45.0%) had two comorbidities, and only two participants (5.0%) had no comorbidity. Nine participants (27.5%) had three comorbidities and nine participants (27.5%) had one comorbidity (Figure 4).

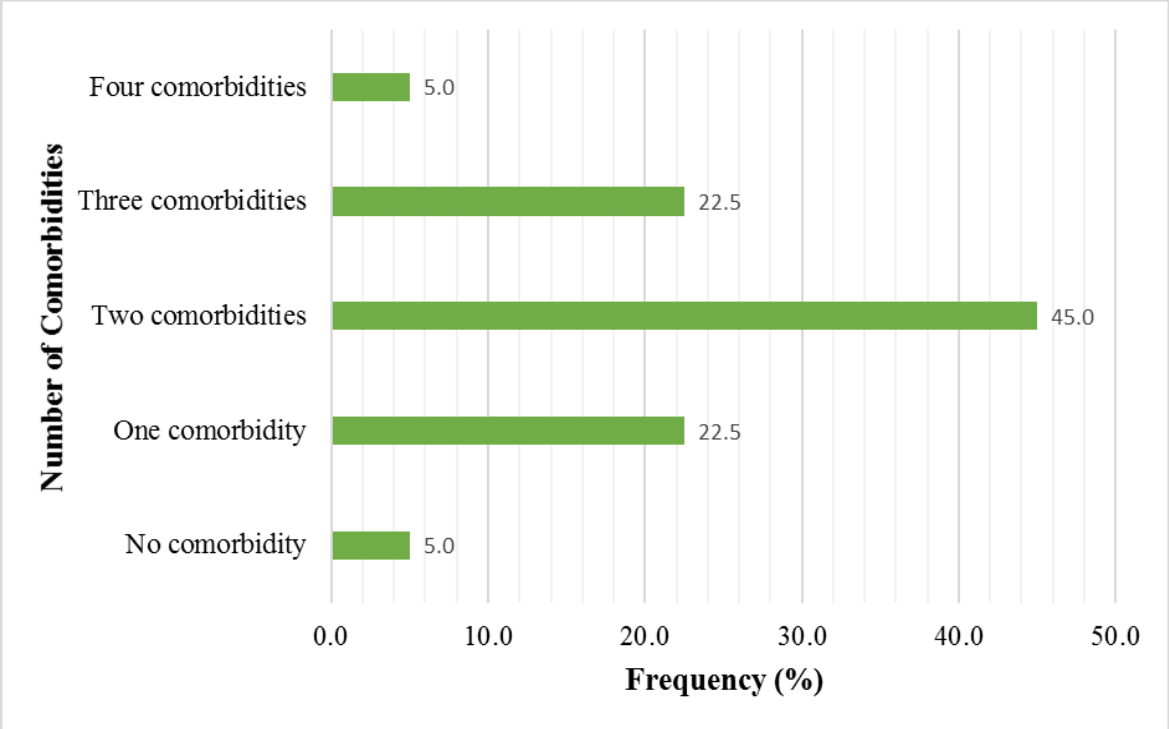

Figure 4: Number of comorbidities amongst the participants admitted at the KNH Medical Critical Care Unit with cardiovascular disease

The most common comorbidities shown in Figure 4 were diabetes mellitus (n=13, 32.5%), chronic kidney disease (n=7, 17.5%), diabetes ketoacidosis (n=6, 15.0%), and acute kidney injury (n=5, 12.5%) among others

(Figure 5).

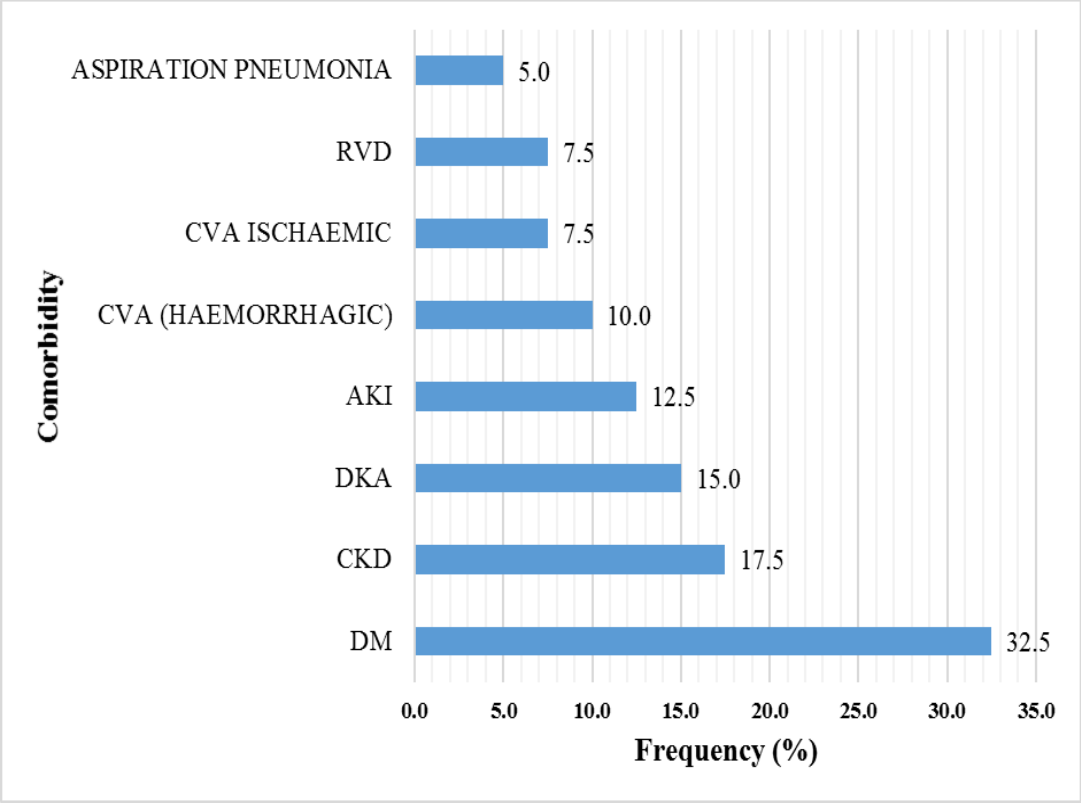

Figure 5: Comorbidities amongst patients admitted at KNH Medical Critical Care Unit with cardiovascular disease

KEY: AKI – Acute kidney injury, CKD – Chronic kidney disease, CVA – Cerebrovascular accident, DKA – Diabetic ketoacidosis, DM – Diabetes mellitus, RVD – Retroviral disease

4.4 Commonly Prescribed Medications among Patients at the KNH Medical Critical Care Unit with a cardiovascular disease

From the 97 prescriptions analysed, a total of 985 drugs were prescribed, hence an average of 10.1 (S D: 3.5) drugs per prescription. Every patient received an average of 24.6 (S D: 6.7) drugs during their stay. The most commonly prescribed class of drugs were cardiovascular (n=248, 25.2%), analgesics (n=97, 9.8%), antibiotics (n=95, 9.6%) and antiplatelets/anticoagulants (n=87, 8.8%) (Table 6). Among the anticoagulants,

enoxaparin (n=51, 5.2%), clopidogrel (n = 20, 2.0%) and aspirin (n= 13, 1.3%) were most widely prescribed. Paracetamol (n=68, 6.9%) was the most widely prescribed analgesic, while ceftriaxone (n=17, 1.7%) was the most commonly prescribed antibiotic. Atorvastatin (n=33, 3.3%) was the only hypolipidemic drug prescribed. Other most commonly used drugs included omeprazole (n=61, 6.2%), different formulations of insulin (n=41, 4.2%) and lactulose (n=40, 4.1%).

Table 6: Commonly prescribed drugs for patients admitted at the KNH Medical Critical Care Unit

Class of Drug (Frequency, %)	**Drug**	**Frequency, % (N = 975)**
Cardiovascular (248, 25.4%)	See table 7	248 (25.4*%)*
Anticoagulants/Antiplatelets (87, 8.9%)	Enoxaparin	51 (*5.2%)*
	Clopidogrel	20 (*2.0%)*
	Aspirin	13 (*1.3%)*
	Warfarin	9 (*0.9%)*
Analgesics (97, 9.9%)	Paracetamol	68 (*6.9%)*
	Tramadol	12 (*1.2%)*
	Morphine	12 (*1.2%)*
Antibiotics (95, 9.7%)	Ceftriaxone	17 (*1.7%)*
	Meropenem	14 (*1.4%)*
	Azithromycin	14 (*1.4%)*
	Amoxiclav	12 (*1.2%)*
	Ceftazidime	10 (*1.0%)*
Hypolipidemics (33, 3.4%)	Atorvastatin	33 (*3.3%)*
Others (352, 36.1%)	Omeprazole	61 *(6.2%)*
	Insulin	41 (*4.2%)*
	Lactulose	40 (*4.1%)*
	Bisacodyl	16 (*1.6%)*
	Ondansetron	11 (*1.1%)*
	Metoclopramide	11 (*1.1%)*

Among the cardiovascular drugs prescribed, diuretics (n=57, 5.8%), calcium channel blockers (n=49, 5.0%), and beta blockers (n=42, 4.3%) were the most common drugs (Table 7). Furosemide (n = 40, 4%), carvedilol (n = 38, 3.8%) and amlodipine (n = 21, 2.1%) were commonly prescribed among the cardiovascular drugs.

Table 7: Summary of the cardiovascular drugs used by patients admitted at the KNH Medical Critical Care Unit

Class of Drugs	Drug	Frequency, %
Inotropes	Noradrenaline	*8 (3.2%)*
Thiazides	HCTZ	*4 (1.6%)*
Diuretics	Furosemide	*40 (16.1%)*
	Spironolactone	*12 (4.8%)*
	Metolazone	*3 (1.2%)*
	Torsemide	*1 (0.4%)*
	Acetazolamide	*1 (0.4%)*
Anti-anginal	Isosorbide mononitrate	*4 (1.6%)*
	Glyceryl trinitrate	*2 (0.8%)*
	Nitroglycerine	*1 (0.4%)*
Antiarrhythmics	Amiodarone	*5 (2.0%)*
	Ketamine	*2 (0.8%)*
Cardiac glycosides	Digoxin	*13 (5.2%)*
Antihypertensives		
Vasodilators	Hydralazine	*19 (7.7%)*
Calcium Channel Blockers (CCBs)	Amlodipine	*21 (8.5%)*
	Nifedipine	*18 (7.3%)*
	Nimodipine	*10 (4.0%)*
Beta blockers	Carvedilol	*38 (15.3%)*
	Nebivolol	*4 (1.6%)*
	Labetalol	*3 (1.2%)*
	Metoprolol	*1 (0.4%)*
Angiotensin-converting enzyme inhibitors (ACEIs)	Enalapril	*13 (5.2%)*
Angiotensin II receptor blockers (ARBs)	Losartan	*9 (3.6%)*
	Telmisartan	*1 (0.4%)*
Centrally acting alpha-2 adrenergic agonist	Methyldopa	*8 (3.2%)*
Alpha 1 agonist	Clonidine	*2 (0.8%)*
Selective sinus node I (Lf) channel inhibitor	Ivabradine	*1 (0.4%)*
Arginine vasopressin V2 receptor blocker	Tolvaptan	*1 (0.4%)*

KEY: ACEIs – Angiotensin converting enzyme inhibitor, ARB – Angiotensin receptor blockers, CCB – Calcium channel blockers.

4.5 Prevalence of Medication Errors

Ninety-seven prescriptions were analysed, from which 985 drugs were administered via the oral and parenteral routes. Seventy-four errors were identified, with a majority of the patients (n=38, 95.0%) experiencing at least one medication errors during the admission period. Two patients (5.0%) had no errors, fifteen patients (37.5%) experienced one error, fourteen patients (35.0%) had two errors, six patients (15.0%) had three errors, two patients (5.0%) had four errors and one patient (2.5%) had five errors.

4.5.1 Types of Medication Errors

Medication errors were classified into six domains according to The Pharmaceutical Care Network Europe (PCNE) classification system (15). The PCNE method describes drug-related problems in six categories, and they are classified as P1, P2, P3, P4, P5 and P6. P1 error describes an adverse reaction where a patient suffers an untoward effect attributable to a pharmaceutical product. A P2 error is a drug choice problem where a patient receives or is going to receive the wrong drug or no drug for an indication. A P3 problem is a dosing problem where the patient receives a higher or lower dose than required. A drug use/administration problem, categorized as a P4 error, occurs when the wrong drug or no drug is administered. A P5 error in an interaction problem, where there is an evident or potential drug-drug interaction or drug-food interaction. A P6 error describes any other medication error that does not fall into the other five categories. For instance, when the prescriber fails to indicate the dose of a drug, this constitutes a P6 error.

Thirty-seven patients (92.5%) had potential drug-drug interactions, eighteen patients (45.0%) had a drug choice problem error, seven patients (17.5%) had a probable adverse

drug reaction, seven patients (17.5%) had dosing problems, three patients (7.5%) had drug use/administration problems, and two patients (5.0%) had others errors not categorized above (Figure 6).

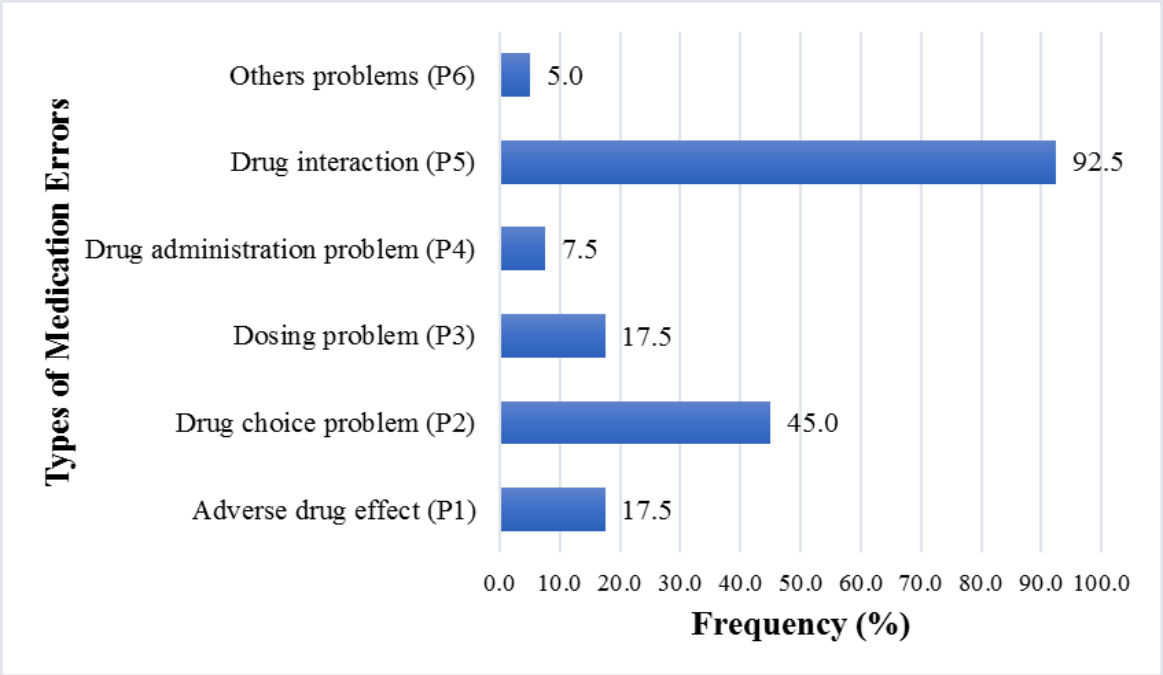

Figure 6: Types of medication errors amongst patients with cardiovascular disorders admitted at the KNH Medical Critical Care Unit

Fifty prescribing errors were identified from the 97 prescriptions. Errors from each class of drugs included using contraindicated drugs in pregnancy, having the dose of a drug not specified in a prescription, failure to administer a prescribed drug, using higher than the recommended dose, and failure to adjust doses in renal insufficiency. The majority of prescribing errors (n=19, 37.3%) were from other classes of drugs shown in Table 8. Fifteen prescribing errors (29.4%) were from antibiotics use and fourteen errors (27.5%) were attributable to cardiovascular medications.

Table 8: Prescribing errors of drugs prescribed at the KNH Medical Critical Care Unit

Class of Drugs	Description of error	No. of errors
Cardiovascular Drugs	Patient with bradycardia receiving carvedilol	5
	Use of contraindicated antihypertensives in pregnancy	3
	Amlodipine dose not specified	3
	Nifedipine not administered	1
	Hypotensive patient on nifedipine	1
	Amlodipine dose too high	1
	Class Subtotal (Frequency, %)	**14 (27.5%)**
Anticoagulants	Enoxaparin dose too high for prophylaxis	1
	Class Subtotal (Frequency, %)	**1 (2.0%)**
Antibiotics	Ceftazidime dose not adjusted in renal failure	6
	Meropenem dose not adjusted in renal failure	3
	Amoxicillin- clavulanic acid dose not adjusted in renal failure	2
	Inappropriate combination of antibiotics (Meropenem, Metronidazole and Ceftriaxone)	2
	Amikacin not administered	1
	Dose of vancomycin not specified	1
	Class Subtotal (Frequency, %)	**15 (29.4%)**
Hypolipidemic	Atorvastatin use in pregnancy	1
	Class Subtotal (Frequency, %)	**1 (2.0%)**
Others	Bisacodyl dose not specified	10
	Cetirizine not administered	4
	Insulin dose not specified	3
	Prophylactic omeprazole dose too high	1
	Lactulose not administered	1
	Class Subtotal (Frequency, %)	**19 (37.3%)**
Total		**50**

4.5.2 Potential Drug-drug Interactions

Potential drug-drug interactions were analysed using the Micromedex drug interactions checker, and the consequences of the interactions were summarized. There were 158 potential drug-drug interactions, with each patient having an average of 3.95 pDDIs. Seventy-nine (50.0%) interactions were classified as major interactions, seventy-four (46.8%) were moderate, three (1.9%) were minor, and there were two incidences of contraindicated drug combinations (Figure 7).

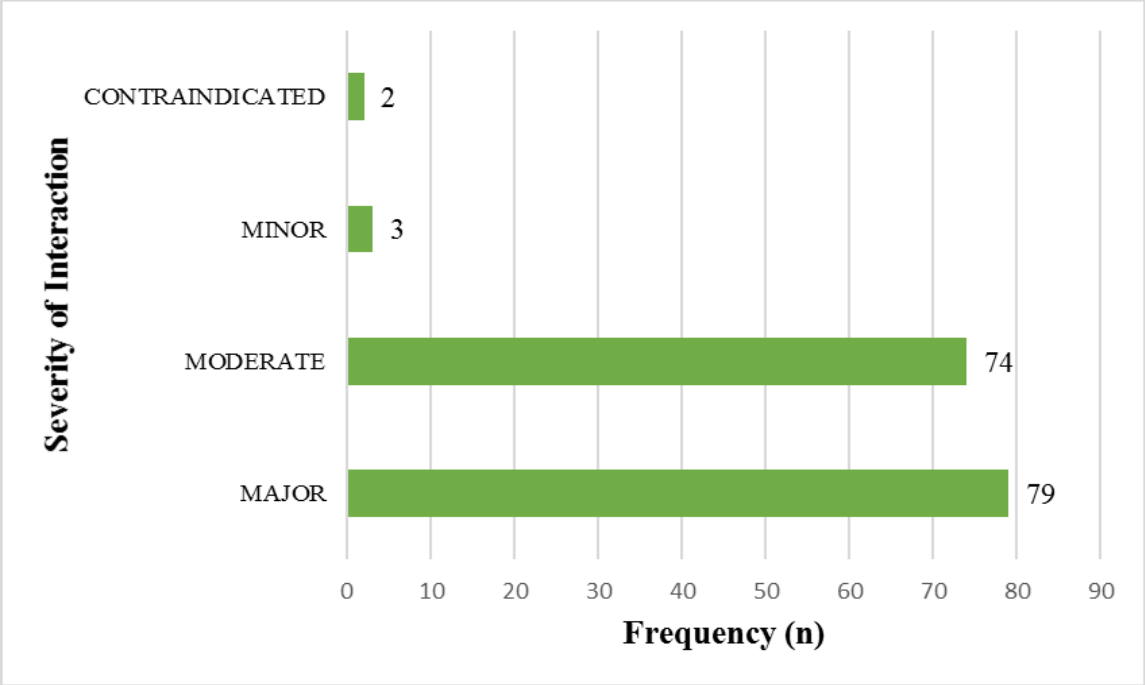

Figure 7: Severity of potential drug-drug interactions among patients admitted at the KNH Medical Critical Care Unit

The possible outcomes of the potential drug-drug interactions are summarized as shown in Table 9. Seventy-eight potential consequences were noted. Thirteen patients (20.6%) were exposed to an increased risk of hyperglycaemia, nine patients (14.2%) were exposed

to increased risk of bleeding, and seven patients (11.1%) were exposed to an increased risk of phenytoin toxicity.

Table 9: Possible Consequences of drug-drug Interactions and their frequency among patients admitted in the critical care unit of KNH with cardiovascular disease

Possible Outcome	Interacting Drugs	Frequency (n)	Prevalence (%)
Hyperglycaemia	Insulin/Furosemide Insulin/Hydrochlorothiazide Empagliflozin/Furosemide	13	20.6
Bleeding	Clopidogrel/Enoxaparin Aspirin/Clopidogrel/Enoxaparin Sodium Valproate/Warfarin Omeprazole/Warfarin Amiodarone/Warfarin/Amoxicillin	9	14.2
Phenytoin toxicity (ataxia, hyperreflexia, nystagmus, and tremors	Phenytoin/Omeprazole Phenytoin/Metronidazole	7	11.1
Hyperkalaemia	Enalapril/Spironolactone Losartan/Spironolactone Enalapril/Cotrimoxazole	6	9.5
Hypoglycaemia	Insulin/Aspirin Insulin/Enalapril Insulin/Cotrimoxazole	6	9.5
QT-interval prolongation	Azithromycin/Fluconazole Azithromycin/Haloperidol Azithromycin/Metronidazole Azithromycin/Ondansetron Ondansetron/Amitriptyline Haloperidol/Aripiprazole	6	9.5
Digoxin toxicity	Digoxin/Furosemide/Omeprazole Digoxin/Metolazone Digoxin/Tolvaptan/Furosemide Digoxin/Spironolactone/Furosemide/Torsemide	5	7.9
Reduced nimodipine exposure and efficacy	Nimodipine/Phenytoin	5	7.9
Reduced paracetamol effectiveness and increased risk of hepatotoxicity	Paracetamol/Phenytoin	5	7.9

4.5.3 Other Medication Errors

Seven patients (17.5%) suffered adverse drug effects, including bleeding events (n=3, 17.5%). Some of the drug choice problems included having no drug prescribed for an indication (n=9, 22.5%), having the wrong drug prescribed for a condition (n=7, 17.5%) and having an inappropriate combination of drugs (n=2, 5.0%) (Table 10). Some of the drug choice problems included having no drug prescribed for an indication (n=9, 22.5%), having the wrong drug prescribed for a condition (n=7, 17.5%) and having an inappropriate combination of drugs (n=2, 5.0%) (Table 10).

Three patients (7.5%) did not receive the drugs prescribed (Table 10). Most patients with dosing errors received higher than the recommended dose of certain drugs. Notably, drugs for patients with end-stage renal disease were not adjusted accordingly (n=4, 10.0%) as shown in Table 10. Other problems included not having the dose of drug indicated (n=3, 7.5%) (Table 10). Some drugs doses were written in terms of tablets instead of doses (Table 10)

Table 10: Description of medication errors occurring among patients admitted at KNH Medical Critical Care Unit

Drug	Frequency (n, %)	Outcome (P1) (Adverse drug effect)
Enoxaparin (SC)	3 (17.5%)	• Bleeding events (GIT bleeding)
Carvedilol (Oral)	2 (5.0%)	• Bradycardia
Potassium chloride (IV)	2 (5.0%)	• Hyperkalaemia
Drug Choice Problem (P2)	**Frequency (n, %)**	**Description**
No drug prescribed for an indication	9 (22.5%)	• No drug to control heart rate • No hematinic administered for low haemoglobin • Hypokalaemia not corrected • Hypertensive patient did not receive antihypertensives
Wrong drug for the condition	7 (17.5%)	• Received antihypertensives contraindicated in pregnancy • Patient with bipedal oedema receiving pregabalin • Hypotensive patient added losartan • Hypotensive patient receiving carvedilol • Cardiac failure patient using ibuprofen
Inappropriate drug combination	2 (5.0%)	Concurrent use of meropenem, ceftriaxone, and metronidazole
Dosing Problem (P3)	**Frequency (n, %)**	**Description**
Higher than the recommended dose	3 (7.5%)	• High dose of omeprazole • High dose of pantoprazole • High dose of amlodipine
Drug not renal adjusted	4 (10.0%)	• Higher than the recommended dose of ceftazidime in ESRD • Higher than the recommended dose of amoxiclav in ESRD • Higher than the recommended dose of vancomycin in ESRD
Drug Use/Administration Problem (P4)	**Frequency (n, %)**	**Description**
Drug not administered	3 (7.5%)	• Antihistamine (cetirizine) not administered • Antihypertensive (nifedipine) for blood pressure control not administered • Lactulose not administered for constipation
Other Medication Problem (P6)	**Frequency (n, %)**	**Description**
Dose of drug not indicated	3 (7.5%)	• Dose of amlodipine not indicated • Dose of bisacodyl not indicated • Dose of amitriptyline not indicated

KEY: ESRD – End-stage renal disease, IV – Intravenously, SC – Subcutaneously.

4.6 Factors Associated with Various Medication Errors

A Fischer's exact or Pearson's chi-square test was done to identify whether there was an association between the occurrence of suspected adverse reactions and the patient's sociodemographic and clinical characteristics at $P \leq 0.05$. There was a significant association between having acute kidney injury and the occurrence of a suspected adverse drug reaction ($P = 0.030$) (Table 11).

Table 11: Factors associated with an adverse reaction

Variable	Prevalence of ADRs	P-value
Sex		
Female	5 (22.7%)	0.427
Male	2 (11.1%)	
Age (Years)		
≤47 years	18(54.5%)	0.407
≥48 years	2(28.5%)	
Education Level		
Primary	22(66.7%)	0.392
Secondary/Tertiary	3(42.9%)	
Employment Status		
Unemployed	7(23.3%)	0.161
Employed	0(0)	
Admission		
From ward	19(57.6%)	1.000
Through outpatient/another hospital	4(57.1%)	
Length of stay in ICU (days)		
≤7 days	13(39.4%)	0.432
≥8 days	4(57.1%)	
HTN (1^0 diagnosis)		
No	9(27.3%)	0.636
Yes	2(28.5%)	
Hypertensive urgency (1^0 diagnosis)		
No	9(27.3%)	0.428
Yes	1(14.3%)	
ADHF (1^0 diagnosis)		
No	3(9.1%)	0.552
Yes	1(14.3%)	
Number of comorbidities		
0-2	7(21.2%)	0.075
3-4	4(57.1%)	
AKI (Comorbidity)		
No	2(6.1%)	**0.030**
Yes	3(42.9%)	
DKA (Comorbidity)		
No	4(12.1%)	0.279
Yes	2(28.5%)	
CKD (Comorbidity)		
No	7(21.2%)	0.317
Yes	0(0)	
DM (Comorbidity)		
No	10(30.2%)	0.662
Yes	3(42.9%)	
CVA (Comorbidity)		
No	7(21.2%)	0.645
Yes	2(28.5%)	

The other medication errors, including drug choice problems (Table 14), dosing problems (Table 15), drug administration problems (Table 16), drug interactions (Table 12), and

other medication errors (Table 17), were also analysed. There was no significant association between these medication errors and the patient's clinical or sociodemographic characteristics.

Table 12: Factors associated with drug-drug interactions

Variable	Prevalence of drug interactions	P-value
Sex		
Female	22 (100.0%)	0.083
Male	15 (83.3%)	
Age (Years)		
≤47 years	17 (51.5%)	1.000
≥48 years	3 (42.9%)	
Education Level		
Primary	23 (69.7%)	0.279
Secondary/Tertiary	2 (28.5%)	
Employment Status		
Unemployed	28 (93.3%)	1.000
Employed	9 (90.0%)	
Admission		
From ward	19 (57.6%)	1.000
Through outpatient/another hospital	4 (57.1%)	
Length of stay in ICU (days)		
≤7 days	1 (33.3%)	1.000
≥8 days	16 (43.2%)	
HTN (1^0 diagnosis)		
No	0 (0)	0.548
Yes	11 (29.7%)	
Hypertensive urgency (1^0 diagnosis)		
No	1 (33.3%)	1.000
Yes	9 (24.3%)	
ADHF (1^0 diagnosis)		
No	0 (0)	1.000
Yes	4 (10.8%)	
Number of comorbidities		
0-2	0 (0)	0.548
3-4	11 (29.7%)	
AKI (Comorbidity)		
No	0 (0)	1.000
Yes	5 (13.5%)	
DKA (Comorbidity)		
No	1 (33.3%)	0.394
Yes	5 (13.5%)	
CKD (Comorbidity)		
No	0 (0)	1.000
Yes	7 (18.9%)	
DM (Comorbidity)		
No	1 (33.3%)	1.000
Yes	12 (31.6%)	
CVA (Comorbidity)		
No	0 (0)	1.000
Yes	9 (24.3%)	

4.7 Risk Factors for Adverse Drug Reactions

Logistic regression was done to establish whether the sociodemographic and clinical characteristics of the patients significantly predicted the occurrence of adverse drug reactions

Table 13: Bivariate logistic regression analysis for risk factors of Adverse Drug Reactions

Variable	Bivariate Analysis		Multivariate Analysis	
	COR	**P-Value**	**AOR**	**P-value**
Sex Male Female	0.226 (0.056 – 1.971)	0.226	-	-
Age (Years) ≤47 ≥48	0.962 (0.908 - 1.019)	0.185	-	-
Education Level Primary Secondary/Tertiary	0.375 (0.071 – 1.978)	0.248	-	-
Employment Status Unemployed Employed	0.304 (0.131 - 0.709)	**0.006**	0.216 (0.156 – 0.654)	0.098
Admission From ward Outpatient/another hospital	0.982 (0.189 – 5.108)	0.983	-	-
Length of stay in ICU (days) ≤7 days ≥8 days	2.051 (0.393 – 10.700)	0.394	1.299 (0.901, 1.872)	0.162
AKI No Yes	11.625 (1.467 – 92.140)	**0.020**	10.321 (1.678 – 75.125)	**0.012**
Number of comorbidities ≤2 ≥3	4.952 (0.892 – 27.488)	0.067	-	-

The significant predictors of adverse drug reactions were employment status, AND having acute kidney injury (Table 13). Those who were employed were 0.304 times likely to have an adverse drug reaction compared to those who were unemployed (p=0.006). Having a higher number of errors in the appropriateness of drugs increased the

chances of adverse drug reactions by 1.495 times ($p<0.001$). Additionally, the presence of acute kidney injury increased the odds of an adverse drug event by 11.625 times ($p = 0.020$). Participants with more than two comorbidities were 4.952 as likely to have an adverse drug reaction, but this finding was not statistically significant ($p = 0.067$). A parsimonious model of these variables using a backward stepwise regression showed that acute kidney injury increased the odds of adverse drug effects by 10.321 after adjusting for employment and length of MCCU stay ($P=0.012$). There were no significant predictors for drug choice problem, dosing, administration errors and other medication errors identified. The findings are in appendix D.

CHAPTER 5: DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1 Discussion

During the study period, a total of 40 patients, comprising 18 (45%) males and 22 (55%) females, were admitted into the CCU with cardiovascular disorders. These findings are similar to an Indian study where the prevalence of cardiovascular diseases was higher in females at 56.6% compared to men at 43.4% (47). However, this contrasted a survey done in the coronary care unit of Dhaka Medical College Hospital 2010 where 56% were males and 44% were females (48). In Africa, females carry a more considerable cardiovascular burden, which has increased by more than 10% since 1990 compared to men (49). A study summarizing findings in sub-Sahara Africa noted that the number of women who live and die from CVD and the number of hospital discharges from CVD-related illnesses exceeds that of men (50). The CVD-related mortality in 2013 was 512269 in women compared to 445,445 in males in sub-Saharan Africa (51). The higher burden in women could be explained by women have increased risk factors such as dyslipidaemia, obesity and overweight, depression, gestational diabetes, preterm delivery, autoimmune disease, and breast cancer treatment (52).

The mean age of the participants was 47.7 ± 15.4, which corresponds to the age of 40 -49 years, where adults are 2.72 times likely to develop hypertension (53). This is similar to the findings in the study done in India, where the mean age for the patients admitted in MICU with cardiovascular conditions was 49.2 ± 15.8 years. In sub-Saharan Africa, cardiovascular diseases such as heart failure has a younger age of onset of about 53 years compared to developed countries (54,55). Some studies suggest that genetics play a role increased predominance of CVD among African Americans, but no specific gene to

support this hypothesis have been isolated. However, a family history of CVD such as hypertension increases the chance of early onset of hypertension (<55years) by 4 times. Poor lifestyle habits that increase the prevalence of diabetes mellitus, hypertension, atherosclerotic diseases, and obesity is also attributable to an earlier age of onset among Africans (56). The difference in age of onset in developing and developed countries is attributable to a lack of adequate healthcare systems and infrastructure, minimal budgetary allocation, insurance coverage, and insufficient number of cardiac professionals in developing countries (57). Therefore, this study emphasises the need for greater allocation of human and financial resources to address the gaps in primary and secondary prevention of cardiovascular conditions.

The primary cardiovascular conditions of the patients admitted in KNH CCU included hypertension at 27.5%. This finding is similar to a study done in India on patients with cardiovascular diseases (CVDs) in a tertiary care hospital in 2016, whereby the main CVD was hypertension at 58.4% (47). Other major cardiovascular conditions leading to CCU admission were hypertensive urgency at 22.5%, followed by acute decompensated heart failure and myocardial infarction each at 7.5%. Most of the patients had two or more coexisting cardiovascular conditions. Hypertension is a major risk for heart failure, and half of the patients with untreated hypertension develop heart failure (58). Rheumatic heart disease is also a common aetiology of heart failure in the African population (54). This finding implies that failure to manage one cardiovascular condition adequately and in good time predisposes one to more cardiovascular illnesses. Therefore, preventive care should be adopted as a key approach in managing non-communicable diseases. Frequent screening of blood pressure, heart functions, proper treatment of infections should be

readily available and encouraged for all adults in Kenya to reduce the burden of cardiovascular diseases (1,59).

The presence of comorbidities such as diabetes, renal failure, and infections worsens the symptoms of heart failure and increases the chances of admission to the MCCU. The co-existence of cardio and renal illness increases mortality and morbidity for patients significantly (60). Early diagnosis and appropriate management of the comorbidities are likely to reduce admissions and mortality among patients with heart failure (61).

In this study, the most utilized cardiovascular drugs were diuretics, antihypertensive drugs, cardiac glycosides, and inotropes. In a similar study done in India medical ICU, inotropes, hypolipidemic agents and diuretics were commonly used (62). Some of the similar findings were atorvastatin was the most commonly used hypolipidemic, furosemide was the most common diuretic and isosorbide mononitrate was the most common antianginal drug. In contrast, the Indian MCCU had a much greater utilisation of inotropes, which was because the commonest primary diagnosis in their ICU was sepsis (62).

Ninety-seven prescriptions were analysed, from which 985 drugs were administered via the oral and parenteral routes. Seventy-seven errors were identified, with a majority of the patients (95%) experiencing at least one medication error during admission. The prevalence was much higher compared to that of an Ethiopian study, where the prevalence of medication errors was 51.8% (63). However, the Ethiopian study focused on a detailed analysis of drug administration errors only, and it included an analysis of the time of administration. In our study, the prevalence of drug administration errors was

7.5%, which could have been much lower because of the availability of drugs at KNH MCCU and better nursing services. A Kenyan study on medication errors in a paediatric inpatient at Kisii level 5 Hospital found a lower prevalence of 75.8%. This could be because the study population was not in critical care and the sample size was ten times bigger than our study (14). This finding points to the need for continuous education of nurses on drug administration, improvement of health systems to facilitate detection and prevention of errors, and deployment of more pharmaceutical personnel in the critical care setup.

Seven patients (17.5%) suffered a probable adverse drug effect. The main adverse effects were major bleeding events, bradycardia and hyperkalaemia. These patients are likely to be on anticoagulants, antiplatelet drugs which are likely to increase bleeding risk. Being critically ill predisposes them to physiological stress ulcers that may increase their chances of gastrointestinal bleeding (64). Antihypertensives, or shock may contribute to lowering of blood pressure, hence the bradycardia. Drugs that are potassium sparing, combined with acute kidney injury may contribute to electrolyte abnormalities, leading to hyperkalaemia (65). A multicentre study done in Spain involving 183,677 adult admissions, estimated the prevalence of adverse events to be 2.2% during hospitalization (52). The difference in prevalence could be explained by the fact that most hospitals in Europe perform routine monitoring (66). This could be implemented in Kenya by equipping the hospitals with the required equipment, utilities, and human resource to enable frequent monitoring of drugs.

Majority of the patients who developed bleeding events were on enoxaparin, which was the main anticoagulant used in the ward. Low molecular weight heparins are associated

with a higher propensity of bleeding events, especially in renal failure and sepsis (67,68). However, in venous thromboembolism, the risk of bleeding with low molecular weight heparin is lower compared to unfractionated heparin (69). The incidence of major bleeding with enoxaparin is estimated at 1.0% - 6.5%, which is determined by the drugs being co-administered, renal insufficiency, obesity, presence of comorbidities, the time of observation, and having advanced age (70). In this study, the incidence of bleeding associated with enoxaparin was 17.5%, which could have been high because of the high number of patients with renal disease. Therefore, dose adjustments depending on renal function is recommended. Some studies suggest that the drug should be withdrawn in stages 4-5 of kidney disease due to lack of safety data in this population, while others suggest dose reduction (71).

In our study, having acute kidney injury was significantly associated with the occurrence of adverse drug effects (p=0.030), which was also an independent predictor (AOR = 10.321, p=0.012) of ADEs. Kidneys play a key role in the clearance of drugs and harmful metabolites, whose accumulation can affect normal homeostasis (72). Inappropriate drug choices and doses and the use of multiple drugs among patients with pre-existing renal dysfunctions could explain why patients with AKI had a high risk of adverse drug effects. This finding was similar to an Ethiopian study that noted a 2.84 increased risk of adverse drug effects among patients with renal disease.

Low eGFR is a known predictor of developing hyperkalaemia experienced by 5% of the patients (65). Therefore, the use of potassium chloride should have been accompanied done through a slow infusion and accompanied by daily monitoring of kidney functions and electrolyte measures. Patients with compromised renal functions should be identified

and monitored closely to ensure that any drugs administered do not worsen the kidney functions further.

Other predictors of the adverse events were being employed (OR = 0.304, p=0.006) and the number of errors in the inappropriateness of the drugs (OR = 1.495, p<0.001). There were contrary findings from a study done in the rural area of India involving 47 patients. Having a higher socioeconomic status was a risk factor for adverse drug events (73). On the contrary, our study showed that being employed reduced the chances of an adverse drug effect by about 30%, a surrogate indicator of a higher socioeconomic status. Probably those who had a higher socioeconomic status had an existing insurance cover or financial ability to conduct the required laboratory monitoring tests in good time to inform clinical decisions. Employed people are also more likely to be educated and aware of their medication even before admission to CCU. However, data on the relationship between socioeconomic status and the occurrence of adverse drug effects is scanty in the ICU setup; hence inconclusive. This association is unexpected and suggests more studies are needed in this area.

About 58% of the patients in the CCU are likely to experience potential drug-drug interactions and are twice as likely to have the interactions compared to patients in the general wards (74). The occurrence of a pDDI is fuelled by the fact that patients could receive up to 30 medications during their ICU stay. In our study, every patient received about 24.6 (SD: 6.7) drugs during their stay. The prevalence of pDDIs was 92.5% in this study group, almost equal to a similar study in India with a sample size of 72 where the incidence of pDDIs was 90.0% (75). This finding was also comparable to a one-year study involving 520 patients in two Pakistan hospitals with a prevalence of 96.5% and

95.7% (76). Two other studies done in the cardiology clinic, one in Pakistan and another in Brazilian reported a prevalence of 91.6% and 70.6% respectively. The low prevalence in Pakistan and Brazil was attributed to the outpatient setting used for both studies, as opposed to the ICU. Some of the recommended monitoring strategies that could help include clinical monitoring, avoiding drug combinations with a high risk of interactions, monitoring the blood counts, and ECG monitoring to reduce adverse outcomes. This study also highlights the importance of monitoring glucose levels, liver function tests, urea and electrolytes and relating these findings to the current medications being used.

Half of the interactions were classified as major, 46.8% were minor, with each patient having 3.95 pDDIs. This finding was slightly different to one study done in an Indian cardiac CCU with 45.2% major interactions and 52.6% moderate interactions. A study in Ethiopia involving 200 admissions related to cardiac problems identified 4.83 pDDIs per patient during admission (77). Drug interactions are highly preventable errors, yet important causes of admission and rehospitalisation (76). The high prevalence of major pDDIs highlight a major gap in the selection of appropriate drug combinations for critically ill patients. There is a need to educate the prescribers on the potential harm of the pDDIs and have a dedicated pharmacist to advise on the suitable alternatives with the aim of optimizing treatment and reducing harm.

The most common possible outcomes from the pDDIs were increased risk of hyperglycaemia, bleeding and phenytoin toxicity. The high incidence of interactions involving insulin could be explained by the high prevalence of diabetes in this sample. Use of diuretics (furosemide) and thiazides (hydrochlorothiazide) impairs glucose tolerance and worsens glucose control (78,79). Studies suggest that thiazide-induced

hypokalaemia stimulates hyperglycaemia (78). Since hypertension precedes diabetes in most cases, there seems to be an unknown mechanism by which thiazides blunt insulin sensitivity (79). This finding implies that diabetic patients might require careful monitoring and possibly insulin dose adjustment to maintain euglycemia.

About 8.9% of the patients were using either one or more anticoagulants and/or antiplatelet agents for prophylaxis or treatment. Use of warfarin, enoxaparin, clopidogrel and aspirin among the patients, especially concomitantly increased the chance of bleeding. A study done in the USA showed that the use of anticoagulants, antibiotics, and hypoglycaemic agents resulted in 46.9% of incidences in emergency department visits attributable to adverse drug effects (80). Concomitant use of aspirin and low molecular weight heparin is associated with more than a two-fold increase in both major bleeding and intracranial bleeding events (81). Combining clopidogrel, aspirin and enoxaparin significantly increases the risk of upper gastrointestinal bleeding within the first seven days (82). Warfarin and omeprazole are known to interact through the cytochrome system, where omeprazole competitively inhibits the metabolism of warfarin through the CYP2C9 and CYP2C19. However, the interaction is not clinically significant since only the less potent warfarin enantiomer (R) is inhibited (83). In summary, in combining anticoagulants and antiplatelet agents should only be used when potential benefits outweigh the risk of bleeding. Patients on triple therapy with LMWH and double antiplatelets should be flagged as high bleeding-risk patients and monitored closely for signs of bleeding.

Dosing errors resulted from a lack of renal dose adjustment and had a prevalence of 10.0%. The use of higher than recommended doses for a defined diagnosis occurred with

a prevalence of 7.5%. In renal failure, the excretion of drugs is compromised, and after loading a normal dose of antibiotics, the subsequent doses should be reduced or the interval should be increased (84). Failure to adjust the dose or interval could increase the risk of toxicities. From a study done at KNH involving 314 patients with chronic kidney disease, patients using antibiotics particularly amoxicillin-clavulanic acid, cefuroxime, amikacin, meropenem, cotrimoxazole, levofloxacin, and piperacillin/tazobactam received inappropriate doses. The study revealed that only 27.7% of the patients received the recommended dose of antibiotics with a 72.3% prevalence of inappropriate prescription (85). In our study, all the incidences of inappropriate doses involved antibiotics, with a lower prevalence to comparable studies. This is probably because this study sample was not focused on patients with CKD. This finding highlights a gap in the renal dose adjustment of patients in the MCCU. Probably if the prescriptions were reviewed by pharmaceutical personnel daily and the clinicians made a daily entry of the eGFR, this omission would be reduced.

Other dosing errors included using a higher than the recommended dose of proton pump inhibitors (PPIs). In the CCU setup, PPIs are used prophylactically for stress ulcers. However, overutilization of PPIs carried potential risks such as increased risks of enteric infections and community-acquired pneumonia, reduced absorption of oral medications and some nutrients and rebound hyperacidity (86,87). The clinicians need to be educated on the indications and the recommended dosing of proton pump inhibitors to reduce their overuse.

Failure to administer the prescribed drug was noted in 7.5% of the patients involving an antihistamine, antihypertensive, and cathartic. From one Ethiopian study, the prevalence

of missed drugs or doses was 8.3% (88). Some of the factors associated with administration errors are the age of the nurse, level of experience, nurse to patient ratio, interruption during medicine administration, lack of drug use guidelines, and being on the night shift as well as drug being out of stock (88,89).

From our study, none of the independent variables predicted drug administration problems. Drug administration problem is related to human resource aspects rather than patient factors, especially in the ICU setup where most of the drugs were availed by the hospital. Therefore, since the scope of this study was limited to the patients' variables, issues related to nursing staff were not explored. Studies recommend that administration errors can be minimized by having continuous training of nurses on safe drug administration, availing guidelines on drug administration, creating a supportive environment for nurses to administer medications safely, and having more experienced nurses (89).

There were incidences of failing to get a drug prescribed for an indication (22.5%), using a wrong drug for a certain indication (17.5%) and use of inappropriate antibiotic combinations (5.0%). Most of the errors involved haematological drugs, cardiovascular drugs. In one study done during the transition of care from the CCU to a non-CCU setting, having an untreated condition accounted for 19.4% of the medication errors (90). An Ethiopian study done in the medical and surgical wards identified 69 (38.1%) untreated indications (91). From the 69 indications, the most commonly involved drugs were cardiovascular, antibiotics, and haematological drugs. One of the factors associated with the error was the presence of comorbidities (91). Untreated condition(s) could increase the duration of admission of a patient and worsen a patient's condition.

Other errors included inappropriate prescribing (incomplete prescriptions) by the clinicians where the dose of the drug was not indicated in a prescription (n=3, 7.5%). Prescription errors are associated with frequent interferences when writing a prescription, distraction, and lack of knowledge (92). In one study done in a paediatric setup at Mbagathi hospital in Kenya, there were three incomplete prescriptions (0.2%) that did not contain the dose of the drug prescribed (32). This figure was similar to the one obtained in our study, but the prevalence could have been higher with larger sample size. An incomplete prescription can lead to misinterpretation by the nurse or pharmacist, and also cause a delay in the filling of a prescription, resulting in delayed intervention or error in drug administration (93). This finding emphasizes the need for having patients' prescriptions verified by a pharmacist and having a clear and efficient communication channel between clinicians and pharmaceutical personnel to solve such omissions promptly.

5.2 Strengths of the Study

This was the first study to investigate and quantify medication errors and their potential risk factors amongst critically ill cardiovascular disease patients in the KNH MCCU. This will provide new information and improve management of these patients, by deploying pharmacists in the CCUs to closely monitor these patients. It will also form a basis for similar larger studies to be conducted in the future.

5.3 Limitations

The study relied on a small sample size, which reduced the generalizability of the study to other settings. Secondly, some aspects of the sociodemographic history collected from the patients or from their medical records could be inaccurate.

The study did not focus on the cause of the medication errors and their interventions; hence more studies are recommended to focus on the two aspects.

The study was limited to the patients' variables, issues related to nursing staffs were not explored. The study did not ascertain causality of adverse drug events so it was not possible to ascribe adverse events do drugs. A larger study assessing causality of ADRs is therefore recommended.

5.4 Conclusion

There was a higher burden of cardiovascular illness among females and the unemployed. Medications errors were highly prevalent in the critical care unit particularly potential drug interactions and drug choice problems. Most errors were attributable to cardiovascular drugs and antibiotics. Being employed reduced the odds of an adverse drug event, while acute kidney injury was an independent predictor of an adverse drug reaction.

Monitoring of patients' clinical signs, conducting the relevant laboratory tests regularly, appropriate choice of drug combinations, and renal dose adjustments is key in mitigating medication errors. The presence of a clinical pharmacist in the MCCU could potentially reduce the occurrence of medication errors and optimize the therapeutic options available for the patients.

5.5 Recommendations

5.4.1 Recommendations for Practice

1. Acutely ill patients with acute kidney injury need keen and frequent monitoring of their electrolyte levels and clinical signs to prevent the occurrence of adverse effects
2. Patients using insulin to manage diabetes and diuretics should have their sugar levels closely monitored to avoid hyperglycaemia and possible diabetic ketoacidosis
3. Clinicians should be keen on writing down a problem list of the patients on a daily basis to avoid having an untreated indication
4. The ICU department should have a standard protocol to ensure every prescription is verified by a clinical pharmacist for appropriateness

5.4.2 Recommendations for Future Studies

1. A study to investigate the most prevalent adverse drug effects in acute kidney injury and their management approaches
2. A study to investigate the actual clinical outcomes of the pDDIs to document their clinical relevancy
3. A study to investigate the health providers' factors that predict the occurrence of medication errors to inform better practices

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APPENDICES

Appendix A: Eligibility Check List

Title: Eligibility Check List

Date:

Screening ID:

Inclusion criteria for cohort study of cardiovascular patients admitted at KNH CCU

	Yes	No
Patients admitted at the KNH CCU for the study period		
Patient above 18 years		
Patient without a cardiovascular diagnosis		

Exclusion criteria for cohort study of cardiovascular patients admitted at KNH CCU

	Yes	No
Patient files with incomplete clinical records		
Patients under the age of 18 years		
Patient without a cardiovascular diagnosis		

Appendix B: Data Collection Tool

PART 1: INFORMED CONSENT FORM

To be read in a language that the respondent is fluent in

ADULT PARTICIPANT INFORMATION AND CONSENT FORM FOR ENROLLMENT IN THE STUDY

Title of Study: MEDICATION ERRORS AMONG CARDIOVASCULAR PATIENTS ADMITTED AT THE CRITICAL CARE UNIT OF KENYATTA NATIONAL HOSPITAL

Principal Investigator\and institutional affiliation:

Mwavu Doryne Mbula, Master of Pharmacy in Clinical Pharmacy student, Department of Pharmaceutics and Pharmacy Practice, School of Pharmacy, University of Nairobi

Supervisors/Co-Investigators and institutional affiliation:

1. Dr. Sylvia Atisa Opanga

   Department of Pharmaceutics and Pharmacy Practice

   University of Nairobi

2. Prof. Faith Apolot Okalebo

   Department of Pharmacology and Pharmacognosy

   University of Nairobi

Introduction:

I request your attention to explain about an ongoing study by the researchers listed above as part of the requirement. This study is part of my assessment for a degree in master of pharmacy in clinical pharmacy at the University of Nairobi. This consent form will inform you about this research and enable you to decide whether to participate in the

study. You are free to ask questions related to the study such as, what will happen to you as a participant, the potential risks, or benefits, the rights you have as a participant or any other information. When you feel satisfied with the study, you are free to enrol into the study by giving your consent. The name of this process is 'informed consent.' When you understand and decide to join in the study, you will sign your initials on this form as proof of consent.

Some of the universal principles that in medical research, which apply to participants are:

i) Participation in this study is totally voluntary

ii) At any point in this study, you are free to withdraw without necessarily explaining your withdrawal

iii) In case you decline to be a participant in the research, you will still enjoy all the normal services you are entitled to. A copy of this form will be provided to you for your records.

May I continue? **YES / NO**

The Kenyatta National Hospital-University of Nairobi Ethics and Research Committee has approved this study via protocol No._____

What is this study about?

This research is targeting adult cardiovascular patients admitted at the critical care unit in Kenyatta National Hospital. This study wants to assess any medication errors experienced by the patients admitted in this unit. About 40 patients will be randomly chosen to participate in this study.

What will happen if you decide to be in this research study?

If you agree to part of this study, the interviewer will access information from your medical file related to your social, medical, and medication history. There will be no direct procedures that will be done to you by the researcher.

Are there any risks or harms discomforts associated with this study?

From this study, you may suffer a loss of privacy. However, all the information collected from your file will be kept confidential. In this study, a code number will be used to refer to you in computer database that is password-protected, and all paper records will be kept in a well-secured cabinet. Please note it could still be possible that someone gains access to the study records and finds out that you were one of the participants since no data storage system can be absolutely secure.

Are there any benefits to being in this study?

You may benefit by being part of this study. If problems are detected, the doctor will be informed and this will be of benefit to you. Also, the results of this study will be useful for improving the quality of care received by you and future patients.

Will being in this study cost you anything?

However, participating in this study will not cost you any money.

Will you get a refund for any money spent as part of this study?

Since there is no foreseeable expenditure for participating in this study, there will be no compensation arising from being a participant.

What if you have questions in the future?

In case you have any additional concerns about being part of this study, please send a text message, or call the investigator on the following number: Doryne Mwavu (+254728478584). If you need additional information about your rights as a research participant, please contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee through the telephone number 2726300 Ext. 44102 or the email address: uonknh_erc@uonbi.ac.ke. The study has ethical approval from this entity.

The researchers in this study should compensate you for the charges you incur if you call these numbers for study-related queries.

What are your other choices?

Participating in this research is voluntary. You have the option to decline to participate or to withdraw from this study at any point without suffering any injustice or losing any benefits and services usually enjoyed at the hospital.

Researcher's statement

Having explained all the relevant details of this study to the above participant, I trust that he/she has understood and voluntarily given his/her consent to participate.

Researcher's Name: _____

Date: _____

Signature: _____

Role in the study: _____

Participant's Statement

This is to confirm that I have read this consent information or have been read to me. I have discussed with the study counsellor in details about this research, and my questions have been addressed in a language that I understand. I am aware of the benefits or risks of being one of the participants. It is clear to me that my participation is voluntary, and at any given point in this study, I am free to withdraw. Therefore, I have agreed to participate in this study freely.

I understand that the research staff will make all efforts possible to maintain the confidentiality of my personal records and identity. I understand that by consenting to

this study, I have not foregone my legal rights, which I am entitled to as a study participant.

Participant/Caregiver initials: _____

Participant/Caregiver signature/thumb stamp: _____

Date: _____

SEHEMU YA 1: FOMU YA KIBALI YA TAARIFA MUHKTASARI WA UHUSIKA WA MTU MZIMA NA FOMU YA IDHINI KWA AJILI YA UTAFITI HUU

Kichwa cha Utafiti: MAKOSA YA DAWA MIONGONI MWA WAGONJWA WA ROHO WALIOLAZWA KATIKA KITENGO CHA UTUNZAJI MUHIMU KATIKA HOSPITALI KUU YA KENYATTA

Mchunguzi Mkuu \ na ushirika wa taasisi:

Mwavu Doryne Mbula, , Mwanafunzi wa shahada ya uzamili ya madawa, Idara ya Pharmaceutics and Pharmacy Practice, Shule ya Famasia, Chuo Kikuu cha Nairobi

Wasimamizi / Wachunguzi wa ushirikiano na ushirika wa kitaasisi:

1. Dk Sylvia Atisa Opanga
   Idara ya Pharmaceutics and Pharmacy Practice
   Shule ya Famasia
   Chuo Kikuu cha Nairobi
2. Profesa Faith Apolot Okalebo
   Idara ya Pharmacology na Pharmacognosy
   Shule ya Famasia
   Chuo Kikuu cha Nairobi

Utangulizi:

Ninaomba umakini wako usikilize nikueleze juu ya utafiti unaoendelea na watafiti walioorodheshwa hapo juu kama sehemu ya mahitaji. Utafiti huu ni sehemu ya tathmini yangu kwa shahada ya uzamili kwa shahada ya dawa katika Chuo Kikuu cha Nairobi. Fomu hii ya idhini itakujulisha juu ya utafiti huu na kukuwezesha kuamua ikiwa utashiriki katika utafiti. Uko huru kuuliza maswali yanayohusiana na utafiti kama vile, nini kitatokea kwako kama mshiriki, hatari zinazoweza kutokea, au faida, haki unazo kama mshiriki au habari nyingine yoyote. Unapohisi kuridhika na utafiti huo, uko huru kujiandikisha katika utafiti huo kwa kutoa idhini yako. Jina la mchakato huu ni 'idhini ya

habari.' Unapoelewa na kuamua kujiunga kwenye utafiti, utasaini jina lako kwenye fomu hii kama uthibitisho wa idhini.

Baadhi ya kanuni za ulimwengu ambazo katika utafiti wa matibabu, ambazo zinatumika kwa washiriki ni:

I. Kushiriki katika utafiti huu ni hiari kabisa
II. Wakati wowote katika utafiti huu, uko huru kujiondoa bila kuelezea uondoaji wako
III. Endapo utakataa kushiriki katika utafiti huo, bado utafurahiya huduma zote za kawaida unazostahiki. Nakala ya fomu hii utapewa kwako kwa kumbukumbu zako.

Naweza kuendelea? **NDIO /LA**

Kamati ya Kitaifa ya Hospitali ya Maadili na Utafiti ya Kenya ya Kenyatta na Chuo Kikuu cha Nairobi imeidhinisha utafiti huu kupitia itifaki nambari_____

Je! Utafiti huu unahusu nini?

Utafiti huu unalenga wagonjwa wazima wa moyo na mishipa waliolazwa katika kitengo cha utunzaji muhimu katika Hospitali ya Kitaifa ya Kenyatta. Utafiti huu unataka kutathmini makosa yoyote ya dawa yanayopatikana na wagonjwa waliolazwa katika kitengo hiki. Karibu wagonjwa 40 watachaguliwa kwa nasibu kushiriki katika utafiti huu.

Ni nini kitatokea ikiwa utaamua kuwa katika utafiti huu?

Ikiwa unakubali sehemu ya utafiti huu, mhojiwa atapata habari kutoka kwa faili yako ya matibabu inayohusiana na historia yako ya kijamii, matibabu, na dawa. Hakutakuwa na taratibu za moja kwa moja ambazo utafanywa kwako na mtafiti.

Je! Kuna hatari yoyote au hudhuru usumbufu unaohusishwa na utafiti huu?

Kutoka kwa utafiti huu, unaweza kupoteza faragha. Walakini, habari yote iliyokusanywa kutoka kwa faili yako itahifadhiwa kwa siri. Katika utafiti huu, nambari ya nambari

itatumiwa kukurejelea kwenye hifadhidata ya kompyuta ambayo inalindwa na nenosiri, na rekodi zote za karatasi zitahifadhiwa kwenye baraza la mawaziri lenye usalama. Tafadhali kumbuka kuwa bado inaweza kuwa mtu anaweza kupata rekodi za utafiti na kugundua kuwa wewe ni mmoja wa washiriki kwani hakuna mfumo wa kuhifadhi data ambao unaweza kuwa salama kabisa.

Je! Kuna faida yoyote kuwa katika utafiti huu?

Unaweza kufaidika kwa kuwa sehemu ya utafiti huu. Ikiwa shida hugunduliwa, daktari atajulishwa na hii itakuwa ya faida kwako. Pia, matokeo ya utafiti huu yatakuwa muhimu kwa kuboresha ubora wa huduma unayopokea wewe na wagonjwa wa baadaye.

Je! Kuwa katika utafiti huu kutagharimu chochote?

Walakini, kushiriki katika utafiti huu hakutakugharimu pesa yoyote.

Je! Utapata marejesho ya pesa yoyote iliyotumiwa kama sehemu ya utafiti huu?

Kwa kuwa hakuna matumizi ya kuonekana kwa kushiriki katika utafiti huu, hakutakuwa na fidia inayotokana na kuwa mshiriki.

Je! Ikiwa una maswali katika siku zijazo?

Ikiwa una wasiwasi zaidi kuhusu kuwa sehemu ya utafiti huu, tafadhali tuma ujumbe mfupi, au piga simu kwa mchunguzi kwa nambari ifuatayo: Doryne Mwavu (+254728478584). Ikiwa unahitaji habari zaidi kuhusu haki yako kama mshiriki wa utafiti, tafadhali wasiliana na Katibu / Mwenyekiti, Hospitali ya Kitaifa ya Kenyatta-Kamati ya Maadili na Utafiti ya Chuo Kikuu cha Nairobi kupitia nambari ya simu 2726300 Ext. 44102 au anwani ya barua pepe: uonknh_erc@uonbi.ac.ke. Utafiti huo una idhini ya kimaadili kutoka kwa chombo hiki.

Watafiti wa utafiti huu wanapaswa kulipia fidia kwa mashtaka unayopata ikiwa utapiga nambari hizi kwa maswali yanayohusiana na utafiti.

Je! Chaguzi zako zingine ni zipi?

Kushiriki katika utafiti huu ni hiari. Una chaguo la kukataa kushiriki au kujiondoa kwenye utafiti huu wakati wowote bila kupata udhalimu wowote au kupoteza faida na huduma ambazo kawaida hufurahiya hospitalini.

Kauli ya mtafiti

Baada ya kuelezea maelezo yote muhimu ya utafiti huu kwa mshiriki hapo juu, ninaamini kwamba ameelewa na kwa hiari yake ameruhusu kushiriki.

Jina la Mtafiti: _____

Tarehe: _____

Sahihi: _____

Jukumu katika utafiti: _____

Taarifa ya Mshiriki

Hii ni kudhibitisha kuwa nimesoma habari hii ya idhini au nimesomewa. Nimejadiliana na mshauri wa utafiti kwa undani juu ya utafiti huu, na maswali yangu yameshughulikiwa kwa lugha ambayo ninaelewa. Ninajua faida au hatari za kuwa mmoja wa washiriki. Ni wazi kwangu kwamba ushiriki wangu ni wa hiari, na wakati wowote katika somo hili, niko huru kujiondoa. Kwa hivyo, nimekubali kushiriki katika utafiti huu kwa uhuru.

Ninaelewa kuwa wafanyikazi wa utafiti watafanya juhudi zote iwezekanavyo kudumisha usiri wa rekodi zangu za kibinafsi na kitambulisho. Ninaelewa kuwa kwa kukubali utafiti huu, sijatangulia haki zangu za kisheria, ambazo ninastahiki kama mshiriki wa utafiti.

Mshiriki / Mlezi aliyechapishwa jina: _____

Saini ya mshiriki / Mlezi / Stempu ya kidole gumba: _____

Tarehe: _____

Part 2: DATA EXTRACTION FORM

Form 1: Patient's Biodata

Instructions

1. Fill one sheet per patient file
2. Fill in the spaces provided or tick against the most appropriate choice provided

Retriever's Initials: ……	**Date: …….**
Unique Identification Number: ……	**Age (years): …….**
Weight (kg): ……	**Gender (M/F): …….**
Height (cm): ……	**BMI: ……....**
Education Status: 0 = Primary and below 1 = Secondary 2 = Tertiary	**Employment Status:** 0 = Unemployed 1 = Employment
Admission: 0 = Transfer from ward 1= Admission through outpatient 2 = Referral from another hospital	**Date of admission at CCU (dd/mm/yyyy):** ……. **Date of discharge from CCU (dd/mm/yyyy):** ……
Patient's chief complaint: ……..…… ……..…. ……...…….	

Patient's Final Diagnosis (Tick appropriately):

Arrhythmias ☐

Rheumatic heart disease ☐

Infective endocarditis ☐

Congenital heart disease ☐

Coronary artery disease ☐

Deep vein thrombosis and pulmonary embolism ☐

Heart attack ☐

Heart failure ☐

Cardiomyopathy ☐

Others (specify)…….

Patient's Comorbidities:

Asthma ☐

Diabetes ☐

COPD ☐

Cancer ☐

Immunocompromised condition ☐

Renal disease ☐

Liver disease ☐

Others (specify)……

……..

Form 2: Laboratory Tests and Monitoring Parameters

Vital Signs and Labs	Day 1	2	3	4	5	6	7	8	9	10
Blood Pressure (mmHg)										
Heart rate										
Oxygen Saturation										
Respiratory rate										
GCS Score										
INR										
ALT										
Bilirubin										
eGFR										
Creatinine										
Sodium										
Potassium										
Haemoglobin										
Calcium										
FBS/HbA1c										

KEY: HbA1c - Haemoglobin A1c, INR - International Normalized Ratio, eGFR - estimated glomerular filtration rate, ALT - alanine aminotransferase

Form 3: Appropriateness of Drug

Class of Drug	Indication	Drug Prescribed (Name, dose (mg), frequency, ROA, and preparation) e.g. Enalapril 10mg BD PO TABLETS	Correct Indication 0=Yes 1=No	Correct Dose 0=Yes 1=No	Correct duration 0=Yes 1=No	Drug administered 0 = No 1 = Yes
Cardiovascular Drugs						
Anticoagulants						
Analgesics						
Antibiotics						
Others						

PART 3: DRUG INTERACTIONS

Are there any potential drug interactions? [NO = 0, YES = 1]			
Interacting drugs		Level of Interaction	Consequences of drug-drug interactions
1			
2			
3.			
4.			
5.			

PART 4: ADVERSE DRUG EVENTS

Are there any adverse drug events? [NO = 0, YES = 1]	
Drug	ADE
1	
2	
3.	
4.	

Appendix C: Checklist for Medication Errors, as adopted from The Pharmaceutical Care Network Europe (PCNE)

		Yes	No
P1	Adverse reaction(s) Patient suffers from an adverse drug event		
P2	Drug Choice Problem Patient gets or is going to get a wrong (or no drug) drug for his/her disease and/or condition		
P3	Dosing problem Patient gets more or less than the amount of drug he/she requires		
P4	Drug Use/Administration Problem Wrong or no drug taken/administered		
P5	Interactions There is a manifest or potential drug-drug or drug-food interaction		
P6	Others		

Appendix D: Supplement Tables

Table 14: Factors Associated with Drug Choice Problems

Variable	Prevalence of drug choice problems	P-value
Sex		
Female	12 (54.5%)	0.216
Male	6 (33.3%)	
Age (Years)		
≤47 years	13 (59.1%)	0.204
≥48 years	7 (38.9%)	
Education Level		
Primary	15 (68.1%)	0.412
Secondary/Tertiary	10 (55.6%)	
Employment Status		
Unemployed	16 (53.3%)	0.082
Employed	2 (20.0%)	
Admission		
From ward	11 (50.0%)	0.348
Through outpatient/another hospital	12 (66.7%)	
Length of stay in ICU (days)		
≤7 days	10 (45.5%)	0.676
≥8 days	7 (38.9%)	
HTN (1^0 diagnosis)		
No	5 (22.7%)	0.498
Yes	6 (33.3%)	
Hypertensive urgency (1^0 diagnosis)		
No	7 (31.8%)	0.464
Yes	3 (16.7%)	
ADHF (1^0 diagnosis)		
No	1 (4.5%)	0.310
Yes	3 (16.7%)	
Number of comorbidities		
0-2	5 (22.7%)	0.498
3-4	6 (33.3%)	
AKI (Comorbidity)		
No	1 (4.5%)	0.155
Yes	4 (22.2%)	
DKA (Comorbidity)		
No	3 (13.6%)	1.000
Yes	3 (16.7%)	
CKD (Comorbidity)		
No	5 (22.7%)	0.427
Yes	2 (11.1%)	
DM (Comorbidity)		
No	10 (45.5%)	0.090
Yes	3 (16.7%)	
CVA (Comorbidity)		
No	4 (18.2%)	0.705
Yes	5 (27.8%)	

Table 15: Factors Associated with Dosing Problems

Variable	Prevalence of dosing problems	P-value
Sex		
Female	5 (22.7%)	0.427
Male	2 (11.1%)	
Age (Years)		
≤47 years	17 (51.5%)	1.000
≥48 years	3 (42.9%)	
Education Level		
Primary	23 (69.7%)	0.081
Secondary/Tertiary	2 (28.6%)	
Employment Status		
Unemployed	6 (20.0%)	0.656
Employed	1 (11.1%)	
Admission		
From ward	19 (57.6%)	1.000
Through outpatient/another hospital	4 (57.1%)	
Length of stay in ICU (days)		
≤7 days	13 (39.9%)	0.432
≥8 days	4 (57.1%)	
HTN (1^0 diagnosis)		
No	8 (24.2%)	0.369
Yes	3 (42.9%)	
Hypertensive urgency (1^0 diagnosis)		
No	8 (24.2%)	1.000
Yes	2 (28.5%)	
ADHF (1^0 diagnosis)		
No	3 (9.1%)	0.552
Yes	1 (14.3%)	
Number of comorbidities		
0-2	7 (21.2%)	0.075
3-4	4 (57.1%)	
AKI (Comorbidity)		
No	3 (9.1%)	0.204
Yes	2 (28.5%)	
DKA (Comorbidity)		
No	4 (12.1%)	0.279
Yes	2 (28.5%)	
CKD (Comorbidity)		
No	5 (15.2%)	0.584
Yes	2 (28.5%)	
DM (Comorbidity)		
No	10 (30.3%)	0.662
Yes	3 (42.9%)	
CVA (Comorbidity)		
No	7 (21.2%)	0.645
Yes	2 (28.5%)	

Table 16: Factors Associated with Drug Use/Administration Problems

Variable	Prevalence of drug administration problem	P-value
Sex		
Female	2 (9.0%)	1.000
Male	1 (5.6%)	
Age (Years)		
≤47 years	19 (51.4%)	1.000
≥48 years	1 (33.3%)	
Education Level		
Primary	23 (62.2%)	1.000
Secondary/Tertiary	2 (66.7%)	
Employment Status		
Unemployed	3 (10.0%)	0.560
Employed	0 (0)	
Admission		
From ward	21 (56.8%)	1.000
Through outpatient/another hospital	2 (66.7%)	
Length of stay in ICU (days)		
≤7 days	16 (43.2%)	1.000
≥8 days	1 (33.3%)	
HTN (1^0 diagnosis)		
No	10 (27.0%)	1.000
Yes	1 (33.3%)	
Hypertensive urgency (1^0 diagnosis)		
No	9 (24.3%)	1.000
Yes	1 (33.3%)	
ADHF (1^0 diagnosis)		
No	4 (10.8%)	1.000
Yes	0 (0)	
Number of comorbidities		
0-2	10 (27.0%)	1.000
3-4	1 (33.3%)	
AKI (Comorbidity)		
No	4 (10.8%)	0.338
Yes	1 (33.3%)	
DKA (Comorbidity)		
No	5 (13.5%)	0.394
Yes	1 (33.3%)	
CKD (Comorbidity)		
No	7 (18.9%)	1.000
Yes	0 (0)	
DM (Comorbidity)		
No	12 (32.4%)	1.000
Yes	1 (33.3%)	
CVA (Comorbidity)		
No	8 (24.2%)	0.545
Yes	1 (33.3%)	

Table 17: Factors Associated with other Medication Errors

Variable	Prevalence of other medication errors	P-value
Sex		
Female	1 (4.5%)	1.000
Male	1 (5.6%)	
Age (Years)		
≤47 years	19 (50.0%)	1.000
≥48 years	1 (50.0%)	
Education Level		
Primary	25 (65.8%)	0.135
Secondary/Tertiary	0 (0)	
Employment Status		
Unemployed	2 (66.7%)	1.000
Employed	0 (0)	
Admission		
From ward	23 (60.5%)	0.174
Through outpatient/another hospital	0 (0)	
Length of stay in ICU (days)		
≤7 days	16 (42.1%)	1.000
≥8 days	1 (50.0%)	
HTN (1^0 diagnosis)		
No	10 (26.3%)	0.479
Yes	1 (50.0%)	
Hypertensive urgency (1^0 diagnosis)		
No	9 (23.7%)	0.442
Yes	1 (50.0%)	
ADHF (1^0 diagnosis)		
No	4 (10.5%)	1.000
Yes	0 (0)	
Number of comorbidities		
0-2	10 (26.3%)	0.479
3-4	1 (50.0%)	
AKI (Comorbidity)		
No	4 (10.5%)	0.237
Yes	1 (50.0%)	
DKA (Comorbidity)		
No	6 (15.8%)	1.000
Yes	0 (0)	
CKD (Comorbidity)		
No	6 (15.8%)	0.323
Yes	1 (50.0%)	
DM (Comorbidity)		
No	13 (46.4%)	1.000
Yes	0 (0)	
CVA (Comorbidity)		
No	8 (21.1%)	0.404
Yes	1 (50.0%)	

Table 18: Covariates of Dosing Problem (P3)

Variable	Bivariate Analysis	
	COR	**P-Value**
Sex Female Male	0.425 (0.072, 2.511)	0.345
Age (Years) ≤47 years ≥48 years	0.978 (0.926, 1.033)	0.419
Education Level Primary Secondary/Tertiary	0.559 (0.161, 1.933)	0.358
Employment Status Unemployed Employed	0.444 (0.047, 4.222)	0.480
Admission From ward Outpatient/another hospital	0.772 (0.198, 3.016)	0.710
Length of stay in ICU (days) ≤7 days ≥8 days	1.398 (0.572, 3.420)	0.463
HTN (1^0 diagnosis) No Yes	2.343 (0.430 – 12.771)	0.325
Hypertensive urgency (1^0 diagnosis) No Yes	1.25 (0.201 – 7.737)	0.810
ADHF (1^0 diagnosis) No Yes	1.667 (0.147 – 18.875)	0.680
Number of comorbidities 0-2 3-4	**4.953** (0.892 – 27.488)	0.067
DKA (Comorbidity) No Yes	2.900 (0.414 – 20.275)	0.283
CKD (Comorbidity) No Yes	2.240 (0.336 – 14.915)	0.830
DM (Comorbidity) No Yes	1.725 (0.324 – 9.172)	0.522
CVA (Comorbidity) No Yes	1.486 (0.236 – 9.356)	0.673

Table 19: Covariates of Drug Use/Administration Problem (P4)

Variable	Bivariate Analysis	
	COR	**P-Value**
Sex Female Male	0.588 (0.049, 7.067)	0.676
Age (Years) ≤47 years ≥48 years	0.967 (0.892, 1.048)	0.415
Education Level Primary Secondary/Tertiary	0.746 (0.135, 4.139)	0.738
Employment Status Unemployed Employed	2.619 (0.394, 17.340)	0.319
Admission From ward Outpatient/another hospital	1.055 (0.293, 3.807)	0.935
Length of stay in ICU (days) ≤7 days ≥8 days	0.909 (0.450, 1.835)	0.789
HTN (1^0 diagnosis) No Yes	1.35 (0.110 – 16.574)	0.815
Hypertensive urgency (1^0 diagnosis) No Yes	1.556 (0.126 – 19.241)	0.731
Number of comorbidities 0-2 3-4	1.35 (0.110 – 16.573)	0.815
AKI (Comorbidity) No Yes	**4.125** (0.301 – 56.385)	0.288
DKA (Comorbidity) No Yes	3.200 (0.243 – 42.182)	0.377
DM (Comorbidity) No Yes	1.042 (0.086 – 12.654)	0.974

Table 20: Covariates of Drug-drug Interactions (P5)

Variable	Bivariate Analysis	
	Crude Odds Ratio	**P-Value**
Age (Years) ≤47 years ≥48 years	 1.015 (0.940, 1.098)	0.693
Employment Status Unemployed Employed	 0.643 (0.052, 7.952)	0.731
Admission From ward Outpatient/Referral from another hospital	0.382 (0.057, 2.536)	0.319
Length of stay in ICU (days) ≤7 days ≥8 days	 1.524 (0.127 – 18.324)	0.740
DM No Yes	 0.960 (0.079 – 11.662)	0.974
Hypertensive urgency (1^0 diagnosis) No Yes	 0.643 (0.052 – 7.951)	0.731
DKA (Comorbidity) No Yes	 0.313 (0.024 – 4.119)	0.377

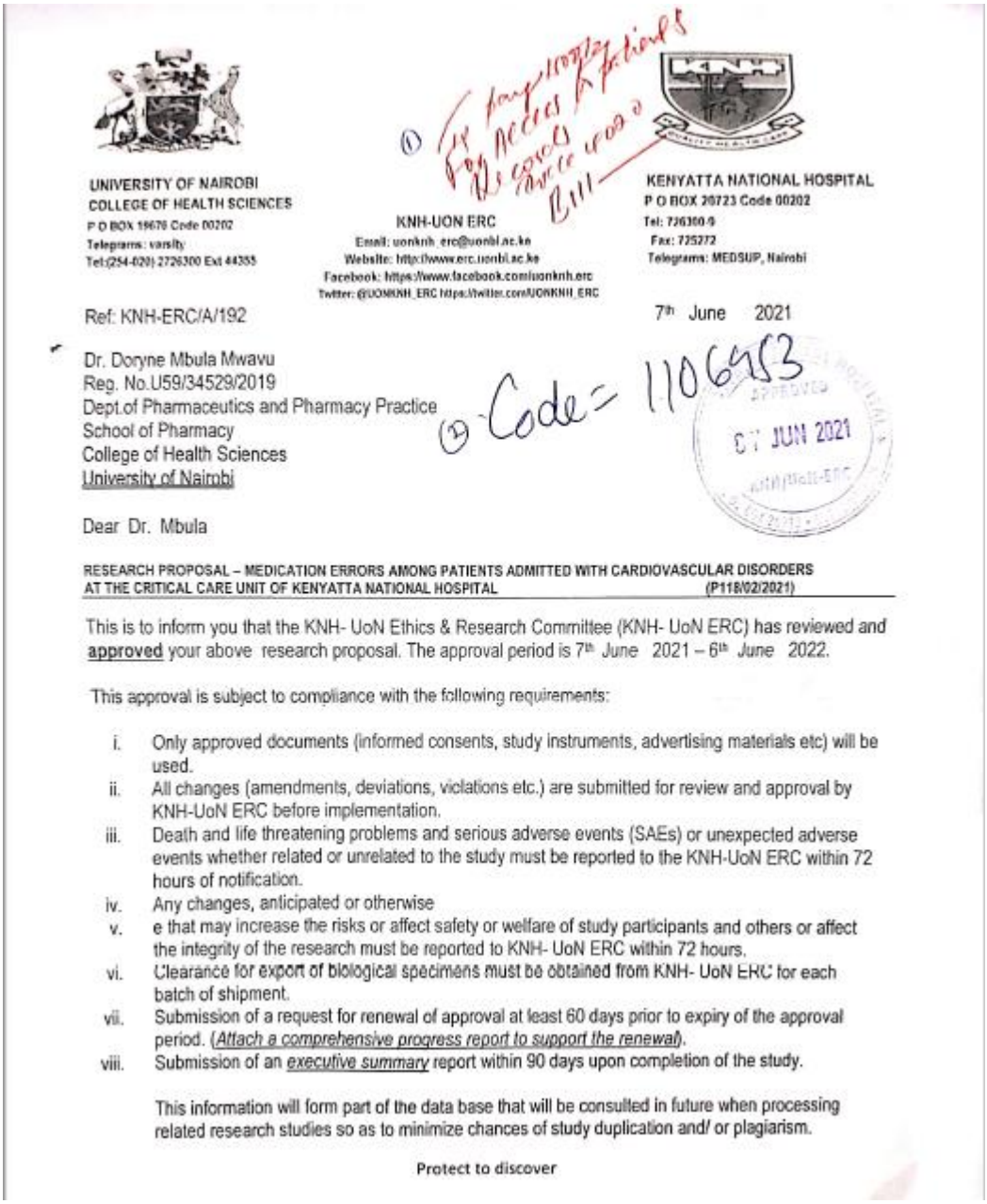
Table 21: Covariates of other medication errors

Variable	Bivariate Analysis	
	Crude Odds Ratio	**P-Value**
Sex **Male** **Female**	1.235 (0.0718, 21.240)	0.884
Age (Years) **≤47 years** **≥48 years**	1.011 (0.919, 1.112)	0.824
Length of stay in ICU (days) **≤7 days** **≥8 days**	1.598 (0.333, 7.674)	0.558
Number of errors in appropriateness of drug	2.009 (0.889, 4.539)	0.093
Hypertensive urgency (1^0 diagnosis) **No** **Yes**	3.222 (0.183 – 56.883)	0.424
Number of comorbidities **0-2** **3-4**	2.8 (0.160 – 49.103)	2.800

Table 22: Covariates of Drug Choice Problem

Variable	Bivariate Analysis		Multivariate Analysis	
	COR	**P-Value**	**AOR**	**P-Value**
Sex Female Male	0.417 (0.114, 1.513)	0.184	-	
Age (Years) ≤47 years ≥48 years	0.441 (0123, 1.573)	0.207	-	
Education Level Primary Secondary/Tertiary	0.583 (0.160 – 0.160)	0.414	-	
Employment Status Unemployed Employed	0.219 (0.040, 1.206)	0.081	0.220 (0.038, 1.289)	0.093
Admission From ward Through outpatient/another hospital	2.000 (0.551 – 7.251)	0.292	-	-
Length of stay in ICU (days) ≤7 days ≥8 days	0.763 (0.215 -2.708)	0.676	-	-
HTN (1^0 diagnosis) No Yes	1.320 (0.921, 1.890)	0.130	-	-
Hypertensive urgency (1^0 diagnosis) No Yes	0.429 (0.093 – 1.980)	0.278	-	-
ADHF (1^0 diagnosis) No Yes	4.200 (0.397 – 44.401)	0.233	-	-
Number of comorbidities 0-2 3-4	1.700 (0.420 – 6.881)	0.457	-	-
AKI (Comorbidity) No Yes	6.000 (0.606 – 59.444)	0.126	-	-
DKA (Comorbidity) No Yes	1.267 (0.223 – 7.199)	0.790	-	-
CKD (Comorbidity) No Yes	0.425 (0.072 – 2.511)	0.345	-	-
DM (Comorbidity) **No** **Yes**	0.240 (0.54 – 1.072)	0.062	0.241 (0.051 – 1.136)	0.072
CVA (Comorbidity) **No** **Yes**	1.731 (0.388 – 7.725)	0.472	-	-

Appendix E: KNH/UON ERC Ethical Approval Letter



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KNH-UON ERC
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Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/192

7th June 2021

Dr. Doryne Mbula Mwavu
Reg. No.U59/34529/2019
Dept.of Pharmaceutics and Pharmacy Practice
School of Pharmacy
College of Health Sciences
University of Nairobi

Code= 1106953

APPROVED
07 JUN 2021

Dear Dr. Mbula

RESEARCH PROPOSAL – MEDICATION ERRORS AMONG PATIENTS ADMITTED WITH CARDIOVASCULAR DISORDERS AT THE CRITICAL CARE UNIT OF KENYATTA NATIONAL HOSPITAL (P118/02/2021)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 7th June 2021 – 6th June 2022.

This approval is subject to compliance with the following requirements:

i. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
ii. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
iii. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
iv. Any changes, anticipated or otherwise
v. e that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
vi. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
vii. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
viii. Submission of an *executive summary* report within 90 days upon completion of the study.

This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

Protect to discover

For more details consult the KNH- UoN ERC website **http://www.erc.uonbi.ac.ke**

Yours sincerely,

PROF. M.L. CHINDIA
SECRETARY, KNH-UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Senior Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information Dept, KNH
The Dean, School of Pharmacy, UoN
The Chair, Dept. of Pharmaceutics and Pharmacy Practice, UoN
Supervisors: Dr. Sylvia Atisa Opanga, Dept.of Pharmaceutics and Pharmacy Practice, UoN
Prof. Faith Apolot Okalebo, Dept.of Pharmacology and Pharmacognosy, UoN

Appendix F: KNH Ethics Study Registration Certificate

KNH/R&P/FORM/01

KENYATTA NATIONAL HOSPITAL
P.O. Box 20723-00202 Nairobi

Tel.: 2726300/2726450/2726565
Research & Programs: Ext. 44705
Fax: 2725272
Email: knhresearch@gmail.com

Study Registration Certificate

1. Name of the Principal Investigator/Researcher
   DR. MWAVU DORYNE MBULA
2. Email address: dmbula@students.uonbi.ac.ke Tel No. 0728478584
3. Contact person (if different from PI) –
4. Email address: – Tel No. –
5. Study Title
   MEDICATION ERRORS AMONG PATIENTS ADMITTED WITH CARDIOVASCULAR DISORDERS AT THE CRITICAL CARE UNIT OF KENYATTA NATIONAL HOSPITAL
6. Department where the study will be conducted MEDICAL UNIT CRITICAL CARE UNITS
   (Please attach copy of Abstract)
7. Endorsed by KNH Head of Department where study will be conducted.
   Name: Dr. K. Korir Signature ... Date 15.6.21
8. KNH UoN Ethics Research Committee approved study number P118/02/2021
   (Please attach copy of ERC approval)
9. I DR. MWAVU DORYNE MBULA commit to submit a report of my study findings to the Department where the study will be conducted and to the Department of Medical Research.
   Signature ... Date 14/06/2021
10. Study Registration number (Dept/Number/Year) Medicine 1229/2021
    (To be completed by Medical Research Department)
11. Research and Program Stamp 18 JUN 2021

All studies conducted at Kenyatta National Hospital **must** be registered with the Department of Medical Research and investigators **must commit** to share results with the hospital.