

SYSTEMATIC REVIEW

OCCURRENCE AND CONTRIBUTING FACTORS ASSOCIATED WITH HYPERKALAEMIA IN EAST AFRICA: A SYSTEMATIC REVIEW

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ABSTRACT

Hyperkalaemia is potentially a life-threatening medical condition characterized by higher-than-normal potassium in the blood. It can result in cardiac arrhythmias which is a serious heart problem and subsequently can lead to a sudden death. Impaired kidney function, such as chronic kidney disease or acute kidney injury, can hinder the proper excretion of potassium, leading to its accumulation in the blood. The prevalence of hyperkalemia in the United States is reported to be 1.55% for the normal population and 6.35% for kidney disease patients. Hyperkalaemia can be too problematic for people with kidney diseases. The prevalence of chronic kidney disease ranges between 2% and 7% in Uganda. The majority of the CKD patients in Uganda are presented late with advanced symptoms such as hyperkalemia. However, a study done by Dorsthorst has found out that it's not only renal-impaired patients who are at the risk of becoming hyperkalemic after deviant consumption of potassium-rich foods, but the healthy humans with normally functioning kidneys are as well at risk. The study also alludes that the severity of hyperkalemia in patients with kidney disease or with normal kidney functionality does not differ. This review work was aimed at finding out the different reported cases of hyperkalemia in the Eastern region of Africa as well as their contributing factors. Articles used in this review were obtained from the internet using two search engines: Scopus and PubMed. Articles written in languages other than English and those which were review papers were excluded. The articles were screened and data were extracted. The results showed that hyperkalemia is caused by factors such as an overdose of potassium pills, chronic kidney disease, drug-to-drug interactions, and renal failure among other factors. Cases of hyperkalemia were reported in Uganda, Ethiopia, Tanzania, and Rwanda. Hyperkalaemia can be managed by responding to its specific cause. The overall prevalence of hyperkalemia has been reported to be approximately 1.1% in the general population (people with normal kidney function). From this review, it can be concluded that hyperkalemia occurs at high rates in people suffering from kidney disease. However, drug-drug interactions, increased intake of potassium, and tumor lysis are other causes.

Keywords: Hyperkalaemia/high serum potassium level, East Africa, cause.***Corresponding Author**

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INTRODUCTION

Hyperkalaemia is a medical condition characterised by increased levels of potassium in the blood. It is known to cause cardiac arrhythmias and hence its life threatening [1]. Generally, serum potassium level that is above 5.0 mmol/l is referred to as hyperkalaemic. The prevalence of hyperkalaemia is reported to be at 1 to 10 percent among the patients who are hospitalized for any other cause [2]. A previous study has shown that patients who have chronic kidney disease (CKD), those who have heart disease, those with diabetes mellitus as well as those who use inhibitors of the renin angiotensin aldosterone system are at about 2 to 3 times increased risk of developing hyperkalaemia [2]. Due to the increasing number of kidney disease and heart failure patients who are taking the Renin-Angiotensin-Aldosterone System inhibitors (RAASi) and mineralocorticoid receptor antagonist, hyperkalaemia is becoming a major concern [3].

Normally, the kidney excretes approximately 90% of the potassium that is ingested on daily basis. Mostly, potassium is filtered freely in the glomerulus and it is reabsorbed in the proximal convoluted tubule (PCT) and the loop of Henle (LH). It is estimated that about 10% of the potassium gets to the distal convoluted tubule (DCT) [4]. There are special principal cells which are located at the distal tubule and the collecting duct which are known to be responsible for excretion of potassium from blood circulation into the lumen of the tubular cells and into urine [4]. This secretion is accomplished by the potassium channels at the luminal membrane which sense and respond to the electrochemical gradient of potassium which is basically generated by the basolateral membrane sodium potassium adenosine triphosphatase (Na⁺/K⁺-ATPase). When potassium quantity is depleted, its production by the principal cells is suppressed, and the hydrogen-potassium adenosine triphosphatase (H⁺/K⁺-ATPase) at the luminal membrane is activated in the intercalated cells to reabsorb the potassium [4].

In this review, the different cases of hyperkalaemia in east African countries are summarised together with the contributing factors.

METHODS

Search from the internet and criteria used in selection

Internet search for articles on studies which were done on causes of hyperkalaemia in east African countries was achieved by typing the key terms, titles, and abstracts in two main search engines: Scopus and PUBMED databases. Articles which were written in a language other than English were excluded from the study. The articles which were included are the ones which were original. The search of the articles and post-search analysis followed the statement given by the Preferred Reporting Items for Systematic Review and Meta-Analyses [5-7]. All available data which was generated from the two mentioned databases reporting cases of developing hyperkalaemia in east African countries were included. The articles were screened by reading through their titles and abstracts. After that, further screening was also done by reading the entire articles.

Research strategy

On 15th February 2023 is when the last document search was done. The inclusion criteria included: identification and use of the key terms, synonyms basing on relevant studies, and the use of boolean operators: "OR", "AND" and " * ". The search was carried out using the following components on both databases:

Pubmed: (hyperkalemia) AND (("east africa") OR Burundi OR Comoros OR Djibouti OR Eritrea OR Ethiopia OR Kenya OR Madagascar OR Malawi OR Mauritius OR Réunion OR Rwanda OR Seychelles OR Somalia OR Somaliland OR Tanzania OR Uganda) NOT (Review[Publication Type])

Scopus: TITLE-ABS-KEY (hyperkalemia AND "east africa" OR burundi OR comoros OR djibouti OR eritrea OR ethiopia OR kenya OR madagascar OR malawi OR mauritius OR réunion OR rwanda OR seychelles OR somalia OR somaliland OR tanzania OR uganda) AND (

EXCLUDE (DOCTYPE , "re")) AND (EXCLUDE (LANGUAGE , "French") OR EXCLUDE (LANGUAGE , "German"))

Study selection

The total number of articles obtained from the Scopus database were 40 whereas the ones obtained from PubMed we found 31, summing up to 71 articles. Among 71 articles, 10 articles were excluded, 6 of which were reviews, 1 was written in Germany language and 3 were written in French language. After this exclusion, 61 articles remained. 15 articles were identified as duplicates and excluded from the 61 leaving a total of 31. The titles and abstracts were then screened and the process resulted into thirteen (13) articles which have been included in this review.

RESULTS AND DISCUSSION

Cases of hyperkalaemia and their causes in East African countries

Acute Kidney Injury

Acute kidney injury (AKI) also known as acute renal failure, refers to a sudden and often reversible loss of kidney function. It is characterized by a rapid decline in kidney function, resulting in a build-up of waste products and electrolyte imbalances in the body. AKI is a crucial widespread health concern in the world and it can either occur at the communities, in hospital setting or in both cases. AKI is expensive to manage and it is linked to increased rate of extended hospitalization and deaths in-hospital. The mortality in hospitals due to AKI is found to be 24% and keeps on increasing with the seriousness of the disease [8]. Basing on the

United Kingdom National Institute for Health and Care Excellence (UK-NICE) report which was published on Acute Kidney Injury (AKI), timely identification, as well as therapy with attentiveness to hydration and treatments could curb up to about 42,000 deaths resulting from AKI every year [8].

An observational study was conducted at Jimma Medical Center in Southwest Ethiopia to investigate the predictors of in-hospital mortality among patients with acute kidney injury (AKI) admitted to the medical ward. Due to limited data on kidney function tests in hospitalized patients and the need to identify contributing factors and outcomes related to AKI in Ethiopia, the study aimed to fill this knowledge gap. The study was carried out prospectively from April to August in 2019, employing a hospital-based approach [8].

Among the patients who lost their lives, the intensity of AKI as per kidney disease improving global outcomes (KDIGO) staging, presence of hyperkalemia, AKI duration, and the length of stay in hospital were significant predictors of in-hospital death cases. The in-hospital death cases of hyperkalemia cases was reported to be 30.7% [8]. In the study, patients with hyperkalemia had higher rates of mortality as compared to normokalemia patients [8]. Another study has also reported that hyperkalaemia patients are associated with higher percentages of mortality than the normokalaemia patients. Consequently, timely identification of patients with high-risk as well as maintenance of serum potassium level within a range that is safe may aid in avoiding the risk of hyperkalemia related-death cases [8].

Following a single centre retrospective study which was carried out in Rwanda to assess impact of introducing haemodialysis on outcomes of patients with AKI (82 patients), hyperkalemia (>6.6 mmol/L) was reported in 40.2% of the patients [9]. The hyperkalemia was associated with death cases [9]. Hyperkalaemia is reported to be a predictor of mortality along with receipt of more than five (5) sessions of haemodialysis[9].

Pseudohypoaldosteronism type II (PHAII)

This is a genetic disorder also referred to as familial hyperkalemic hypertension or Gordon syndrome. It is characterized by hyperchloremic metabolic acidosis, hyperkalemia, hypertension, low renin, and high sensitivity to thiazide diuretics in absence of renal failure. This disease results from mutations in the WNK1, WNK4, KLHL3 or CUL3 genes [19].

It is reported that pendrin hyperactivity is necessary to drive hyperchloremic metabolic acidosis and hyperkalemia in PHAII. This is due to the fact that both of these symptoms are corrected by pendrin genetic ablation [19].

Chronic kidney disease

Chronic kidney disease (CKD) is epitomized by its nature of being symptomless until the end stage. It is reported to be among the most regular problem of the public health worldwide. A regular check-up therefore, is very essential more so for the people with high risks, and to whom screening has been carried out and

findings obtained from a laboratory [10]

A cross-sectional study was conducted between July 1 and October 28, 2018 to screen the levels of electrolytes and estimate the glomerular filtration rate (eGFR) in the staff members of the Ethiopian Public Health Institute (EPHI). The aim of the study was to detect chronic kidney disease (CKD) in a timely manner and identify the factors associated with it. [10].

The study results indicated that 3.6% and 1.9% of the participants had stage II CKD based on the MDRD and CKD-EPI equations, respectively, as reported by Molla et al. [10]. Furthermore, hyperkalemia, defined as a serum potassium level above 5.0 mmol/L, was detected in 9.5% of the participants [10].

Serum electrolytes and risk factors in Diabetic patients

Electrolytes are substances that ionise in solutions and acquire the capability to conduct electricity. They are important constituents in many processes including the regulation of body fluid volume as well as osmotic pressure (sodium, potassium and chloride ions), rhythms of myocardial muscles, contractility and neuromuscular excitability (e.g., K^+) and acid-base balance (e.g., K^+ , Cl^-) chloride and sodium ions are the major electrolytes found in the extracellular fluid while magnesium, potassium and phosphate are the major electrolytes in the intracellular fluid [11].

The movement of potassium ions out of cells and sodium ions into cells occurs through diffusion, which is driven by trans-membrane electrical gradients. The sodium-potassium ion (Na^+-K^+) pump is activated by hormones like catecholamine and insulin, and it counteracts

the movement of these electrolytes to maintain their balance within and outside cells. Changes in the levels of catecholamine and insulin can alter the electrolyte levels in the serum, disrupting. Changes in the total amount of extracellular solute, osmotic diuresis, and intake of water caused by thirst, and influences from associated conditions are the mechanisms that have been considered by which fluid and solute abnormalities occur in hyperglycaemic patients [11].

Following a study carried out in Ethiopia on 279 diabetic patients from 1st February to 1st April 1, 2019, 10.9% of the diabetic patients were reported to be hyperkalemic, that is, they had potassium concentration levels in serum which was higher than 5.1 mmol/L [11]. From the study, the total serum electrolyte concentration levels in patients with diabetic was highly abnormal hence diabetes interferes with electrolyte balance potassium being one of them hence resulting into hyperkalaemia [11].

Drug-drug interactions

Following a study which was conducted in Ethiopia, Drug-drug interactions are reported to cause hyperkalaemia. These includes use of Enalapril and spironolactone whose prevalence of interaction is 73% and use of Enalapril and losartan whose prevalence of interaction is 1.6% [12]. This study was an hospital based and a retrospective cross sectional and it was done on 384 elderly (60 years and above) cardiovascular disease patients. The main aim was to check on polypharmacy, drug-

drug interactions as well as drug appropriateness, among these patients [12].

Renal failure

Renal disorder is a common problem in the whole world. Chronic Kidney Disease (CKD) is reported to affect approximately 16% of people in the population worldwide while AKI is reported to account for about 5–20% of hospital admissions [13]. Renal failure causes increased death rate in high as well as low income countries. When patients experience acute kidney injury or complications related to chronic kidney disease, they often seek care at emergency departments. Proper management of these conditions can be crucial to saving lives. In both developing and high-income countries, the prevalence of chronic kidney disease is approximately 13.9%, while the prevalence of acute kidney injury is 7% [13].

According to a prospective cohort study which was carried out on patients aged 15 years and above and who were presented at the emergence department at the national referral hospital in Tanzania with acute symptoms of renal failure and in need of emergent dialysis, Patients were reported to have deadly imbalances of electrolytes, basically hyperkalemia. The major complication presented and diagnosed among the study participants was hyperkalemia 77(53%). This study was carried out from September 2017 to February 2018 [13].

HIV patients live for a long period of time. As a result, they face a challenge of increased morbidity due to non-communicable diseases (NCDs). Diseases of the kidney which manifests as renal dysfunction are among the

emerging NCDs worldwide, with a varying prevalence of 13.9 to 48.5% [14]. The rising prevalence of renal dysfunction in Sub-Saharan Africa is raising concerns about the impact of the HIV epidemic in the region [14].

A cross-sectional study was carried out at an outpatient clinic at Mulago hospital in Uganda in 2018. The study involved patients who were on Tenofovir disoproxil fumarate (TDF) for at least 6 months who were 18 years and above. Patients who had documented kidney disease as well as pregnancy were excluded [14]. Among 278 patients who were enrolled for the study, 15(5.26%) had hyperkalaemia which could be explained by the possibility of the patients having had acute kidney injury, chronic kidney disease and medications such as Cotrimoxazole [14].

Drug therapy problems

Drug therapy problems (DTPs) are reported to be big worries in the health sector and they have been reported to cause negative clinical effects [16]. The occurrence of DTPs in patients with heart failure is known to worsen the outcome. A study was carried out in Ethiopia to assess DTPs, the associated factors and patient satisfaction among patients of ambulatory heart failure. This was done at Tikur Anbessa Specialized Hospital (TASH) [16]. The results showed that around 20% (n = 84) of patients experienced medication unpleasant effects [16]. The study found that warfarin use was associated with bleeding of gums, while ACEIs were linked to dry cough and

angioedema, and nifedipine caused peripheral edema. In addition, the study identified other adverse drug reactions, such as penicillin allergy, upper gastrointestinal bleeding caused by dual antiplatelet therapy, atenolol induced bradycardia, high dose of furosemide induced bronchospasm & hypotension, myopathy related to atorvastatin, and spironolactone induced gynecomastia and hyperkalemia.. [16]. Adverse drug events in metabolic and endocrine systems were also reported to cause 21.5% cases of hyperkalemia [15]

Tumour lysis syndrome

Tumour lysis syndrome (TLS) is a deadly emergency disease which results from hurried release of intracellular metabolites following death of a tumour cell. Its manifested by a series of metabolic signs, more specifically hyperkalemia, hyperphosphatemia, hyperuricemia and hypocalcemia [17]. An hospital based prospective cohort study was done in Ethiopia for 6 months on 61 newly diagnosed paediatric oncology patients with the aim evaluating and characterizing the incidence of tumor lysis syndrome among pediatric oncology patients before and after treatment. Among the 61 pediatric oncology patients, 4.9% and 6.6% cases had hyperkalemia incidences before and after treatment respectively [17].

Cell death leads to release of potassium into the systemic circulation and when the renal clearance of these chemical substances is overwhelmed, hyperkalemia results [17].

CONCLUSION

Hyperkalemia is a medical condition

characterized by a high level of potassium in the blood. There are several causes of hyperkalemia, including:

- i. **Kidney disease or failure:** Kidneys play an important role in regulating potassium levels in the body, so any impairment or damage to the kidneys can lead to hyperkalemia.
- ii. **Medications:** Certain medications such as RAASi (renin-angiotensin-aldosterone system inhibitors) and mineralocorticoid receptor antagonists (MRAs) used to treat hypertension, heart failure, and other conditions can cause hyperkalemia.
- iii. **Acidosis:** Acidosis is a condition in which there is an excess of acid in the blood, which can cause potassium to shift out of cells and into the bloodstream, leading to hyperkalemia.
- iv. **Trauma or injury:** Trauma or injury to muscles can cause potassium to leak out of cells and into the bloodstream, leading to hyperkalemia.
- v. **High potassium intake:** Consuming high amounts of potassium-rich foods or supplements can cause hyperkalemia, especially in people with kidney disease or other underlying medical conditions.
- vi. **Adrenal insufficiency:** Adrenal glands produce hormones, including aldosterone, which helps regulate potassium levels. In adrenal insufficiency, there is a deficiency of aldosterone, leading to hyperkalemia.
- vii. **Other medical conditions:** Certain medical conditions such as diabetes, congestive heart failure, and rhabdomyolysis can also cause hyperkalemia.

In East Africa, most of the cases of hyperkalaemia are reported to be caused by: Acute kidney injury (AKI), Chronic kidney disease, Serum electrolytes and risk factors in Diabetic patients, Drug-drug interactions, Renal failure, Drug therapy problems, Tumour lysis syndrome and Post-Cardiac Arrest as shown in the table of results. In Uganda, majority of chronic kidney diseases are presented at late stages when they have already developed advanced complications like electrolyte imbalances such as hyperkalaemia [20] and it has been reported that people with normally functioning kidneys have equal chances of developing hyperkalaemia [21].

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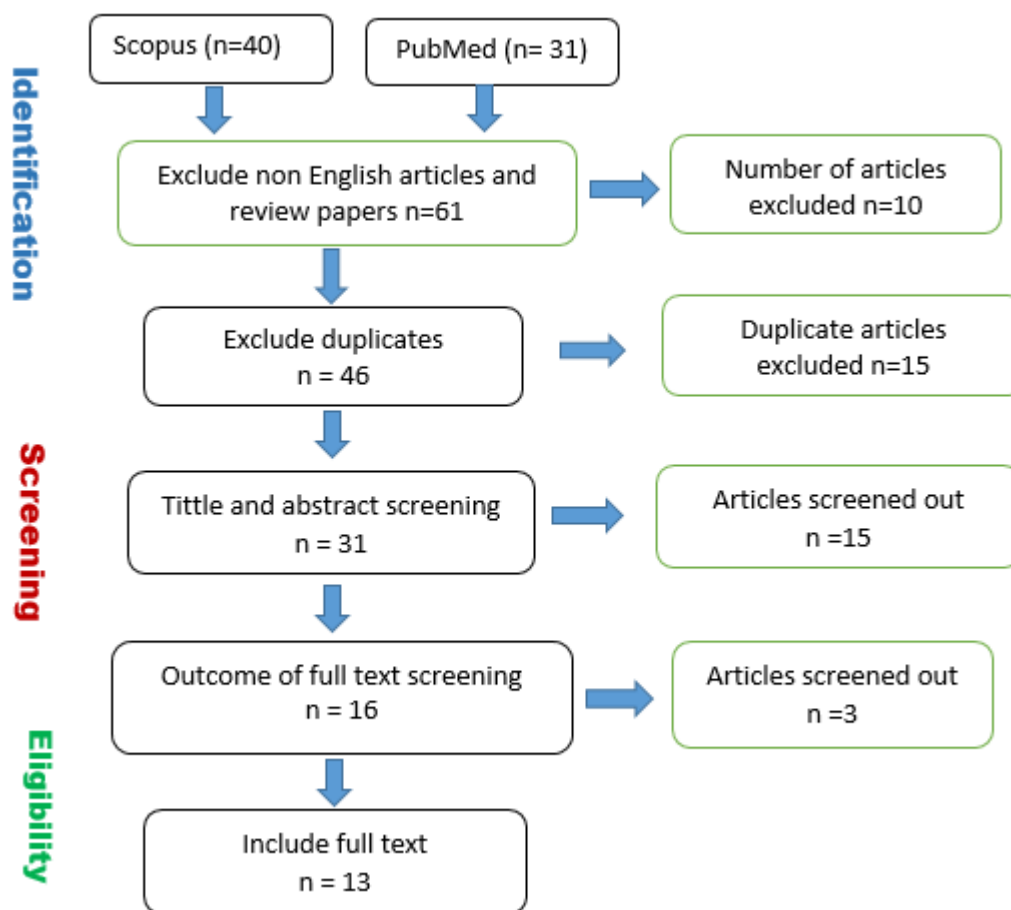


Figure 1: The procedure used in selecting the articles

Table 1: The different cases of hyperkalaemia and their causes in the east African countries

Cause of hyperkalemia	country	Type of study	Year of the study	Cases of hyperkalemia	References
Acute kidney injury (AKI)	Ethiopia	A prospective and observational study which was hospital-based	April 2019 to August 2019	The mortality rate of hyperkalemia patients which occurred at the hospital was reported to be 30.7%.	[8]
	Rwanda	A single center retrospective study	September 2014 to December 2016	hyperkalemia was reported in 40.2% of the patients and it was associated with death	[9]
Chronic kidney disease	Ethiopia	A cross-sectional study	1 st July to 28 th October, 2018	9.5% of the participants had hyperkalemia	[10]
Serum electrolytes and risk factors in Diabetic patients	Ethiopia	A cross sectional study	1 st February to 1 st April 2019	10.9% of the diabetic patients were reported to be hyperkalemic	[11]
Drug-drug interactions	Ethiopia	A hospital based retrospective cross sectional		Drug-drug interactions are reported to cause hyperkalaemia.	[12]
Renal failure	Tanzania	A prospective cohort study	September 2017 to February 2018	Hyperkalemia 77(53%) was the main complication that was diagnosed among study participants.	[13]
	Uganda	A cross-sectional study	2018	15(5.26%) had hyperkalaemia	[14]
Drug therapy problems	Ethiopia	A hospital based, prospective and cross-sectional study	20 th June to 20 th August 2017	21.5% cases of hyperkalemia Myopathy related to atorvastatin and spironolactone induced gynecomastia and hyperkalemia	[15] [16]
Tumour lysis syndrome	Ethiopia	An hospital based prospective cohort study	October 2016 to July 2017	4.9%(before treatment) and 6.6% (after treatment)cases had hyperkalemia	[17]
Post–Cardiac Arrest	Uganda	A descriptive study		6(8.22%) had hyperkalaemia	[18]

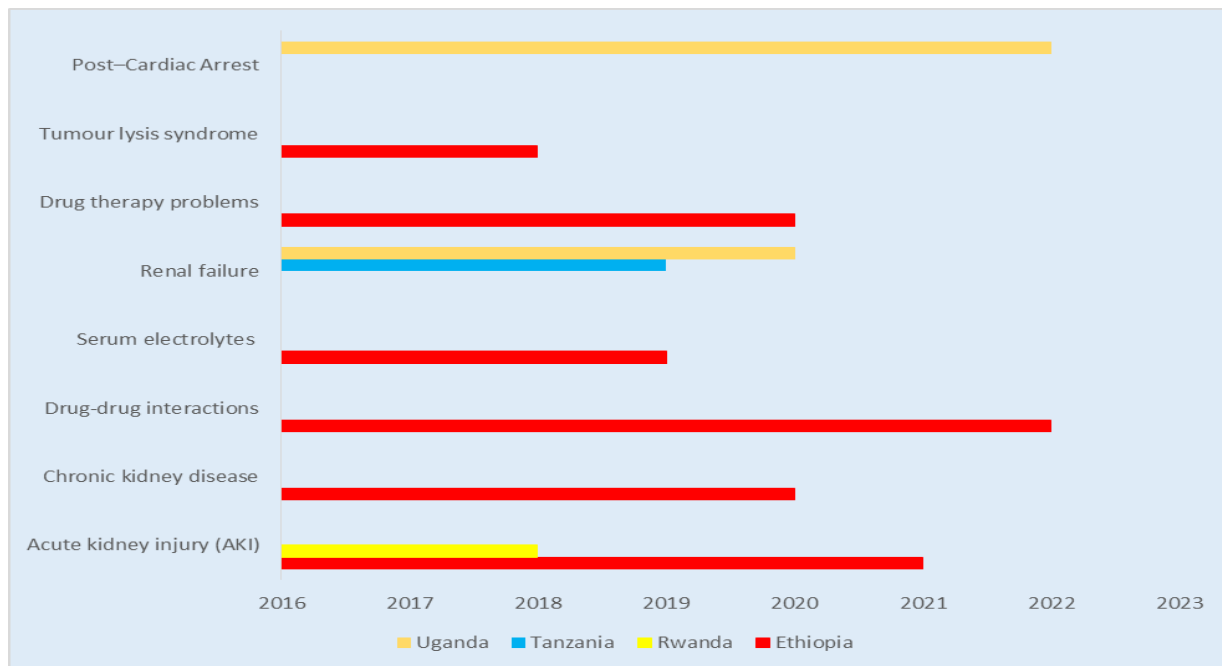


Figure 2: Causes of hyperkalaemia in East African countries