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## Research Article

# Hyperkalemia in the Emergency Department: Different Phenotypes

# Noemí Del Toro-Cisneros, Adela Uribe-Pérez, Olynka Vega-Vega*

Department of Nephrology and Mineral Metabolism, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico

*Corresponding author: Olynka Vega-Vega, Department of Nephrology and Mineral Metabolism, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Vasco de Quiroga 15, Belisario Domínguez Sección XVI, Tlalpan, Mexico City, 14080, Mexico

## Abstract

**Background:** Hyperkalemia is a common electrolyte disorder in the emergency department, its presence is associated with increased morbidity and mortality. The main causes reported are related to decreased excretion as in patients with impaired renal function and associated with drug intake. Our objectives were to know the prevalence, etiology, management, and outcomes in these patients. **Methods:** This is a retrospective and observational study. All adult patients admitted to the emergency department with a diagnosis of hyperkalemia from June 2018 to December 2019 were included. We identified 4 groups associated with the development of hyperkalemia: Acute Kidney Injury (AKI) or decompensated Chronic Kidney Disease (CKD), associated with drugs, inadequate dialysis, and others. Demographic data, comorbidities, home medications, clinical and laboratory findings at presentation, management, and patient outcomes were collected from these patients. **Results:** We included 175 patients; the prevalence of hyperkalemia was 2.1%. In 59% of the cases, hyperkalemia was attributed to AKI or decompensated CKD, 15% to inadequate hemodialysis, 18% associated with medications, and the remaining 8% to dehydration and gastrointestinal bleeding. The general mortality of patients admitted to the Emergency Department (ED) of our institution in the same study period was 7.5% and among the patients included in this study it was 17%. **Conclusions.** Mortality in patients admitted to the emergency department with hyperkalemia is higher. We found that those with drug-associated hyperkalemia and hyperkalemia attributed to AKI or decompensated CKD have a longer hospital stay and mortality than hyperkalemia associated with inadequate dialysis and dehydration.

**Abbreviations:** ED: Emergency Department; AKI: Acute Kidney Injury; SCr: Serum Creatinine; CKD: Chronic Kidney Disease; eGFR: Estimated Glomerular Filtration Rate; DM: Diabetes Mellitus; SAH: Systemic Arterial Hypertension; CHF: Chronic Heart Failure; EKG: Electrocardiogram; RRT: Renal Replacement Therapy; RAAS: Renin-Angiotensin-Aldosterone System; NSAIDs: Non-Steroidal Anti-Inflammatory Drugs

## Background

Hyperkalemia is one of the most common electrolyte disorders in the Emergency Department (ED) and is associated with life-threatening cardiac dysrhythmias and arrest, which significantly increase morbidity and all-cause mortality [1]. This term refers to an elevation in potassium concentration; although there is no universal cut-off point to define hyperkalemia, the term is used when the Serum Potassium (SK) concentration is >5 to 5.5 mmol/L [2,3]. Hyperkalemia usually develops due to increased intake or administration, decreased excretion, or to a shift of potassium from the intracellular to the extracellular compartment [3]. It is less frequent in patients with normal renal function; however, its incidence increases with impaired kidney function [4]. The main risk factors for its development are worsening kidney function, the presence of comorbidities such as Diabetes Mellitus (DM), Chronic Heart Failure (CHF), Coronary Artery Disease (CAD), among others [3,5]. In addition, many drugs induce hyperkalemia, such as mineralocorticoid antagonists, β-blockers, antibiotics, antifungals, and particularly Renin-Angiotensin-Aldosterone System (RAAS) inhibitors [1,3]. This study aimed

to determine the prevalence, main etiology, management, and outcomes of patients with hyperkalemia in the ED of a tertiary care hospital in Mexico City.

## Methods

This is a single-center, retrospective, and observational study performed at the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán in Mexico City. The study was approved by the local Human Research and Ethics Boards (reference NMM-4000-21-22-1). All adult patients admitted to the ED with a diagnosis of hyperkalemia from June 2018 to December 2019 were included. We excluded patients who were transferred to another hospital or with incomplete data. All data was obtained from an electronic medical record and followed up to their discharge. The collected variables included demographic data, comorbidities, home medications, clinical and laboratories findings at presentation, management, and patient outcomes.

## Variable Definitions

Hyperkalemia was defined as a SK concentration >5.0 mmol/L. Acute Kidney Injury (AKI) was defined and staged according to the Kidney Disease Improving Global Outcomes (KDIGO) criteria [6]. Baseline Serum Creatinine (SCr) was defined as the mean SCr in the previous 6 months before hospitalization, or the minimum SCr value during hospitalization if previous values were unavailable [7]. Chronic Kidney Disease (CKD) was defined by the KDIGO CKD guidelines based on previously documented findings or during evaluation in the ED [8]. The eGFR was calculated using the Chronic Kidney Disease Collaboration creatinine equation [9].

## Statistical Analysis

For continuous variables, their distribution was assessed by the Kolmogorov-Smirnov test. Descriptive statistics are expressed as number (percentage), median (interquartile range) or mean (standard deviation) as appropriate. Baseline characteristics of patients among those with AKI or decompensated CKD and associated with medications were analyzed using U-Mann-Whitney. Chi-square or Fisher's exact test was used for categorical variables. All statistical tests were two-sided, and a p-value below 0.05 was considered statistically significant. All analyses were performed using SPSS 24.0 (IBM, Armonk, NY, USA).

## Results

From June 1st, 2018, to December 31st, 2019, a total of 8,342 patients were admitted to our Institution in the ED. Among them, 175 patients (2.1%) were admitted to the ED with the diagnosis of and hyperkalemia (Figure 1). The baseline characteristics of all the patients included in this study are provided in Table 1. In a total of 103 patients (59%), the cause of hyperkalemia was attributed to AKI or decompensated CKD, in 15% inadequate hemodialysis

(HD), in 18% associated with medications, and the remaining 8% dehydration and gastrointestinal bleeding were attributed. Of the patients in the dehydration and gastrointestinal bleeding group, 87% of the patients rapidly improved their condition and were discharged [median length of hospital stay 2 days (1 to 3 days)]. All these patients received hydration treatment, and only 3 patients required intravenous administration of calcium gluconate and polarizing solution to manage hyperkalemia. Two patients in this group died (13%), both during a surgical procedure.
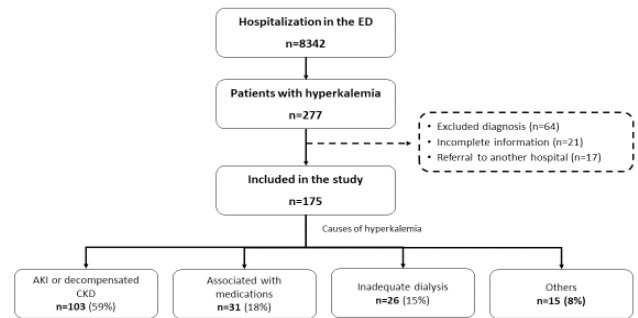


**Figure 1:** Flow chat of the studied population.

| | n=175 |
|---|---|
| **Demographics** | |
| Age, years | 60 (± 19) |
| Male, n (%) | 90 (51) |
| **Comorbidities** | |
| >3 Comorbidities, n (%) | 97 (55) |
| Diabetes, n (%) | 85 (48) |
| Hypertension, n (%) | 107 (61) |
| Chronic kidney disease, n (%) | 89 (51) |
| ESRD, n (%) | 35 (20) |
| Hepatic cirrhosis, n (%) | 31 (18) |
| **Admission treatment** | |
| RAAS inhibitors, n (%) | 56 (32) |
| Beta-blockers, n (%) | 58 (33) |
| Spironolactone, n (%) | 26 (15) |
| Acetaminophen, n (%) | 23 (13) |
| NSAIDs, n (%) | 5 (3) |
| Others, n (%) | 46 (26) |
| **Causes of hyperkalemia** | |
| AKI/decompensated CKD, n (%) | 103 (59) |
| Associated with medications, n (%) | 31 (18) |
| Inadequate hemodialysis, n (%) | 26 (15) |
| Others, n (%) | 15 (8) |
| **Laboratory at ED admission** | |
| SCr, mg/dL | 3.5 (2.2-8.2) |
| SK, mmol/L | 6.1 (5.6-6.7) |
| Change in ECG, n (%) | 48 (27) |
| **Outcomes** | |

| | |
|---|---|
| Length of hospitalization, days | 6 (2-11) |
| Withdrawal of RAAS inhibitors, n (%) | 16 (9) |
| Discharged, n (%) | 146 (83) |
| Mortality, n (%) | 29 (17) |

**Note:** Continuous variables are expressed as median (interquartile range) or mean (standard deviation) depending on their distribution.
**Abbreviations:** ESRD: End-Stage Renal Disease; RAAS: Renin-Angiotensin-Aldosterone System Inhibitors; NSAIDs: Non-Steroidal Anti-Inflammatory Drugs; AKI: Acute Kidney Injury; CKD: Chronic Kidney Disease; SK: Serum Potassium; SCr: Serum Creatinine; ECG: Electrocardiogram

**Table 1:** Clinical characteristics of the patients included in this study.

### Hyperkalemia secondary to AKI or decompensated CKD

Of the patients with inadequate HD, 69% received one extra HD session during the first 24 hours in ED and were discharged with modifications to their chronic HD schedule, [median length of hospitalization 1-day (1 to 3)]. In the remaining 8 patients, an infectious process was diagnosed and remained hospitalized in their chronic HD schedule. Two patients died of infectious complications. The other two phenotypes of hyperkalemia, with completely different behavior, were: attributed to AKI or decompensated CKD, and associated with medications.

Hyperkalemia secondary to AKI or decompensated CKD Of the total population studied, 103 (59%) patients had hyperkalemia associated with AKI or decompensated CKD. The median age in this group of patients was 65 (53-78) years, and 50% were male. The main comorbidities of these patients were: DM in 48%, systemic arterial hypertension (SAH) in 62%, CHF in 13%, liver cirrhosis in 17%, CKD KDIGO stage G3 or higher in 38%, and 49% had 3 or more comorbidities. On admission to the ED, the median SCr was 3.4 mg/dL (2.4-5.8), SK levels was 6.2 mmol/L (5.8-6.7), and 30% presented some alterations in the EKG. This was the group with the highest SK levels (p=<0.001).

Forty-six percent of these patients were receiving different drugs associated with the development of hyperkalemia; however, renal function deterioration predominated, so they were categorized into this phenotype (Table 2).The causes of hospitalization among patients who had impaired renal function were: infectious in 37%, dehydration associated with gastrointestinal losses in 16%, gastrointestinal bleeding in 7%, acute myocardial infarction in 4%, diabetic ketoacidosis in 3%, and the rest attributed to progression of kidney disease. The main treatments used in these patients were: calcium gluconate in 45%, polarizing solution (glucose plus insulin) in 41%, sodium bicarbonate in 21%, and finally, 7 patients (8%) required initiation of HD. This hyperkalemia phenotype in patients with impaired renal function presented mortality of 20%, this outcome was related to infectious and cardiovascular complications.

| | AKI or decompensated CKD n=103 | Associated with medications n=31 | *p-Value* |
|---|---|---|---|
| Age, years | 65 (53-78) | 64 (53-75) | 0.62 |
| Male, n (%) | 52 (50) | 14 (45) | 0.68 |
| Diabetes, n (%) | 50 (48) | 20 (65) | 0.09 |
| Serum potassium, mmol/L | 6.2 (5.8-6.7) | 5.6 (5.3-6) | <0.001 |
| RAAS inhibitors, n (%) | 38 (37) | 8 (26) | 0.29 |
| Beta-blockers, n (%) | 31 (30) | 19 (61) | 0.003 |
| Spironolactone, n (%) | 19 (18) | 5 (16) | 0.80 |
| Length of ED stay, days | 2 (1-3) | 1 (1-2) | 0.009 |
| Length of hospitalization stay, days | 7 (4-12) | 5 (1-10) | 0.56 |
| Discharge, n (%) | 84 (82) | 27 (87) | 0.42 |
| Mortality, n (%) | 21 (20) | 4 (13) | 0.37 |

**Note:** Categorical variables are expressed as number of patients (percentage). Continuous variables are expressed as median (interquartile range).

**Table 2:** Characteristics of the patients in the studied groups.

**Hyperkalemia associated with medications**

Of the total population, 31 (30%) patients had hyperkalemia associated with drug use. The median age in this group was 64 (53-75) years, and 45% were male. The main comorbidities of these patients were: DM and SAH in 65%, CHF in 16%, liver cirrhosis in 32%, kidney transplant in 6%, and 52% had 3 or more comorbidities. On admission to the ED, the median SCr was 1.6 mg/dL (1.1-2.4), SK levels was 5.6 mmol/L (5.3-6.0), and only 13% presented some alterations in the EKG.

The main cause of hospitalization was infection in 55% of the cases. Four of these patients presented AKI stage 1, however, it resolved within 24 hours of admission. Most of their cause of hospitalization was related to hyperkalemia and they were discharged with treatment adjustment. The treatments used in these patients were: loop diuretics 23%, calcium gluconate in 19%, and polarizing solution in 13%. One patient (3%) presented persistent hyperkalemia and started HD. The mortality of these patients was 13%, all these patients died of infectious complications related to decompensation of their comorbidities (diabetic foot ulcer and soft tissue infection, spontaneous bacterial peritonitis, among others).

**Serum Potassium and Electrocardiogram**

Twenty-seven percent of our study population had EKG abnormalities consistent with hyperkalemia. We looked for an association of these with serum potassium levels, dividing the population into those with serum potassium <6 mmol/L and ≥6 mmol/L. In the first group, 79 patients were found and only 6% of them presented EKG alterations compatible with hyperkalemia. In this group of patients, there was one death that occurred 9 days after hospital admission and was associated with infectious complications. Ninety-six patients had potassium equal to or greater than 6mmol/L and 45% had EKG abnormalities. In this group there were 4 deaths that occurred in the first 48 hours of admission. All these patients had potassium levels > 6.5mmol/L.

**Outcomes**

The days of hospital stay in the ED were different between the two commented phenotypes, patients with hyperkalemia secondary to deterioration of renal function were longer than secondary to drugs (p=0.009). However, on the days of total hospital stay, discharge or death, no differences were observed (Table 2). The survival at 7 days seems to be worse in those who presented deterioration in renal function (Figure 2), although no statistical difference was observed. At hospital discharge, a total of 25 patients (14%) underwent a change in treatment, predominantly the withdrawal of drugs related to RAAS 64%.
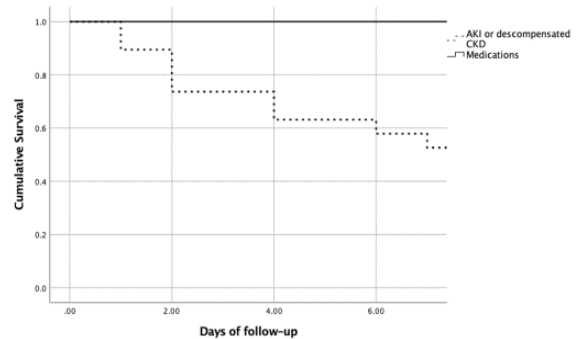


**Figure 2:** Cumulative survival probability of patients according to phenotypes.

## Discussion

The prevalence of hyperkalemia there is depending on the cut-off value used and the population studied. In the general population, a cut-off value greater than 5 mEq/L has been described in 1.5% and even reaches >6% among those patients with CHF and CKD [10]. In this study we observed a prevalence of 2.1% in the analyzed period. In our study, as it was a tertiary care center, all patients had at least one comorbidity, the most frequent being SAH, DM, CKD, ESRD, and cirrhosis, all of them independent risk factors for the development of hyperkalemia [5,11,12]. In addition, many of these patients were receiving drugs potentially associated with hyperkalemia, such as RAAS inhibitors, beta-blockers, NSAIDs, mineralocorticoid inhibitors, antibiotics, among others. According to the mechanisms associated with the development of hyperkalemia, we divide the population into the following groups: AKI or decompensated CKD, inadequate HD, associated with medications, and others. In this last group, dehydration prevailed as a cause of hyperkalemia. The most patients with inadequate HD received and extra HD therapy in ED and were discharged without any complications. However, those with impaired renal function were the patients with the highest severity and length of hospital stay. Of those associated with the use of medications, hyperkalemia resolved rapidly with the suspension of the medication, only 4 presented mild deterioration in renal function with subsequent improvement, relevantly they had a shorter stay in the ED (p= 0.009) and were discharged, although the length of hospital stay was not different compared to those with impaired eGFR, this was attributed to the fact that 17 of these patients required a longer stay due to infectious diseases.

On admission to the ED, hyperkalemia-related EKG abnormalities were detected in 48 patients (27%), in other series,

alterations in the EKG have been reported in around 50% [13]. We consider that our low detection of alterations may be due to the absence of reports of non-classical or minor alterations and, furthermore, it is recognized that patients with CKD or ESRD often do not present EKG alterations even with very high potassium values. Ninety-seven (55%) of our patients, based on serum potassium levels and regardless of EKG findings, received at least one of the widely used treatments for hyperkalemia [2,3,14]. It's important to point out that in this series, 25 patients changed their course of treatment because they considered the former was the cause of hyperkalemia, with the most frequent being elimination the use of RAAS inhibitors. Previous reports have documented that their suspension is associated with increased morbidity and mortality [15-18], which makes it imperative to establish some prevention measures or chronic treatment for the hyperkalemia in the future. The mortality of the patients admitted to the ED in our institution in the same study period was 7.5% and among the patients included in this study it was 17%. However, given the nature of the study, this mortality cannot be attributed to this single factor, we consider that this population could probably present greater severity. Our main limitation is the retrospective nature of the study, in addition, these data only reflect the type of patients treated at our institution. In the future, these data could guide preventive measures, especially in those patients with known deterioration in renal function and those on chronic replacement therapy.

## Conclusions

We found worse outcomes in the phenotypes of hyperkalemia associated with the use of medications and that attributed to an alteration in renal function, which could reflect a more serious condition of the patients. Patients with inadequate HD and hyperkalemia associated with dehydration due to gastrointestinal losses predominantly had short hospital stays and discharge.

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