Incidence and Risk Factors of Hyperkalemia in Pediatric Patients in a Large North European Healthcare System

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Introduction

Homeostatic maintenance of serum potassium (K^+) is important for many physiologic processes, such as cardiac electrical conduction and inotropy, smooth muscle tone, neuronal signaling, and acid-base balance. Hyperkalemia is a relatively common electrolyte abnormality that can result in severe arrhythmias and increased risk of death.

Little data exist on the burden of hyperkalemia in pediatric clinical settings. Here, we estimate hyperkalemia incidence and determinants among healthcare users from the Stockholm CREAtinine Measurements (SCREAM) project, a healthcare utilization cohort of the Stockholm region in Sweden.

Methods

- This project is based on the SCREAM project,[1] a healthcare utilization cohort including all residents in the region of Stockholm, Sweden, undertaking at least one measurement of serum creatinine in inpatient or outpatient care during 2006–2011. Thereafter, data were linked with regional and national administrative databases
- Pediatric patients (<18 years) undergoing K^+ testing during 2009–2011 were included. The index date was set at January 1, 2009, the point at which the study covariates were calculated. An additional inclusion criterion was the existence of ≥1 ambulatory measurement of serum creatinine within the preceding year
- Hyperkalemia was defined as serum K^+ >5.0 mmol/L, and moderate-to-severe hyperkalemia as serum K^+ >5.5 mmol/L
- Incidence proportion and incidence rates were estimated overall, by comorbid conditions and use of renin–angiotensin–aldosterone system inhibitors (RAASis)
- Logistic regression models were used to identify baseline risk factors of hyperkalemia

Results

- Of the 15,177 pediatric patients registered, 5228 underwent K^+ testing at least once per year. Of these, 5168 individuals were followed for the whole period (98.9%), 33 died before the end of follow-up (0.63%), and the remaining 27 individuals migrated from the county before the end of follow-up (0.52%)
- K^+ levels >5.0 mEq/L and >5.5 mEq/L occurred in 6.4% and 2.8% of all patients, respectively, over the 3-year period. Most cases of hyperkalemia (68%) occurred only once during follow-up

Table 2. Risk Factors (Defined as K^+ >5.0 mmol/L) in Persons Aged <18 Years

Risk Factor	Odds Ratios (95% CI)
Age	0.81 (0.79–0.83)
Female	0.71 (0.53–0.94)
Renal disease	3.25 (2.01–5.24)
Diabetes mellitus	2.86 (1.28–6.37)
Hypertension	1.13 (0.54–2.35)
RAASi use	2.09 (0.9–4.85)
NSAID use	0.92 (0.45–1.86)
K^+ measurements	
(0–2]	REF
(2–4]	4.01 (2.66–6.05)
>4	23.18 (15.96–33.65)

CI, confidence interval; K^+, potassium; NSAID, nonsteroidal anti-inflammatory drug; RAASi, renin–angiotensin–aldosterone system inhibitor; REF, reference value. Adjusted odds ratios with 95% CIs from logistic regression on hyperkalemia. Models are adjusted by demographics, number of K^+ measurements, and the following drugs/comorbidities (others were discarded because of quasi-complete data separation): RAASi use, NSAID use, diabetes mellitus, hypertension, and renal disease.

- Older age (odds ratio [OR], 0.81; 95% confidence interval [CI], 0.79–0.83, per year increase) and female sex (0.71; 0.53–0.94) were associated with lower risk of hyperkalemia
- Comorbid CKD (OR, 3.25; 95% CI, 2.01–5.24) or diabetes (2.86, 1.28–6.37) were associated with higher hyperkalemia risk
- Although not statistically significant, hypertension (OR, 1.13; 95% CI, 0.54–2.35) and RAASi use (2.09, 0.90–4.85) were also associated with increased risk of hyperkalemia

Table 1. Crude and Adjusted IRs of Hyperkalemia by Risk Factors, for Persons Aged <18 Years, per 1000 Patient-Years

Category	Crude IR K^+ >5.0 mmol/L	Adjusted IR K^+ >5.0 mmol/L	Crude IR K >5.5 mmol/L	Adjusted IR K^+ >5.5 mmol/L
Overall	46.52 (43.25–50.03)	7.80 (5.63–9.97)[a]	18.84 (16.81–21.12)	1.96 (0.67–3.24)
Creatinine tertile				
T1	41.71 (36.61–47.53)	—	15.76 (12.75–19.49)	—
T2	16.07 (12.97–19.92)	—	6.19 (4.4–8.74)	—
T3	82.82 (75.25–91.15)	—	35.07 (30.28–40.63)	—
Renal disease				
No	21.53 (19.31–24.00)	7.30 (5.22–9.38)	8.04 (6.73–9.61)	1.87 (0.63–3.12)
Yes	720.91 (653.86–794.94)	39.10 (15.41–62.79)	310.24 (267.39–360.07)	6.50 (0.00–15.78)[a]
Cardiovascular disease				
No	46.01 (42.76–49.52)	7.82 (5.62–10.01)	18.77 (16.73–21.06)	1.73 (0.58–2.87)
Yes	96.14 (58.61–158.56)	6.19 (0.00–14.33)[a]	25.64 (10.41–65.64)	3.74 (0.00–8.78)[a]
Diabetes mellitus				
No	45.8 (42.54–49.32)	7.63 (5.48–9.78)	18.63 (16.6–20.92)	1.89 (0.59–3.20)
Yes	88.48 (59.15–132.76)	28.79 (0.00–61.30)[a]	30.78 (15.83–60.64)	10.60 (0.00–33.14)[a]
RAASi				
No	31.33 (28.65–34.27)	7.88 (5.60–10.16)	13.04 (11.35–14.99)	1.85 (0.62–3.09)
Yes	707.02 (624.43–800.71)	3.33 (0.00–14.10)[a]	270.83 (221.69–331.08)	15.14 (0.00–38.23)[a]
K^+ samplings per year				
(0–2]	9.33 (7.85–11.09)	5.55 (3.71–7.39)	2.91 (2.14–3.97)	1.21 (0.23–2.19)
(2–4]	66.04 (52.65–82.91)	35.20 (17.20–53.20)	22.31 (15.16–32.93)	17.22 (6.13–28.32)
>4	685.38 (629.2–746.66)	236.41 (161.82–311.00)	299.53 (263.21–340.94)	129.38 (67.02–191.74)

IR, incidence rate; K^+, potassium; RAASi, renin–angiotensin–aldosterone system inhibitor; T, tertile.
[a]Adjusted IRs were obtained from a zero-inflated negative binomial model and were adjusted by continuous age, sex, renal disease by ICD-10 code, history of cardiovascular disease, hypertension status, diabetes mellitus, use of RAASi, and number of K^+ tests per year as a categorical variable. Adjusted IRs are presented fixing the value of the adjustment factors to their mean value.

- The incidence rate of hyperkalemia was 46.5/1000 patient-years (PYs), with higher rates observed in individuals with diabetes (88.5), chronic kidney disease (CKD; 720.9), or cardiovascular disease (96.1), or RAASi users (707.0)
- Moderate-to-severe hyperkalemia had an overall incidence rate of 18.8/1000 PYs, with rates ranging from 25.6 among patients with cardiovascular disease to 310.0 among those with CKD

Conclusions

- Among pediatric patients undergoing K^+ testing, hyperkalemia was common, being experienced by more than 6% of patients
- The risk of hyperkalemia significantly increased in the presence of CKD, diabetes, and RAASi use, conditions in which frequent K^+ monitoring is advocated

Reference
1. Runesson B, et al. *Clin Kidney J.* 2016;9(1):119–127.

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