BRIEF ARTICLE

Prevalence of Hyperkalemia in a Cohort of Patients with Heart Failure with Reduced Ejection Fraction in a Specialized Unit

Prevalencia de hiperkalemia en una cohorte de pacientes con insuficiencia cardíaca con fracción de eyección reducida en una unidad especializada

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ABSTRACT

Background: Hyperkalemia is a common condition in patients with heart failure (HF), impacting treatment and prognosis. However, its prevalence and risk factors in our region are not clearly defined.
Objective: The aim of the study was to determine the prevalence of hyperkalemia in a specialized HF unit and its association with clinical and pharmacological variables.
Methods: An observational, analytical, and retrospective study was conducted including 693 patients with heart failure with reduced ejection fraction (HFrEF) treated at the Multidisciplinary Heart Failure Unit (UMIC) of a university hospital between 2018 and 2022. Hyperkalemia was defined as serum potassium > 5.0 mEq/L and classified according to tis level, as mild (>5.0–<5.5 mEq/L), moderate (5.5–6.0 mEq/L), or severe (>6.0 mEq/L). Chi-square and Mann-Whitney tests were used to assess associations.
Results: The prevalence of hyperkalemia was 27%, with a predominance of mild cases (85%). A significant association was found with chronic kidney disease (CKD), but not with diabetes. No significant relationship was either found with the use of disease-modifying drugs, including renin-angiotensin-aldosterone system inhibitors.
Conclusions: The prevalence of hyperkalemia in this cohort is high and is primarily associated with CKD. The absence of an association with disease-modifying treatments reinforces the importance of continuing these therapies, given their role in improving morbidity and mortality in HFrEF.

Key words: Hyperkalemia - Heart failure - Renin-angiotensin-aldosterone system - Chronic kidney disease

RESUMEN

Introducción: La hiperkalemia es una condición frecuente en pacientes con insuficiencia cardíaca (IC), con impacto en el tratamiento y pronóstico. Su prevalencia y factores de riesgo en nuestra región no están claramente definidos.
Objetivo: El objetivo del estudio fue determinar la prevalencia de hiperkalemia en una unidad especializada de IC y su asociación con variables clínicas y farmacológicas.
Material y métodos: Estudio observacional, analítico y retrospectivo en 693 pacientes con insuficiencia cardíaca con fracción de eyección reducida (ICFEr) atendidos en la Unidad Multidisciplinaria de Insuficiencia Cardíaca (UMIC) de un hospital universitario entre 2018 y 2022. La hiperkalemia se definió como potasio sérico > 5,0 mEq/L y se clasificó según el nivel: leve (>5,0 -<5,5 mEq/L), moderada (5,5-6,0 mEq/L) o grave (>6,0 mEq/L). Se aplicaron pruebas Chi-cuadrado y Mann-Whitney para evaluar asociaciones.
Resultados: La prevalencia de hiperkalemia fue del 27%, con predominio de casos leves (85%). Se halló asociación significativa con la enfermedad renal crónica (ERC), no así con la diabetes. No se encontró relación significativa con el uso de fármacos modificadores de la enfermedad, incluyendo inhibidores del sistema renina-angiotensina-aldosterona.
Conclusiones: La prevalencia de hiperkalemia en esta cohorte es elevada y se vincula principalmente con la ERC. La ausencia de asociación con tratamientos modificadores de la enfermedad refuerza la importancia de mantenerlos, dado su papel en mejorar la morbimortalidad en la ICFEr.

Palabras clave: Hiperkalemia - Insuficiencia cardíaca - Sistema renina-angiotensina-aldosterona - Enfermedad renal crónica

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INTRODUCTION

Heart failure (HF) is a disease with high prevalence and morbidity and mortality. One of its prognostic and therapeutic challenges is hyperkalemia, which is one of the most common electrolyte disturbances in this population, with a reported incidence of up to 25%. It is classified as mild (>5.0–<5.5 mEq/L), moderate (5.6–6.0 mEq/L), or severe (>6.0 mEq/L). (1–3) Recent evidence demonstrates a U-shaped relationship between serum potassium levels and mortality in patients with HF, with increased risk at both low and high levels. (4,5)

The standard treatment for heart failure with reduced ejection fraction (HFrEF) includes drugs that act on the renin-angiotensin-aldosterone system. (6) Despite strong evidence supporting their use, a significant proportion of patients do not reach target doses, mainly due to the onset of hyperkalemia, symptomatic hypotension, or worsening renal function. (7–11)

This scenario presents a therapeutic dilemma between the long-term prognostic benefits of disease-modifying drugs and the immediate risks associated with hyperkalemia. (12,13) The coexistence of comorbidities such as chronic kidney disease (CKD) and diabetes mellitus further increases this risk. (14–16) In this context, the present study aimed to determine the prevalence of hyperkalemia and its associated risk factors in a cohort of patients with HFrEF treated at a specialized unit in Montevideo.

METHODS

An observational, analytical, descriptive, and retrospective study was conducted including outpatients over 18 years of age with HFrEF (left ventricular ejection fraction, LVEF, ≤ 40%) treated at the Multidisciplinary Heart Failure Unit (UMIC) of Hospital de Clínicas, The study period spanned from 2018 to 2022. Patients with acute kidney injury and stage D HF were excluded.

Definition of variables

Data were collected by reviewing the UMIC electronic databases. Hyperkalemia was defined as serum potassium ≥5.0 mEq/L, and severity ranges were based on those proposed by the European Society of Cardiology (ESC). (17)

Statistical analysis

Qualitative variables were expressed as frequencies and percentages, while continuous quantitative variables were reported as mean and standard deviation (SD) or median and interquartile range (IQR). The chi-square test was used to assess the association between qualitative variables. Student's t-test was used for differences in normally distributed continuous variables, and the Mann-Whitney U test for non-normally distributed variables. The level of significance was set at alpha = 0.05.

Ethical considerations

The study was conducted in accordance with the ethical considerations of the World Medical Association's Declaration of Helsinki. (18) and the project was approved by the Hospital de Clínicas ethics committee.

RESULTS

Among a total cohort of 1050 patients with heart failure, 693 meeting the inclusion criteria were included in the study, 69.8 % (478) of whom were women. The median population age was 73 years (IQR 64–81.5) and the prevalence of hyperkalemia was 27% (95% CI 23–30). Mean potassium level was 4.55 ± 0.61 mEq/L. The analysis of subgroups showed that patients with hyperkalemia had a mean potassium level of 5.28 mEq/L vs. 4.29 mEq/L in the rest of patients. Regarding disease severity, the most common presentation was mild (85.5%), compared with 12.9% moderate and only 1.6% severe (Figure 1).

The association between hyperkalemia and relevant clinical variables is presented in Table 1. The prevalence was 28.2% (135/478) for females and 23.7% (51/215) for males, with no significant difference (p = 0.214). Neither significant difference was observed between patients with and without hyperkalemia in terms of age (p = 0.654) or presence of diabetes (p = 0.324).

Notably, there was a statistically significant association between hyperkalemia and the presence of CKD (OR 1.469, 95% CI 1.046–2.062, p = 0.026) (Figure 2).

Regarding renal functional parameters, there was a clear association with reduced glomerular filtration rate and increased azotemia (Table 2).

Fig. 1. Degree of hyperkalemia. Most patients presented mild hyperkalemia, while only a very limited number of cases were severe

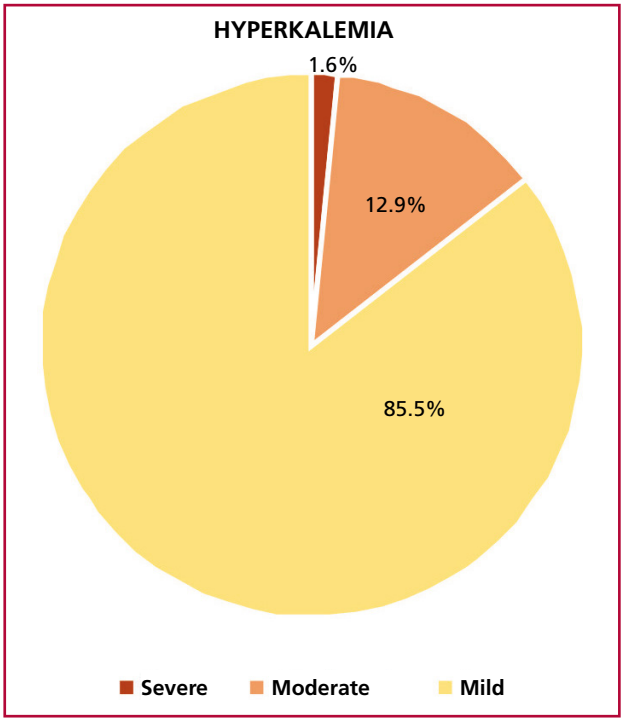

Table 1. Prevalence of hyperkalemia and clinical variables

Clinical variable	All (n=693)	Hyperkalemia YES (n=186)	Hyperkalemia NO (n=507)	p
Age, years, mean ± SD	75 (± 13.02)	72.47 (± 12.54)	71.48 (± 13.20)	0.654
Diabetes Mellitus, n (%)	225 (32.5)	55 (29.6)	170 (33.5)	0.324
Hypertension, n (%)	596 (86.0)	161 (86.6)	435 (85.8)	0.798
CKD, n (%)	280 (40.4)	88 (47.3)	192 (37.9)	0.026
FC Dyspnea, n (%)				
0	3 (0.4)	----	3 (0.6)	----
1	217 (31.3)	60 (32.3)	157 (31.0)	0.816
2	314 (45.3)	87 (46.8)	227 (44.9)	0.702
3	147 (21.2)	38 (20.4)	109 (21.5)	0.841
4	11 (1.6)	1 (0.5)	10 (1.9)	0.319
Ischemic heart disease, n (%)	397 (57.3)	114 (61.3)	283 (55.9)	0.206

CKD: chronic kidney disease; FC: functional class; SD: standard deviation

Fig. 2. Hyperkalemia and CKD. The relative frequency of hyperkalemia is higher, though not exclusive, in patients with chronic kidney disease (CKD). The absence of hyperkalemia is associated more closely with absence of CKD.

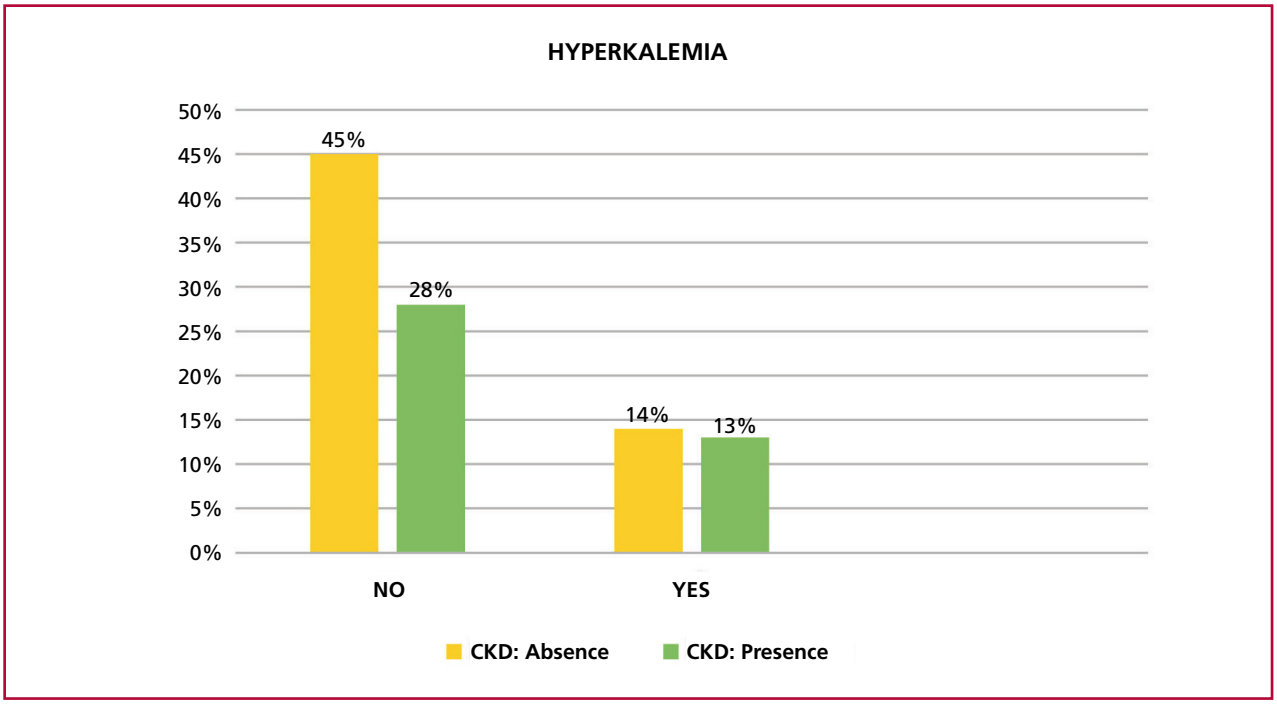

Table 2. Presence of hyperkalemia and other parameters studied

	All (n=693)	Hyperkalemia YES (n=186)	Hyperkalemia NO (n=507)	p
Creatinine (mg/dL)*	1.1 (0.9 – 1.4)	1.2 (0.9 – 1.5)	1.1 (0.9 – 1.4)	0.523
eGFR CKD/EPI**	67.0 ± 1.4	62.7 ± 1.7	68.6 ± 1.2	0.007
Azotemia g/L*	45.5 (34.3 – 62.0)	50.0 (38.0 – 67.0)	44.0 (33.0 – 60.0)	0.003

*values expressed as median (IQR); **values expressed as mean ± SD
eGFR CKD/EPI: glomerular filtration rate according to the CKD/EPI formula

Table 3 presents the relationship between hyperkalemia and stages of glomerular filtration rate. A strong association with stage 3B is notable.

The relationship between the presence of hyperkalemia and standard therapy for HF is detailed in Table 4. No statistically significant difference was observed in any of the cases.

DISCUSSION

Hyperkalemia in patients with HFrEF is common and is associated with increased morbidity and mortality. (19, 20) This first study in the UMIC cohort (Montevideo) found a prevalence of 27%, a figure higher than the 8–25% range reported internationally. (21, 22). Most cases were mild and were significantly associated with stage 3B CKD, a stage at which potassium excretion is significantly impaired. (23)

No significant association was found in stages 4–5 CKD. This could be explained by the small sample size in this subgroup, or by marked clinical caution and therapeutic inertia, characterized by low prescription of disease-modifying drugs (DMDs) due to the risk of severe hyperkalemia. (9, 16, 24) These findings underscore the clinical dilemma of balancing the benefits of DMDs against the risk of complications related to impaired potassium homeostasis in patients with advanced kidney disease, a group frequently excluded from clinical trials. (24)

Regarding treatment, the lack of an association between the use of ACEI/ARB II or mineralocorticoid antagonists and hyperkalemia differs from international reports describing a significantly higher incidence of hyperkalemia events in patients on triple therapy. (25) This finding may be attributed to the homogeneity of the sample due to the high local prescription rate, but it also suggests the success of optimized treatment regimens. The concomitant use of SGLT2i s likely exerts a compensatory diuretic effect that neutralizes the risk of elevated potassium. (26) Therefore, the risk associated with these drugs appears manageable under close monitoring in specialized units.

Among the study's strengths are the availability of a large, well-characterized cohort with standardized definitions according to international guidelines, allowing for precise risk stratification by CKD stage. As limitations, the retrospective observational design and the setting in a specialized unit may introduce selection and referral biases. These factors, along with therapeutic adjustment based on the risk of low baseline potassium levels, should be considered when generalizing the results.

Table 3. Presentation of the relationship between hyperkalemia and glomerular filtration rate stages

Stage	All (n=693)	Hyperkalemia YES (n=186)	Hyperkalemia NO (n=507)	p
1, n (%)	133 (19.3)	27 (14.8)	106 (21.0)	0.071
2, n (%)	262 (38.1)	64 (35,0)	198 (39.2)	0.287
3 A, n (%)	152 (22.1)	45 (24.6)	107 (21.2)	0.458
3 B, n (%)	94 (13.7)	37 (20.2)	57 (11.3)	0.005
4, n (%)	34 (4.9)	8 (4.4)	26 (5.1)	0.796
5, n (%)	13 (1.9)	2 (1.1)	11 (2.2)	0.528

Table 4. Occurrence of hyperkalemia and standard HF therapy

Stage	All (n=693)	Hyperkalemia YES (n=186)	Hyperkalemia NO (n=507)	p
ACEI – ARB II* , n (%)	585 (84.4)	156 (83,9)	429 (84,6)	0.966
Beta-blockers, n (%)	621 (89,6)	172 (92,5)	449 (88,6)	0.135
Loop diuretics, n (%)	429 (61,9)	109 (58,6)	320 (63,1)	0.278
Thiazides, n (%)	26 (3,8)	4 (2,2)	22 (4,3)	0.183
Spironolactone, n (%)	184 (26,6)	52 (28,0)	132 (26,0)	0.612
ARNI, n (%)	19 (2,7)	5 (2,7)	14 (2,8)	0.958
Statins, n (%)	408 (58,9)	115 (61,8)	293 (57,8)	0.339
Antiplatelet agents, n (%)	292 (42,1)	86 (46,2)	206 (40,6)	0.185
SGLT2i n (%)	26 (3,8)	9 (4,8)	17 (3,4)	0.362

ACEI: angiotensin-converting enzyme inhibitors ARB II: angiotensin II receptor blockers; ARNI: angiotensin receptor neprilysin inhibitors; SGLT2i: sodium-glucose cotransporter 2 inhibitors

* 577 ACEI patients, 8 ARA II patients.

CONCLUSIONS

The prevalence of hyperkalemia in patients with HFrEF in our cohort is high, with the majority of cases being mild. Hyperkalemia is primarily associated with the presence of CKD, especially in 3B stage. The absence of a significant association between hyperkalemia and the use of DMDs highlights the importance of maintaining disease-modifying therapy, aimed at reducing morbidity and mortality in this patient group.

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web).

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