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FREQUENCY OF HOSPITAL-ACQUIRED HYPONATREMIA IN CHILDREN RECEIVING MAINTENANCE INTRAVENOUS FLUIDS AT A TERTIARY-CARE HOSPITAL IN KARACHI, PAKISTAN: A CROSS-SECTIONAL STUDY

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Hospital-acquired hyponatremia; children; maintenance intravenous fluids; isotonic fluids; hypotonic fluids; Pakistan.

Abstract

Background: *Hospital-acquired hyponatremia (HAH) is a common and potentially preventable electrolyte abnormality in hospitalized children. It may lead to cerebral edema, seizures, encephalopathy, and death. Reported frequencies vary widely across settings, and contemporary Pakistani data remain limited.*
Objective: *To determine the frequency of HAH and its association with age, sex, place of admission, and type of maintenance intravenous fluid among children admitted to a tertiary-care hospital.*
Methods: *This cross-sectional study was conducted in the Department of Pediatrics, Dr. Ruth K.M. Pfau Civil Hospital, Karachi, Pakistan, from 30 December 2021 to 30 June 2022. Children aged >1 month to 14 years, admitted for >48 hours, with admission serum sodium >135 mEq/L and requiring maintenance intravenous fluids, were enrolled through non-probability consecutive sampling. Serum sodium was measured at admission and 48 hours later. HAH was defined as serum sodium <135 mEq/L at 48 hours in a child with normal sodium at admission. Data were analyzed using IBM SPSS version 23. Chi-square or Fisher's exact tests were applied, and $p<0.05$ was considered statistically significant. Institutional approval and informed consent were obtained.*
Results: *Of 121 children, 42 (34.7%) developed HAH. The mean age was 3.4 ± 3.1 years; 68 (56.2%) were male and 53 (43.8%) were female. HAH was significantly more frequent among female children (45.3% vs. 26.5%; $p=0.030$) and among children receiving 0.45% dextrose saline (DS) compared with 0.9% DS (46.8% vs.*

27.0%; p=0.026). No significant association was found with age <7 years (37.6% vs. 20.0%; p=0.130) or admission to the pediatric ward versus ICU (37.6% vs. 25.0%; p=0.210). Common diagnoses among HAH cases were gastrointestinal and infectious diseases (28.6% each), respiratory disease (21.4%), and malnutrition with sepsis (14.3%).

Conclusion: *HAH occurred in approximately one-third of hospitalized children receiving maintenance intravenous fluids. Female sex and hypotonic fluid (0.45% DS) were significantly associated with HAH. These findings support careful maintenance-fluid selection and regular serum sodium monitoring. Larger multicenter studies with adjusted analyses are needed to confirm these associations.*

INTRODUCTION

Hyponatremia is one of the most frequently encountered electrolyte abnormalities in hospitalized children and is clinically important because an acute fall in serum sodium concentration can produce cerebral edema and neurological manifestations ranging from irritability, nausea, and altered consciousness to seizures, encephalopathy, permanent neurological injury, and death [1–3]. Children may be particularly vulnerable to neurological complications because acute changes in serum osmolality can result in rapid movement of water into brain cells. Hospital-acquired hyponatremia (HAH) refers to the development or worsening of hyponatremia during hospitalization in a patient who was not hyponatremic, or who had a normal serum sodium concentration, at admission. Its occurrence is influenced by the underlying illness, fluid therapy, medications, postoperative status, and the timing and frequency of electrolyte monitoring [1, 4].

The diagnostic approach to hyponatremia involves initial assessment of plasma osmolality and volume status, followed by evaluation of volume state and urinary sodium excretion (Figure 1).

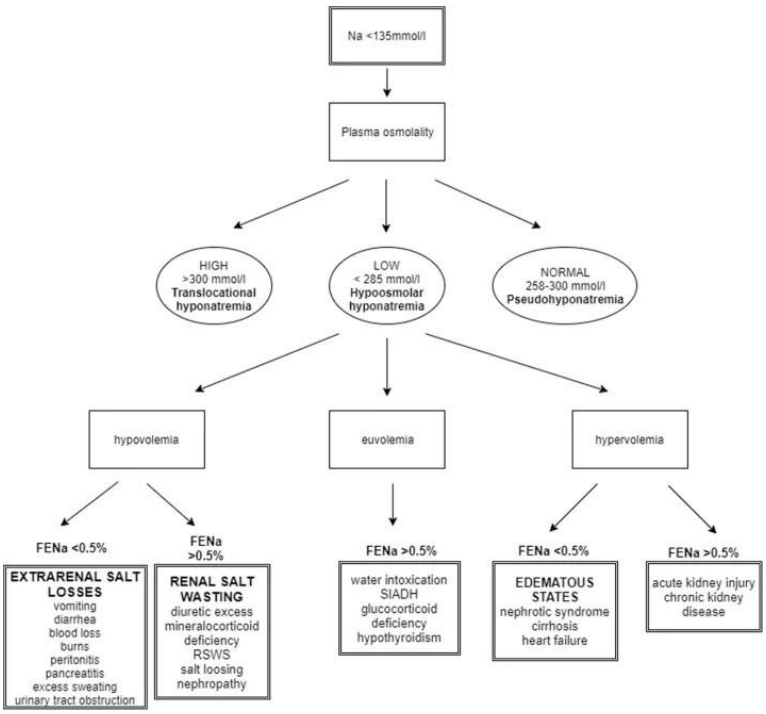
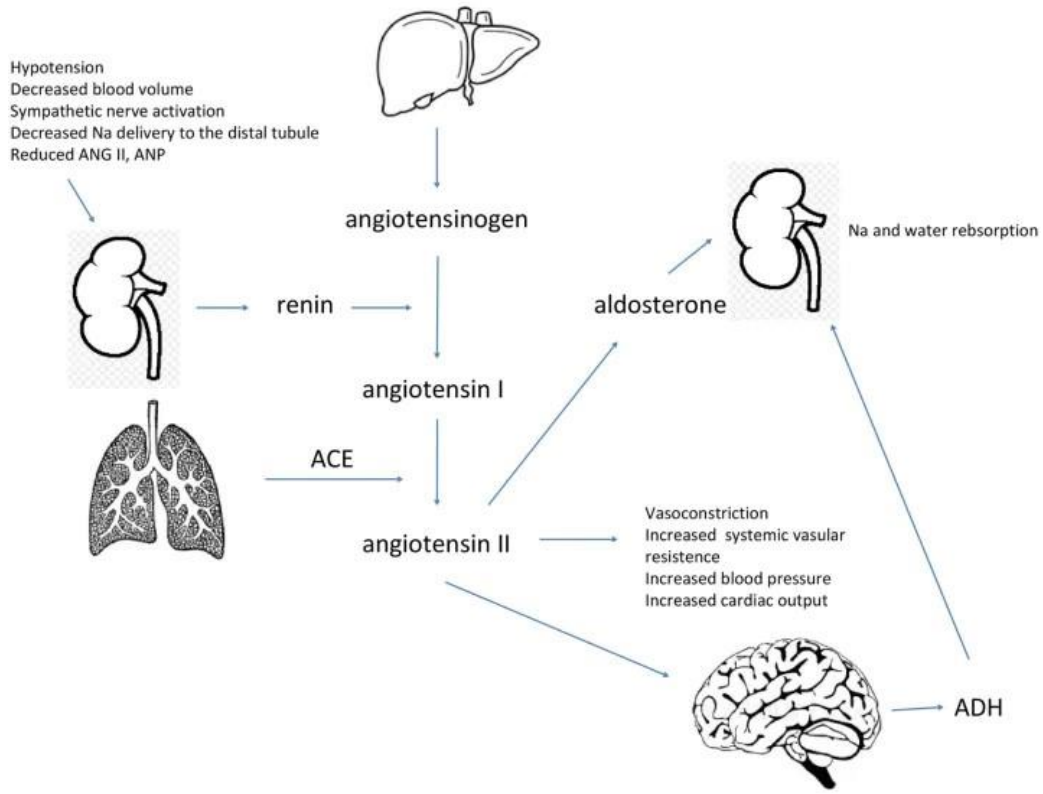


Figure 1. Diagnostic algorithm for hyponatremia based on plasma osmolality and volume status. Adapted from Zieg J. Pathophysiology of hyponatremia in children. Front Pediatr. 2017;5:213. doi:10.3389/fped.2017.00213.

The development of HAH is multifactorial. Acute illness can stimulate non-osmotic secretion of arginine vasopressin (AVP), impairing renal free-water excretion despite a normal or reduced plasma osmolality. Pain, nausea, vomiting, stress, surgery, pulmonary disease, central nervous system disorders, hypoxemia, and several medications can act as stimuli for AVP release [2, 4-5]. When free-water intake exceeds the kidney's ability to excrete water, serum sodium concentration falls. This mechanism is particularly relevant in hospitalized children because several AVP-stimulating conditions may occur simultaneously during acute illness [4-5]. Excessive administration of maintenance fluid may further aggravate water retention, particularly when the administered solution contains a relatively low concentration of sodium.

The traditional approach to pediatric maintenance fluid therapy originated from the Holliday–Segar method, introduced in 1957 to estimate daily water requirements according to body weight [6]. Although this approach represented an important development in pediatric fluid therapy, subsequent clinical experience demonstrated that the routine use of hypotonic maintenance solutions in acutely ill children could contribute to iatrogenic hyponatremia. Hospitalized children frequently have increased AVP activity, and administration of hypotonic fluids in this setting provides additional free water that may not be adequately excreted [4-5,7]. Reports of severe hyponatremic encephalopathy and neurological injury in otherwise healthy children further emphasized the potential consequences of hospital-acquired sodium disturbances [8].



Neurohormonal mechanisms such as the renin–angiotensin–aldosterone system (RAAS) and vasopressin secretion play a central role in sodium and water homeostasis (Figure 2).

Figure 2. Renin–angiotensin–aldosterone system regulating sodium and water balance. Adapted from Zieg J. Pathophysiology of hyponatremia in children. Front Pediatr. 2017;5:213. doi:10.3389/fped.2017.00213.[1]

Evidence accumulated over the last two decades has consistently demonstrated an association between hypotonic maintenance fluids and HAH. Early randomized studies showed that children receiving hypotonic solutions developed hyponatremia more frequently than those receiving isotonic solutions. In a randomized controlled trial involving hospitalized children, hyponatremia occurred in 14.3% of children receiving 0.18% saline at standard maintenance rates compared with 1.72% among those receiving 0.9% saline [9]. Similarly, studies in postoperative and critically ill children reported that

hypotonic maintenance therapy was associated with an increased risk of developing hospital-acquired hyponatremia [10-11]. A systematic review and meta-analysis of randomized trials subsequently confirmed that hospitalized children receiving hypotonic fluids had a higher risk of hyponatremia than those receiving isotonic fluids, with the increased risk also observed for more clinically significant degrees of hyponatremia [12].

More recent evidence has strengthened the rationale for isotonic maintenance therapy. A 2021 systematic review and meta-analysis involving 22 randomized controlled trials and 3,795 hospitalized children found that isotonic maintenance fluids were protective against hyponatremia, whereas hypotonic fluids significantly increased the risk of developing hyponatremia during both the first 24 hours and after 24 hours of therapy [13]. An updated systematic review and meta-analysis published in 2024 included 33 randomized controlled trials involving 5,049 children and similarly demonstrated that isotonic maintenance fluids significantly reduced the risk of mild hyponatremia during both early and prolonged treatment periods [14]. Although isotonic fluids may have disadvantages in selected populations, including an increased risk of hypernatremia in neonates and potential effects on renal function, the overall evidence supports their use for most hospitalized children requiring maintenance intravenous fluid therapy [14].

These findings have resulted in changes in pediatric clinical practice. The American Academy of Pediatrics recommended isotonic maintenance intravenous fluids, with appropriate dextrose and potassium supplementation when indicated, for children aged 28 days to 18 years who require maintenance intravenous fluid therapy [15]. Similarly, the European Society of Pediatric and Neonatal Intensive Care guidelines recommend isotonic balanced solutions containing glucose for most acutely and critically ill children and emphasize regular monitoring of plasma electrolytes, serum glucose, and fluid balance [16]. Contemporary reviews have also described the transition from routine hypotonic maintenance fluids toward isotonic therapy as an important quality-improvement development in pediatric inpatient care [17]. Nevertheless, the use of isotonic fluid does not completely eliminate HAH, because sodium disturbances may still arise from persistent AVP secretion, excessive fluid administration, underlying disease, medications, renal impairment, or other factors affecting water balance [1, 4, 14].

The frequency of HAH also varies considerably among pediatric populations and clinical settings. In a prospective observational study of postoperative children, hospital-acquired hyponatremia was observed among children receiving hypotonic maintenance fluids, highlighting the contribution of postoperative physiology and fluid prescribing to sodium disturbances [10]. In a pediatric intensive care unit study, 19.6% of patients developed HAH, and increased fluid intake, use of antidiuretic hormone-stimulating drugs, and postsurgical status were identified as significant associated factors [11]. These findings indicate that HAH is not attributable to fluid tonicity alone and that the risk may differ according to patient characteristics, illness severity, treatment exposure, and hospital setting.

More recent population-based pediatric evidence also demonstrates variability in the reported frequency of hospital-acquired and community-acquired hyponatremia. Rius-Peris et al. analyzed 5,550 pediatric admissions and reported an overall incidence of 15.8% for community-acquired hyponatremia and 1.4% for hospital-acquired hyponatremia in a general pediatric ward [18]. Most cases were mild, whereas severe hyponatremia was uncommon. The relatively low frequency of HAH in this population compared with earlier reports may reflect differences in patient characteristics, definitions, monitoring practices, and contemporary fluid management. Therefore, estimates from one healthcare setting cannot necessarily be generalized to other pediatric populations.

The situation is particularly relevant in low- and middle-income settings where clinical practices, availability of laboratory monitoring, patient case-mix, and intravenous fluid prescribing practices may differ from those in high-income countries. Evidence from Pakistan remains limited. In a pediatric tertiary-care study conducted at Aga Khan University Hospital, Karachi, Bibi et al. evaluated 865 children receiving maintenance intravenous fluids and reported hospital-acquired hyponatremia in 240 children (27.7%). Most affected children had mild hyponatremia, although moderate and severe cases were also documented [19]. The study also reported that a substantial proportion of affected children were receiving hypotonic intravenous solutions. These findings provided important local evidence that HAH represents a clinically relevant problem among hospitalized Pakistani children.

In addition to patient-level risk, local prescribing practices may influence the occurrence of HAH. A multicenter survey of pediatric residents from ten Pakistani hospitals found considerable variation in the selection of maintenance intravenous fluids. Among respondents, 45.8% selected 0.9% saline, whereas 43.98% selected 0.45% saline and 10.92% selected 0.2% saline in the clinical scenarios presented. Hypotonic fluids were particularly frequently selected for younger children and for conditions such as pneumonia and meningitis. Although most respondents reported monitoring fluid balance, substantially fewer reported routine electrolyte monitoring [20]. These findings suggest that inappropriate fluid composition and insufficient electrolyte surveillance may remain relevant considerations in pediatric inpatient care.

Taken together, available evidence indicates that hospital-acquired hyponatremia is a multifactorial complication of pediatric hospitalization in which underlying illness, non-osmotic AVP secretion, intravenous fluid composition and volume, medications, postoperative status, and monitoring practices may all contribute [1,4,10-11]. Although international evidence has substantially changed recommendations for pediatric maintenance fluid therapy, the reported frequency of HAH differs across populations and healthcare settings [13-14, 18]. Furthermore, the principal Pakistani study documenting the burden of HAH was conducted more than a decade ago, while subsequent local evidence has focused largely on maintenance-fluid prescribing knowledge rather than the contemporary frequency of HAH itself [19-20]. Updated local data are therefore needed to determine the current burden of this potentially preventable electrolyte abnormality and to provide evidence for appropriate monitoring and fluid-management practices in hospitalized children.

This study was undertaken to determine the frequency of hospital-acquired hyponatremia among children admitted to a tertiary-care hospital. The findings are expected to provide locally relevant evidence on the burden of this condition and contribute to improved recognition, monitoring, and prevention of sodium disturbances in pediatric inpatients.

Methods

Study design and setting

A cross-sectional study was conducted in the Department of Pediatrics, Dr. Ruth K.M. Pfau Civil Hospital, and Karachi. The study was carried out over six months, from 30 December 2021 to 30 June 2022, following approval of the study synopsis.

Sample size and sampling

The sample size was calculated using the OpenEpi sample size calculator. Based on a previously reported frequency of hospital-acquired hyponatremia of 27.7% [19], a 95% confidence level and an absolute precision of 8% were used, yielding a required sample size of 121 children. Participants were recruited through non-probability consecutive sampling.

Eligibility criteria

Children aged >1 month to 14 years were eligible for inclusion. Children were required to have been admitted for more than 48 hours, have a serum sodium concentration >135 mEq/L at admission, and require maintenance intravenous fluids.

Children with an admission duration of less than 48 hours, serum sodium <135 mEq/L at admission, or chronic kidney disease for more than three months were excluded. Children whose parents or guardians did not provide consent were also excluded.

Data collection

After obtaining informed consent, a baseline serum sodium measurement was obtained at admission. Children fulfilling the eligibility criteria were enrolled and received supportive and definitive treatment according to the hospital's clinical protocols. At 48 hours after admission, 2 mL of venous blood was collected in a serum bottle by trained staff and transported to the laboratory of Dr. Ruth K.M. Pfau Civil Hospital, Karachi, for serum sodium measurement.

Serum sodium concentrations were recorded on a structured data collection proforma together with relevant participant characteristics and the type of intravenous fluid administered during hospitalization. Children who developed hyponatremia received appropriate symptomatic management in addition to treatment of the underlying illness. Participant identities and laboratory results were kept confidential throughout the study.
Hospital-acquired hyponatremia was assessed using the serum sodium measurement obtained 48 hours after admission among children who had a normal serum sodium concentration at admission.

Statistical analysis
Data were entered and analyzed using IBM SPSS Statistics version 23. Quantitative variables, including age and serum sodium concentration, were assessed for distribution. Normally distributed variables were summarized as mean ± standard deviation (SD), whereas non-normally distributed variables were presented as median with interquartile range (IQR). Categorical variables, including sex, mode of admission, and hospital-acquired hyponatremia, were summarized using frequencies and percentages.
Potential effect modifiers, including age, sex, and mode of admission, were assessed through stratification. Following stratification, the chi-square test or Fisher's exact test was applied, as appropriate, to examine associations between categorical variables. A two-sided p-value <0.05 was considered statistically significant.

Results
Baseline characteristics of the study population
A total of 121 children fulfilling the eligibility criteria were included in the analysis. The mean age of the study population was 3.4 ± 3.1 years. There were 68 (56.2%) male and 53 (43.8%) female children, indicating a slight predominance of males in the study population. The majority of participants were admitted to the pediatric ward, accounting for 93 (76.9%) children, while 28 (23.1%) were admitted to the intensive care unit (ICU).
With regard to maintenance intravenous fluid therapy, 74 (61.2%) children received 0.9% dextrose saline (DS), whereas 47 (38.8%) received 0.45% DS. Thus, isotonic fluid therapy represented the more frequently administered fluid regimen in the study population. The baseline characteristics of the hospitalized children are summarized in Table 1, while the distribution of age is presented graphically in Figure 3.

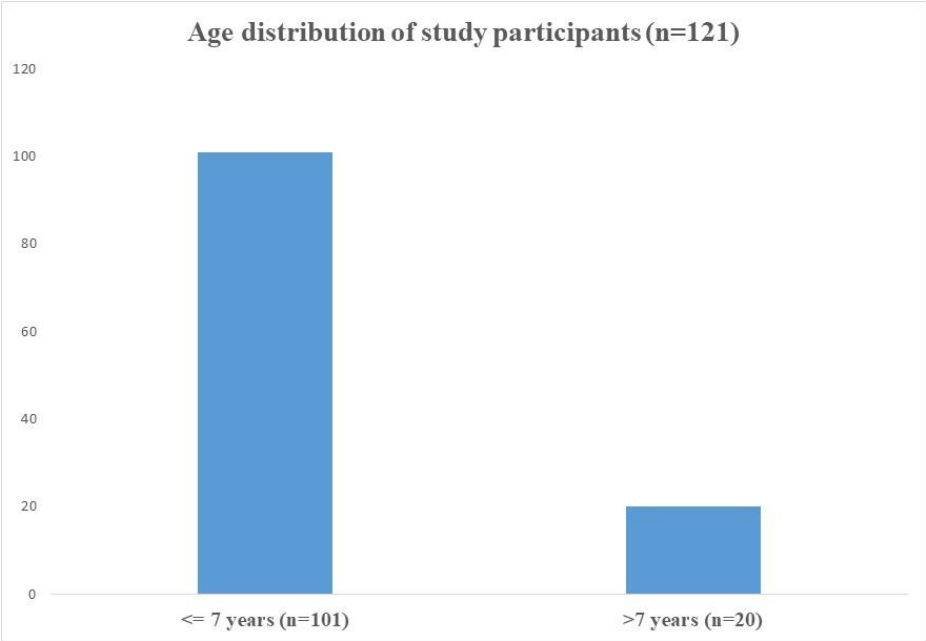


Figure 3. Age Distribution of study participants (n=121)

Table 1. Baseline characteristics of hospitalized children (n=121)

Variable	n	%
Age (years)	3.4± 3.1	
Gender		
Male	68	56.2%
Female	53	43.8%
Place of admission		
Pediatric ward	93	76.9%
ICU	28	23.1%
Type of intravenous fluid		
0.45% DS	47	38.8%
0.9% DS	74	61.2%

Frequency of hospital-acquired hyponatremia

Of the 121 children followed during hospitalization, 42 developed hospital-acquired hyponatremia after admission, corresponding to an overall frequency of 34.7%. The remaining 79 (65.3%) children did not develop hyponatremia during the observation period. Thus, approximately one in three children included in the study developed a hospital-acquired reduction in serum sodium concentration. The distribution of children according to the development of hospital-acquired hyponatremia is shown in Figure 4.

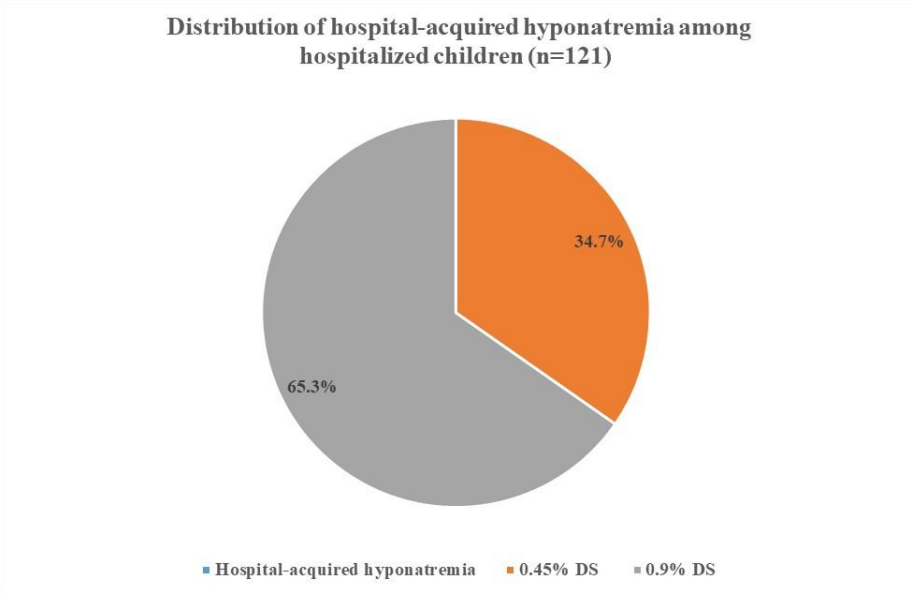


Figure 4. Distribution of hospital-acquired hyponatremia among hospitalized children (n=121)

Clinical diagnoses among children with hospital-acquired hyponatremia

The clinical diagnoses of the 42 children who developed hospital-acquired hyponatremia are presented in Table 2. Gastrointestinal and infectious diseases were the most frequently represented diagnostic categories, with 12 (28.6%) children in each category. Together, these two groups accounted for 24 of the 42 cases of hospital-acquired hyponatremia.

Table 2. Clinical diagnoses among children with hospital-acquired hyponatremia (n=42)

Diagnosis	n	%
Gastrointestinal disease	12	28.6
Infectious disease	12	28.6

Respiratory Disease	9		21.4
Malnourished children with sepsis	6		14.3
Neurological disease	2		4.8
Burn	1		2.4
Total		**42**	**100**

Respiratory disease was the next most frequent diagnosis, occurring in 9 (21.4%) children. Six (14.3%) children who developed hyponatremia were described as malnourished children with sepsis. Neurological disease was recorded in 2 (4.8%) cases, while 1 (2.4%) child had a burn injury. The six diagnostic categories collectively accounted for all 42 children who developed hospital-acquired hyponatremia.

Hospital-acquired hyponatremia according to age

The occurrence of hospital-acquired hyponatremia was compared between two age groups. Among the 101 children aged <7 years, 38 (37.6%) developed hyponatremia, whereas 63 (62.4%) did not. Among the 20 children aged ≥7 years, 4 (20.0%) developed hyponatremia and 16 (80.0%) remained without hyponatremia.

Although the proportion of hyponatremia was higher among children aged <7 years than among those aged ≥7 years (37.6% vs. 20.0%), the difference did not reach statistical significance (p=0.130). Therefore, age group was not significantly associated with hospital-acquired hyponatremia in the present analysis.

Hospital-acquired hyponatremia according to gender

Gender showed a statistically significant association with hospital-acquired hyponatremia. Among the 68 male children, 18 (26.5%) developed hyponatremia and 50 (73.5%) did not. In comparison, 24 (45.3%) of the 53 female children developed hyponatremia, while 29 (54.7%) did not.

Thus, the proportion of hospital-acquired hyponatremia was higher among female children than male children (45.3% vs. 26.5%). The difference between the two groups was statistically significant (p=0.030).

Hospital-acquired hyponatremia according to place of admission

The frequency of hospital-acquired hyponatremia was also examined according to the place of admission. Of the 93 children admitted to the pediatric ward, 35 (37.6%) developed hyponatremia, while 58 (62.4%) did not. Among the 28 children admitted to the ICU, 7 (25.0%) developed hyponatremia and 21 (75.0%) did not.

Although the proportion of hyponatremia was higher among children admitted to the ward compared with those admitted to the ICU (37.6% vs. 25.0%), this difference was not statistically significant (p=0.210).

Hospital-acquired hyponatremia according to type of intravenous fluid

The association between the type of maintenance intravenous fluid and hospital-acquired hyponatremia was also assessed. Among the 47 children who received 0.45% DS, 22 (46.8%) developed hospital-acquired hyponatremia, while 25 (53.2%) did not. Among the 74 children receiving 0.9% DS, 20 (27.0%) developed hyponatremia and 54 (73.0%) did not.

The frequency of hospital-acquired hyponatremia was therefore higher among children receiving 0.45% DS than among those receiving 0.9% DS (46.8% vs. 27.0%). This difference was statistically significant (p=0.026).

Summary of observed associations

Overall, hospital-acquired hyponatremia was identified in 42 (34.7%) of the 121 hospitalized children. Among the characteristics examined, gender and type of intravenous fluid showed statistically significant associations with hospital-acquired hyponatremia. The proportion of hyponatremia was higher among female children and among children receiving 0.45% DS. In contrast, differences according to age group

and place of admission were not statistically significant. The complete comparison of hospital-acquired hyponatremia across the assessed characteristics is presented in Table 3.

Table 3. Hospital-acquired hyponatremia according to risk factors (n=121)

Factors	Hyponatremia Present n (%)	Hyponatremia Absent n (%)	p-value
Age group			
< 7 years (n=101)	38 (37.6)	63 (62.4)	0.13
≥ 7 years (n=20)	4 (20.0)	16 (80.0)	
Gender			
Male (n=68)	18 (26.5)	50 (73.5)	0.03
Female (n=53)	24 (45.3)	29 (54.7)	
Place of admission			
Ward (n=93)	35 (37.6)	58 (62.4)	0.21
ICU (n=28)	7 (25.0)	21 (75.0)	
Type of intravenous fluid			
0.45% DS (n=47)	22 (46.8)	25 (53.2)	0.026
0.9% DS (n=74)	20(27)	32 (73)	

Discussion

Hospital-acquired hyponatremia remains an important electrolyte abnormality among hospitalized children, particularly because it may develop during treatment in children who have a normal serum sodium concentration at admission. In the present study, 42 of 121 hospitalized children developed hospital-acquired hyponatremia, giving an overall frequency of 34.7%. This finding indicates a substantial burden of HAH in the study population and is considerably higher than the frequency reported in several recent international pediatric studies. However, direct comparison should be made cautiously because the reported frequency of HAH varies according to the patient population, clinical setting, duration of follow-up, frequency of sodium measurements, definition of HAH, and type of intravenous fluid used.

The frequency observed in the present study is higher than that reported by Rius-Peris et al. in a large pediatric cohort from Spain. In that study, 3,102 children who had at least one plasma sodium measurement were analyzed from a total of 5,550 pediatric admissions. Hospital-acquired hyponatremia occurred in 42 children, corresponding to an incidence of 1.4%, while community-acquired hyponatremia occurred in 15.8% [21]. In contrast, our study identified HAH in 34.7% of children. The difference is substantial despite both studies distinguishing hyponatremia present at admission from that developing during hospitalization. One possible explanation is the difference in study populations and surveillance. The Spanish study included children from a general pediatric ward over a prolonged period and relied on available sodium measurements, whereas our study specifically enrolled children requiring maintenance intravenous fluids and followed children with normal admission sodium for development of HAH. The latter approach may have enriched the study population for children at risk of iatrogenic or illness-associated sodium disturbances. Thus, our findings should not be interpreted as representing the incidence of HAH in all pediatric admissions.

A more recent regional study from Iran reported an intermediate frequency. Bakhtiari et al. conducted a longitudinal study of hospitalized children with normal serum sodium at admission and reported HAH in 22.1% of 456 children [22]. Female sex was identified as an independent factor in their analysis, with an odds ratio of 3.83 (95% CI 1.08–13.59), while children younger than one year showed a borderline association with HAH [22]. The 22.1% frequency reported in Iran is lower than the 34.7% observed in our study but remains substantially higher than the 1.4% reported in the Spanish cohort. The difference between these estimates reinforces the influence of hospital setting, patient characteristics, monitoring intensity, and fluid-management practices on the observed frequency of HAH.

The present finding is also higher than the frequency of severe HAH reported in a population-based Finnish study. Lehtiranta et al. evaluated 46,518 acutely ill children and found severe hyponatremia, defined as serum sodium <125 mmol/L, in 27 children (0.06%). Among an estimated 6,984 children who received moderately hypotonic intravenous fluids after admission, severe HAH developed in 7 children (0.1%), generally within the first 8 hours of hospitalization [23]. These findings cannot be directly compared with our overall HAH frequency because our study did not classify the outcome according to severity and included all hyponatremia below the normal sodium threshold. Nevertheless, the Finnish study demonstrates that while severe HAH is uncommon at the population level, clinically important sodium disturbances can develop rapidly after initiation of intravenous fluid therapy.

The frequency observed in our study is also higher than that reported in a recent Turkish prospective observational study. Pınarbaşı et al. followed pediatric inpatients who were normonatremic at admission and received intravenous fluids for at least 24 hours. Among 8,065 hospitalized children, 373 fulfilled the study criteria, and HAH occurred in 4.6% [24]. Hyponatremia developed earlier in children younger than 100 days, with a median time to occurrence of 6 days compared with 10.5 days in older children. The investigators also reported that moderate-to-severe hyponatremia was more frequent among younger infants and that inadequate sodium supplementation was common among affected infants [24]. The considerably lower frequency than that observed in our study may partly reflect differences in age distribution, fluid composition duration of observation, and the clinical population included.

The difference between our findings and recent international estimates may also be considered in the context of changes in pediatric intravenous fluid practice. A 2021 systematic review and meta-analysis involving 22 randomized controlled trials and 3,795 children found that isotonic maintenance fluids were associated with a lower risk of hyponatremia than hypotonic fluids. The reported prevalence of hyponatremia was 5.7% versus 23.3% within 24 hours and 6.0% versus 26.3% after 24 hours in the isotonic and hypotonic groups, respectively [25]. An updated meta-analysis published in 2024 expanded the evidence to 33 randomized controlled trials involving 5,049 children. Isotonic maintenance fluids significantly reduced the risk of mild hyponatremia within 24 hours (RR 0.38, 95% CI 0.30–0.48) and after 24 hours (RR 0.47, 95% CI 0.37–0.62). Isotonic fluids also reduced the risk of moderate hyponatremia at both time periods [26]. These findings provide a strong biological and clinical context for the association observed in our study between intravenous fluid type and HAH.

In the present study, HAH occurred in 46.8% of children receiving 0.45% DS compared with 27.0% of those receiving 0.9% DS, and the difference was statistically significant (p=0.026). The direction of this finding is consistent with the recent evidence showing greater protection against hyponatremia with isotonic compared with hypotonic maintenance solutions [25-26]. The ESPNIC clinical practice guideline similarly recommends isotonic balanced solutions containing glucose for most acutely and critically ill children and emphasizes regular monitoring of plasma electrolytes, glucose, and fluid balance [27]. The current findings therefore support the importance of careful selection of maintenance fluid composition in hospitalized children. However, because our study was cross-sectional and observational, the association between fluid type and hyponatremia should not be interpreted as proof of causality. Fluid selection may have been influenced by the underlying disease severity or clinical condition of the child, which could itself influence the risk of hyponatremia.

Recent Pakistani evidence also supports the importance of intravenous fluid composition. A 2025 case-control study from the Children's Hospital and Institute of Child Health, Multan, evaluated children in a pediatric intensive care setting and found that exposure to hypotonic fluids was significantly more common among children with HAH than among controls. The reported odds of previous hypotonic-fluid exposure were 9.2 times higher among cases (95% CI 4.3–19.7), while exposure to antidiuretic-hormone-stimulating drugs was also more frequent among cases [28]. Although this study was conducted in a PICU and used a case-control design, rather than the general pediatric population studied here, its findings provide contemporary Pakistani evidence supporting an association between hypotonic fluid exposure and HAH. Importantly, the authors themselves noted that their reported associations were unadjusted and that multivariable analysis was not performed [28]. This reinforces the need to interpret associations from both studies cautiously.

The clinical diagnoses observed among children who developed HAH in our study provide additional information about the patient groups in which sodium disturbances occurred. Gastrointestinal and infectious diseases were the most frequent categories, each accounting for 28.6% of HAH cases, followed by respiratory disease (21.4%) and malnutrition with sepsis (14.3%). Neurological disease accounted for 4.8%, while burns accounted for 2.4%. This pattern is broadly compatible with the clinical spectrum described in recent pediatric literature. In the Spanish cohort, infections and gastrointestinal disorders were among the diagnostic groups associated with hyponatremia, while the authors reported that age and discharge diagnosis were important factors associated with the occurrence of hyponatremia [21]. The concentration of cases in gastrointestinal and infectious illnesses in our study may reflect the high prevalence of these conditions among children requiring inpatient treatment and the potential for vomiting, diarrhea, reduced oral intake, inflammation, and non-osmotic antidiuretic hormone secretion to accompany acute illness.

The present study also found a higher frequency of HAH among children younger than 7 years. Hyponatremia occurred in 37.6% of children aged <7 years compared with 20.0% among those aged ≥7 years, although the difference was not statistically significant (p=0.130). This direction of association is consistent with the findings of several recent studies suggesting that younger children may be particularly susceptible to sodium disturbances during hospitalization. In the 2025 Iranian study, children younger than one year had an increased but borderline risk of HAH [22]. Similarly, the 2025 Turkish study demonstrated earlier development of HAH in infants younger than 100 days and a greater frequency of moderate-to-severe hyponatremia in this group [24]. The absence of statistical significance in our study may reflect the relatively small number of children aged ≥7 years, with only 20 participants in this category, limiting the statistical power to detect differences between age groups.

A statistically significant association was observed between gender and HAH in the present study. Hyponatremia developed in 45.3% of female children compared with 26.5% of male children (p=0.030). This finding is notable because a similar association has been reported in the recent Iranian longitudinal study, in which female sex was associated with HAH with an odds ratio of 3.83 (95% CI 1.08–13.59) [22]. The contemporary Pakistani PICU study also included gender in its stratified analyses, although its principal reported associations concerned hypotonic fluid exposure, antidiuretic-hormone-stimulating medication, and recent hospitalization [28]. The consistency of the female predominance between our study and the Iranian study is noteworthy; however, the biological or clinical explanation for this observation remains uncertain. Further studies with larger samples and adjusted analyses are required before gender can be considered an independent determinant of HAH.

The place of admission was not significantly associated with HAH in our study. Hyponatremia occurred in 37.6% of children admitted to the pediatric ward compared with 25.0% of those admitted to the ICU (p=0.210). This finding differs from the expectation that critically ill children may have a greater risk of sodium disturbances because of severe illness, non-osmotic antidiuretic hormone secretion, multiple medications, and intensive fluid therapy. However, the ICU subgroup in our study comprised only 28 children, which limits the ability to detect a statistically significant difference. In addition, the study was conducted in a single tertiary-care hospital, and the composition and severity of ICU admissions may differ from those in other pediatric centers. Recent studies have demonstrated that clinical setting is an important source of heterogeneity in HAH estimates. For example, the Finnish study specifically examined severe HAH among acutely ill children receiving hypotonic fluids, whereas the Turkish and Iranian studies included broader pediatric inpatient populations [23-24].

The present findings should also be considered in light of the distinction between HAH frequency and severity. Our study was designed primarily to determine the frequency of HAH and did not provide a detailed severity classification of the 42 cases. Therefore, the observed frequency of 34.7% should not be interpreted as indicating that one-third of hospitalized children developed clinically severe hyponatremia. This distinction is important because recent population-based evidence demonstrates that severe HAH is much less common than mild biochemical hyponatremia [23]. Similarly, the Spanish study reported that most hyponatremia cases were mild, with 90.8% classified as mild and 8.6% as moderate [21]. Future studies from similar settings should therefore report both the frequency and severity of HAH to better characterize its clinical importance.

The present findings can also be viewed against the only directly comparable earlier Pakistani study identified in the literature. Bibi et al., in a tertiary-care pediatric setting in Karachi, reported HAH in 240 of 865 children (27.7%), with 79.6% of cases classified as mild, 14.6% as moderate, and 5.8% as severe [19]. The frequency of 34.7% observed in our study is higher than the 27.7% previously reported in Karachi. Although the two studies were conducted in the same broad geographic setting and included children requiring maintenance intravenous fluids, differences in hospital population, clinical practice, fluid prescribing, monitoring, and study period may account for the difference. Importantly, the earlier study was conducted before the widespread incorporation of contemporary isotonic maintenance-fluid recommendations. The persistence of a substantial HAH burden in the present study therefore suggests that changing fluid practices alone may not completely eliminate hospital-acquired sodium disturbances.
Several factors should be considered when interpreting the findings. First, this was a single-center study conducted in a tertiary-care pediatric hospital, and the results may not be generalizable to other hospitals or to children managed in primary or secondary care settings. Second, the sample size was relatively small, particularly for subgroup analyses such as ICU admission and age ≥7 years. Third, participants were selected using consecutive non-probability sampling, which may introduce selection bias. Fourth, the study assessed serum sodium at admission and after 48 hours; therefore, transient changes occurring earlier than 48 hours may not have been captured. Fifth, the analysis was based on unadjusted comparisons. Consequently, the observed associations with gender and intravenous fluid type may be influenced by underlying disease, severity of illness, medication use, nutritional status, or other clinical factors that were not included in an adjusted model. Finally, the study did not evaluate detailed fluid volume, sodium intake from enteral sources, urine sodium, urine osmolality, or antidiuretic hormone-related factors, which limits assessment of the mechanisms underlying HAH.
Despite these limitations, the study provides contemporary data on HAH among hospitalized children in a tertiary-care setting in Karachi. The finding that more than one-third of the enrolled children developed HAH, together with the significant association observed with intravenous fluid type, emphasizes the need for careful fluid prescription and electrolyte surveillance. The results also suggest that children with gastrointestinal, infectious, and respiratory illnesses constitute an important proportion of affected patients. Future multicenter Pakistani studies with larger sample sizes should use standardized definitions of HAH, assess severity, record fluid volume and sodium content in detail, and apply multivariable analysis to identify independent predictors. Such studies would help determine whether the high frequency observed in the present study reflects a broader pattern in Pakistani pediatric hospitals and could inform locally appropriate strategies for prevention and monitoring.
In conclusion, hospital-acquired hyponatremia occurred in 34.7% of children in this study. It was more frequent among female children and among those receiving 0.45% dextrose in saline (DS), whereas age group and admission location were not significantly associated with HAH. The overall frequency was higher than that reported in several recent international cohorts but remained within the broad range reported in regional pediatric studies. These findings highlight HAH as an important inpatient pediatric problem and support continued attention to appropriate maintenance-fluid selection and timely monitoring of serum electrolytes.

Conclusion

This study found hospital-acquired hyponatremia in 34.7% of hospitalized children receiving maintenance intravenous fluids. It was more frequent among girls and among children given 0.45% dextrose in saline than among those given 0.9% dextrose in saline. Age group and place of admission were not significantly associated with HAH. The frequency was higher than in several international studies but within the range reported regionally. These findings show that HAH remains a common and potentially preventable problem in hospitalized children. Careful maintenance-fluid selection and regular serum sodium monitoring are needed. As this was a single-center, observational study with unadjusted analyses, larger multicenter studies are required to confirm these findings and identify independent risk factors.

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