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Original Article

Paediatrics Section

Hyponatremia in Children Hospitalised with Community-acquired Pneumonia: A Prospective Observational Study

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ABSTRACT

Introduction: Community-acquired Pneumonia (CAP) is a common cause of mortality and morbidity among the under-5 years age population. Hyponatremia (HN) is common in patients with CAP, it is usually asymptomatic but it is associated with severe disease and poor outcome. Its monitoring and early identification can guide proper fluid therapy in patients with CAP.

Aim: To evaluate the occurrence of Hyponatremia (HN) in paediatric patients with CAP and to analyse its association with severity of pneumonia.

Materials and Methods: This prospective observational study was conducted in MGM Medical College and Hospital Aurangabad, India, over a period of 2 years. Serum sodium concentration was measured in 76 hospitalised children with clinically and radiologically confirmed CAP. Those with hyponatremia were identified. Statistical analysis was done by chi-square test for categorical variables and t-test for continuous variables to study the relationship of hyponatremia with various clinical parameters and inflammatory markers.

Results: Out of 76 patients, 41(54%) had hyponatremia on the day of admission. In the majority of patients (38.2%), HN was mild (mild HN 131-134 mEq/L moderate HN 126-130 mEq/L, severe HN less than 125 mEq/L). None of the patients had neurological symptoms due to HN. On admission, hyponatremic patients had higher white blood cell count (40 vs. 28 p 0.013), neutrophil count (38 vs. 25 p 0.014) and serum C-reactive protein (39 vs. 28 p 0.032) than normonatremic ones. No association was found with the type of intravenous fluid (0.45% DNS or Isolyte P) used and hyponatremia (P 0.6471).

Conclusion: It can be concluded that hyponatremia is common in CAP and it is associated with the disease severity.

Keywords: Electrolyte disturbances, Hypernatremia, IV fluid therapy

INTRODUCTION

Community-acquired pneumonia accounts for nearly one-fifth of childhood deaths worldwide [1]. Hyponatremia (HN) is one of the most common electrolyte disturbances, presenting in approximately 20-50% of patients with pneumonia [2-5]. It may be asymptomatic or it can cause serious neurological problems like seizures, encephalopathy, coma or even death [6-9]. HN is easy to diagnose but its etiology is usually difficult to find [2,3].

HN may result from Syndrome of Inappropriate Secretion of Antidiuretic Hormone (SIADH); cerebral salt wasting or it may be iatrogenic due to use of hypotonic maintenance fluids [2-4,10]. Serum osmolality may be low, normal or high in the case of HN [2]. SIADH is one of the most important causes of HN with hypo-osmolality [4,6,11]. It is usually caused by respiratory, CNS diseases or drugs. In children, pulmonary disorders that may cause SIADH includes infections (e.g. pneumonia, empyema, abscess), asthma, cystic fibrosis and positive-pressure ventilation [2-5,10]. On the other hand, hyperglycemia causes HN with elevated serum osmolality [11,12], It can cause hyponatremia in patients with severe CAP. Symptomatic hyponatremia has been reported with the use of hypotonic maintenance fluid [13,14]. It has been proposed that isotonic maintains fluids may reduce incidence and complications associated with hyponatremia in various studies [15-21].

Association between pneumonia and hyponatremia was first described in 1962 by Stormont and Waterhouse [22], the studies done in the last 2 decades, there are wide variations in its incidence. HN was seen in 8% to 45% of children hospitalised due to pneumonia [2,23-27]. In most cases, HN found in CAP is mild (Don M et al., Sakellaropoulou A et al.,) [2,28]. It has been studied that HN is related to severity of pneumonia measured with serum inflammatory markers [2,28], higher body temperature on admission [2], longer duration of hospital stay, frequency of complications and mortality [2,23,28]. Any correlation between HN and type of radiological consolidation or etiology of CAP has not been found by Don M et al., but in the study done by Park SW et al., they found incidence of hyponatremia differs according to infecting microorganism and radiological findings [29].

There are wide variations in the occurrence of HN in patients with pneumonia as per the above studies. So the need was felt to have data from the region of Marwathwada in Maharashtra state of India on this topic as it has the potential for neurologic injury and complications.

MATERIALS AND METHODS

This prospective observational study was conducted at the Department of Paediatrics MGM Medical College and Hospital Aurangabad (MS), India over a period of two years from Nov 2016 to Oct. 2018. The protocol was approved by the Ethics Committee (Letter No. MGM-ECRHS/2016/30; dated 25.11.2016). Informed consent was obtained from the parents of all children.

In all, 76 hospitalised children (2-59 months age group) for presumed CAP were eligible for the study. The sample size was estimated using Open Epi as 72 at 80% confidence interval and anticipated frequency of HN 15% in average of 500 patients of CAP per year in this hospital.

Pneumonia was diagnosed and classified as per 2014 revised WHO criteria [1]. Patients showing signs and/or symptoms compatible with respiratory infection with or without radiological infiltrations consistent with pneumonia i.e., dense, fluffy consolidation of entire lung or portion of a lobe; often with air bronchograms and possibly pleural effusion [1] were included. Newborns, children presenting with symptoms suggestive of asthma, and those with chronic underlying illness or hospital-acquired pneumonia were excluded, also patients with diabetes insipidus or Diabetes mellitus, on peritoneal dialysis and patients with CNS infections were excluded.

Socio-demographic data and clinical characteristics of each patient were noted. On admission using aseptic technique, 2 mL of blood from cubital region was collected. The blood samples were then tested for complete blood cell count, C-reactive Protein (CRP), serum concentrations of sodium (Na).

All children were again screened for hyponatremia on day 3 and on day of discharge. Other investigations were done whenever required.

Study Definitions

Serum sodium level less than 135 mEq/L on day 1 was taken as hyponatremia [1-3,9]. The severity of hyponatremia was classified as mild (131 to 134) moderate (126 to 130) severe (125 and less) [9], whereas hypernatremia was defined as a serum sodium concentration >145 mEq/L [1,2]. Reference values for other hematological parameters were as follows:

Platelet count- normal (1.5 lac/cmm to 5 lac/cmm)

Thrombocytopenia <1.5 lac/cmm

Thrombocytosis >5 lac/cmm

WBC count- normal 6000-1500/cmm,

High >50000/cmm

Neutrophil- normal 40-60%

High >60%

CRP- Normal less than 6 mg per dL.

High more than 6 mg/L

The severity of pneumonia was classified as per revised WHO classification [1], it includes only two categories of pneumonia; "pneumonia" with fast breathing and/or chest in drawing, and "severe pneumonia", pneumonia with any general danger sign, like not able to drink, persistent vomiting, convulsions, lethargic or unconscious, stridor in a calm child or severe malnutrition.

STATISTICAL ANALYSIS

The data entry and results analysis was done with the Microsoft Excel Version 2013. All the relevant categorical variables were compared with the chi-square test. For continuous variables t-test, paired t-test was used when applicable. Significance was set at <0.05. Statistical analysis was performed by using SPSS software.

RESULTS

Baseline characteristics of all the children are shown in [Table/Fig-1]. The mean age was 2.74±1.23 years with 55 (72%) males and 21 (28%) females.

Clinical parameter	No. of cases	Percentage
Respiratory distress	71	93
Shock	11	14.5
Ventilator required	3	3.9
Pneumonia	50	76
Severe pneumonia	26	34

[Table/Fig-1]: Baseline characteristics of 76 children with community-acquired pneumonia. Data are presented as numbers and percentage.

Out of 76 patients, 41 (54%) had HN on the day of admission. It was mild in 29 (70.7%), moderate in 09 (21.9%) and severe in 03 (7.3%) cases [Table/Fig-2].

Serum sodium level (mEq/L)	No. of patients	Percentage
Normal (135-145 mEq/L)	35	46.0%
Mild HN (131-134 mEq/L)	29	38.2%
Moderate HN (126-130 mEq/L)	09	11.8%
Severe HN (<125 mEq/L)	03	3.9%
Total	76	100%

[Table/Fig-2]: Serum Sodium levels at the time of admission.

The mean sodium level at admission was 134.21 mEq/L with a standard deviation of 4.46. The mean sodium level at day 3 was 135.17 mEq/L with a standard deviation of 4.55 and the mean sodium level at discharge was 136.92 mEq/L with a standard deviation of 4.20. No patient had hypernatremia.

As seen in [Table/Fig-3,4], a significant association was found between the presence of HN and elevated levels of CRP, WBC count and neutrophil levels. Children with or without HN did not differ in age, gender, presence of shock.

Lab parameters	Number of cases	Percentage
WBC (≥15,000/uL)	26	89.5
Neutrophillia (>60%)	63	82.8
Thrombocytosis (>500000/cmm)	17	22.4
Thrombocytopenia (<150000/cmm)		
CRP (>6 mg/lit)	67	88.2

[Table/Fig-3]: Laboratory parameters of 76 children with community-acquired pneumonia. Data are presented numbers and percentage.

Variable		With hyponatremia (N=41)	With normonatremia (N=35)	p-value
Gender	Male	30	25	0.868
	Female	11	10	
Mechanical ventilation (No. of cases)	Yes	3	0	0.012
	No	38	35	
Pneumonia severity	Pneumonia	21	29	0.004
	Severe pneumonia	20	6	
C-reactive protein (mg/L)	Normal (0-6 mg/l)	2	7	0.032
	Increased (>6 mg/l)	39	28	
Platelet count (nummber/cmm)	Normal	33	19	0.024
	Thrombocytopenia (<150000/cmm)	1	6	
	Thrombocytosis (>500000/cmm)	7	10	
WBC (number/cmm)	Normal (6000-15000/cmm)	1	7	0.013
	Increased (>15000/cmm)	40	28	
Neutrophil (%)	Normal (40-60%)	3	10	0.014
	Increased (>60%)	38	25	
Length of hospital stay (days)	<5	2	11	0.005
	5-10	34	23	
	>10	5	1	

[Table/Fig-4]: Characteristics of 76 children with hyponatremia vs. children with normal levels of serum sodium on admission. Data are presented number of cases with abnormal value.

No correlation was found between the type of maintenance fluid used and serum sodium concentrations. The analyses was continued by dividing the children into two groups: those on 0.45% DNS (17 cases) and those on ISOLYTE P (59 cases) as maintenance fluid. Out of total 41 HN cases the number of patients with HN in 0.45% DNS group was 10 vs. 31 in patients on ISOLYTE P maintenance fluid and this difference was not statistically significant (p=0.6471).

The length of hospital stay was categorised into 3 groups as less than 5 days, 5-10 days and more than 10 days. In normonatremic group (total 35 patients) 11 children required admission for less than 5 days, 23 were admitted for 5-10 days and one patient was in the hospital for more than 10 days. In the HN group (total 41 patients) distribution in the above 3 categories were two patients, 34 patients, and five patients respectively. This difference was statistically significant (p<0.05) showing CAP with HN required more days of hospitalisation as compared to CAP without HN [Table/Fig-4].

Out of 76 patients, 50 (65.8%) patients had non-severe pneumonia and 26 (34.2%) patients had severe pneumonia. in non-severe pneumonia group, 21 were hyponatremic and 29 were normonatremic. In severe pneumonia group, 20 had HN and 6 had normal sodium concentration. The association between severe pneumonia and hyponatremia was statistically significant (p=0.003758) as shown in [Table/Fig-4].

DISCUSSION

The study found HN to be common among CAP children, though it was mild in severity (131-134 mEq/L).

The frequency of HN was 54% (41 cases). It was higher than 27-45% found in earlier studies [2,23,25,27,28]. The low prevalence of HN (8%) reported by Zilberberg MD et al., was due to use of more stringent definition which required second serum sodium measurement within 24 hours of admission for inclusion in study [26]. In a recent study by Park SW et al., on a large cohort of 3938 cases, HN was found in 13.5% of patients with respiratory infection [29]. They also demonstrated the degree of HN varies with microorganisms causing respiratory infection, anatomical site of infection and radiological finding. This may account for differences in the prevalence of HN in the different studies.

In the present study 70% of them had mild HN (serum sodium 131-134 mEq/L), 21.9% had moderate and 7.3% had severe HN. In previous studies the prevalence of mild forms of HN was 92%-96% which reflects a very low proportion of moderate to severe HN [2, 28,27]. The index study findings are close to the study done by Singhi S and Dhawan A, in which the percentage of moderate and severe HN was higher i.e., 27%, 4.5% and that of mild HN was 68.5% [23]. The higher percentage of moderate and severe HN in this study may be due to more number of severe pneumonia cases (34%) in comparison to previous studies like Nair V et al., in which 14% had severe pneumonia [Table/Fig-5] [25].

Study	Frequency of HN (%)	Mild HN (%)	HN and severity of pneumonia (p-value)	HN and CRP (p-value)	HN and WBC count (p-value)	HN and length of hospital stay (p-value)
Singhi S and Dhawan A, [23]	27	68.5	–	–	–	<0.05
Nair V et al., [25]	28	–	0.05		<0.0001	
Wrotek A and Jackowska T, [27]	33.3	96		< 0.01	0.02	0.01
Ziberberg MD et al., [26]	8	–	<0.001	–	–	<0.07
Don M et al., [2]	45.4	92	–	0.014	0.008	–
Park SW et al., [29]	13.5	–	–	0.0001	0.037	0.02
Present study	54	70	0.004	0.032	0.013	0.014

[Table/Fig-5]: Showing comparison of present study with previous studies [2,23,25-27,29].

Among the laboratory parameters studied in present study like CRP value, WBC Count, Neutrophil count, which is surrogate markers of severity of illness, they were on the higher side in the majority of pneumonia patients. In present study Hyponatremia was significantly associated with increased neutrophil count (p=0.014), total leukocyte count (p=0.013), increased platelet count (p=0.024) and raised C-reactive protein levels (p<0.032) of patients. Similar findings were also noted by Don M et al., and Nair V et al., as seen in [Table/Fig-5] [2,25].

It has been noted in previous studies [2,26] that CAP patients with HN had more severe disease, longer hospital stay, complications and higher mortality rates than in those patients without HN.

In the present study, all the children (3 children) who required mechanical ventilation were found to be hyponatremic, indicating that hyponatremia is associated with the requirement of mechanical ventilation (p=0.012) and prolonged hospital stay (p=0.005).

Nair V et al., also found hyponatremia to be associated with more severe illness and extended hospital stays [25]. Crude length of hospital stay was increased by 2.3 days in the hyponatremic group (8.7 vs. 6.4 days <0.0001) as compared to the normonatremic group. Similar findings were observed by Don M et al., and Wrotek A and Jackowska T, [2,27]. In this study, patients were divided in 3 groups as per the duration of hospital stay, CAP patients with hyponatremic required significantly longer hospital stay than normonatremic patients (p<0.005) as seen in [Table/Fig-5].

It is important to highlight that hyponatremia was associated not only with a longer duration of hospitalisation but also with increased mortality. Nair V et al., found that hospital mortality was significantly greater among patients admitted with hyponatremia (9.5 vs. 3.4%, p=0.05) and the presence of hyponatremia was associated with a 7% increased risk of death (p=0.03) [25].

According to Singhi S and Dhawan A there is a correlation between HN and a higher rate of complications, higher mortality, and longer duration of hospitalisation [23]. However, in that study, only patients with moderate-to-severe HN were analysed, so the groups are different. In the present study, one patient (2.4%) in HN group died but not in the normonatremic group but because of a small number of patients who had complications and unfavorable outcome, statistical significance concerning the association of HN with mortality could not be established.

None of the patients developed neurological complications due to hyponatremia or features of dehydration or over-hydration. In previous studies done by Nair V et al., Don M et al., Wrotek A and Jackowska T, [2,25,27] they noted hyponatremia to be commonly associated with CAP but it was asymptomatic and none of their patient developed neurological problems associated with HN.

LIMITATION

Serum osmolarity was not calculated; comparison of serum sodium with serum osmolarity would have given a clue to the etiology of HN. Blood glucose levels were not monitored, it would have helped in knowing the proportion of hyponatremic patients caused by hyperglycemia. Although the type of maintenance fluid given to patients was documented, the total amount received per day was not noted, it is needed to analyse the contribution of hypotonic intravenous fluids in the causation of HN. Study design could not ascertain the cause and effect relationship of severity of pneumonia and hyponatremia.

CONCLUSION

The results confirm that mild HN is common in children with CAP and that the degree of HN is associated with the severity of CAP. Thus, serum electrolytes should be monitored in children hospitalised for pneumonia.

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