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Occurrence of Hyperkalemia in Patients with Chronic Kidney and Liver Diseases

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ABSTRACT

Hyperkalemia is a common and potentially life-threatening electrolyte imbalance in patients with Chronic Kidney Disease (CKD) and Chronic Liver Disease (CLD), often exacerbated by comorbid conditions such as hypertension and diabetes. **Objective:** To assess the frequency and risk factors associated with hyperkalemia in patients with Chronic Kidney Disease (CKD) and Chronic Liver Disease (CLD) at a tertiary care hospital in Karachi, Pakistan. **Methods:** This cross-sectional study was carried out from March 2024 to May 2024, including 120 adult patients diagnosed with CKD (stage 3 or above) or CLD. Data on demographics, disease duration, comorbidities, previous hyperkalemia episodes, and medication compliance were collected. Serum potassium levels were measured, with hyperkalemia severity classified as mild (K+ 5.0–5.5 mEq/L), moderate (K+ 5.5–6.0 mEq/L), or severe (K+ >6.0 mEq/L). Statistical analysis was performed using SPSS version 24.0, with Spearman correlation and Chi-square tests applied. **Results:** The average age of the patients was 53.33 years, with 55% being male. The mean serum potassium level was 5.42±0.92 mEq/L. Medication compliance was high in 74.2% of patients. Hyperkalemia was present in 70.8% of patients, with 22.5% exhibiting severe hyperkalemia. Significant association was found between severity of hyperkalemia and age ($p<0.01$). Hypertension ($p=0.001$) and diabetes mellitus ($p=0.001$) were significantly associated with severity of potassium levels. **Conclusions:** The study highlighted a high prevalence of hyperkalemia in CKD and CLD patients, significantly associated with age, hypertension, and diabetes mellitus.

INTRODUCTION

Chronic Kidney Disease (CKD) and Chronic Liver Disease (CLD) affect millions worldwide, with significant morbidity and mortality [1-3]. In CKD, the kidney's ability to excrete potassium is diminished, predisposing patients to hyperkalemia. Similarly, in liver diseases, especially in cirrhosis, alterations in potassium handling, due to changes in renal function and the metabolism of medications, also predispose patients to elevated potassium levels [1-3]. Hyperkalemia, an abnormally high potassium level in the blood is one of the most common life-threatening condition that poses a significant clinical challenge [4]. The regulation of potassium is highly relying on hepatic and renal functions, which are greatly compromised in hyperkalemia [4, 5]. Studies have consistently shown medications to be a major contributing factor in hyperkalemia cases. Research suggests that medications are a primary or contributing factor in 35-75% of hospitalized patients with hyperkalemia [6]. The risk of hyperkalemia increases furthermore when patients had pre-existing CKD and liver diseases [7]. Both conditions independently impair the body's capacity to regulate potassium levels, creating a double jeopardy situation. Drugs such as potassium-sparing diuretics, commonly prescribed for hypertension in CKD patients, exacerbate this issue. These diuretics, while effective in eliminating excess fluid, also retain potassium in the body, potentially pushing potassium levels beyond safe limits in CKD patients [6-8]. While liver disease presents a different

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challenge to potassium balance. Liver damage can indirectly affect potassium homeostasis by diminishing the production of proteins that control the movement of potassium between cells and the bloodstream. Healthy cells maintain a delicate equilibrium of potassium within their walls. However, impaired protein production due to liver disease can disrupt this balance, allowing excessive potassium to accumulate inside cells [9, 10]. Furthermore, some liver diseases can impair blood flow to the kidneys, further hindering their ability to excrete potassium effectively [6, 8]. The combined presence of CKD or CLD significantly increases the risk of hyperkalemia induced by these medications. The impaired excretory capacity in CKD and the altered potassium handling in CLD create a precarious environment where even a modest medication-induced potassium increase can lead to clinically significant hyperkalemia. Despite the recognition of hyperkalemia as a complication in CKD and CLD, the specific risk factors associated with hyperkalemia in these patient populations remain incompletely understood. Existing studies often lack sufficient power or focus primarily on specific medications or disease severities.

Therefore, the objective of current study was to assess the frequency of hyperkalemia in patients with chronic kidney and liver diseases presenting at a tertiary care hospital, Karachi, Pakistan.

METHODS

It was a cross-sectional study conducted at the nephrology and hepatology clinics at Jinnah Medicare hospital, Karachi, Pakistan from March 2024 to May 2024. Sample size of 120 was estimated using Open Epi Sample Size Calculator by taking statistics of hyperkalemia as 35% in CKD, margin of error as 8.5% and 95% confidence level [6]. Adult patients aged 18 years or older diagnosed with CKD (stage 3 or above) or CLD (any stage) were included in the study. Patients with primary hyperparathyroidism or any other endocrine disorder known to directly affect potassium levels, patients who had treatment with bisphosphonates or denosumab within last 6 months and having pregnancy or breastfeeding females were excluded from the study. Patients were selected using non-random convenience sampling method. The study was conducted in accordance with the Declaration of Helsinki and approved by the institutional review board of the hospital, Ref No. ERC-1436/2024. Informed consents were obtained from all participants after a thorough explanation of the study's purpose, procedures, potential risks, and benefits. Data regarding age, gender, duration of disease, comorbidities, and previous episodes of hyperkalemia was collected. Laboratory test was performed to evaluate the phosphate, and potassium (K+) levels. The severity of hyperkalemia was defined as mild if K+ was >5.0 to <5.5 mEq/L, moderate if K+ was 5.5–6.0 mEq/L, and if severe K+ was >6.0 mEq/L. Compliance with medication was also reported. Data were analyzed using SPSS version 24.0, Descriptive statistics (mean, standard deviation, frequency, and percentage) was used to summarize patient characteristics. Spearmen correlation and Chi-square test was applied to assess the relationship between with hyperkalemia with age, gender, and comorbidities. A p-value<0.05 was considered as statistically significant.

RESULTS

The table 1 provides a summary of the baseline characteristics of the patients in the study. The average age of the patients was 53.33 years, with a standard deviation of 13.77 years. Of 120 patients, most of the patients were male (n=66, 55%). The median duration of disease was 5.23 years, with an interquartile range from 2.82 to 7.05 years. Of 120 patients, 25% were diabetic and 37.5% were hypertensive. About 30.8% of the patients have had previous episodes of potassium disorder, however, 74.2% of the patients showed high medication compliance.

Table 1: Descriptive Statistics of Baseline Characteristics (n=120)

Variables	Descriptive Statistics Mean ± SD / N (%)
Age (Years)	53.33 ± 13.77
Gender	
Male	66 (55.0%)
Female	54 (45.0%)
Duration of Disease (Years)	5.23 (2.82-7.05%)
Comorbidities	
Diabetes	30 (25.0%)
Hypertension	45 (37.5%)
Previous Episodes of Potassium Disorder	
Yes	37 (30.8%)
No	83 (69.2%)
Medication Compliance	
Low	31 (25.8%)
High	89 (74.2%)

The mean K+ of the patients with CLD and CKD was 5.42 ± 0.92 mEq/L. Majority of the patients had hyperkalemia (70.8%), whereas, 29.2% patients had normal K+ levels. Of 85 patients with hyperkalemia, 25% had mild hyperkalemia, 22.5% had moderate hyperkalemia and 23.3% had severe hyperkalemia, respectively (Figure 1).

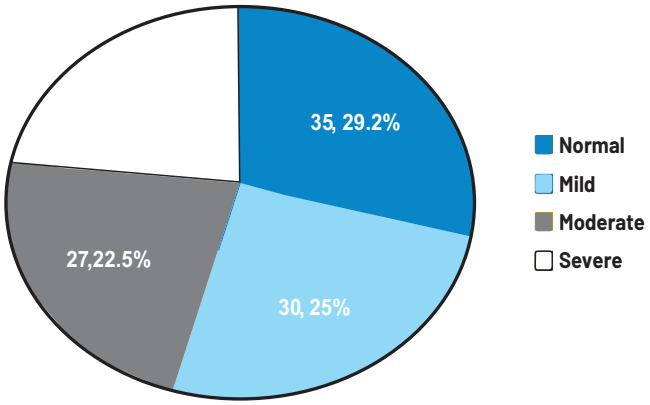

Figure 1: Frequency Distribution of Potassium Status (Hyperkalemia)

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Patients aged >50 years had a higher proportion of severe hyperkalemia (39.7%) compared to those aged≤50 years (0%). Similarly, proportion of moderate hyperkalemia was higher in age>50 years (38%) as compared to age≤50 years (0%). There was significant association between severity of hyperkalemia and age groups (p<0.01). Females had higher proportion of severe hyperkalemia and males had higher proportion of moderate hyperkalemia. However, there was insignificant association between severity of hyperkalemia and gender (p=0.22) (Table 2).

Table 2: Relationship between Severity of Hyperkalemia and Age Groups

Variables	Severity of Hyperkalemia N (%)				p-Value
	Normal	Mild	Moderate	Severe	
Age Groups					
≤50 Years	35 (71.4%)	14 (28.6%)	0 (0.0%)	0 (0.0%)	<0.01
≤50 Years	0 (0.0%)	16 (22.5%)	27 (38.0%)	28 (39.4%)	
Gender					
Male	16 (29.6%)	16 (29.6%)	14 (25.9%)	8 (14.8%)	0.22
Female	19 (28.8%)	14 (21.2%)	13 (19.7%)	20 (30.3%)	

Individuals with hypertension have a higher percentage of moderate to severe potassium levels compared to those without hypertension. This relationship was statistically significant with a p-value<0.01. Moreover, individuals with diabetes mellitus also have a higher percentage of moderate to severe potassium levels compared to those without diabetes mellitus.This relationship was statistically significant with a p-value<0.01 (Table 3).

Table 3: Relationship between Severities of Hyperkalemia with Comorbidities

Comorbidities		Severity of Hyperkalemia N (%)				p-Value
		Normal	Mild	Moderate	Severe	
HTN	No	29 (38.7%)	12 (16%)	17 (22.7%)	17 (22.7%)	<0.01
	Yes	6 (13.3%)	18 (40%)	10 (22.2%)	11 (24.4%)	
DM	No	31 (34.4%)	15 (16.7%)	19 (21.1%)	25 (27.8%)	<0.01
	Yes	4 (13.3%)	15 (50%)	8 (26.7%)	3 (10%)	

DISCUSSION

The present study investigates the occurrence of hyperkalemia in patients with Chronic Kidney Disease (CKD) and Chronic Liver Disease (CLD) at a tertiary care hospital in Karachi, Pakistan. The study's findings reveal a high prevalence of hyperkalemia among these patients, with significant correlations between hyperkalemia and age, as well as comorbid conditions such as hypertension and diabetes mellitus. Specifically, 70.8% of the studied population exhibited hyperkalemia, with 22.5% experiencing severe hyperkalemia. This study underscores the heightened vulnerability of CKD and CLD patients to hyperkalemia, especially when subjected to certain medications. The detailed analysis of the key outcomes indicates several significant findings. Firstly, the high prevalence of hyperkalemia in the patient cohort aligns with existing literature, which highlights the compromised ability of CKD and CLD patients to regulate potassium levels. Recent studies have consistently demonstrated the increased risk of hyperkalemia in CKD patients due to impaired renal potassium excretion [11, 12]. Furthermore, medications such as potassium-sparing diuretics exacerbate this risk by retaining potassium within the body [13, 14]. Similar mechanisms were at play in CLD patients, where hepatic dysfunction interferes with potassium homeostasis [15, 16]. Secondly, there was significant association between severity of hyperkalemia and age (p=0.001). Older patients (>50 years) exhibited a higher incidence of moderate to severe hyperkalemia, consistent with the notion that aging kidneys have a diminished capacity to excrete potassium efficiently [17, 18]. Moreover, there was statistically significant association between comorbid conditions and severity of potassium levels. This observation aligns with previous research indicating that comorbidities further strain the body's potassium regulatory mechanisms, thereby increasing the likelihood of hyperkalemia [19, 20]. The study's most significant achievement lies in its comprehensive assessment of hyperkalemia in a combined CKD and CLD patient population. Previous research often focused on either condition independently, with limited exploration of their concurrent impact on potassium regulation [20-21]. By addressing this gap, the study provides valuable insights into the compounded risks these patients face, highlighting the critical need for careful medication management and monitoring in this vulnerable group. Additionally, the study's robust methodology, including the use of a cross-sectional design and comprehensive statistical analyses, strengthens the reliability of its findings. The use of non-random convenience sampling may introduce selection bias, potentially limiting the generalizability of the results. Future research should employ randomized sampling methods to validate these findings in broader populations. Further studies should investigate these mechanisms to develop targeted interventions for preventing hyperkalemia in CKD and CLD patients. Lastly, the study's exclusion criteria, such as the exclusion of patients treated with bisphosphonates or denosumab, may overlook other potential contributors to hyperkalemia, necessitating a more inclusive approach in future research.

CONCLUSIONS

Study shows high prevalence of hyperkalemia and significant association of age, hypertension and DM with hyperkalemia in CKD and CLD patients.

Authors Contribution

Conceptualization: FAS, AR
Methodology: FAS, AR
Formal analysis: MQ[1]
Writing, review and editing: FAS, AR, MQ[1], Mq[2]

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All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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