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Comprehensive Assessment OfDrug-Induced HypokalemiaIn Hospitalized Patients: Insights From A Tertiary Care Hospital

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Abstract
Background:
Hypokalemia, defined as a serum potassium concentration below 3.5 mmol/L, is a common electrolyte disturbance, often resulting from increased renal excretion, gastrointestinal losses, or drug-induced factors. This condition is frequently observed in hospitalized patients and can lead to serious complications if left untreated. Medications such as diuretics and antibiotics are known to cause hypokalemia, but the spectrum of drugs involved and the population characteristics remain underexplored.
Aims:
This study aimed to evaluate the incidence and characteristics of drug-induced hypokalemia in hospitalized patients at a tertiary care hospital. It also sought to determine the demographic profile of affected patients and assess the severity and potential mechanisms of hypokalemia caused by various medications.
Methodology:
A prospective observational study was conducted over six months in a tertiary care hospital. Data were collected from 111 hospitalized patients aged 18 years and above, across various wards. Patient demographics, medication histories, and potassium levels were documented. The Naranjo scale was applied to assess the probability of adverse drug reactions (ADR) leading to hypokalemia, and descriptive statistics were used for analysis.
Results:
Of the 111 patients, 40.50% experienced drug-induced hypokalemia, with Furosemide (23.07%) and Ceftriaxone (17.30%) being the most common causative agents. Males were slightly more affected than females (55.50% vs. 44.50%). Most cases of hypokalemia were moderate in severity (65.38%), with mild (21.15%) and major cases (13.46%) being less frequent. The probability of ADR was classified as probable in 50% of cases.
Conclusion:
Drug-induced hypokalemia is prevalent among hospitalized patients, particularly with medications like Furosemide and Ceftriaxone. The study underscores the importance of early detection and management to prevent complications. Future research should focus on the mechanisms of lesser-known drugs causing hypokalemia and strategies for prevention in at-risk populations.
Keywords: *Hypokalemia, drug-induced hypokalemia, Furosemide, Ceftriaxone, electrolyte imbalance, adverse drug reaction (ADR), hospitalized patients.*

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I. Introduction

Potassium and sodium are essential electrolytes with contrasting roles in maintaining physiological balance. Sodium raises blood pressure and cardiovascular risks, while potassium relaxes blood vessels, promotes sodium excretion, and lowers blood pressure. However, typical Western diets often contain more sodium than potassium, contributing to an imbalance that increases the risk of chronic diseases, particularly cardiovascular disorders[1]. Potassium, the most abundant intracellular cation, is crucial for cellular metabolism, maintaining intracellular volume, and regulating membrane potential, which are vital for muscle and nerve function[2]. The kidneys, influenced by hormones such as aldosterone, insulin, and catecholamines, play a

primary role in maintaining potassium homeostasis[2]. Plasma potassium levels between 3.5 and 5.5 mmol/L are necessary for proper function, with deviations increasing the risk of mortality from cardiac, renal, and pulmonary diseases[3]. Hypokalemia, defined as a serum potassium concentration below 3.5 mmol/L, is often caused by increased renal excretion, gastrointestinal losses, or shifts within cells, and is frequently induced by medications like diuretics and laxatives[4] . It is highly prevalent in hospitalized patients and can lead to muscle weakness, cramps, constipation, and, if untreated, life-threatening arrhythmias[5] . Treatment focuses on restoring potassium levels and addressing the underlying cause, with severe cases requiring intravenous potassium and milder cases managed through dietary changes or oral supplements[6] . This study is significant as it highlights the critical mechanisms of potassium regulation, identifies key causes of hypokalemia, and underscores the importance of early diagnosis and effective management in preventing serious complications.

Objective

Primary Objective:

- To assess and evaluate drugs induced hypokalemia at a tertiary care hospital.

Secondary Objective:

- To evaluate population of patients with hypokalemia induced by drugs, among patients reported or found with hypokalemia.
- To evaluate the possibility of relations between drug and hypokalemia as effect of that medicine.
- To assess the male and female mapping of the hypokalemia induced by drug

Methodology

Study Design: This study was a prospective, observational study conducted at a tertiary care teaching hospital. The study was carried out over a 6-month period (24 weeks) in various inpatient wards.

Study Population: The study population consisted of 111 hospitalized patients aged 18 years and above from various departments, including HICU, ICU, cardiac, medicine, and surgery wards.

Data sources: Data was gathered from the following sources:

- Inpatient prescription records
- Medication charts
- Medication history charts
- Medicine strips
- Medication history interviews with patients

Inclusion Criteria

- Hospitalized patients aged 18 years and above
- Both male and female patients
- Patients with documented hypokalemia due to pharmacological causes

Exclusion Criteria

- Pediatric patients (under 18 years of age)
- Pregnant women
- Patients treated in the outpatient department (OPD)

Data Collection

A specifically designed data collection form was used to record all medically relevant patient information. This included demographic details, diagnosis, admission reasons, medical history (past, present, family, personal, and drug history), and potassium levels. Drug-induced hypokalemia was the primary focus of the study. Tools like Micromedex and Medscape were used to evaluate the severity of hypokalemia, and the Naranjo Scale was applied to assess the probability of hypokalemia as an adverse drug reaction (ADR).

Study Procedure

After data collection, patient information was recorded in an Excel database for further analysis. Descriptive statistics, including means, standard deviations, frequencies, and percentages, were calculated using the Statistical Package for Social Sciences (SPSS) software, version 22.0.

Ethical Considerations

Ethical approval for the study was obtained from the Institutional Human Ethics Committee of Karnataka College of Pharmacy, Bangalore. Approval was also submitted to Rajiv Gandhi University of Health Sciences, Bangalore.

II. Results

Sociodemographic details of populations:

The study included 111 patients, with a gender distribution of 59.49% male (n=66) and 40.50% female (n=45). The majority of patients were aged 61-70 years (39.63%), followed by those aged 31-60 years (31.53%), over 70 years (20.72%), and 18-30 years (8.10%). Regarding past medical history, 51.35% had infectious diseases, 36.93% had cardiovascular diseases, 31.53% had respiratory diseases, 23.42% had endocrine/metabolic disorders, 20.72% had gastrointestinal diseases, and 18.91% had urinary tract infections. Among diagnosed diseases, infectious diseases were most prevalent (68.46%), followed by cardiovascular (41.44%), respiratory (37.83%), urinary tract (35.13%), and endocrine/metabolic (29.72%) disorders, details are depicted in Table 1.

Table 1: Sociodemographic details of populations

Category	**Sub-Category**	**Number (N)**	**Percentage (%)**
Gender Distribution (Total: 111)	Male	66	59.49%
	Female	45	40.50%
Age Distribution (Total: 111)	18-30 years	9	8.10%
	31-60 years	35	31.53%
	61-70 years	44	39.63%
	70+ years	23	20.72%
Past Medical History/ Co-Morbidities	Cardiovascular Diseases	41	36.93%
	Infectious Diseases	57	51.35%
	Respiratory Diseases	35	31.53%
	Endocrine/Metabolic Disorders	26	23.42%
	Urinary Tract Infections	21	18.91%
	Gastrointestinal Diseases	23	20.72%
Diagnosed Diseases categories	Cardiovascular	46	41.44%
	Infectious	76	68.46%
	Respiratory	42	37.83%
	Endocrine/Metabolic	33	29.72%
	Urinary Tract	39	35.13%

Evaluation of Hypokalemia Causes in a Sample Population: Pharmacological, Non-Pharmacological, and Drug-Induced Factors:

Hypokalemia, or low potassium levels, can be caused by both pharmacological and non-pharmacological factors. Among 111 cases, 40.50% were due to drugs, with males (55.50%) slightly more affected than females (44.50%). Among drugs inducing hypokalemia (52 cases), the most common were Furosemide (23.07%) and Ceftriaxone (17.30%). Other drugs contributing include Hydrocortisone (11.52%), Azithromycin (9.61%), Meropenem, and Metronidazole (each 5.76%), with lower incidences linked to Ciprofloxacin, Levofloxacin, Gentamycin, Prednisolone, and Carvedilol. These medications likely cause potassium depletion through mechanisms like increased renal excretion or intracellular shifting of potassium, details are depicted in Table 2.

Table 2: Evaluation of Hypokalemia

Hypokalemia Type (Total: 111)	Pharmacological Hypokalemia	45	40.50%
	Non-Pharmacological Hypokalemia	66	59.50%
Hypokalemia by Drugs (Total: 45)	Male	25	55.50%
	Female	20	44.50%
****Drugs Inducing Hypokalemia (Total: 52)**	Furosemide	12	23.07%
	Ceftriaxone	9	17.30%
	Hydrocortisone	6	11.52%
	Azithromycin	5	9.61%
	Ciprofloxacin	1	1.9%
	Meropenem	3	5.76%
	Metronidazole	3	5.76%
	Levofloxacin	1	1.9%
	Gentamycin	1	1.9%
	Prednisolone	2	3.8%
	Carvedilol	2	3.8%
	Ampicillin/Sulbactam	1	1.9%
	Hydrochlorothiazide	3	5.76%
	Insulin	1	1.9%

	Salbutamol	1	1.9%
	Acetazolamide	1	1.9%

Probability of ADR and Severity of Hypokalemia in Affected Patients:

In an analysis of adverse drug reactions (ADR) leading to hypokalemia, the probability of ADR was classified as **defined** in 23.07% of cases, **probable** in 50%, and **possible** in 26.92%. Regarding the severity of hypokalemia, among 52 cases, the majority were classified as **moderate** (65.38%), while **mild** cases accounted for 21.15%, and **major** cases were less frequent at 13.46%. This suggests that while most cases were not severe, moderate hypokalemia was the most common presentation, details are depicted in Table 3.

Table 3: Probability of ADR and Severity of Hypokalemia

Probability of ADR	Defined	12	23.07%
	Probable	26	50%
	Possible	14	26.92%
Severity of Hypokalemia (Total: 52)	Major	7	13.46%
	Moderate	34	65.38%
	Mild	11	21.15%

III. Discussion

This study aimed to evaluate drug-induced hypokalemia in a tertiary care hospital, focusing on the demographic characteristics of the affected population and the drugs contributing to this condition. The study found that hypokalemia was prevalent in hospitalized patients, with a considerable proportion being drug-induced. Furosemide and Ceftriaxone were the most common culprits, and the majority of hypokalemia cases were classified as moderate in severity. The findings underscore the importance of early identification and treatment of drug-induced hypokalemia to prevent complications.The gender distribution showed that men were slightly more affected by drug-induced hypokalemia than women, which aligns with some earlier studies, such as that by Kim et al. (2014), who reported similar male predominance in hospitalized patients with hypokalemia[7]. However, other studies, such as Khan et al. (2017), found no significant gender difference[8], indicating that while gender may be a factor, its impact may vary depending on the population studied.The most commonly implicated drugs were Furosemide, followed by Ceftriaxone, which mirrors findings from prior studies like those by Gennari et al. (2011), who also highlighted the role of loop diuretics like Furosemide in causing potassium depletion[9]. Furosemide, through its mechanism of action, increases renal potassium excretion, leading to hypokalemia[10]. The role of Ceftriaxone, however, is less commonly emphasized in literature, making this study's finding an interesting addition to the body of knowledge on drug-induced hypokalemia.Compared to the study by Mount (2020), which found corticosteroids and antibiotics as common causes of hypokalemia, this study aligns well, with hydrocortisone and azithromycin also contributing to hypokalemia in the present sample[11]. However, the frequency of corticosteroids causing hypokalemia was lower here than in Mount's findings, which may be due to differences in patient populations or prescribing patterns in different regions.Additionally, this study classified the severity of hypokalemia, finding most cases to be moderate, which contrasts with some earlier reports, such as by Rose et al. (2013), who reported more severe cases of hypokalemia in ICU settings[12]. This difference could be attributed to the study's broader inclusion criteria, encompassing a wider range of hospitalized patients rather than focusing solely on critically ill populations.

In conclusion, this study's findings are consistent with previous research on the primary causes and risks associated with hypokalemia, particularly drug-induced cases. However, the identification of drugs like Ceftriaxone as significant contributors adds a novel dimension to the current understanding. Future research could further investigate the mechanisms by which lesser-known drugs induce hypokalemia and explore prevention strategies in hospital settings.

Limitations of the Study

This study has several limitations. First, the relatively small sample size of 111 patients may not be fully representative of the broader hospitalized population, which could limit the generalizability of the findings. Additionally, the study was conducted at a single tertiary care hospital, which may introduce bias related to local prescribing practices and patient demographics. The study also relied on data from inpatient prescription records and medication histories, which may be subject to inaccuracies or incomplete information. Furthermore, while the Naranjo scale was used to assess the probability of drug-induced hypokalemia, this method is not without limitations and may not fully capture the complex interactions between medications and patient conditions. Lastly, the study did not explore long-term outcomes of patients with drug-induced hypokalemia, leaving gaps in understanding the full clinical impact of this electrolyte disturbance. Future research should address these limitations by including larger, more diverse populations, multi-center studies,

and long-term follow-up data to better understand the consequences and management of drug-induced hypokalemia.

IV. Conclusion

This study highlights the significant prevalence of drug-induced hypokalemia in hospitalized patients, with Furosemide and Ceftriaxone being the most frequently implicated medications. The finding that most cases were of moderate severity emphasizes the need for early detection and intervention to prevent more severe complications. The gender distribution, showing a slight male predominance, aligns with some previous studies, although inconsistencies in gender-related susceptibility suggest further research is needed. The identification of less commonly recognized drugs like Ceftriaxone as causes of hypokalemia adds valuable knowledge to clinical practice, encouraging more vigilant monitoring of electrolytes in patients on such medications. Future research should explore the underlying mechanisms by which these drugs cause potassium depletion, as well as strategies to prevent hypokalemia in at-risk populations. This study contributes to the broader understanding of hypokalemia, particularly in drug-induced cases, and highlights the importance of integrating electrolyte management into routine care for hospitalized patients.

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