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CLINICAL STUDY

Community-acquired hyperkalemia in elderly patients: risk factors and clinical outcomes

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ABSTRACT

Background: Although the risk and related factors of hyperkalemia developed in the hospital are known in elderly, risk and related factors of community-acquired hyperkalemia (CAH) in this population are not well known. This study was performed to investigate the risk of CAH in elderly and evaluate the related factors and clinical outcomes.

Study design, setting and participants, intervention: Patients (aged ≥65 years) with hyperkalemia were screened. Group 1 (young-old); 65–74 years/old, Group 2 (middle-old); 75–84 years/old, Group 3 (oldest-old); ≥85 years/old, and Group 4 (control group); ≥65 years/old (normal serum potassium levels). The relation between CAH and hospital expenses (HE), the number of comorbid diseases (NCD), and all-cause of mortality rates (MR) were evaluated. We also investigated whether drugs, sex, and NCD are risk factors for the development of CAH.

Results: There was a positive correlation between serum potassium levels and length of hospital stay, MR, HE, and NCD ($p < 0.001$). Risk factors for CAH were the use of non-steroidal-anti inflammatory drugs (NSAIDs) (Odds Ratio [OR]: 2.679), spironolactone (OR: 2.530), and angiotensin converting enzyme inhibitors (ACEI) (OR: 2.242), angiotensin receptor blockers (ARB) (OR: 2.679), ≥2 comorbid diseases (OR: 2.221), female gender (OR: 2.112), and renal injury (OR: 5.55). CAH risk was found to be increased 30.03 times when any of ACEI, ARB, NSAIDs, or spironolactone is given to a patient with a renal injury.

Conclusion: Use of NSAIDs, ACEI, ARB, spironolactone and increased NCD are all independent risk factors for CAH in the elderly, especially in patients with kidney diseases.

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Community-acquired hyperkalemia; elderly; risk factors; mortality; hospital expenses

Introduction

World Health Organization reports that elderly population grows faster compared to other age groups and in 2025 there will be a total of 1.2 billion persons aged over 60 years.[1] It is also estimated that by 2050, there will be 2 billion elderly and 80% of this population will be living in developing countries. As elderly population is growing rapidly in the whole world, it is essential to understand their health problems for providing appropriate health care.

In all the stages of aging defined by gerontologists (young-old: 65–74 years, middle-old: 75–84 years, oldest-old: >85 years), functional reserve capacity was diminished in multiple organ systems.[2–4] The elderly population is susceptible to electrolyte disorders like potassium imbalance due to the physiological changes. Hyperkalemia is accepted as a life-threatening electrolyte disorder.[5] Potassium secretion may be diminished due to diseases like heart failure, hypertension, chronic, and acute renal injury which may present more often with advancing age in the elderly. In addition, polypharmacy which may cause electrolyte disorders like hyperkalemia may also arise due to increased number of comorbidities.[6] Use of the drugs which may cause hyperkalemia in the presence of renal failure may be another risk factor for hyperkalemia.[7] It has been stated that there is an evident relation between hyperkalemia and morbidity and mortality in elderly.[8] Hyperkalemia in this population may increase the need for hemodialysis, mechanic ventilation, hospitalization, and intensive care follow-up. All these may increase health expenses and have serious *economic impacts in especially developing* countries.

Although the risk and related factors of hyperkalemia developed in the hospital are known in elderly, risk and related factors of community-acquired hyperkalemia

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(CAH) in this population are not well known. We performed this study to determine the risk of CAH, related factors, and clinical outcomes in young-middle-oldest-old patients.

Patients and methods

This study was approved by Human Research Ethics Committee (20.08.2015, 2015/261). Written informed consent was taken from patients for their participation in the study.

Patients (aged ≥65 years) admitted to our hospital between 1 January 2014 and 31 December 2014 were screened and the patients presenting with hyperkalemia were evaluated. The patients with pseudohyperkalemia, intravascular hemolysis, severe thrombocytosis (platelets >1.000.000/mL), or severe leucocytosis (white blood cells >70.000/mL), transfusion reactions, sickle cell crisis, and hemolytic reactions induced by drugs and the patients who developed hyperkalemia during hospital stay were excluded from the study.

Patients were grouped according to age; Group 1 (young-old) consisted of patients aged between 65 and 74 years, Group 2 (middle-old) between 75 and 84 years, and Group 3 (oldest-old) over 85 years. Of the patients admitted to our clinic in that period, the patients aged ≥65 years with normal serum potassium levels (3.5–5.5 mEq/L) were included in Group 4 (control group). Systolic blood pressure, diastolic blood pressure, and pulse rate of each patient were also recorded at admission to the hospital.

The patients with hyperkalemia were evaluated thoroughly for underlying etiology and presence of comorbid diseases like diabetes mellitus, hypertension, chronic obstructive lung disease, acute-chronic kidney disease (AKI-CKD), coronary artery disease, cerebrovascular event, and malignancies were investigated. Hospital expenses (HEs) were recorded for each patient (Unites States Dollars [USD]). Potassium levels and all-cause mortality rates (MRs) in all groups were also noted. In addition, use of drugs, which may cause hyperkalemia, like non-steroid anti-inflammatory drugs (NSAIDs), angiotensin converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), spironolactone, beta blocker, heparin, digoxin, potassium supplements, trimethoprim-sulfamethoxazole were recorded. Drug use was considered to be a significant factor if it was administered within 24–36 h prior to the diagnosis of hyperkalemia.

The need for hemodialysis, mechanical ventilation, and intensive care, the total cost of hospital stay, the length of hospital stay, the number of comorbid diseases (NCDs) were evaluated and their relation with serum potassium level was investigated. The relationship between CAH and all-cause of mortality was evaluated.

Risk analysis of CAH was performed for the drugs which may cause hyperkalemia, age, gender, and NCD.

AKI was defined as ≥0.3 mg/dL increase in serum creatinine in last 48 h or increase in serum creatinine more than 1.5 times the baseline, which is known or presumed to have occurred within the prior 7 d; or urine output <0.5 mL/kg/h for the last 6 h.[9] CKD was defined as estimated glomerular filtration rate (eGFR) < 60 mL/dk/1.73 m^2 or presence of renal functional and structural impairment for at least 3 months although eGFR is >60 mL/dk/1.73 m^2 or presence of glomerular hematuria or proteinuria lasting for at least 3 months.[10]

Laboratory tests

Serum potassium, sodium, fasting plasma glucose, blood urea nitrogen (BUN), serum creatinine (Normal: 0.6–1.1 mg/dL), magnesium, albumin, calcium, phosphor, arterial blood gases, high sensitive c-reactive protein (hsCRP), hemoglobin, parathyroid hormone (PTH), eGFR, and 24 h urine protein excretion were evaluated in all groups. Serum sodium, plasma glucose, BUN, and creatinine were measured by Olympus AU 640 Chemistry Immunoanalyzer (Tokyo, Japan). Serum potassium, magnesium, calcium, phosphor, albumin, hsCRP levels were measured by Cobas Integra 800 Chemistry Analyzer (Basel, Switzerland) and eGFR was calculated by Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) Formula as $141 \times \min(Scr/\kappa,1)\alpha \times \max(Scr/\kappa,1) - 1.209 \times 0.993$ age $\times 1.018$ [female] $\times 1.159$ [black].

Electrocardiogram (ECG) was performed for all patients with hyperkalemia using 12 derivation ECG devices with a 25 mm/s velocity. ECGs were evaluated for the presence of peaked T waves, short QT interval, prolonged PR interval, prolonged QRS duration, and ventricular fibrillation.

During management of hyperkalemia, the patients who did not need hospitalization were reevaluated 48 h later. Medical treatment was discontinued in patients if serum potassium level was found in normal range.

Treatment of hyperkalemia

In patients with serum potassium levels between 5.5 and 6 mEq/L without ECG changes, potassium-restricted diet was suggested, medications associated with hyperkalemia were discontinued, and the patients were followed closely. Medical treatment was started for the patients with serum potassium levels of 6–6.5 mEq/L

with ECG changes. In addition to beginning potassium restricted diet and withdrawal of the drugs associated with hyperkalemia, 5–10 mL 10% calcium gluconate (iv) was administered in 2–5 min to prevent cardiac complications of hyperkalemia. The dose was repeated after 15 min if ECG abnormalities persisted. Oral Kayexalate 1 g/kg (max. 30–40 mg), $NaHCO_3$ 1–2 mEq/kg or 1 mL/kg were given in 10–30 min. When serum potassium level was above 6.5 mEq/L; calcium gluconate, $NaHCO_3$, insulin-glucose infusion, and nebulized albuterol (10–20 mg) were administered for the first 30 min. Dialysis was performed for the patients whose peaked T waves were not improved despite the medical treatment. Glucose and insulin infusion (iv) (10% dextrose 500 cc +10 unit regular insulin) was given in 30 min to 1 h. Insulin infusion was administered without using dextrose when glucose level was above 200 mg/dL.[11]

Statistical methods

MedCalc packet statistical software program (Ostend, Belgium) was used for statistical analysis. Shapiro–Wilk test was used to identify whether variables were normally distributed. The mean ± standard deviation was used for descriptive statistics for non-normally distributed variables. For the mean comparisons of the groups, where more than two groups involved, one-way analysis of variance was applied. Chi-square test was used to investigate the association between need for hemodialysis, mortality, categoric variables of mortality, and age groups in hospitalized patients.

The odds ratio was calculated for risk analysis from logistic regression and chi-square analysis. ROC curve analysis was performed to investigate the association between potassium value and mortality. Sensitivity and specificity values were calculated to assess the diagnostic performance of potassium values. Linear association between potassium and age values was investigated by Pearson correlation analysis. $p < 0.05$ was accepted as the level of statistical significance for all comparisons.

Results

There were 40,092 patients aged 65 years and older, and 1180 of these had CAH, which constituted 2.94% of all patients. There were 249 patients meeting inclusion criteria and these were included in the study. The patients were grouped according to their ages as follows; Group 1, $n = 129$ (57 male [M], 72 female [F]), Group 2, $n = 75$ (25 M, 50 F), and Group 3, $n = 45$ (23 M, 22 F). Group 4, $n = 182$ (109 M, 73F) included patients who were admitted to our clinic in the mentioned period and had normal potassium levels, this group is used as a control.

Demographic and laboratory data of the groups are shown in Table 1. There was a significant difference between groups for age, serum potassium values, duration of hospitalization, hsCRP, proteinuria, arterial blood gases HCO_3, pH, eGFR, HEs, need for hospitalization, MR, and the need for hemodialysis ($p < 0.05$).

Of the 249 patients in all groups, 73 patients in Group 1 (45.9%), 45 patients in Group 2 (43.7%), and 38 patients in Group 3 (74.5%) needed hospitalization. Need for mechanic ventilation of patients in hospitalized patients was shown in Table 2. Need for mechanic ventilation was higher in Group 3 compared to Group 2 and it was also higher in Group 2 compared to Group 1 ($p < 0.05$).

Use of the drugs that may cause CAH was evaluated in each group. In Group 1, 13.8% of patients had history of use of ARB, 12.6% beta blocker, 10.7% spironolactone, 10% ACEI, 4.4% NSAIDs, and 11.2% other drugs, in Group 2, 22.4% of patients had history of taking beta blocker, 22.3% spironolactone, 20.4% ACEI, 20.4% ARB, 15.6% NSAIDs, 10.2% other drugs, and in Group 3, 31.4% gave history of use of spironolactone, 25.5% NSAIDs, 23.4% ACEI, 19.6% ARB, 19.6% beta blocker, 9.6% other drugs. In total, 59.7%, 75.8%, and 86.7% of patients were found to be using drugs, which may cause CAH in Groups 1, 2, and 3, respectively. Only 3.2% of patients in Group 4 had the history of above-mentioned drugs. Oldest-old patients were using significantly more drugs compared to middle and young-old patients, and middle-old patients were found to be using significantly more drugs compared to young-old patients ($p < 0.001$).

Comorbid disease were recorded in all patients and it was detected that 61.3%, 66.7%, 89.9%, 3.4% of patients had two or more comorbid diseases in Groups 1, 2, 3, and 4, respectively ($p < 0.001$).

Related factors with CAH

There was a positive linear correlation between serum potassium levels and duration of hospital stay in Groups 1, 2, and 3 (for all groups $p < 0.001$, $r = 0.684$, $r = 0.629$, $r = 0.900$, respectively).

There was a positive correlation between serum potassium levels and HEs in Groups 1, 2, and 3 (for all groups $p < 0.001$, $r = 0.577$, $r = 0.615$, $r = 0.712$, respectively). There was a positive correlation between serum potassium levels and need for hemodialysis in Groups 1, 2, 3 (for all groups $p < 0.001$, $r = 0.612$, $r = 0.730$, $r = 0.598$). There was a positive relation between serum

Table 1. Laboratory and demographic data of the patients.

	Group 1 ($n = 129$)	Group 2 ($n = 75$)	Group 3 ($n = 45$)	Group 4 ($n = 252$)
Age (years)	$68.7 \pm 6.3^{b,c,d}$	$77.6 \pm 9.1^{a,c}$	$87.9 \pm 2.1^{a,b,d}$	$75.1 \pm 7.7^{a,c}$
SBP (mmHg)	132.2 ± 14.6	134.5 ± 13.8	131.6 ± 11.9	119.5 ± 12.0
DBP (mmHg)	85.5 ± 6.9	86.3 ± 7.2	84.5 ± 6.6	82.3 ± 3.6
Pulse	84.3 ± 4.7	85.7 ± 5.2	85.9 ± 6.1	84.6 ± 6.1
Potassium, mEq/L	$5.96 \pm 0.28^{b,c,d}$	$6.79 \pm 0.30^{a,c,d}$	$7.70 \pm 0.32^{a,b,d}$	$4.40 \pm 0.55^{a,b,c}$
FPG, mg/dL	148.4 ± 88.5	138.1 ± 73.6	142 ± 74.4	100.9 ± 33.8
BUN, mg/dL	56.6 ± 32.5	55.5 ± 31.0	62.18 ± 3	20.12 ± 3
Creatinine, mg/dL	2.64 ± 1.8	2.56 ± 1.9	3.1 ± 1.9	0.5 ± 0.2
Magnesium, g/dL	2.37 ± 0.6	2.74 ± 1.0	2.84 ± 0.8	2.83 ± 0.6
Hemoglobin, g/dL	10.6 ± 2.3	10.8 ± 2	10.65 ± 2.1	11.4 ± 1.7
hCRP, mg/L	$7.56 \pm 9.8^{b,c,d}$	$25.1 \pm 45^{a,c,d}$	$40.89 \pm 38.9^{a,b,d}$	$3.6 \pm 0.3^{a,b,c}$
Sodium, mmol/L	135.4 ± 6.5	136.9 ± 5.9	135.8 ± 7.8	136.3 ± 5.5
Albumin, g/dL	3.25 ± 0.8	3.14 ± 0.6	2.92 ± 0.7	3.97 ± 0.2
Calcium, mg/dL	7.75 ± 1.2	8.25 ± 0.7	8.82 ± 3.5	8.50 ± 1.0
Phosphor, mg/dL	7.09 ± 1.1	7.22 ± 0.4	7.86 ± 1.3	5.3 ± 1.4
PTH, pg/mL	211.09 ± 122.6	213.97 ± 219.14	202.96 ± 157.3	35.51 ± 15.2
Proteinuria, mg/gün	$1379.8 \pm 136.4^{b,c,d}$	$1937.2 \pm 1297.2^{a,d}$	$1830.6 \pm 1544.5^{a,d}$	$98.6 \pm 23.7^{a,b,c}$
ABG pH	$7.30 \pm 0.03^{b,c,d}$	$7.22 \pm 0.04^{a,c,d}$	$7.12 \pm 0.03^{a,b,d}$	$7.44 \pm 0.01^{a,b,c}$
ABG HCO_3, mEq/L	$20.43 \pm 3.57^{b,c,d}$	$15.97 \pm 1.78^{a,c,d}$	$11.33 \pm 1.43^{a,b,d}$	$25.04 \pm 2.1^{a,b,c}$
ABG SO_2, mmHg	97.48 ± 1.33	96.42 ± 2.08	95.69 ± 13.28	98.12 ± 23.3
ABG PCO_2, mmHg	37.41 ± 7.05	35.68 ± 6.27	37.51 ± 1.03	39.81 ± 4.02
eGFR, mL/dak	$35.45 \pm 24.85^{b,c,d}$	$32.81 \pm 19.16^{a,c,d}$	$23.60 \pm 17.95^{a,b,d}$	$96.01 \pm 4.4^{a,b,c}$
MR, %	$30.1^{b,c,d}$	$53.3^{a,c,d}$	$65.8^{a,b,d}$	$5.3^{a,b,c}$
DR, %	$28.8^{b,c,d}$	$75.9^{a,c,d}$	$81.2^{a,b,d}$	$1.12^{a,b,c}$
LHS, days	$6.21 \pm 4.2^{b,c,d}$	$9.36 \pm 2.8^{a,c,d}$	$13.55 \pm 3.6^{a,b,d}$	$5.93 \pm 2.4^{a,b,c}$
NH, %	$56.5^{b,c,d}$	$60^{a,c,d}$	$84.4^{a,b,d}$	$12.3^{a,b,c}$
HE, USD $	$482.6 \pm 311.1^{b,c,d}$	$821.68 \pm 312.1^{a,c,d}$	$1050.67 \pm 224.5^{a,b,d}$	$322.2 \pm 114.7^{a,b,c}$
LT, days	$4.83 \pm 3.7^{b,c,d}$	$8.20 \pm 2.9^{a,c,d}$	$13.71 \pm 3.3^{a,b,d}$	$9.04 \pm 8.3^{a,b,c}$

SBP: systolic blood pressure; DBP: diastolic blood pressure; FPG: fasting plasma glucose; BUN: blood urea nitrogen; hCRP: high sensitive c-reactive protein; PTH: parathyroid hormone; ABG: arterial blood gas; HCO_3: bicarbonate; eGFR: estimated glomerular filtration rate; MR: all-cause of mortality rate; DR: dialysis requirement; LHS: length of hospital stay; NH: need for hospitalization; HE: hospital expenses; LT: length of treatment; USD $: American dollar.
[a]Shows the statistically significant difference when a parameter in Group 1 is compared with the same parameter in another group.
[b]Shows the statistically significant difference when a parameter in Group 2 is compared with the same parameter in another group.
[c]Shows the statistically significant difference when a parameter in Group 3 is compared with the same parameter in another group.
[d]Shows the statistically significant difference when a parameter in Group 4 is compared with the same parameter in another group.

Table 2. Distribution of hospitalized patients according to the need for mechanic ventilation.

	Group 1	Group 2	Group 3	Total	*p* Value
Need for mechanic ventilation, % (*n*)	19.2 (14)	44.4 (20)	65.8 (25)	37.8 (59)	<0.001
No need for mechanic ventilation, % (*n*)	80.8 (59)	55.6 (25)	34.2 (13)	62.2 (97)	<0.001
Total	100 (73)	100 (45)	100 (38)	100 (156)	<0.001

potassium levels and need for mechanical ventilation, intensive care in Groups 1, 2, 3 (for all groups $p < 0.001$, $p < 0.001$, respectively).

There was statistically significant relation between CAH and all-cause of MR in Groups 1, 2, and 3. Its sensitivity was 74.07% and specificity was 85.29% in Group 1 (AUC = 0.849; 95% CI: 0.775–0.906; $p < 0.001$), its sensitivity was 91.7% and specificity was 96.1% in Group 2 (AUC = 0.976; 95% CI: 0.911–0.998; $p < 0.001$), and sensitivity was 80% and specificity was 85% (AUC = 0.916; 95% CI: 0.794–0.978; $p < 0.001$) in Group 3. There was no statistically significant relation between serum potassium level and MR in Group 4. The sensitivity of this relation was 92.9%, and specificity was 25% (AUC = 0.588; 95% CI: 0.513–0.660; $p = 0.269$). The area under ROC curve values for MR in groups is shown in Table 3. ROC curve for CAH and mortality in all groups 1, 2, 3, and 4 are shown in Figures 1, 2, 3, and 4, respectively.

There was a positive statistically important relation between age and NCDs ($p < 0.05$).

Risk factors for CAH

Based on the data obtained, NSAIDs, spironolactone, ACEI, ARB, and beta-blockers were found to be independent risk factors for 2.679, 2.530, 2.242, 2.679, and 2.136 times more respectively for hyperkalemia. In addition to this, the risk of developing CAH is increased by 2.221, 2.112, and 5.5 times more in patients with two or more comorbid diseases, female gender, and renal failure, respectively. If a patient with renal failure was taking ACEI, ARB, NSAIDs, beta blocker, or spironolactone risk of CAH was found to be increased by 30.03 times

Table 3. Area under ROC curve for mortality.

	Group 1	Group 2	Group 3	Group 4
Area under the ROC curve (AUC)	0.849	0.976	0.916	0.588
Standard error	0.0489	0.0145	0.0387	0.0797
95% CI	0.775–0.906	0.911–0.998	0.794–0.978	0.513–0.660
Z-statistic	7.122	32.831	10.763	1.104
p Value	<0.0001	<0.0001	<0.0001	0.2695

CI: confidential interval; ROC: receiver operator characteristics curve.

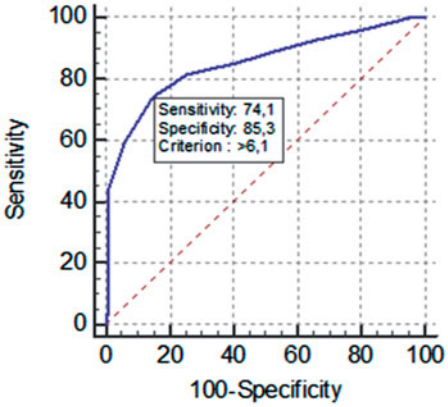

Figure 1. ROC curve between CAH and mortality in Group 1.

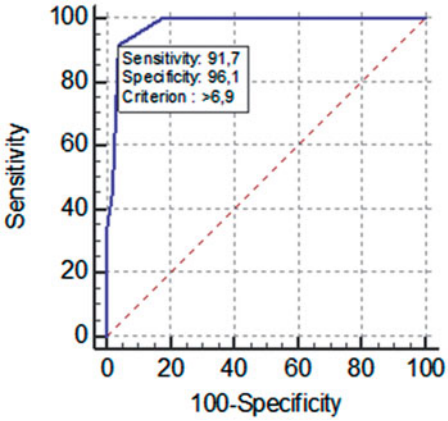

Figure 2. ROC curve between CAH and mortality in Group 2.

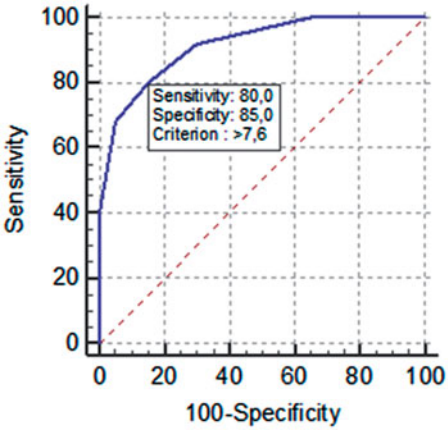

Figure 3. ROC curve between CAH and mortality in Group 3.

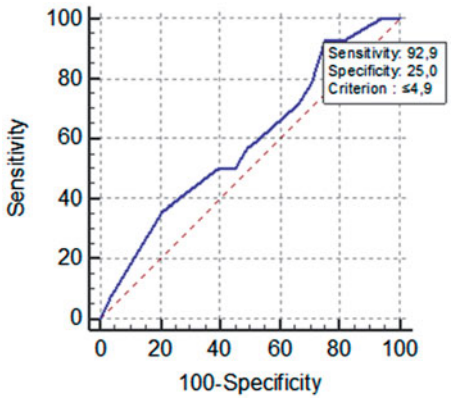

Figure 4. ROC curve between potassium and mortality in Group 4.

Table 4. Independent risk factors for CAH.

		95% Confidence interval (CI)	
	Odds ratio (OR)	Lower	Upper
NSAID	2.679	2.304	3.115
Spironolactone	2.530	2.134	3.000
ACEI	2.242	1.975	2.975
ARB	2.679	2.304	3.115
Beta blocker	2.1363	2.690	3.426
≥2 comorbid diseases	2.221	2.104	3.162
Female gender	2.112	2.432	3.012
Renal failure	5.55	4.192	7.348

CAH: community-acquired hyperkalemia; NSAID: non-steroidal anti-inflammatory drug; ACEI: angiotensin converting enzyme inhibitor; ARB: angiotensin 2 receptor blocker.

(95% CI: 21.598–166.863). Risk factors of CAH in elderly are shown in Table 4. Age was not an independent risk factor for CAH ($p = 0.761$).

Discussion

Although there is studies about hyperkalemia in general population, to the best of our knowledge, this is the first study carried out to investigate risk and related factors of CAH in the elderly.

Functional and anatomical changes in aged kidneys make elderly susceptible to electrolyte abnormalities like hyperkalemia. In this study, we found that CAH causes an increase in mortality and morbidity rates. Frequency and severity of CAH in elderly may be associated with underlying renal dysfunction, a number of

comorbidities, and use of medications causing hyperkalemia.

With increasing age, structural and functional changes, which may cause potassium imbalance, may arise. Reduction in GFR and tubular transport functions may cause reductions in potassium excretion. However, remaining nephrons will try to compensate this. In the presence of medications associated with hyperkalemia or in the presence of risk factors like underlying renal disease, the risk of hyperkalemia is increased in elderly patients compared to younger patients.[11] In our study, although positive relation was obtained between the age and CAH, age was not found as an independent risk factor for CAH. This may be related to the common use of the drugs like ACEI, ARB, NSAIDs, spironolactone, and increased number of comorbidities, which may cause hyperkalemia in the elderly. Mukete et al. reported that the NCDs increases in patients older than 65 years and this may cause polypharmacy which may cause adverse effects.[12] Buurman et al. also reported that NCDs increases in elderly patients as they get older.[13] Comorbid diseases like heart failure, hypertension, chronic, and acute kidney injury may lead to tubular dysfunction and reduction in GFR which may decrease the renal excretion of potassium. In addition, comorbid diseases may affect potassium secretion, which is already impaired in the elderly.[14] Besides, increase in the NCDs may cause increased use of drugs decreasing potassium secretion and thus increase the risk of hyperkalemia.[15] In our study, number of comorbidities was higher in oldest old patients compared to middle and young-old patients and was found higher in middle-old patients than the young-old patients. Besides, use of the drugs causing hyperkalemia was found to be higher in oldest and middle-old patients who had more comorbid diseases compared to young-old patients. Number of comorbid disease was found to be an independent risk factor for CAH.

NSAIDs increase serum potassium level due to hyporeninemic hypoaldosteronism secondary to inhibition of prostaglandin E_2 (PGE_2) and prostacyclin I_2 (PGI_2). PGE_2 and PGI_2 may increase the number of potassium channels in distal tubulus, therefore inhibition of these agents may also lead to hyperkalemia.[16] Mamdani et al. reported that frequency of NSAIDs use was 20–30% and this also increases with increasing age. Incidence of hyperkalemia in elderly patients who use potassium-sparing diuretic was reported to be 10–19% in various studies.[17–19] Angiotensin II is a major stimulator of adrenal aldosterone synthesis. Inhibition of angiotensin II may cause hypoaldosteronism and thus, cause a reduction in potassium secretion in collector tubules. It also decreases eGFR and contributes to decreased potassium excretion.[20] Elgendy et al. carried out a meta-analysis consisting of 113,386 patients older than 65 years and concluded that ARBs are the risk factor for the development of hyperkalemia (RR: 1.57, 95% CI: 1.13–2.19, $p = 0.008$).[21] Beta blockers decrease *catecholamine-induced renin release*, which decreases angiotensin II and aldosterone secretion and cause hyperkalemia. They also decrease potassium shift into the cell and contribute to hyperkalemia.[22] Potassium-sparing diuretics like spironolactone increase serum potassium level as they block the potassium secreting effect of aldosterone in distal tubulus.[23] Takaichi et al. tried to determine the risk factors of hyperkalemia in 9117 patients whose mean age was above 60 years old and with a serum creatinine level of more than 5 mg/dL and showed that serum creatinine level, diabetes mellitus, use of ACEI, ARB, and beta blocker, male gender, and age were all independent risk factors for hyperkalemia. In our study, we did not exclude the patients with serum creatinine level more than 5 mg/dL. We also found that ACEI, ARB, beta blocker, spironolactone, NSAIDs use, and the presence of renal failure are risk factors for hyperkalemia supporting the results of previous studies.[24] However, age was not found as an independent risk factor for hyperkalemia in our study. This may be related to the compensation of age-related reduced potassium secretion by the remaining nephrons. In addition, we found that female gender is a risk factor for CAH. In our study, oldest-old patients were using more drugs causing hyperkalemia in compared to middle-young-old patients, whereas middle-old patients were using more drugs causing hyperkalemia in compared to young-old patients. We found that NSAIDs, spironolactone, ACEI, ARB, and beta blocker increase the risk of CAH by 2.679, 2.530, 2.242, 2.679, and 2.1363 times, respectively. In addition, use of a drug that may cause hyperkalemia in an elderly patient with renal injury was found to increase the risk of CAH by 30.03 times.

In a meta-analysis study consisting of patients (mean age: 64.46 ± 11.04/years) with hyperkalemia and cardiovascular disease, who are under antihypertensive treatment, hyperkalemia was found to be related with increased mortality and hospitalization rate, which were 6.25% and 7.8%, respectively.[25] Unlike this meta-analysis, eight other comorbid diseases in addition to cardiovascular disease were also evaluated in our study. Our results suggested that hospitalization and MRs were higher in study groups compared to control group and hyperkalemia was related with mortality and hospitalization rate. Also, hospitalization and MRs were higher in oldest-old patients compared to middle and young-old patients. Positive correlation was present

between duration of hospitalization and serum potassium values in oldest, middle and young-old patients. This increased the HEs in study groups. Shorr et al. found average HEs as 11.109 USD in 6117 patients with severe hyponatremia (mean age: 74.4/years) and 10.033 USD in 18,445 patients with moderate hyponatremia (mean age: 74.3/years).[26] A similar study by Turgutalp et al., hospital costs in patients with community-acquired hyponatremia, aged above 65 and 75 years was investigated. Hospital cost were 1.034.4 ± 452.2 USD, 1.499.1 ± 627.4 USD, respectively. In the same study, the need for mechanic ventilation was found to be 19.3% and 35.9%, respectively. They stated that the need for mechanic ventilation increases in elderly patients due to this electrolyte disorder.[27] Community-acquired hyponatremia is an important electrolyte imbalance and there have been many studies performed to find out the economic cost and need for mechanic ventilation in these patients. However, there is not available data about HEs and the need for mechanic ventilation due to CAH in the elderly. We found hospital cost for oldest, middle, and young-old patients to be 1050.67 USD, 821 USD, and 482 USD, respectively. Need for mechanic ventilation for hospitalized patients were 19.2%, 44.4%, 65.8% for young, middle, and oldest-old patients, respectively.

Limitations

The first limitation of the study is its retrospective design and the second limitation is the small sample size. In addition, mortality reasons could not be evaluated separately due to the retrospective design of the study. Instead, all-cause mortality was reported.

Conclusion

Elderly patients are susceptible to CAH. Increased NCDs cause polypharmacy and eventually hyperkalemia in elderly patients, especially in very old patients. CAH is more common in oldest-old patients compared to middle and young-old patients and it is also more common in middle-old patients in compared to young-old patients. Drugs like NSAIDs, ACEI, ARB, and spironolactone are risk factors for CAH in elderly patients, especially in patients with kidney diseases. Increased serum potassium level is related to increased mortality, morbidity, and HEs. Thus, they should be prescribed more carefully.

Disclosure statement

The authors declare that they have no conflict of interest.

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