Sodium Abnormalities in Children Admitted to Paediatric Intensive Care Unit - A Cross Sectional Study

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ABSTRACT

Objective: Fluid and electrolyte disorders are commonly seen in patients admitted to the intensive care unit. Hyponatremia and hypernatraemia can develop and exacerbate during hospitalization. To determine the aetiology and outcome of hyponatraemia and hypernatraemia in children admitted to the paediatric intensive care unit (PICU) of a tertiary hospital.

Design: A hospital based cross sectional study

Setting: This cross-sectional study was carried out in a tertiary care hospital, Chennai, India between March 2012 and June 2013.

Method: All children admitted to the PICU who developed hyponatraemia or hypernatraemia on admission, or during their period of illness, were included in the study. If hyponatremia or hypernatremia was confirmed, on or after admission to the PICU, samples were collected and sent for plasma osmolality, urine osmolality and urine sodium for further classification into the syndrome of inappropriate anti-diuretic hormone (SIADH) and diabetes insipidus (DI). Serum sodium levels were monitored till normalization.

Result: The study observed 130 patients admitted in PICU for a period of 15 months. Seventy-five patients had hyponatraemia and 55 had hypernatraemia. Hypernatraemic patients had a mortality rate of 29.1% compared to 8% for hyponatraemic patients and this was statistically significant (p=0.002). In hyponatraemic patients 29.3% had SIADH and in hypernatraemic patients 32.7% had DI. Overall, severity assessed between hyponatraemic and hypernatraemic patients based on the Glasgow Coma Scale (GCS) and mechanical ventilation showed that hypernatraemic patients tended to be significantly more critical and unwell than hyponatraemic patients (p=0.000).

Conclusion: The study reported a higher mortality rate in hypernatraemic patients compared to the hyponatraemic patients. Presence of SIADH was noted in hyponatraemic patients and DI in hypernatraemic patients.

Keywords: Hyponatraemia, hypernatraemia, osmolality, syndrome of inappropriate anti diuretic hormone, SIADH, diabetes insipidus, DI, Glasgow Coma Scale, GCS.

INTRODUCTION

Fluid and electrolyte disorders are commonly encountered by patients in the intensive care unit. Such disorders are characterized by relative water excess or deficiency causing a change of the effective plasma osmolality[1]. Osmo-receptors help perceive the alterations in osmolality. Downward transduction of the signals from the osmo-receptors results in synthesis and transportation of arginine vasopressin (AVP) or anti-diuretic hormone to the posterior lobe of the pituitary gland[2,3].

The pathological condition characterized by the presence of an unusually high or low amount of sodium in the blood is termed dysnatraemia. Hypernatraemia, defined as serum sodium exceeding 145 meq/L, may be due to increased free water loss with no adequate replacement, lack of circulating AVP, or inadequate renal response to AVP[1,4].Symptoms of hypernatraemia mainly include restlessness, irritability, lethargy, confusion, and drowsiness[1,5].Hyponatraemia is defined as plasma sodium <136meq/L. Hyponatraemia and hypernatraemia are usually reported to develop and exacerbate during hospitalization. Further, an association has been established with greater length of stay (LOS) and mortality[3]. When there is a rapid fall in plasma sodium to <110-125 mEq/L, seizures and coma develop. Cerebral oedema has been identified as the most dreaded outcome in a patient suffering from acute hyponatraemia[1]. Compared to adults, incidence of hyponatraemia is more frequent in sick hospitalized children[6].

OBJECTIVE

To determine the aetiology and outcome of hyponatraemia and hypernatraemia in children admitted to the paediatric intensive care unit (PICU) of a tertiary care hospital.

METHODOLOGY

This cross-sectional study was carried out in a tertiary care hospital in Chennai, India for a period of fifteen months from March 2012 to June 2013. Institutional ethics approval was obtained before the conduction of the study (CSP-MED/11/Aug/12/03). The research objectives

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were explicated to the children and their caregivers, and they were assured about the confidentiality of the study data. Informed consent is obtained from the caregivers of the children and in addition assent was taken from children more than 12 years of age before the beginning of the study. A primary caregiver is usually a parent, who accompanies the child to every clinic visit. All children of age groups one month to 18 years, admitted to the PICU, who developed hyponatraemia or hypernatraemia on admission or during their period of illness, were included in the study. All children on diuretics and patients requiring PICU care for post-surgical procedures and for minor procedures were excluded.

On admission, once hyponatraemia or hypernatraemia was confirmed, samples were collected and sent for plasma osmolality, urine osmolality and urine sodium for further classification into syndrome of inappropriate anti-diuretic hormone (SIADH) and diabetes insipidus (DI). If hyponatraemia or hypernatraemia developed after admission, samples were taken before any change in patient management. Serum sodium levels were monitored till normalization. All these children were treated according to our PICU protocols.

Hyponatraemia is defined as a serum sodium concentration below 135meq/L. It was graded as:
- 130-134 mEq/L
- 125-129 mEq/L
- <125 mEq/L

Grading was done according to Singhi S, et al[7].

Hypernatraemia is defined as serum sodium concentration above 145meq/L. It was graded as:
- 145-150 mEq/L
- 151-155 mEq/L
- 156-160 mEq/L
- >160 mEq/L

Grading was done according to Darmon M, et al[8].

Serum sodium was measured by the ion-specific electrode technique. The normal range is 135-145meq/L.

Plasma osmolality was measured using an osmometer and its normal range is 270-290osm/kg.
Urine sodium is the measurement of concentration of sodium in urine, expressed as mmol/L.

Urine osmolality is a measure of urine concentration and its normal range is 500-800osm/kg and was measured using an osmometer.

SIADH is defined as serum sodium <135meq/L, plasma osmolality <270osm/kg, urine osmolality >100osm/kg and urine sodium >25mmol/L.

DI is defined as: serum sodium >145meq/L, plasma osmolality >300osm/kg, urine osmolality <300osm/kg, and urine sodium >30mmol/L.

The paediatric Glasgow Coma Scale (GCS) is used to assess the level of consciousness in children. It comprises three tests: eye, verbal and motor responses. All the 3 values and their sum are considered. The lowest possible value is 3 (deep coma or death) whilst the highest value is 15 (fully awake and aware person). In our study we divided the GCS values into 1-5, 6-10, and 11-15 groups and compared it with the sodium values of the children.
Statistical analysis was done with Chi-square tests with SPSS version 17.

RESULTS

In our study period of 15 months in the PICU, 130 patients developed sodium abnormalities of whom 75 had hyponatraemia and 55 had hypernatraemia.

Hyponatraemia (n=75): Of the 75 hyponatraemic patients, 66.7% were male and 33.3% were female with a mean age of 5.4 years and a standard deviation of 4.887. A majority (58.7%) had serum sodium levels in the range of 130–135meq/L and the mean serum sodium level was 128.9meq/L with a standard deviation of 5.163. Acute febrile illness (38.6%) and central nervous system (CNS) disorders (32%) were the most common illness found in these children and 24% of children presented with seizures. GCS for 61 (81.3%) individuals was in the 11-15 range, indicating mild brain injuries. For 6 (8%) patients, GCS value ranged between 1-5 and 8 (10.7%) patients belonged to the 6-10 group. Fourteen (18.7%) patients required mechanical ventilation.

SIADH was present in 22(29.3%) patients of whom10 (13.3%) had GCS values in the 11-15range, 6 (8%) had GCS values in the 6-10 range and 6 (8%) had GCS values in the 1-5 range. In the 53 patients without SIADH, 38 (71.7%)had serum sodium levels in the range of 130–134meq/L with a mean serum sodium of 132.1meq/L. In the 22 patients with SIADH,10 (45.5%) had serum sodium levels in the range of 125-129meq/L with a mean sodium of 127meq/L. This was statistically significant (p=0.000).

When the outcome was correlated with serum sodium levels, death was recorded in 6 patients with 50% of children having a mean serum sodium level of 126.6meq/L. However, in the 69 patients who were alive, 60.9% of children had 132.1meq/L as their mean serum sodium level. This was not statistically significant (p= 0.276). Correlation between SIADH and outcome revealed that patients without SIADH were thriving well. On the contrary, for the 22 patients with SIADH, 16 (72.7%) were alive and 6(27.3%) patients died. This was statistically significant (p = 0.000). In the 75 hyponatraemic patients, duration of stay ranged from 1–70 days with a mean of 10.1 days. Table 1 tabulates the correlation between serum sodium, SIADH and outcome and they are not statistically significant (p =0.527).

Table 1: Correlation of serum sodium, SIADH and outcome

SIADH				Outcome		Total
				Alive	Death	
Yes	Serum sodium (mEq/L)	<125	Count	5	1	6
			% of Total	22.7	4.5	27.3
		125-129	Count	7	3	10
			% of Total	31.8	13.6	45.5
		130-134	Count	4	2	6
			% of Total	18.2	9.1	27.3
	Total		Count	16	6	22
			% of Total	72.7	27.3	100.0
No	Serum sodium (mEq/l)	<125	Count	3	0	3
			% of Total	5.7	0	5.7
		125-129	Count	12	0	12
			% of Total	22.6	0	22.6
		130-134	Count	38	0	38
			% of Total	71.7	0	71.7
	Total		Count	53	0	53
			% of Total	100.0	0	100.0

Hypernatraemia (n=55): In the hypernatraemic group with 55 children, 33 (60%) were males and 22 (40%) were females with a mean age of 5.4 years and a standard deviation of 6.277. The serum

sodium levels ranged from 146–177meq/l with a mean of 151.67meq/l and a standard deviation of 6.137. In the hypernatraemic group, 49.1% of children had serum sodium in the range of 145-150meq/L with a mean sodium of 147meq/L, 44% had CNS disorders and 40% presented with seizures. Among the three subdivisions of GCS, 16 (29.1%) individuals belonged to the 1-5 group, 17 (30.9%) to the 6-10 group and 22 (40%) to the 11-15 group. Thirty-three (60%) patients required mechanical ventilation.

In the hypernatraemic group 18 (32.7%) patients had DI. When correlated with serum sodium levels, 20% of the patients having DI had serum sodium levels in the range of 151-155meq/l with a mean serum sodium level of 153.5meq/L. However, 45.5% of the patients without DI had serum sodium levels in the range of 145-150meq/l with 147meq/L as the mean serum sodium. This was statistically significant (p= 0.001). Further, a low GCS value ranging from 1-5 was noted in 10 (18.2%) children with DI and this was statistically significant (p=0.001).

Outcome, when correlated with serum sodium, revealed that 21 (38.2%) of the individuals who were alive had serum sodium in the range of 145–150 mEq/l with a mean sodium of 147.1meq/L. On the contrary, 12 (21.8%) children who died had serum sodium in the range of 145-155 mEq/l with 150mEq/L as mean sodium. This was not statistically significant (p=0.695). When DI and outcome were compared, equal distribution was seen in children with DI- 16.4% survived and 16.4% died and mortality due to DI was statistically significant (p= 0.017). The duration of hospital stay ranged from 1-68 days with a mean of 13.2 days. Table 2 tabulates the correlation of serum sodium, DI and outcome and it is not statistically significant (p=0.053). The duration of hospital stays between hyponatraemic patients and hypernatraemic patients was statistically not significant with Mann Whitney Test.

Comparison of hyponatraemia and hypernatraemia revealed 29.1% deaths in children with hypernatraemia as opposed to 8% deaths in children with hyponatraemia. About 29.1% of the hypernatraemic patients had GCS values in the range of 1-5. On the contrary, only 8% of the hyponatraemia patients had GCS value in the 1-5 range. Compared to 18.7% of hyponatraemia patients, about 60% of hypernatraemia patients required mechanical ventilation.

Table 2: Correlation of serum sodium, diabetes insipidus and outcome

Outcome				Diabetes Insipidus		Total
				Yes	No	
Alive	Serum sodium (mEq/l)	145-150	Count	1	20	21
			% of Total	2.6	51.3	53.8
		151-155	Count	6	6	12
			% of Total	15.4	15.4	30.8
		156-160	Count	0	4	4
			% of Total	0	10.3	10.3
		>160	Count	2	0	2
			% of Total	5.1	0	5.1
	Total		Count	9	30	39
			% of Total	23.1	76.9	100.0
Death	Serum sodium (mEq/l)	145-150	Count	1	5	6
			% of Total	6.3	31.3	37.5
		151-155	Count	5	1	6
			% of Total	31.3	6.3	37.5
		156-160	Count	2	1	3
			% of Total	12.5	6.3	18.8
		>160	Count	1	0	1
			% of Total	6.3	0	6.3
	Total		Count	9	7	16
			% of Total	56.3	43.8	100.0

Table 3 tabulates the severity analysis for hyponatraemia and hypernatraemia patients in terms of GCS and mechanical ventilation.

Table 3: Severity analysis for hyponatraemia and hypernatraemia in terms of Glasgow Coma Scale and mechanical ventilation

			Group	
			Hyponatremia	Hypernatremia
GCS	1-5	(n)	06	16
		%	8.0	29.1
	6-10	(n)	08	17
		%	10.7	30.9
	11-15	(n)	61	22
		%	81.3	40.0
Total		(n)	75	55
		%	100.0	100.0
Mechanical Ventilation	Yes	(n)	14	33
		%	18.7	60.0
	No	(n)	61	22
		%	81.3	40.0
Total		(n)	75	55
		%	100.0	100.0

Table 3 Severity assessed with GCS and mechanical ventilation show hypernatremia was more severe than hyponatremia and is statistically significant (p value – 0.000).

The spectrum of illness among the patients with hyponatraemia was predominantly acute febrile illness and CNS disorders (Table 4). Again, CNS disorders were principally found in patients with hypernatraemia. Among the hypernatraemic patients with CNS diseases, the most common disorder was acute symptomatic status epilepticus.

Table 4: Systemic distribution of children with hyponatraemia and hypernatraemia

System	Hyponatremia*(n=75)* *n (%)*	Hypernatremia*(n=55)* *n (%)*
CNS	24(32)	24(44)
Respiratory	03(04)	04(07)
Renal	04(05)	02(03.6)
Gastrointestinal	04(05)	07(12.7)
Acute Febrile Illness	29(39)	06(11)
Haemato-oncology	02(02.6)	04 (07.2)
Sepsis/septic shock	04(05)	05(09)
Others	05(06)	03(05.4)

DISCUSSION

The current study identified hypernatraemia to be more severe than hyponatraemia. The study consisted of 1012 sick children seeking emergency care in the PICU, admitted over a period of 15 months. Among these patients 7.4% were reported to be hyponatraemic. The incidence of hospital acquired hyponatraemia varies between 10% and 50% in different studies depending on the definition of hyponatraemia and methodology used[9].Stelfox et al[10]. found ICU acquired hyponatraemia (plasma sodium<133mEq/l) in 11% of patients. Funk et al[4].found hyponatraemia in 17.7% of adult ICU admissions. A prospective study of 727 sick children, by Singhi et al[7] found hyponatraemia in 29.8%. Incidence of hypernatremia was established as 5.4% in our PICU.

The incidence of hypernatraemia was between 6% and 26% and 4% and 10% of adult patients admitted in medical and surgical ICUs respectively, during treatment for their illness[11].In a study by Athvale

et al[12], on hypernatremia in paediatric ICU admissions for a period of one year, the incidence of hypernatremia was 10%[11]. This is similar to study by Subba Rao et al[13]on paediatric ICU admissions. Majority of the hyponatraemic patients in our study had sodium levels in the range of 130-134mEq/l, which is similar to studies by Sachdev A, et al[9], Bibi S, et al[14] and LuuR, et al[15].In hypernatraemic patients, mean serum sodium level was 151.7mEq/l. while Subba Rao et al[13] reported a mean sodium level of 159.8mEq/l.

A spectrum of illnesses leads to the development of both hyponatremia and hypernatremia. The most frequent ones for hyponatraemia noted were acute febrile illness and CNS disorders. Subba Rao,et al[13] identified infectious diseases (27%) as the major cause of hyponatremia in children admitted in PICU. This was akin to studies by Padhi R, et al[16], which concluded that sepsis was the major cause in hyponatraemic children. In a study by Al Naama LM, et al[17].the most common (25.3%) acute CNS disease was meningoencephalitis. In our study, the spectrum of illness with hypernatraemia included predominantly CNS disorders, the commonest of which was acute symptomatic status epilepticus. In a study by Forman S, et al[18], the most common aetiology of hypernatremia in children was dehydration secondary to infection, and overall, 14% had underlying chronic neurological disorder. Subba Rao et al[13] stated that CNS disorders (26.7%) and infections (26.7%) were seen in 15 hypernatraemic children.

Analysis of the severity of the patients in terms of GCS revealed that out of 75 hyponatraemic patients, majority had a GCS value within the 11-15 range. There were no studies comparing the severity of GCS score and hyponatraemia in children. Conversely, for the 55 hypernatraemic patients, GCS values were as follows: 29.1% had 1-5, 30.9% had 6-10, and 40% had 11-15 ranges. A higher GCS value corresponds to less severity as opposed to a lower value signifying an alarming situation that calls for immediate action. The current study revealed that compared to the hyponatremic patients, the hypernatraemic ones were more vulnerable to morbidities. In this regard a study by Stelfox et al[10] reported a mean GCS score of 8 for the hypernatraemic adult patients. Again, studies comparing GCS and hypernatraemia in children were limited and these studies included children with traumatic brain injury with GCS<8[19]. Further, the need for mechanical ventilation was also higher in hypernatraemic patients compared to the hyponatraemic ones. Several studies in children and adults have also indicated the greater requirement for mechanical ventilation in hypernatraemic patients[10,20]. Alharfi et al[19] observed that children with traumatic brain injury with hypernatraemia had reduced ventilator free days.

SIADH is a common cause of hyponatremia. In the current study, about 29.3% of the hyponatremic population had SIADH. This is similar to studies done by Babaliche et al[21], Laczi et al[22], and Panicker et al[23]. When related to plasma sodium levels and outcome, out of 22 patients having SIADH, maximum mortality was recorded for 45.5% of patients having serum sodium values within 125–129mEq/l. Thus, low serum sodium levels with SIADH were all related with mortality due to hyponatraemia.

DI is linked with hypernatraemia. In the current study, out of the 55 hypernatraemic patients, 32.7% had DI. In a study by Dagget et al[24], of 20 hypernatraemic patients with sodium values >150meq/l, 8 patients had intracranial disorders and all 8 had DI. In children and adults, a definitive diagnosis of DI is needed as effective therapy is available[11]. When compared to serum sodium levels and outcome, death was recorded for 31.3% of the patients having DI and serum sodium levels in the range of 151-155 mEq/l. Mortality rates of 69–86% have been reported in both children and adults with central DI after traumatic brain injury. The increased mortality in these studies can be due to inclusion criteria of having children with traumatic brain injury[25,26].

Overall comparison of the hyponatraemic patients and hypernatraemic patients revealed increased severity for the hypernatraemic patients compared to the hyponatraemic ones. Mortality was higher in hypernatraemic patients. Severity assessed with GCS and mechanical ventilation also identified the hypernatraemic patients to be more critical and sicker than hyponatraemic ones. The observed results were statistically significant. There is a need for appropriate random trials for general acceptance of the results. The data is limited by the size of the sample population. To get a global view, a large-scale study is required to be conducted.

CONCLUSION

The current study reported a significantly higher mortality rate in hypernatraemic patients (29.1%) compared to hyponatraemic patients (8%). SIADH was noted in 29.3% of hyponatraemic patients whilst 32.7% of hypernatraemic patients had DI. Severity analysis with GCS and mechanical ventilation revealed that hypernatraemic patients were significantly sicker than hyponatraemic patients.

Authorship Contribution: Dr. Krithika Prabaharan: involved in conceptualization, methodology, data curation and formal analysis of the study. Dr. Shuba Sankaranarayanan: involved in conceptualization, methodology, supervision and writing – Original draft of the study. Dr. Vinoth N Ponnurangam: involved in formal analysis, writing – review and editing of the study.

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Competing Interest: None.

Sponsorship: None.

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Informed Consent: Informed consent is obtained from the caregivers of the children and in addition assent was taken from children more than 12 years of age before the beginning of the study.

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