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Determinants of Serum Sodium Status in Critically Ill Pediatrics Patients

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ABSTRACT

INTRODUCTION- Hyponatremia is common occurrence in hospitalized Sick children. Presence of hyponatremia generally indicates a serious illness and poor outcome in sick children attending emergency services. Hyponatremia can eventually lead to seizure and death depending magnitude and severity of onset. Management of hyponatremia mainly depends on the duration of hyponatremia and volume status of the patients. There is serious neurologic sequel if hyponatremia is inappropriately treated.

MATERIAL AND METHODS- The Present retrospective observational study was conducted in the Pediatric ICU ward of Department of Pediatrics at Dr. B.R.A.M. Hospital associated Pt. J.N.M. Medical College, Raipur (C.G.), India during study period from April 2015 to September2015. The study was carried out hyponatremia in children between the age group of >1 months to 13 years presenting with critically illness need mechanical ventilation admitted in ICU were included in the study. Sample size was fixed at 84. The patient's clinical data were recorded in all the cases. Investigations were done on the day of admission in who were clinically critically ill and had an initial serum sodium value <135mEq/L.

OBSERVATIONS- Study subjects were also divided into groups based on whether hyponatremia (Group I), Nonrmonatremia (Group II) or Hypernatremia (Group III) was noted in them. Three groups were found to be age matched. It was noted that no significant difference existed between groups in terms of fluid administered when compared to other fluids administered. Significantly higher frequency (41.81 %) of MODS (Multiorgan dysfunction syndrome) was noted in subjects with hyponatremia compared to other two groups. Also significantly difference distribution of systems involved was noted in study groups when all systems were compared.

CONCLUSION-We can conclude from findings of this study that hyponatremia is a common finding in critically sick patients; it is more common in infants and patients with MODS (Multiorgan dysfunction syndrome) & Meningoencephalitis.

KEYWORDS Hyponatremia, Critically ill, Children

INTRODUCTION-

Hyponatremia, a very common electrolyte abnormality in hospitalized patients, is a serum sodium level <135 mEq/L. Development of hyponatremia in critically ill patients is associated with positive balance of electrolyte free fluid either through the administration or disturbances in renal mechanisms of urinary dilution. Both total body sodium and total Body Water determine the serum sodium concentration. Hyponatremia is common occurrence in hospitalized Sick children[1, 2]. The common causes are acute diarrhea, acute infectious disease, like (pneumonia, meningitis, septicemia) heart failure, renal disease, and hepatic failure. Presence of hyponatremia generally indicates a serious illness and is associated with poor outcome in sick children attending emergency services[2].

Acute hyponatremia occurs when serum sodium fails rapidly, in less than 48 hrs. The brain does have not the opportunity to adjust to the change, and brain stem herniation may occur. Chronic hyponatremia occurs when serum sodium falls slowly over 48 hrs. In this case, the brain will compensate by extruding the solutes into the ECF compartment. Hence a patient with chronic hyponatremia will be less symptomatic than acutely hyponatremic patient with the same serum sodium level.

Hyponatremia causes a decrease in the osmolality of the extracellular space. Because the intracellular space then has a higher osmolality, water moves from the extracellular space to the intracellular space to maintain osmotic equilibrium. The increase in intracellular water causes cells to swell. Although cell swelling is not problematic in most tissues, it is dangerous for the brain, which is confined by the skull. As brain cells swell, there is an increase in intracranial pressure, which impairs cerebral blood flow. Acute, severe hyponatremia can cause brainstem herniation and apnea; respiratory support is often necessary. Brain cell swelling is responsible for most of the symptoms of hyponatremia. Neurologic symptoms of hyponatremia include anorexia, nausea, emesis, malaise, lethargy, confusion, agitation, headache, seizures, coma, and decreased reflexes. Patients may have hypothermia and Cheyne-Stokes respirations[3]. Hyponatremia can cause muscle cramps and weakness; rhabdomyolysis can occur with water intoxication. The symptoms of hyponatremia are mostly a result of the decrease in extracellular osmolality and the resulting movement of water down its osmotic gradient into the intracellular space. Brain swelling can be significantly obviated if the hyponatremia develops gradually, because brain cells adapt to the decreased extracellular osmolality by reducing intracellular osmolality. This reduction is achieved by extrusion of the main intracellular ions (potassium and chloride) and a variety of small organic molecules. This process explains why the range of symptoms in hyponatremia is related to both the serum sodium level and its rate of decrease. A patient with chronic hyponatremia may have only subtle neurologic abnormalities with a serum sodium level of 110 mEq/L, but another patient may have seizures because of an acute decline in serum sodium level from 140 to 125 mEq/L. [4, 5, 6]

Management of hyponatremia mainly depends on the duration of hyponatremia and volume status of the patients. Removal of non osmotic stimuli for vasopressin secretion, judicious use of hypertonic saline and close monitoring of plasma and urine electrolytes are essential components of management. There are scarcities of data available on whether the presence of hyponatremia in intensive care unit (ICU) admission is independently associated with excess mortality. The present study was conducted to assess the distribution of hyponatremia in critically ill mechanically ventilated children and its association with other factors in critically ill patients admitted to the ICU with hyponatremia especially the use of hypotonic or isotonic intravenous fluids.

MATERIAL AND METHODS

The Present retrospective observational study was conducted in the Pediatric ICU ward of Department of Pediatrics at Dr. B.R.A.M. Hospital associated Pt. J.N.M. Medical College, Raipur (C.G.), India during study period from April 2015 to September2015. Ethical clearance was taken from institutional ethics committee.

INCLUSIONCRITERIA –

- All critically ill who were mechanically ventilated child.
- Age more than 1 month to 13 yrs.

EXCLUSION CRITERIA-

- Age less than 1 month & more than 13 yrs.

The study was carried out hyponatremia in children between the age group of >1 months to 13 years presenting with critically illness need mechanical ventilation admitted in ICU were included in the study.

Calculation of Sample Size

It is calculated using formula- 4PQ/L2, where –

P= prevalence of hyponatremia

Q= 1-P, L= Level of error, Confidence level=95% .Taking P=23%, L=5%, we see that minimum sample size =283. We have taken 33% that is 84.Sample size exceeded the sample size calculated for power of the study 0.8, α error to be 0.05 and population mean as seen in previous study.[7]

Predesigned proforma was used for the study. At the time of admission, one venous blood samples were collected & used for the estimation of serum sodium. The patient's clinical data including age, sex diagnosis were recorded in all the cases. Serum sodium concentration <135mEq/L was considered as hyponatraemia. Serum sodium concentrations of 131-134mEq/L represent mild hyponatremia, 126-130mEq/L moderate hyponatremia and ≤125mEq/L severe hyponatremia. Hypernatremia was defined as a serum sodium concentration >145mEq/L.

Investigations were done on the day of admission in who were clinically critically ill and had an initial serum sodium value <135mEq/L, data were analyzed in between age group <1 yr &>1 yr, natremic status hypo, normo and hypernatremia. Results were analyzed by using appropriate statistical methods.

Data was expressed as mean ± S.D. and percentage depending on distribution of data and as percentage. Kolmogorove-Smirnov analysis was used to check if data follows the normal distribution. Fischer exact test or Chi-square test was used to check the significance of difference between frequency distribution of data in different groups. ANOVA followed by post hoc Tukey's HSD test was used to study significance of difference between more than two groups in case of parametric data. p Value < 0.05 was considered to be statistically significant.

OBSERVATIONS-

Table 1: Comparison of age between study groups

Characteristics	Group I Hyponatremia N=55	Group II Normonatremia N=22	Group III Hypernatremia N=7	p Value
Age (in Years) (Mean ± S.D.)	3.6 ± 4.1	4.8 ± 4.6	4.6 ± 3.5	>0.05

Study subjects were also divided into groups based on whether hyponatremia (Group I), Nonrmonatremia (Group II) or Hypernatremia (Group III) was noted in them. Three groups were found to be age matched. **[Table-1]**

Table 2: Comparison of sex distribution between study groups

Characteristics Hyponatremia N=55		Group I Normonatremia N=22	Group II Hypernatremia N=7	Group III	p Value
Sex	Male	35	10	3	>0.05
	Female	20	12	4	

These three study groups were also found to be matched for frequency of sex distribution. **[Table-2]**

Table 3: Comparison between fluids administered in study groups

Characteristics Hyponatremia N=55		Group I Normo-natremia N=22	Group II Hypernatremia N=7	Group III	p Value*	p Value
Fluid Administered	DNS	32 (58.18)	15 (68.1)	6 (85.8)	0.3	>0.05
	ISO-P	10 (18.18)	2 (9.09)	1 (14.2)	0.7	
	N/5	7 (12.7)	0 (0)	0 (0)	0.2	
	Others	8 (14.5)	5 (22.7)	0 (0)	0.4	

*Vs subjects in which other fluids were administered

Distribution of fluids administered in study groups was studied. It was noted that no significant difference existed between groups in terms of fluid administered when compared to other fluids administered, neither the difference was noted when distribution of all fluids administered was studied in study groups. **[Table-3]**

Table 4: Comparison between systems involved in study groups

Characteristics Hyponatremia N=55		Group I Normonatremia N=22	Group II Hypernatremia N=7	Group III	p Value	P Value
Systems involved	CNS	14 (25.4)	9 (40.1)	3 (42.8)	0.4	<0.05
	Hepatobiliary	5 (9.09)	0 (0)	0 (0)	0.4	
	MODS(-Multiorgan dysfunction syndrome)	23 (41.81)	2 (9.09)	1(14.2)	0.01	
	Respiratory	5 (9.09)	5 (22.7)	1 (14.2)	0.2	
	Others	8 (14.5)	6 (27.3)	2 (28.4)	0.2	

Various systems involved were assessed in different study groups. No significant difference was noted in distribution of systems involved between study groups in CNS (p=0.4), Hepatobilliary (p=0.4), respiratory (p=0.2) or others (p=0.2) when compared with distribution of other systems involved.

Significantly higher frequency (41.81 %) of MODS (Multiorgan dysfunction syndrome) was noted in subjects with hyponatremia compared to other two groups (9.09 % and 14.2 %) (p=0.01). Also significantly difference distribution of systems involved was noted in study groups when all systems were compared. **[Table-4]**

Table 5: Comparison between hrs of stay in study groups

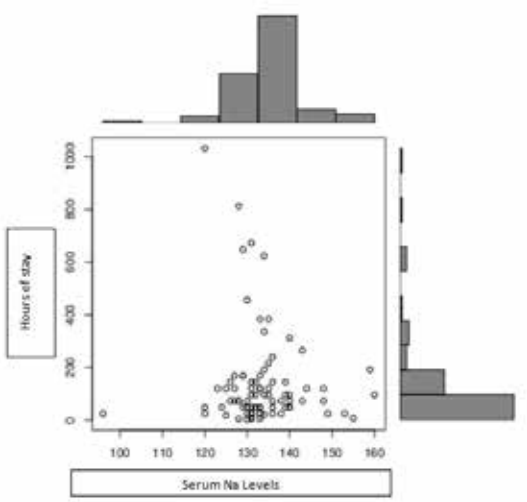
Characteristics	Group I Hyponatremia N=55	Group II Normonatremia N=22	Group III Hypernatremia N=7	p Value
Hours of stay (Mean ± S.D.)	151.7 ± 218.07	125.5 ± 97.9	76.6 ± 65.6	>0.05

Table 6: Comparison between hrs of stay in study groups

Characteristics Hyponatremia N=55		Group I Normonatremia N=22	Group II Hypernatremia N=7	Group III	P Value
Hrs Of stay	<24	16	2	3	>0.05
	25-48	9	4	0	
	49-72	5	4	1	
	73-96	3	3	1	
	>96	22	9	2	

No significant difference was noted in hours of stay in study groups. [Table-5, 6]

Fig 1: Pearson's correlation analysis between Hours of stay and serum Na levels



Pearson's r: -0.105, p value: 0.3

Pearson's correlation analysis was performed to assess association between serum Na levels and hours of hospital stay, very weak negative correlation was found to exist between two parameters (Pearson's r: -0.105, p Value: 0.3). **[Figure-1]**

DISCUSSION-

In the current study, subjects were divided into groups based on whether hyponatremia (Group I), Norma anthemia (Group II) or Hypernatremia (Group III) was noted in them. Three groups were found to be age matched and Sex matched. Hyponatremia is a very common finding in critically ill patients even before administration of IV Fluids. Although it may be contributed by dilution due to SIADH and sustained by natriuresis. But, as suggested by Singhi et al. translocation and redistribution can also be possible mechanisms.[8]

In the present study the fluid administered prior to admission was studied. It was noted that no significant difference existed between groups in terms of fluid administered when compared to other fluids administered , Neither the difference was noted when distribution of all fluids administered was studied in study groups.. A study by Singhi S also suggests that there are many other mechanisms of hyponatremia in critically sick patients as well other than use of hypotonic fluid.[8]

Choong et al[9(2011)] conducted a randomized, controlled trial comparing isotonic (NS) with hypotonic (½NS) parenteral maintenance fluid for 48 hours in postoperative pediatric patients who underwent elective surgery. Children ages 6 months to 14 years were randomized to receive either hypotonic or isotonic saline IV fluids. Fifty-three patients (40.8%) in the hypotonic saline group and 29 patients (22.7%) in the isotonic saline group developed hyponatremia ($p<0.01$) the risk of hyponatremia was greater with hypotonic IV fluids than with isotonic IV fluids. However, the risk of hypernatremia was not significantly different between the two groups. The authors concluded that an isotonic IV fluid is a safer empirical choice than hypotonic IV fluids in protecting against acute postoperative hyponatremia in children. Baseline Na^+ concentrations were not obtained in all patients to determine whether patients developed hyponatremia from IV fluids.

Au et al[10(2008)] performed a retrospective observational study of postoperative patients ages 42 days to 23 years old admitted to the PICU. The authors reviewed the incidence of hyponatremia in children receiving isotonic (RL or NS) or hypotonic. The authors concluded there was a trend toward increased incidence of hyponatremia in patients receiving hypotonic IV fluids, but this study lacked the power necessary to determine the exact cause of hyponatremia.

Fluid management in the pediatric critical care population is especially complex as many patients require multiple continuous infusions and excess fluid volume due to hypovolemic shock or blood pressure instability. The choice of IV fluids and rate are very important in preventing dysnatremia in the pediatric critical care population.

Rey et al[11(2011)] studied the effects of hypotonic and isotonic IV fluids on the incidence of dysnatremia in critically ill children. One hundred twenty-five patients were randomized to either a hypotonic saline group or an isotonic saline group No differences were found in the incidence of dysnatremia when surgical and nonsurgical patients were compared or in patients who were on mechanical ventilation and those who were not ventilated. The authors concluded that hypotonic IV fluids increased the incidence of hyponatremia by 5.8-fold.

Montañana et al[12(2008)] randomized 122 patients admitted to the pediatric intensive care unit (PICU) to receive either isotonic (NaCl = 140 mEq/L) or hypotonic (NaCl <100 mEq/L) IV fluids. The primary endpoint was the percentage of patients who were hyponatremic at 6 and 24 hours after fluid therapy. The authors concluded that isotonic IV fluids prevent iatrogenic hyponatremia in PICU patients.

Various systems involved were assessed in different study groups. Significantly higher frequency (41.81 %) of MODS was noted in subjects with hyponatremia compared to other two groups (9.09 % and 14.2 %) ($p<0.01$). Multi organ dysfunction is more frequent than death in pediatric Intensive Care Unit, and it has been a consistent observation that mortality correlates with the number of failing organ systems and the degree of dysfunction within any given organ system.[13]

F Shann and S Germer in prospective study found 46% children were hyponatremic in patients with pneumonia & meningitis.[14] Guruswamy N T et al (2014) also found similar frequency of hyponatremia that is 46% in children presenting with acute respiratory tract infection in their prospective study.[15] In our study also meningitis was associated with hyponatremia in 25.4% cases.

In the present study, no significant difference was noted in hours of stay in study groups, but on Pearson's correlation analysis was performed to assess association between serum Na levels and hours of hospital stay, very weak negative correlation was found to exist between two parameters (Pearson's r: -0.105, p-value: 0.3).

CONCLUSION-

We can conclude from findings of this study that hyponatremia is a common finding in critically sick patients; it is more

common in infants and patients with MODS (Multiorgan dysfunction syndrome) & Meningoencephalitis. A regular check on the electrolyte levels has to be done and the type and rate of intravenous fluids should be individualized for each patient.

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Conflict of interest:
None declared

Ethical approval:
The study was approved by the institutional ethics committee

BIBILIOGRAPHY

1. Arieff AI, Defronzo RA. In: Fluids, Electrolytes and Acid-base Disorders.Churchil l Livingstone, New York, 1994 second edition, 1995.
2. Prasad SVSS, Singhi S, Chugh KS. Hyponatremia in Sick children seeking emergency care. Indian Pediatri 1994; 31:287-294
3. Nelson's text book of paediatrics, 20th edition, South-Asian edition.
4. Sterns RH, Silver SM, Spital A.Hyponatremia .in: Seilden DW, Giebish G,eds. The Kidney: Physiology and Pathophysiology. Philadelphia: Lipincott Williams & Wikins; 2000.p. 1117-1138
5. Singhi S, M Jayashree Free water excess is not the main cause of hyponatremia in Critically Ill Patients Receiving Conventional Maintenance fluids: Indian Pediatr;2009; 46:577-583
6. Fenk GC, Linder G, Druml W, et al. Incidence and Prognosis of dysnatremia present on ICU admission. Intensive care Med. 2010; 36:304-311
7. http://www.surveysystem.com/sample-size-formula.html
8. Singhi S ,Marudkar A: Hyponatremia in a Pediatric Intensive Care Unit. Indian Pediatr,1996
9. Choong K, Arora S, Cheng J. Hypotonic versus isotonic maintenance fluids after surgery for children: a randomized controlled trial. *Pediatrics*. 2011;125(5):857–866. et al. [PubMed]
10. Au AK, Ray PE, McBryde KD. Incidence of postoperative hyponatremia and complications in critically ill children treated with hypotonic and normotonic solutions. *J Pediatr*. 2008;(1):152, 33–38. et al. [PubMed]
11. Rey C, Los-Arcos M, Hernandez A. Hypotonic versus isotonic maintenance fluids in critically ill children: a multicenter prospective randomized study. *Acta Paediatr*. 2011;100(8):1138–1143. et al.[PubMed]
12. Montañana PA, Alapont VM, Ocon AP. The use of isotonic fluid as maintenance therapy prevents iatrogenic hyponatremia in pediatrics: a randomized, controlled open study. *Pediatr Crit Care Med*.2008;9(6):589–597. et al.
13. Thukral A, Kohil V, Lodha R; et al. Validation Of PELOD score for Multi Organ Dysfunction in Children . Indian Pediatr 2007: 44 . 683-686
14. F Shann and S Germer. Hyponatraemia associated with pneumonia or bacterial meningitis. Archives of Disease in Childhood, 1985, 60, 963-966
15. Guruswamy N T et al. "Correlation of hyponatremia in children presenting with acute lower respiratory tract infection in a tertiary care hospital".