Original Research Article

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Study of association of mortality with electrolyte abnormalities in children admitted in pediatric intensive care unit

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ABSTRACT

Background: Electrolyte abnormalities are common in critically ill children. In view of importance of electrolyte homeostasis and its significant impact on the final outcome of patient, the present study was undertaken. Objective of this study was to determine the prevalence of electrolyte abnormalities in children admitted in Pediatric Intensive Care Unit at the time of admission and its association with mortality and primary organ system involvement.

Methods: The study enrolled all the patients from 29 days to 12 years admitted in PICU of a tertiary care hospital during April 2015 to September 2016 (total 18 months). The children were classified according to presence or absence of electrolyte abnormality. The children were further divided into subgroups based on electrolyte values and mortality and organ system involvement was analyzed in each of the sub groups.

Results: The prevalence of electrolyte abnormality in terms of sodium or potassium abnormality in the present study was 44.31% (323 of 729). Hyponatremia (27.43%) was the most common electrolyte abnormality followed by hypokalemia (13.99%). The mortality in children with electrolyte abnormality was found to be 28.8% which was significantly higher than mortality in those without electrolyte abnormality. Maximum children with hyponatremia had central nervous system involvement (48.5%) and those with hypernatremia had gastrointestinal involvement (65.4%). Hypokalemia was most frequently observed with gastrointestinal involvement (54.9%) and hyperkalemia with renal involvement (34.8%).

Conclusions: Present study has demonstrated significant association of electrolyte abnormalities at admission in PICU with mortality and primary organ system involvement. Close monitoring and correction of electrolyte abnormalities is essential to reduce morbidity and mortality.

Keywords: Critically ill, Hyponatremia, Intensive care unit, Mortality, Water electrolyte imbalance

INTRODUCTION

Electrolyte abnormalities are common in critically ill children and occur in a wide range of conditions resulting in morbidity and mortality irrespective of primary problem.¹

Early recognition with a thorough understanding of common electrolyte abnormalities and their prompt management definitely pose an implication on the final outcome of the patient.² These electrolyte disturbances

may aid in diagnosis of the illness and can also act as markers of disease severity and potential of recovery from disease.^{3,4}

Sodium is the predominant cation in the extracellular fluid, ranging from 135-145 mEq/l. It is the major determinant of serum osmolality and hence, is responsible for maintenance of intravascular volume. The presence of either hypernatremia or hyponatraemia (dysnatraemias) in the intensive care unit have a prevalence approaching 30% and are an independent risk

factor for poor prognosis on admission or during ICU stay.^{3,7}

Hyponatremia is serum sodium level less than 135 mEq/l.⁶ It occurs in about 3% of hospitalized patients. The incidence in the PICU, however, may be as high as 30%.⁴ Euvolemic hyponatremia is the most common dysnatremia in critically ill patients.⁷

Hypernatremia is serum sodium concentration more than 145 mEq/l. Some define it as levels more than 150mEq/l. The incidence of hypernatremia in the intensive care setting approaches 6%. ^{4,6} Excessive sodium is mostly iatrogenic. Infants presenting with severe hypernatremia mostly are a result of inappropriate dilution of infant formula feeds, inadequate breastfeeding or high sodium content in the insufficient amount of breast milk. ⁸

Potassium is predominantly present in intracellular compartment ranging from 150-160 mEq/l while serum concentration ranges from 3.5-5 mEq/l. This normal ratio between extracellular and intracellular concentrations is important for maintenance of the resting membrane potential and neuromuscular functioning.⁶

Hypokalemia is serum potassium concentration below 3.5 mEq/l.⁹ It occurs in about 15% children admitted to PICU.¹⁰ The most common causes of hypokalemia in the PICU is the use of diuretics and alkalosis.⁴

Hyperkalemia is serum potassium levels more than 5.5 mEq/l. 11 It occurs in about 3.3% of all hospitalized patients and can carry a high rate of mortality. 9

Electrolyte abnormalities that are present on admission can further additionally complicate the course of stay in the intensive care setting, irrespective of the primary disease process. In view of the importance of electrolyte homeostasis and its significant impact on the final outcome of the patient, the present study was undertaken to study the association of electrolyte abnormalities at admission with mortality in children admitted in pediatric intensive care unit. Since sodium and potassium are the electrolytes most frequently deranged in critically ill patients, we have studied these electrolytes in the present study. We also studied the association of primary organ system involvement with electrolyte abnormalities present at admission.

METHODS

The study was carried out in the Pediatric Intensive Care Unit at a tertiary care hospital after obtaining approval and waiver of consent from the Institutional Ethics Committee. We enrolled all the patients admitted in PICU of age 29 days to 12 years during April 2015 to September 2016 excluding those children who were referred from other hospitals after any form of treatment. At the time of admission, the patients' clinical picture was recorded in a prefixed case record form consisting of

age, sex, date of admission, provisional clinical diagnosis, duration of PICU stay, organ system primarily involved and final outcome in terms of discharge from PICU or death. Information of blood investigations like serum electrolytes (sodium, potassium) was collected from the hospital records. We classified the children into groups according to presence or absence of electrolyte abnormality. The children were then, divided into subgroups based on electrolyte values and mortality was analysed in each of the sub groups.

Definitions

Hyponatremia and hypernatremia were defined as serum sodium concentration below 135 mEq/L and above 145 mEq/L respectively. Hypokalemia and hyperkalemia were defined as potassium level below 3.5 mEq/L and above 5.5 mEq/L, respectively.⁶

Statistical methods

All data was entered in a master chart in Microsoft Excel sheet and was analyzed in SPSS 16.0 software. Qualitative data was represented in form of frequency and percentage and analyzed using Chi Square test or Fischer's F test as per the normality test. P value less than 0.05 was considered to be statistically significant. Results were graphically represented wherever deemed necessary.

RESULTS

We studied 729 children admitted in the PICU of a tertiary care hospital, of which infants constituted the maximum number of admissions (43.76%). Maximum number of admissions had respiratory system involvement (29.49%) followed by central nervous system (26.75%).

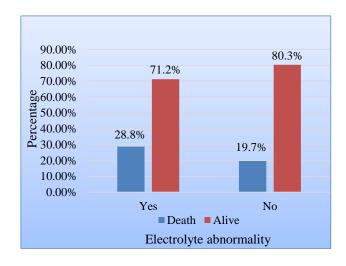


Figure 1: Outcome of the study population in terms of death or survival, and presence or absence of electrolyte abnormality.

The prevalence of electrolyte abnormality in terms of sodium or potassium abnormality in our study was 44.31% (323 out of 729). Hyponatremia (27.43%) was the most common electrolyte abnormality followed by hypokalemia (13.99%). Hypernatremia was observed in 3.57% and hyperkalemia in 6.31% cases. The mortality in the group with electrolyte abnormality was found to be 28.8% as compared to 19.7% in the group without electrolyte abnormality. The association was statistically significant (P value = 0.004; Odd's ratio: 1.640; 95% confidence interval: 1.169-2.322) (Figure 1).

The mortality in patients with hyponatremia and hypernatremia was 32.5% and 38.5% respectively, which was significantly higher than the mortality in normonatremic patients which was 19.5%. The association of hyponatremia and hypernatremia at admission with mortality was found to be statistically significant. (Hyponatremia - Odd's ratio: 1.990; 95% confidence interval 1.376-2.878; P value = 0.00; Hypernatremia - Odd's ratio: 2.583; 95% confidence interval 1.137-5.866; P value = 0.019). The mortality rates were observed to rise significantly as serum sodium

values increased above the normal range (P value = 0.000) (Figure 2).

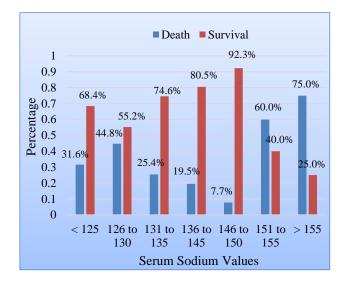


Figure 2: shows the outcome in the subgroups of patients that are divided according to serum sodium values.

Table 1: Association of the sodium values in the study population with the primarily involved organ system.

Involved angen austen.		Sodium values			Tatal	
Involved organ system		Hyponatremia	Normonatremia	Hypernatremia	Total	
Central nervous system	No.	97	91	7	195	
	%	48.5	18.1	26.9	26.7	
Respiratory system	No.	45	170	0	215	
	%	22.5	33.8	0.0	29.5	
Renal	No.	6	19	1	26	
	%	3.0	3.8	3.8	3.6	
Cardiovascular system	No.	3	47	0	50	
	%	1.5	9.3	0.0	6.9	
Gastrointestinal system	No.	11	52	17	80	
	%	5.5	10.3	65.4	11.0	
Hepatobiliary	No.	5	27	0	32	
	%	2.5	5.4	0.0	4.4	
Endocrine	No.	0	7	0	7	
	%	0.0	1.4	0.0	1.0	
Infections	No.	19	42	0	61	
	%	9.5	8.3	0.0	8.4	
Haematology	No.	1	30	0	31	
	%	0.5	6.0	0.0	4.3	
Genitourinary	No.	1	0	0	1	
	%	0.5	0.0	0.0	0.1	
Poisoning	No.	0	1	0	1	
	%	0.0	0.2	0.0	0.1	
Sepsis	No.	12	17	1	30	
	%	6.0	3.4	3.8	4.1	
Total	No.	200	503	26	729	
	%	100.0	100.0	100.0	100.0	

The mortality in the group with hypokalemia and hyperkalemia was found to be 24.5% and 30.4% which was higher than the mortality in the group with normokalemia which was 23.1%. However, the association was not statistically significant. (Hypokalemia - Odd's Ratio: 1.083; 95% confidence interval 0.663-1.769; P value = 0.750; Hyperkalemia - Odd's Ratio: 1.459; 95% confidence interval 0.757-2.815; P value = 0.257).

The association of primary organ system involvement with the presence of electrolyte abnormality was found statistically significant. Maximum number of study participants with hyponatremia had central nervous system involvement (48.5%) and those with hypernatremia had gastrointestinal system involvement (65.4%) (P value <0.001) (Table 1).

Table 2: Association of the potassium values in the study population with the primarily involved organ system.

Involved organ system		Potassium values			T-4-1
		Hypokalemia	Normokalemia	Hyperkalemia	Total
Control manners and an	No.	9	184	2	195
Central nervous system	%	8.8	31.7	4.3	26.7
Descriptors suctors	No.	8	207	0	215
Respiratory system	%	7.8	35.6	0.0	29.5
Danal	No.	2	8	16	26
Renal	%	2.0	1.4	34.8	3.6
Candianasanlan santan	No.	8	41	1	50
Cardiovascular system	%	7.8%	7.1%	2.2%	6.9%
Control of the standard of the standard	No.	56	23	1	80
Gastrointestinal system	%	54.9%	4.0%	2.2%	11.0%
II. matabilia	No.	5	27	0	32
Hepatobiliary	%	4.9%	4.6%	0.0%	4.4%
Endersine	No.	1	0	6	7
Endocrine	%	1.0%	0.0%	13.0%	1.0%
Infantiana	No.	1	60	0	61
Infections	%	1.0%	10.3%	0.0%	8.4%
Haamatalaav	No.	3	14	14	31
Haematology	%	2.9%	2.4%	30.4%	4.3%
Garitanai na ma	No.	1	0	0	1
Genitourinary	%	1.0%	0.0%	0.0%	0.1%
Determine	No.	0	1	0	1
Poisoning	%	0.0%	0.2%	0.0%	0.1%
Canais	No.	8	16	6	30
Sepsis	%	7.8%	2.8%	13.0%	4.1%
Total	No.	102	581	46	729
Total	%	100.0%	100.0%	100.0%	100.0%

Hypokalemia was most frequently observed in patients with gastrointestinal involvement (54.9%) and hyperkalemia with renal involvement (34.8%) (P value <0.001) (Table 2).

DISCUSSION

In the present study which was done in a tertiary care set up including 729 study participants, the overall mortality of patients was 23.73%. Similar mortality rate was observed in the study done by Jain M et al which was 22.8% (16/70) and the study was conducted in a tertiary care hospital in Ahmedabad, India. 12

Present study showed electrolyte abnormality (sodium, potassium) in 44.31% patients (n = 323). The prevalence of electrolyte abnormality in the present study was found to be higher than the study done by Rao SSD et al which had 32.45% patients with electrolyte abnormality and by Jain M et al which had 31.4% patients. This difference in prevalence may be attributed to the different subset of study population catered by our tertiary centre. The mortality in patients with electrolyte abnormality was found to be 28.8% in the present study, similar to a study by Rao SSD et al which showed 24.2% mortality in patients with electrolyte abnormalities. Of the total 173

deaths in the present study, 93 patients (53.7%) had electrolyte abnormality.

We found hyponatremia in 27.43% of patients, it being the most common electrolyte abnormality in patients, admitted to PICU at the time of admission and hypernatremia in 3.57% of patients. Similar results were found in a study conducted by Ebrahim SAE et al which showed 23.33% (28 out of 120) patients with hyponatremia on admission to PICU.13 However, hypernatremia in their study was seen in 11.66% patients, which was higher than the present study. In the study by Jain M et al, hyponatremia and hypernatremia were seen in 12.85% and 5.71% patients respectively. 12 Fewer patients with hyponatremia in their study could be explained by the exclusion of acute diarrhoeal diseases in their study population. A higher frequency of hyponatremia of 29.8% was observed in a prospective study of 727 sick children conducted in PGIMER, Chandigarh, India by Singhi S et al which was similar to the present study.² In the present study, it was observed that mild hyponatremia (131-135 mEq/l) was most common with 15.64% patients. In a Kenyan study done on 1026 children by Ibinda F et al, 46.6% children had blood sodium disturbances with 44.4% hyponatremic and 2.1% hypernatremic.¹⁴ Most children had mild (41.9%) rather than moderate (2.2%) or severe hyponatremia (0.3%).

Present study found a significant association of mortality with the presence of hyponatremia and hypernatremia at admission. The mortality was seen to rise significantly as serum sodium values rose above 155 mEq/l and between 126-130 mEq/l. In the study done by Rao SSD et al the mortality with hyponatremia and hypernatremia was observed to be 20.7% and 33.33% respectively. Jain M et al studied patient population where the mortality associated with hyponatremia and hypernatremia was found to be 55.55% and 50% respectively. 12 Singhi et al, showed that among hospitalized patients, 15-20% had a serum sodium level of <135 mEq/L, while only 1-4% had a serum sodium level of less than 130 mEq/L.¹⁵ The prevalence of hyponatremia was lower in the ambulatory setting and severe hyponatremia (<125 mEq/L) had a high mortality rate. In instances when the serum sodium level was less than 105 mEq/L, the mortality was over 50%. Funk GC et al, showed an independent mortality risk rising with increasing severity of both hyponatremia and hypernatremia. 16 Similar to the present study, another study done by Lindner et al, found that incidence of hypernatremia at the center's intensive care unit was 9% of the total cases of which 23% had hypernatremia on admission with 39% mortality, compared to 24% in patients without hypernatremia.¹⁷ Darmon et al, reported mortality rates ranging from 30-48% in critically ill patients with hypernatremia more than 150 mEq/l.18 Alharfi IM et al, performed a cohort study of 165 all severely injured trauma patients admitted to a Pediatric Critical Care Unit of which 76% had normonatremia (135-150 mmol/L), 18% had hypernatremia (151-160 mmol/L), and 6% had severe hypernatremia (>160 mmol/L) with mortality rates four-fold greater with hypernatremia and six-fold with severe hypernatremia.¹⁹

In the present study, hyponatremia and hypernatremia was observed in higher number of study participants less than 1 year of age, which was 42.0% and 65.4% respectively. Jain M et al also showed that electrolyte imbalance was more frequently seen in infants (48%).¹² Infants are thus, overall more susceptible to electrolyte abnormalities that too, more specifically sodium abnormalities. Thus, a lower threshold should be kept for intervention of electrolyte abnormalities. The mean duration of PICU stay was prolonged in patients with hyponatremia (5.93±5.05) as compared to normonatremic (4.58±4.74) and hypernatremic patients (4.50±3.41) in our study. Rao SSD et al found similar results with mean duration of PICU stay prolonged in hyponatremic (4.69±4.04) in comparison with hypernatremic (3.35 ± 3.24) and normonatremic (2.63 ± 3.02) .

In the present study, hypokalemia was found in 13.99% cases, being the second most common electrolyte abnormality and hyperkalemia in 6.31% cases. Rao SSD et al and Jain M et al however, found hypokalemia as the least common abnormality in their study consisting only 3.6% and 5.7% of all cases respectively.^{1,12} This difference could possibly be explained by exclusion of diarrheal diseases in their studies. Hyperkalemia in their studies comprised of 14.4% and 11.42% cases respectively. In a study of 727 sick children by Singhi S et al results were similar to the present study with hypokalemia observed in 13.9% cases and hyperkalemia in 5.4% cases.²⁰ Much higher percentage of potassium abnormality was observed by Cummings BM et al in their study with hypokalemia affecting 40% of all admissions and hyperkalemia in 29% admissions.21 Similarly, Ebrahim SAE et al found hypokalemia in 38.33% cases and hyperkalemia in 22.5% cases in their study. 13 Such higher percentage of potassium abnormality in their studies could be explained by the electrolyte measurements being recorded throughout the course of illness in the patients. In the present study, we have considered electrolyte values at admission to PICU.

Mortality was higher in the hypokalemic and hyperkalemic group i.e. 24.5% and 30.4% as compared to normokalemic group which was 23.1, the association being not statistically significant. In a study by Singhi S et al, the mortality rate among hypokalemic (15%) as well as hyperkalemic children (10.3%) was higher than that of normokalemic children (4.4%).²⁰ Presence of concomitant hyponatremia with hypokalemia further aggravated the risk of mortality. In the present study, the higher mortality in the normokalemic group could be attributed to the presence of concomitant sodium abnormalities in 175 patients out of 581 normokalemic patients. The mortality was significantly higher in patients with associated hyponatremia and hypernatremia with mortality rates being 30.9% and 30.0% respectively,

compared to 19.7% in the normokalemic-normonatremic group and this association was found to be statistically significant.

In the present study, hypokalemia was most commonly found in infants (58.8%) and hyperkalemia in children above 5 years of age (60.9%). Singhi S et al also found that hypokalemia was more common in infants with 18 children under 1 year of age, 14 between 1-5 years and 11 were above 5 years of age.¹⁰

We found significant association of the involved organ system with hyponatremia and hypernatremia in the present study. Hyponatremia was associated most commonly with central nervous system affection followed by respiratory system. Out of the CNS cases, most patients were cases of tuberculous meningitis (34%) and meningoencephalitis (32.9%). Similar results were found in the study by Rao SSD et al, where 41.4% cases with hyponatremia had central nervous system involvement.1 respiratory Amongst cases hyponatremia in the present study, 60% cases had pneumonia and 33.33% had bronchiolitis. Respiratory diseases and central nervous system diseases formed the bulk of the present study population, which possibly explains hyponatremia being the most common electrolyte abnormality in the present study. Hypernatremia was associated most commonly with gastrointestinal involvement of which all patients had diarrhea with severe dehydration.

We found significant association of potassium abnormalities with the primary organ system involved. More than 50% patients with hypokalemia had gastrointestinal system involvement with most cases being acute watery diarrhoea. Amongst patients with hyperkalemia, 34.8% had renal involvement in form of acute or chronic renal failure, closely followed by haematological involvement (30.4%) out of which 3 were cases of vasculotoxic snake bite and the rest were haematological malignancies. The maximum number of patients with hyperkalemia being above 5 years of age could be explained by fact that most of the patients with renal failure in our study were above 5 years of age. In the study by Rao S et al, 18.8% patients with hypokalemia each had central nervous system and gastrointestinal involvement, and 27.4% of hyperkalemia patients had renal involvement.1 Lower incidence of hypokalemia associated with GIT involvement could be attributed to the exclusion of diarrhoeal diseases from the study population.

Present study emphasizes the significant association of mortality with sodium abnormality in children admitted in PICU. The association of mortality with potassium abnormality on admission was not found statistically significant in the present study, however, mortality was observed in higher percentage of cases with potassium abnormality as compared to normal population. Thus, electrolyte abnormality on admission should be taken

seriously and appropriate and aggressive measures should be taken to correct the electrolyte abnormality and maintain homeostasis. The electrolyte levels should be diligently monitored thereafter. Clinicians should be wary of spurious reports and should judge a patient clinically, rather than only relying on laboratory findings. We would like to emphasis on the electrolyte measurements at admission to intensive care unit because, with early recognition of electrolyte disturbances, risk factors may be ameliorated through supportive therapy to improve outcome in the patients.

There are certain limitations of the present study. We have not recorded the serial electrolyte measurements. Thus, we might have missed subsequent electrolyte derangements which could have had implications on the final outcome of the patient. We have conducted the study in a tertiary care centre that acts as a referral centre for many peripheral hospitals. Thus, the results cannot be applied to the general population or other peripheral centre hospitals. We require randomized control trials for applying the results to general population. We also did not record the number of cases with electrolyte abnormalities that were symptomatic for the underlying abnormality and the management that was instituted for the same. Further large scale randomized trials are required to ascertain the exact implications of electrolyte abnormality at admission on eventual fate of the child.

CONCLUSION

Electrolyte abnormalities are common in children admitted to intensive care unit. They develop or are frequently exacerbated during hospitalization and are associated with increased length of stay and mortality. Thus, vigilant monitoring of electrolytes and timely optimal correction of electrolyte abnormalities are the keys to survival in a critically ill child. Our study has demonstrated significant associations of electrolyte abnormalities with mortality, age group and primary organ system involvement. The prognostic and therapeutic implications of these findings, as well as the ability to define causality shall need further prospective studies.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

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