Received: 15 February 2022 | Revised: 30 March 2022 | Accepted: 31 March 2022

DOI: 10.1111/apa.16348

ACTA PÆDIATRICA NURTURING THE CHILD WILEY

ORIGINAL ARTICLE

The incidence, hospitalisations and deaths in acutely ill children with dysnatraemias

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Funding information
The study was supported by the Alma and K A Snellman Foundation, Finland (Saara Lehtiranta); the Foundation for Paediatric Research, Finland (Saara Lehtiranta, Minna Honkila, Terhi Tapiainen) and the Academy of Finland (Terhi Tapiainen)

Abstract

Aim: The aim was to evaluate the incidence, hospitalisations and deaths in acutely ill children with dysnatraemias.

Methods: This was a register-based cohort study of 46 518 acutely ill children aged <16 years who visited a paediatric emergency department. Risk factors were assessed using two nested case–control studies.

Results: Moderate to severe hypernatraemia occurred in 92 children (0.20%; 95% confidence interval [CI]: 0.16%–0.24%) and moderate to severe hyponatraemia in 131 children (0.28%; 95% CI: 0.24%–0.33%). Underlying medical conditions increased the risk of both moderate to severe hypernatraemia (odds ratio [OR]: 17; 95% 5.5–51) and moderate to severe hyponatraemia (OR: 3.5; 95% CI: 2.0–5.9). The use of a feeding tube (OR: 14; 95% CI: 3.2–66) and intellectual disability (OR: 7.3; 95% CI: 3.0–18) was associated with moderate to severe hypernatraemia. The risk of death was associated with moderate to severe hypernatraemia (OR: 19; 95% CI: 2.0–2564) and moderate to severe hyponatraemia (OR: 33; 95% CI: 3.7–4311).

Conclusions: Severe dysnatraemias were more prevalent in acutely ill children with underlying medical conditions and were markedly associated with the risk for death.

KEYWORDS
hypernatraemia, hyponatraemia, sodium disturbances, water-electrolyte imbalance

1 | INTRODUCTION

Severe sodium abnormalities are potentially life-threatening conditions in acutely ill children. Moderate to severe hypernatraemia (serum or plasma sodium ≥150 mmol/L) has been reported to occur in 0.04% of acutely ill children assessed for electrolyte values[1] and moderate to severe hyponatraemia (serum or plasma sodium <130 mmol/L) in approximately 1%.[2] Mild hyponatraemia (serum or plasma sodium 130–134 mmol/L) is the most common electrolyte imbalance, with an occurrence of 17%–45% amongst patients presenting at paediatric emergency departments (ED).[3,4]

Patient characteristics related to moderate to severe hypernatraemia have been reported earlier in two uncontrolled patient series, which showed associations with dehydration and pre-existent neurological disability.[1,5] Moderate to severe hypernatraemia often develops during hospitalisation and has been shown to be

Abbreviations: CI, confidence interval; ED, emergency department; IQR, interquartile range; OR, odds ratio; PICU, paediatric intensive care unit.

associated with high mortality in acutely ill children.[1,5,6] The risk factors for hyponatraemia in children are well characterised including febrile response,[3,4,7] increased levels of inflammation markers[4,7–11] and greater severity of their acute illness.[7,10–16] Most of the previous studies, however, have included mainly patients with mild hyponatraemia and only a few with moderate to severe hyponatraemia.[4,7–10,17] There is, thus, limited evidence from controlled research settings for the risk factors for both moderate to severe hypernatraemia and hyponatraemia.

We set out a controlled study of acutely ill children presenting at a paediatric ED to investigate the risk factors for moderate to severe sodium disturbances. In addition, we report hospitalisations and deaths and in children with moderate to severe hypernatraemia or hyponatraemia.

Key Notes

- In this register-based cohort study, moderate to severe hypernatraemia occurred in 0.20% and moderate to severe hyponatraemia in 0.28% of acutely ill children.
- In two nested case–control studies, severe sodium disturbances were more prevalent in acutely ill children with underlying medical conditions.
- The risk of death was 19-fold in children with moderate to severe hypernatraemia and 33-fold in children with moderate to severe hyponatraemia as compared to those with normal sodium values.

2 | PATIENTS AND METHODS

2.1 | Study design and population

This was a register-based cohort study into the occurrence and development in the time of sodium abnormalities in a population of 46 518 acutely ill children. Two nested case–control studies were carried out to assess risk factors, hospitalisation and deaths for moderate to severe hyper- and hyponatraemia and mild hyponatraemia in 1074 of these children. The study plan was approved by the Ethics Committee for Human Sciences at the University of Oulu, Finland. According to Finnish legislation, individual informed consent is not required for register-based medical research. All the data were collected and analysed according to the current European Union data protection requirements and legislation. We have earlier reported the occurrence of severe hyponatraemia (serum sodium <125 mmol/L) in children receiving moderately hypotonic fluid therapy based on the same cohort.[18]

The total cohort included all the acutely ill children who visited the paediatric ED at Oulu University Hospital, Finland, during the years 2007–2017. During the study period, moderately hypotonic fluid therapy with 60–80 mmol/L of sodium was used. Approximately 15% of the patient who visited paediatric ED received intravenous fluid therapy.[18] All sodium measurements for these children were retrieved from the electronic laboratory system of NordLab, Oulu, Finland. In addition to the measurements made at the ED itself, sodium values were also retrieved for the children hospitalised after attending the ED.

Moderate to severe hypernatraemia was defined as serum sodium ≥150 mmol/L and moderate to severe hyponatraemia as serum sodium <130 mmol/L at the ED or within 7 days during hospitalisation. Mild hyponatraemia was defined as serum sodium 130–134 mmol/L and normonatraemia as serum sodium 135–145 mmol/L. Two age-matched control subjects with normal sodium values during hospitalisation were selected for each patient with moderate to severe hypernatraemia, and three age-matched controls with mild hyponatraemia and three with normal sodium values during hospitalisation were selected for each patient with moderate to severe hyponatraemia.

The nested case–control study of risk factors, deaths and hospitalisation associated with moderate to severe hypernatraemia included children aged between 1 month and 16 years, whereas that assessing moderate to severe hyponatraemia included all children aged less than 16 years. Elective postoperative patients, patients with active oncological treatment and surgical trauma patients were not included because they had not been treated at the paediatric ED.

The medical records were systematically reviewed for risk factors, deaths and hospitalisation by physicians engaged in this research, and the data entry sheet was designed on the basis of a review of the literature on hypernatraemia and hyponatraemia.

2.2 | Statistical methods

Occurrence figures were calculated for moderate to severe hyper- and hyponatraemia with 95% confidence intervals (CI). The sample size for the assessment of risk factors and outcomes for moderate to severe hypernatraemia was estimated on the basis of an odds ratio (OR) of 3.0, regarded as a clinically significant finding, with an alpha error of 5% and a power of 80%. With two controls per subject, 92 cases were required. The sample size for assessing the risk factors and outcomes for moderate to severe hyponatraemia was based on an OR of 2.5 with an alpha error of 5% and a power of 80%, so that with three controls per subject, 117 cases were required. The controls were selected randomly from the whole cohort and matched for age within 2 weeks for children aged 0–3 months, 1 month for children aged 3–6 months, 2 months for children aged 6–12 months, 4 months for children aged 12–36 months, 6 months for children aged 3–6 years, 12 months for children aged 6–12 years and 24 months for children older than 12 years. The difference in the 1st day of hospitalisation, i.e., the date of hospitalisation, between the cases and their controls, was no more than 60 days. The

logistic regression model, or Firth's logistic regression, when zero counts occurred in the outcome variable, was designed separately for hypernatraemia and hyponatraemia, and the outcomes were evaluated separately for moderate to severe hyponatraemia versus normonatraemia and for moderate to severe hyponatraemia versus mild hyponatraemia. We performed a subgroup analysis by excluding patients with hyponatraemia and diabetes to present results separately for patients with hypoosmolar hyponatraemia. In all the analyses, the controls were matched for age and sampling time and adjusted for sex.

The analyses were performed using the following statistical programs: StatsDirect, Version 3 (StatsDirect Ltd, Merseyside, UK), IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp, Armonk, New York, USA), Stata, Version 16 (StataCorp LLC, College Station, Texas, USA) and R (R Foundation for Statistical Computing, Vienna, Austria).

3 | RESULTS

3.1 | Study cohort

There had been 46 518 visits made to the paediatric ED during the period concerned, and the data set retrieved from the laboratory comprised 59 283 electrolyte measurements (Figure 1). At least one sodium measurement was performed for 11 753 children.

Moderate to severe hypernatraemia occurred in 92 children who visited the ED (0.20%; 95% CI: 0.16%–0.24%) and moderate to severe hyponatraemia in 131 children (0.28%; 95% CI: 0.24%–0.33%). For moderate to severe hypernatraemia, the median sodium value was 151 mmol/L (interquartile range [IQR]; 25%–75%: 151–154 mmol/L) and for moderate to severe hyponatraemia, the median sodium value was 128 mmol/L (IQR; 25%–75%: 126–129 mmol/L).

3.2 | Moderate to severe hypernatraemia

The mean age of the 92 children with moderate to severe hypernatraemia was 4.8 (SD 5.1) years and the most common reasons for their hospitalisation were gastroenteritis (29%), a viral infection (16%) and a neurological disorder (16%) (Table 1). The patients presenting with alcohol intoxication were teenagers with a mean age of 14 years (SD 1.2). Moderate to severe hypernatraemia was observed in 46 children (50%) at presentation in the ED and 9 children (10%) developed this condition during the first 24 h of hospitalisation (Figure 2). The mean length of stay in the hospital was 10 days (SD 17) (Table 1). Altogether, four children with hypernatraemia died during the hospitalisation, whereas there were no deaths in the control group. The reasons for deaths were viral infection in two patients, pulmonary hypertension in one patient and traumatic asphyxia in one patient.

The nested case–control assessment of risk factors for moderate to severe hypernatraemia showed more than one underlying medical condition (OR: 17; 95% CI: 5.5–51; $p < 0.001$), intellectual disability (OR: 7.3; 95% CI: 3.0–18; $p < 0.001$), use of a feeding tube (percutaneous endoscopic gastrostomy, PEG) (OR: 14; 95% CI: 3.2–66; $p = 0.001$) and more than one ongoing course of medication (OR: 9.0; 95% CI: 3.2–25; $p < 0.001$) to be associated with moderate to severe hypernatraemia as compared with the age-matched control subjects having normal sodium values (Table 2).

When assessing the hospitalisation for children with moderate to severe hypernatraemia relative to the control subjects, moderate to severe hypernatraemia was found to be significantly associated with a risk of hospitalisation (88 of 92 patients [96%] vs. 136 of 181 patients [75%], OR: 7.4; 95% CI: 2.6–21; $p < 0.001$) and treatment in the paediatric intensive care unit (PICU) (49 of 92 patients [53%] vs. 7 of 181 patients [4%], OR: 31; 95% CI: 13–76; $p < 0.001$). A neurological symptom during hospitalisation (OR: 3.4; 95% CI: 1.8–6.5; $p < 0.001$) and death during hospitalisation (OR: 19; 95% CI:

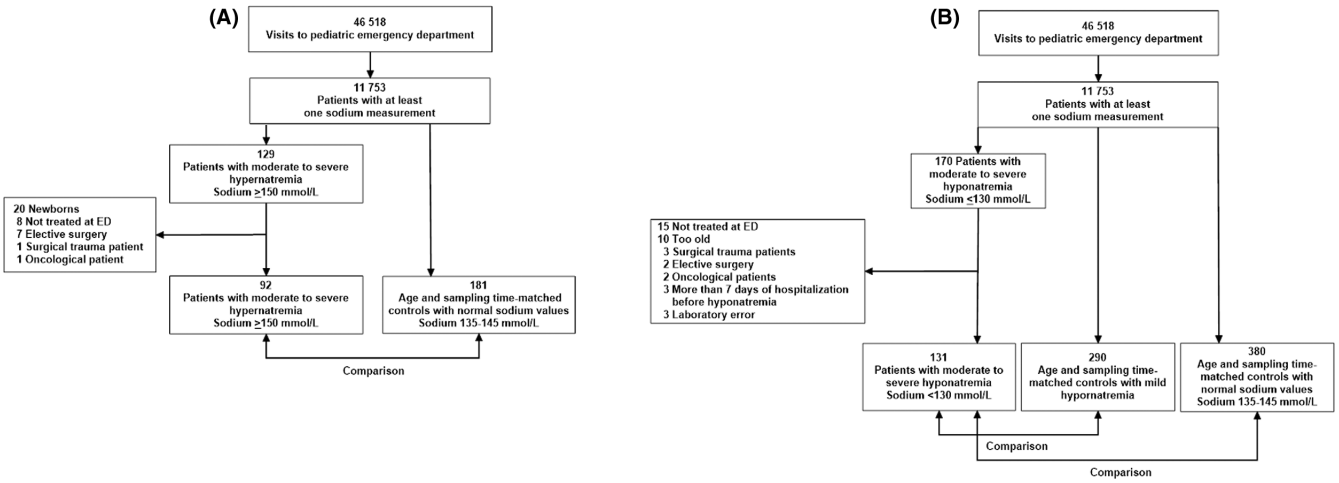

FIGURE 1 Study design. (A) Case–control cohort study of risk factors, deaths and hospitalisation for moderate to severe hypernatraemia. (B) Case–control study of risk factors, deaths and hospitalisation for moderate to severe hyponatraemia in the same cohort

TABLE 1 Baseline characteristics of the children with moderate to severe hypernatraemia and the control subjects with normal sodium values

	Moderate to severe hypernatraemia cases (sodium ≥150 mmol/L)	Control cases (sodium 135–145 mmol/L)
	n = 92	*n* = 181
Age, mean (SD), y	4.8 (5.1)	4.8 (5.2)
Gender, No. (%)		
Girls	44 (48)	78 (43)
Boys	48 (52)	103 (57)
Acute illness, No. (%)		
Gastroenteritis	27 (29)	37 (20)
Viral infection	15 (16)	37 (20)
Neurological disorder	15 (16)	10 (5.5)
Alcohol intoxication	8 (8.7)	1 (0.6)
Diabetes mellitus, type 1	6 (6.5)	7 (3.9)
Pneumonia	5 (5.4)	12 (6.6)
Post-resuscitation	4 (4.3)	0 (0)
Acute heart disease	1 (1.1)	1 (0.6)
Acute kidney disease	1 (1.1)	2 (1.1)
Severe bacterial infection	1 (1.1)	5 (2.8)
Acute surgical abdomen	0 (0)	5 (2.8)
Pyelonephritis	0 (0)	10 (5.5)
Other	9 (10)	54 (30)
Underlying medical condition, No. (%)		
None	52 (57)	151 (83)
One	17 (19)	26 (14)
More than one	23 (25)	4 (2.2)
Ongoing medication, No. (%)		
None	67 (72)	169 (93)
One	7 (7.6)	7 (3.9)
More than one	18 (20)	5 (1.7)
Hospital length of stay, d (SD)	10 (17)	2.4 (5.2)

2.0–2564; $p = 0.007$) were also associated with moderate to severe hypernatraemia.

3.3 | Moderate to severe hyponatraemia

The mean age of the 131 children with moderate to severe hyponatraemia was 5.2 (SD 4.5) years and the most common reasons for hospitalisation were type 1 diabetes (19%), acute kidney disease (13%) and viral infection (11%) (Table 3). The patients presenting with alcohol intoxication were teenagers with a mean age of 14 years (SD 0.4). Most of the children ($n = 86$, 66%) had moderate to severe hyponatraemia upon presentation at the ED and 26 children (20%) developed this during the first 24 h of hospitalisation (Figure 2). The mean length of stay in the hospital was 11 days (SD 13) (Table 3).

Altogether, five children with hyponatraemia died during the hospitalisation, whereas there were no deaths in control groups. The reasons for deaths were myocarditis in one patient, whooping cough in one patient, cerebral venous sinus thrombosis due to severe dehydration caused by gastroenteritis in one patient, brain tumour in one patient and acute surgical abdomen in one patient.

The nested case–control assessment of risk factors for moderate to severe hyponatraemia showed an underlying medical condition (OR: 3.5; 95% CI: 2.0–5.9; $p < 0.001$) and ongoing medication (OR: 2.4; 95% CI: 1.2–5.1; $p = .02$) to be associated with hyponatraemia as compared with the age-matched controls with normal sodium values (Table 4). Also, the children with moderate to severe hyponatraemia more often had a decline in their general condition (OR: 5.9; 95% CI: 3.7–9.3; $p < 0.001$) and were more often critically ill whilst at the ED (OR: 17; 95% CI: 8.6–33; $p < 0.001$).

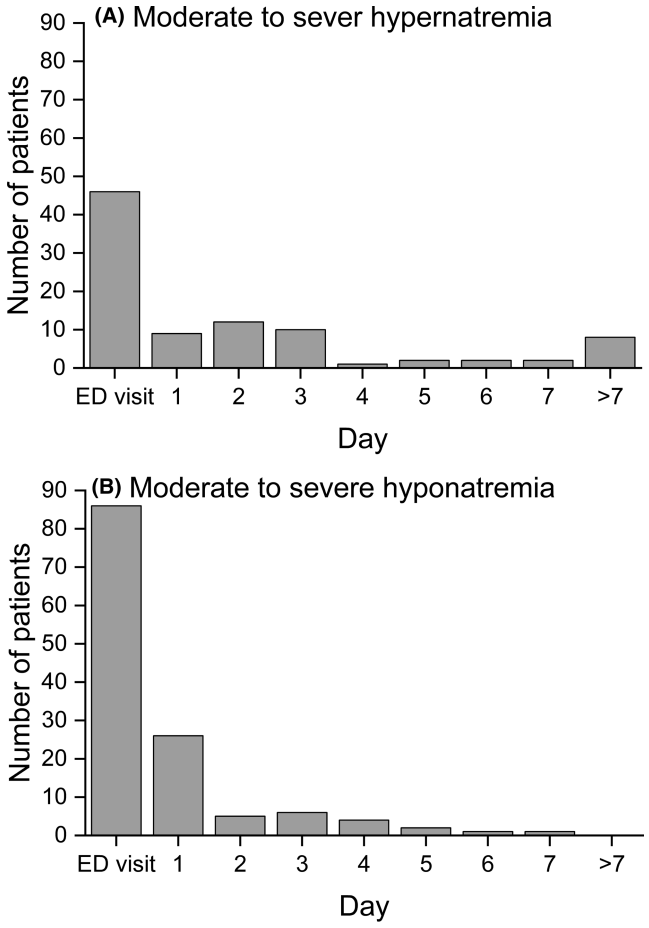

FIGURE 2 Time to the development of moderate to severe hypernatraemia (sodium ≥150 mmol/L) and moderate to severe hyponatraemia (sodium <130 mmol/L) in acutely ill children. Day 0 refers to the presentation at the ED and day 1 to the first 24 h of hospitalisation

When assessing the hospitalisation for children with moderate to severe hyponatraemia relative to the normonatraemic control subjects, hyponatraemia was associated with an increased risk of hospitalisation (128 of 131 patients [98%] vs. 266 of 380 patients [70%], OR: 18; 95% CI: 5.7–59; $p < 0.001$) and treatment at the PICU (74 of 131 patients [56%] vs. 14 of 380 patients [4%], OR: 34; 95% CI: 18–65; $p < 0.001$). A neurological symptom during hospitalisation (OR: 1.8; 95% CI: 1.1–3.1; $p = .02$) and death during hospitalisation (OR: 33; 95% CI: 3.7–4311; $p = 0.001$) were also associated to moderate to severe hyponatraemia (Table 5).

When assessing the need for hospitalisation in children with moderate to severe hyponatraemia relative to the children with mild hyponatraemia, moderate to severe hyponatraemia was associated with an increased risk of hospitalisation (128 of 131 patients [98%] vs. 243 of 290 patients [84%], OR: 8.2; 95% CI: 2.5–27; $p = .001$) and treatment at the PICU (74 of 131 patients [56%] vs. 24 of 290 patients [8%], OR: 15; 95% CI: 8.8–26; $p < .001$). A neurological symptom (OR: 1.8; 95% CI: 1.0–3.0; $p = .04$) and death during hospitalisation (OR: 25; 95% CI: 1.4–455; $p = .03$) were also associated more to moderate to severe hyponatraemia than to mild hyponatraemia (Table 5).

TABLE 2 Risk factors, deaths and hospitalization for moderate to severe hypernatremia compared with randomly selected control subjects with normal sodium values (135–145 mmol/L) ($n = 181$) matched for age and sampling time* and adjusted for sex

	Moderate to severe hypernatremia (sodium ≥150 mmol/L)	
	n = 92	
	aOR (95% CI)	*p* value
Risk factor		
Underlying medical condition		
One	1.9 (0.9–3.8)	0.07
More than one	17 (5.5–51)	<0.001
Intellectual disability	7.2 (3.0–18)	<0.001
PEG tube	14 (3.2–66)	0.001
Ongoing medication		
One	2.6 (1.0–7.6)	.09
More than one	9.0 (3.2–25)	<0.001
Need for surgery	5.8 (2.3–15)	<0.001
Outcome		
Need for hospitalization	7.4 (2.6–21)	<0.001
Need for PICU treatment	31 (13–76)	<0.001
Neurological symptom[a]	3.4 (1.8–6.5)	<0.001
Death[a]	19 (2.0–2564)	0.007

*During hospitalization.

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; PEG, percutaneous endoscopic gastrostomy; PICU, paediatric intensive care unit.

3.4 | Subgroup analysis of patients with moderate to severe hypoosmolar hyponatraemia

There were 25 (19%) patients with moderate to severe hyponatraemia treated because of type 1 diabetes. After excluding the patients with diabetes, moderate to severe hyponatraemia was associated with the need for hospitalisation (OR: 15; 95% CI: 4.7–49; $p < .001$), treatment at PICU (OR: 33; 95% CI: 17–64; $p < .001$) and death during the hospitalisation (OR: 33, 95% CI: 1.8–596; $p = .02$), but not with neurological symptoms during the treatment (OR 1.6, 95% CI: 0.9–3.0, $p = .1$) when compared to those with normal sodium values.

3.5 | Mild hyponatraemia

Mild hyponatraemia was not associated with any underlying medical condition or ongoing medication, but the children concerned more often had a decline in their general condition (OR: 2.9; 95% CI: 2.1–4.0; $p < .001$) and were more often critically ill whilst at the ED (OR: 3.0; 95% CI: 1.5–6.1; $p = .002$) than the age-matched controls with normal sodium values (Table 4).

When the deaths and hospitalisation of the children with mild hyponatraemia were considered relative to normonatraemic

TABLE 3 Baseline characteristics of the children with moderate to severe hyponatraemia and control subjects with mild hyponatraemia and normal sodium values

	Moderate to severe hyponatraemia (sodium <130 mmol/L)	Mild hyponatraemia (sodium 130–134 mmol/L)	Control subjects (sodium 135–145 mmol/L)
	n = 131	*n* = 290	*n* = 380
Age, mean (SD), y	5.2 (4.5)	5.0 (4.3)	5.0 (4.3)
Gender, No. (%)			
Girls	55 (42)	155 (53)	167 (44)
Boys	76 (58)	135 (47)	213 (56)
Acute illness, No. (%)			
Diabetes mellitus, type 1	25 (19)	32 (11)	5 (1.3)
Acute kidney disease	17 (13)	6 (2.1)	8 (2.1)
Viral infection	15 (11)	49 (17)	114 (30)
Gastroenteritis	12 (9.2)	60 (21)	45 (12)
Pneumonia	12 (9.2)	38 (13)	27 (7.1)
Neurological disorder	10 (7.6)	31 (11)	36 (9.5)
Acute surgical abdomen	9 (6.9)	11 (3.8)	12 (3.2)
Pyelonephritis	8 (6.1)	31 (11)	29 (7.6)
Severe bacterial infection	7 (5.3)	16 (5.5)	20 (5.3)
Acute heart disease	6 (4.6)	2 (0.7)	2 (0.5)
Other	10 (7.6)	14 (4.8)	82 (22)
Underlying medical condition, No. (%)			
None	90 (69)	249 (86)	340 (90)
One	33 (25)	33 (11)	46 (12)
More than one	8 (6.1)	8 (2.8)	4 (1.1)
Ongoing medication, No. (%)			
None	104 (80)	265 (91)	354 (93)
One	13 (10)	15 (5.2)	18 (4.7)
More than one	14 (11)	10 (3.4)	8 (2.1)
Highest CRP, mean (SD)	86 (100)	82 (94)	43 (64)
Length of stay, mean (SD), d	11 (13)	3.4 (5.4)	1.8 (3.2)

Abbreviations: CRP, C-reactive protein; SD, standard deviation.

patients, mild hyponatraemia was seen to increase the risk of hospitalisation (243 of 290 patients [84%] vs. 266 of 380 patients [70%], OR: 2.2; 95% CI: 1.5–3.3; $p < .001$) and treatment at the PICU (24 of 290 patients [8%] vs. 14 of 380 patients [4%], OR: 2.3; 95% CI: 1.2–4.6; $p = .01$) but was not associated with neurological symptoms during hospitalisation and no deaths were recorded (Table 5).

4 | DISCUSSION

In this register-based cohort study of 46 518 visits in a paediatric ED, moderate to severe hypernatraemia occurred in 0.20% and moderate to severe hyponatraemia in 0.28% of acutely ill children. Two nested case–control studies showed that both moderate to severe hypernatraemia and hyponatraemia were more prevalent in children with previous underlying medical conditions and medications. The risk of death was 19-fold in children with moderate to severe hypernatraemia and 33-fold in children with moderate to severe hyponatraemia as compared to those with normal sodium values.

Limited data have been available previously on risk factors for moderate to severe hypernatraemia in acutely ill children,[1,5] but the present results show moderate to severe hypernatraemia to be clearly associated with underlying medical conditions, the need for a feeding tube, ongoing medication and intellectual disability. Acutely ill children with such problems may be unable to express their thirst and therefore are at risk of insufficient oral water intake. Our finding is in line with a previous observation that hypernatraemia was associated with dehydration and intellectual disability.[1] Eight (8%) patients with moderate to severe hypernatraemia had diagnosis of alcohol intoxication, which has not been reported to cause hypernatraemia previously.[1]

TABLE 4 Risk factors for moderate to severe hyponatraemia and mild hyponatraemia relative to randomly selected control subjects with normal sodium values (135–145 mmol/L) ($n = 380$) matched for age and sampling time and adjusted for sex

	Moderate to severe hyponatraemia (sodium <130 mmol/L)		Mild hyponatraemia (sodium 130–134 mmol/L)	
	$n = 131$		$n = 290$	
	aOR (95% CI)	*p* value	aOR (95% CI)	*p* value
Risk factor				
Underlying medical condition				
One	3.5 (2.0–5.9)	<0.001	1.3 (0.8–2.1)	0.35
More than one	7.6 (2.2–26)	0.001	2.7 (0.8–9.2)	0.10
Ongoing medication				
One	2.4 (1.2–5.1)	.02	1.1 (0.6–2.3)	0.73
More than one	6.0 (2.4–15)	<0.001	1.7 (0.6–4.2)	0.29
Clinical appearance at admission				
Decline in general condition	5.9 (3.7–9.3)	<0.001	2.9 (2.1–4.0)	<0.001
Critically ill	17 (8.6–33)	<0.001	3.0 (1.5–6.1)	0.002
Need for surgery	7.1 (3.6–14)	<0.001	1.7 (0.8–3.4)	0.17

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval.

TABLE 5 Deaths and hospitalisation in children with moderate to severe hyponatraemia (sodium <130 mmol/L) ($n = 131$) and mild hyponatraemia (sodium 130–134 mmol/L) ($n = 290$)

Outcome	aOR (95% CI)	*p* value
Moderate to severe hyponatraemia vs control subjects with normal sodium values		
Need for hospitalisation	18 (5.7–59)	<0.001
Need for PICU treatment	34 (18–65)	<.001
Neurological symptom[a]	1.8 (1.1–3.1)	.02
Death[a]	33 (3.7–4311)	.001
Moderate to severe hyponatraemia vs children with mild hyponatraemia		
Need for hospitalisation	8.2 (2.5–27)	.001
Need for PICU treatment	15 (8.8–26)	<.001
Neurological symptom[a]	1.8 (1.0–3.0)	.04
Death[a]	25 (1.4–455)	.03
Mild hyponatraemia vs control subjects with normal sodium values		
Need for hospitalisation	2.2 (1.5–3.3)	<.001
Need for PICU treatment	2.3 (1.2–4.6)	.01
Neurological symptom[a]	1.0 (0.7–1.6)	.89
Death[b]	No deaths	

Notes: Control subjects were matched for age and sampling time and analyses were adjusted for sex.

[a]During hospitalisation.

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; PICU, paediatric intensive care unit.

Moderate to severe hypernatraemia was hospital acquired in half of the children in the present cohort and was closely associated with treatment at the PICU and with death. Our findings thus support active fluid balance monitoring and electrolyte measurements in severely ill children and other children who are unable to maintain oral water intake during acute illness.

Hyponatraemia has earlier been associated with greater severity of acute illness in cohorts consisting mainly of patients with mild hyponatraemia.[7,10,11,13–16] Accordingly, moderate to severe hyponatraemia was found here to be associated with a decline in general condition and critical illness on presentation at the ED. The same associations were observed for mild hyponatraemia, but their effect was significantly smaller than that for moderate to severe hyponatraemia.

The risk of hospitalisation and death in children with moderate to severe hyponatraemia is a matter of some concern. The risk for PICU treatment and for death was more than 30-fold in children with less than 130 mmol/L sodium as compared with control subjects having normal sodium values. The association may be bidirectional, however, because severe illness may result in severe sodium abnormality, and severe sodium abnormality may impair the outcome. Thus, a very low sodium value may be a predictive sign of a critical illness.[15,16] Children with severe sodium abnormalities appear to be high-risk patients who need careful clinical follow-up. According to previous studies, approximately half of the patients may develop seizures if their sodium level falls below 125 mmol/L.[19] In the present instance, moderate to severe hyponatraemia was associated with neurological symptoms during hospitalisation.

One strength of the present work is that it is one of the first studies to describe risk factors and outcomes for severe dysnatraemias in acutely ill children in a controlled setting. We were able to retrieve all the electrolyte measurements made for a large cohort of paediatric ED visits from the electronic laboratory system. Our sample size enabled meaningful analyses to be made of moderate to severe hyper- and hyponatraemia. Furthermore, we were able to

compare the risk factors, deaths and hospitalisation for moderate to severe hyponatraemia and with those for mild hyponatraemia and report their effects in the same cohort. Finally, we focused on moderate to severe dysnatraemias. Since most of the studies about hyponatraemia have included patients with mild hyponatraemia, we had a separate control group for mild hyponatraemia.

There are some limitations to this study, however. Surgical trauma patients, who are known to both have risk for hyponatraemia and benefit for isotonic fluid therapy,[20] were not treated at our paediatric ED during the period concerned. In surgical paediatric patients, the incidence of moderate to severe hyponatraemia may be higher than in the present study.[21] Also, we were unable to compare patients treated with different fluid regimes because the population was drawn from the era before isotonic fluid therapy was adopted in clinical practice,[20] so that the patients almost exclusively received moderately hypotonic maintenance fluid therapy. In all the analyses, the controls were matched for age and sampling time and adjusted for sex. There may be, however, other confounding variables that were not controlled in this observational study.

In conclusion, severe sodium abnormalities were associated with deaths and more severe course of acute illness in acutely ill children. Acute illness was less severe in children with mild hyponatraemia when compared to those with moderate to severe hyponatraemia.

CONFLICT OF INTEREST

All authors declare no conflict of interest.

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How to cite this article: Lehtiranta S, Honkila M, Anttila S, Huhtamäki H, Pokka T, Tapiainen T. The incidence, hospitalisations and deaths in acutely ill children with dysnatraemias. Acta Paediatr. 2022;111:1630–1637. doi:10.1111/apa.16348