

Original Article

Hyponatremia of children of two months to five years of age with community-acquired pneumonia and its correlation with severity of illness and its outcome.

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ABSTRACT

Background: Pneumonia is an acute respiratory infection of the lungs where alveoli become inflamed and are filled with pus and fluid, leading to impaired oxygen exchange, respiratory distress, and painful breathing. Community-acquired pneumonia (CAP) remains the leading single cause of mortality in the pediatric age group worldwide. This study aims to study hyponatremia in community-acquired pneumonia among children of 2 months to 5 years of age and its correlation with severity of illness, course, outcome and length of stay in hospital. **Material and Methods:** This was a prospective observational study conducted in the pediatric inpatient ward & pediatric intensive care unit (PICU) of North Bengal Medical College. The study was conducted from July 2023 to December 2024 with a duration of 18 months. Children admitted to the pediatric inpatient ward or PICU with a clinical diagnosis of CAP according to the WHO criteria were included in the present study. **Results and Conclusion:** The present study highlights that hyponatremia is a common finding in children with CAP. This study also highlights the significant association of hyponatremia with severe pneumonia, the association of severe hyponatremia with severe pneumonia, increased need for ventilation, prolonged hospital stays, and higher mortality in children with CAP.

Key words: Community Acquired Pneumonia, C-Reactive Protein, Healthcare Associated Pneumonia, Pediatric Interquartile Range (IQR), Syndrome of Inappropriate Antidiuretic Hormone (SIADH)

Pneumonia is an acute respiratory infection of the lungs where alveoli become inflamed and are filled with pus and fluid, leading to impaired oxygen exchange, respiratory distress, and painful breathing. It is caused by a variety of pathogens, including viruses, bacteria, and fungi. Community-acquired pneumonia (CAP) is defined as an acute infection of the lung parenchyma in a previously healthy child, acquired outside of the hospital settings, and not hospitalised within 14 days before onset of symptoms [1]. According to the World Health Organisation (WHO), 740180 deaths in children under five years occurred due to pneumonia, accounting for 14% of all under-five deaths and 22% of deaths among those aged 1 to 5 years in 2019. Mortality due to pneumonia is disproportionately higher in Southern Asia and sub-Saharan Africa [2]. In India, pneumonia is the leading cause of mortality among affected children. According to UNICEF data from December 2018, India has an under-five mortality rate of 39.4 per 1,000 live births [3]. “Fighting for Breath”, a report by the non-profit organisation ‘Save the Children’ published that in

2015, 178717 under-five children died in India because of pneumonia, which means that every hour, 20 children died due to pneumonia in the country [4].

Hyponatremia, a common electrolyte abnormality found in CAP. Hyponatremia is defined as a serum sodium level of less than 135 mEq/dL [5]. Most children with hyponatremia require intravenous fluid, as breathlessness, fatigue, and the risk of aspiration often limit adequate oral fluid intake. This can further cause hemodilution and acute hyponatremia, causing a rapid shift of fluids into brain cells, resulting in cerebral oedema [6]. Association between pneumonia and hyponatremia was first described in 1962 by Stormont and Waterhouse [7]. Several studies have reported a high prevalence of hyponatremia in community-acquired pneumonia and have linked it to increased mortality and indicators of severe illness [8-10]. According to the study by Singhi and Dhawan, hyponatremia in CAP resulted in longer duration of hospital stay, a two-fold increase in complications and 3.5 times higher

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mortality than those with normal sodium levels [11].

The current study was conducted at North Bengal Medical College in Darjeeling, a tertiary care centre serving a broad region of West Bengal, including populations from neighbouring states such as Bihar and countries like Nepal and Bangladesh. Given the resource-limited setting, early identification is crucial to optimise resource allocation and ensure appropriate management of pediatric patients. This study aims to investigate the occurrence of hyponatremia in children aged 2 months to 5 years with community-acquired pneumonia and to examine its correlation with the severity of the illness.

METHODS

A descriptive observational study with a prospective design was conducted in the pediatric inpatient ward & Pediatric Intensive Care Unit (PICU) of North Bengal Medical College & Hospital, Darjeeling, from July 2023 to December 2024, for 18 months. Children admitted to the pediatric inpatient ward or PICU with a clinical diagnosis of community-acquired pneumonia (CAP) according to the WHO criteria were included in the present study. The inclusion criteria were children aged two months to five years, children admitted to the pediatric ward and the intensive care unit who fulfilled the WHO criteria of pneumonia, or severe/very severe pneumonia. The exclusion criteria were children with acute gastroenteritis, known renal disease, pre-existing cardiac disease, respiratory morbidity, CNS infections and malignancies, children on medication that can cause electrolyte disturbances, e.g., diuretics, anticonvulsants, children diagnosed with pneumonia due to nosocomial infection, aspiration pneumonia, and severe acute malnutrition.

Sample Size and Technique

The sample size was estimated based on the following formula as below:

Sample size (n) was calculated using the following formula: $n = (Z_{1-\alpha/2})^2 P(1-P) / d^2$

Where, P = proportion of hyponatremia in CAP children, d = Allowable absolute error, $Z_{1-\alpha/2}$ = Constant; $1-\alpha$ = desired confidence level, taken as 95%. Taking 46.3% proportion with 10% absolute error, 95% confidence interval and assuming a 10% non-response rate, the calculated minimum sample size was 106.

Systematic random sampling was applied for the selection of participants. According to the previous year's data on outpatients, a weekly average of 10 children were diagnosed. Data were collected for 32 weeks. Approximately 520 children were diagnosed with CAP during this period. Per week, $106/32=3.3\sim4$ patients' data were collected. Systematic random sampling was used to recruit 4 patients per week. Sampling interval was calculated as $520/106=4.9$, rounded off to 5. A

random number selection was made between 1 and 5, and the first child with CAP was selected from the lists according to the random number in the first week. Then, every fifth alternate eligible child was selected till the required sample size was reached.

Following the receipt of ethics committee approval from the institution (Memo No: IEC/NBMC/M-07/033/2023), data collection commenced. Informed consent from the parents of children were taken before proceeding. After obtaining informed consent from parent detailed history and clinical examination were conducted in all children included in the study admitted with pneumonia. Pneumonia and severe pneumonia were defined according to the WHO guidelines. At the time of admission, blood samples (2 ml) were collected in a sterile vial before starting intravenous fluids or antibiotics for serum sodium level, Total Leucocyte Count (TLC), C-reactive protein (CRP) and analysed using an automated system of the central laboratory in the hospital. A chest X-ray was done to identify lung infiltrates. Children were followed up for ventilation requirement, duration of hospital stay, and the outcome (death or discharge) and recorded for all children. All children included in the study were treated appropriately per hospital protocol.

Statistical Analysis

The collected data of 106 children were checked for consistency, completeness and entered into a Microsoft Excel data sheet. Data were organised and presented using the principles of descriptive and inferential statistics. Categorical variables were expressed as a percentage of the total participants. Continuous variables were expressed as Mean \pm Standard Deviation. The Pearson Chi-Square value was used for inferential statistics. Bar diagrams and pie diagrams were used to present the data. The statistical software IBM-SPSS version 22 was used for the analysis. An alpha level of 5% was taken into consideration; thus, a *p*-value less than 0.05 was considered statistically significant.

RESULTS

In Table 1, the majority of the children were older than 12 months (84%). male (56.6%). All children enrolled in the study had fast breathing, 58.5% had the presence of chest in-drawing, which was statistically significant, and 25.5% had the presence of danger signs. Almost half of the children (50.9%) had lung infiltrates on chest X-ray, and 17% of children required statistically significant ventilation support. Around 42.5% of children had hyponatremia; of those, the majority had mild hyponatremia (75.6%). 15.5% had moderate hyponatremia, while only 8.9% had severe hyponatremia. The majority of the children had a CRP level of more than 10 mg/L (82.1%) with a mean CRP level of 51.5 ± 50.6 mg/L and an average total leucocyte count of 12118.8 ± 3456.8 cells per microliter.

Table 1: Baseline Characteristics and Laboratory Data

Characteristics	n (%)
Age	
≤ 12years	17 (16)
> 12years	89 (84)
Danger Signs	
Fast Breathing	106 (100)
Chest Indrawing	62 (58.5)
Lung Infiltrates on Chest X-Ray	54 (50.9)
Requirement of Ventilation	
Mechanical	5 (4.7)
Non-invasive	13 (12.3)
No ventilation	88 (83)
Severity of Hyponatremia	
Mild	33 (73.3)
Moderate	5 (11.1)
Severe	7 (15.6)
CRP Level(mg/dL)	
≤ 10	19 (17.9)
> 10	87 (82.1)
Total Leucocyte Count	
Median (IQR)	11500.0 (4225.0)
Mean ± SD	12118.8 ± 3456.8

In Table 2, 74.5% of children had pneumonia and 25.5% had severe pneumonia, which was statistically significant. 91.5% of children were discharged from the hospital after getting cured.

Table 3 shows that among the children, 85.7% in the severe hyponatremia category had severe pneumonia, compared to 60.0% in the moderate hyponatremia category and 33.3% in the mild hyponatremia category. This difference was found to be statistically significant (p = 0.03)

Table 3: Association between severity of hyponatremia and severity of pneumonia in children

WHO Classification of Pneumonia	Hyponatremia severity n (%)			Total n (%)	Pearson Chi-Square value	p value
Pneumonia	Mild	Moderate	Severe	25 (55.6)	6.9	0.03*
	22 (66.7)	2 (40.0)	1 (14.3)			
Severe pneumonia	11 (33.3)	3 (60.0)	6 (85.7)	20 (44.4)		
Total	33 (100.0)	5 (100.0)	7 (100.0)	45 (100.0)		

n represents the number of samples; % represents the frequency of distribution; p value ≤ 0.05 is considered statistically significant

DISCUSSION

The demographic distribution in the present study showed that the maximum children were older than 12 months (84%), with a mean age of 26.9 ± 13.2 months, having a slight male

But 8.5% of children died. 50.9% of children stayed more than 7 days in the hospital, and both were statistically significant.

Table 2: Characteristics of Children with Hyponatremia vs Children with no Hyponatremia

	Hyponatremia n (%)		p value
Severity of Pneumonia			
Pneumonia	54 (88.5)	25 (55.6)	0.000**
Severe Pneumonia	7 (11.5)	20 (44.4)	
Outcome			
Death	2 (3.3)	7 (15.6)	0.02*
Discharged	59 (96.7)	38 (84.4)	
Length of Hospital Stay			
≤ 7 days	35 (57.4)	17 (37.8)	0.04*
> 7 days	26 (42.6)	28 (62.2)	

n represents the number of samples; % represents the frequency of distribution; p value ≤ 0.05 is considered statistically significant; p value ≤ 0.000 is considered highly statistically significant.

predominance (56.6%). Mandal et. al. conducted a study in Safdarjung Hospital, New Delhi, to see the association of hyponatremia in pneumonia in children, found the mean age as 18.52 ± 18.1 months [10]. Similarly, research from Bangalore observed a comparable distribution of community-acquired

pneumonia (CAP) cases, with 42% occurring in children aged 2 months to 2 years and 46% in those aged 2 to 5 years [8]. Preschool-aged children experienced a similar frequency of atypical bacterial lower respiratory infections as older children, likely due to the decline in maternal antibody-derived passive immunity and their still-developing immune system [12].

Among the included children with CAP in the present study, around 1/4th of the children had severe pneumonia (25.5%), fast breathing (100%), chest in-drawing (58.5%), and danger signs (25.5%) were commonly seen. Almost half of the children (50.9%) revealed lung infiltrates on chest X-ray, and 17% required ventilation support due to respiratory difficulty. Similar studies reported slightly higher proportions of severe pneumonia. Praneetha CK et al. showed 45% severe pneumonia cases with 12.3% requiring ventilation support [8]. A study from Assam reported ~44% severe pneumonia among children with CAP and 13% required ventilation support [9].

The present study showed that although a relatively smaller proportion of pneumonia severity but respiratory support was needed in a comparatively higher proportion. These differences might be due to variation in clinical assessment, differences in study setting or differences in time to reach healthcare settings due to resource accessibility. In a study from Gujrat, severe CAP was observed in 32.69% of cases according to PIDS criteria, indicating ICU admission. Bronchopneumonia (40.38%) was the most common chest X-ray finding, followed by lobar pneumonia (32.69%). The children presented with fast breathing (94.23%), tachypnoea (83.65%), chest indrawing (64.42%), tachycardia (58.65%), hypoxia (20.91%), grunting (9.61%), and cyanosis (11%) [13]. A study from Uttar Pradesh reported that hypoxic pneumonia is significantly linked to higher hospital mortality [14].

Hypoxic pneumonia (35.9%) with higher susceptibility observed among infants (2–11 months), females, and those exposed to biomass fuel. Also, having risk factors as pallor, wheezing, tachypnoea, low pulse volume, severe malnutrition, and critical danger signs such as inability to breastfeed, lethargy, and convulsions, presence of infiltration on chest X-rays [14].

Blood parameters in CAP

The study revealed the presence of inflammation among the children with CAP, having an average CRP level of 51.5 ± 50.6 mg/L and an average total leucocyte count of 12118.8 ± 3456.8 cells per microliter. Mandal PP et al. in their study reported WBC count among children with CAP as 12076.00 ± 5548.28 cells per microliter, 47% of children having CRP level more than 10 mg/L. Leukocyte count in CAP patients showed a significant correlation with inflammatory markers such as IL-1ra and sTNF-RI levels, both initially and after 24 hours [15].

Hyponatremia in CAP

Hyponatremia is the most common electrolyte abnormality seen in children having pneumonia. The current study observed

that 42.5% of the children with CAP had hyponatremia, with the majority having mild hyponatremia (73.3%), 11.1% had moderate hyponatremia, while 15.6% had severe hyponatremia. Similar findings were reported from Assam, as 46.32% of children had hyponatremia, mostly being mild. A study from Bangalore reported 43.5%, from Bihar 35.3% hyponatraemic cases in children with CAP [16]. Few Indian studies have documented lower rates, ranging from 21% to 27%. Studies from other countries, such as Greece, reported the prevalence of hyponatremia as 35.2% in CAP, 30% in Spain [17, 18].

The reason behind hyponatremia in pneumonia can be due to various factors, such as the illness itself, difficulty in removing excess water, abnormal vasopressin release, use of certain medications, and intake of hypotonic fluids. It can be caused by either a lack of sodium or too much water in the body. Some literature also suggested that Atrial natriuretic peptide (ANP), a hormone produced by the heart, may also contribute. ANP helps regulate urine production, sodium balance, and blood pressure. Higher levels of ANP, commonly found in lung diseases, are associated with low oxygen levels, lung blood vessel constriction, high blood pressure in the lungs, and heart strain [19].

Hyponatremia and disease severity

Gender and age distribution did not significantly differ between the hyponatremic and normonatremic groups, comparable to the findings of the study by Praneetha CK et al. [8]. Error! Bookmark not defined. Severe pneumonia was significantly more frequent in the hyponatremic group (44.4% vs. 11.5%, $p = 0.000$), indicating the role of sodium in respiratory function. Furthermore, within the severe hyponatremia subgroup, the proportion of severe pneumonia was even higher (85.7%), with a significant association between the severity of pneumonia and with severity of hyponatremia ($p = 0.03$). Similarly, hyponatremia with a much higher proportion in severe pneumonia was reported by with a statistically significant difference. Another study found that hyponatremia was more common in severe pneumonia (70%) than in pneumonia (30%) ($P < 0.01$). While mild hyponatremia was the most frequent in both groups, severe hyponatremia was more prevalent in severe pneumonia (16%) compared to pneumonia (6%), which is similar to the present study [8].

It indicates that hyponatremia can predict the severity of pneumonia. Recent studies are exploring the exact cause of hyponatremia in community-acquired pneumonia (CAP). Swart et al. suggested that the non-osmotic release of vasopressin may contribute to significant hyponatremia [20]. However, Tagarro et al. found that true SIADH is rare in CAP patients with hyponatremia, though it correlates well with inflammatory markers [21]. Hausman-Kedem et al. concluded that B-type natriuretic peptide (BNP) is unlikely to be a cause [22]. Despite varying potential mechanisms, multiple studies, including the present one, consistently identify hyponatremia

as a common electrolyte imbalance in CAP.

A critical finding of this study was the significantly higher requirement for ventilation in hyponatremic children than the normonatremic group (31.1% vs. 6.6%, $p=0.002$). Among those requiring ventilation, 12.3% needed non-invasive and 4.7% required mechanical ventilation. This highlights the significance of hyponatremia as a marker of impending respiratory failure. Similar findings have been reported where electrolyte imbalances contribute to poor lung compliance and increased need for respiratory support. Rabha J *et al.* in their study reported that ~90% of children were in the hyponatremic group among the required ventilation in CAP children, suggesting the hypothesis that patients with hyponatremia had a higher likelihood of developing shock, requiring mechanical ventilation, and experiencing an extended hospital stay [9]. These findings are also consistent with other studies.

The inflammatory markers in our study, such as Elevated CRP levels and total leucocyte counts, did not show a significant difference between the two groups. This suggests that CRP alone may not be a reliable predictor of hyponatremia. Studies on serum sodium disorders in pediatric CAP are scarce, but hyponatremia appears common. Sakellaropoulou *et al.* found that sodium levels at admission had an inverse significant correlation with C-reactive protein and leukocyte count. Some studies have hypothesised that cytokine-mediated renal water retention contributes to hyponatremia in respiratory infections, independent of CRP levels. Hyponatremia is a marker of systemic inflammatory response, leading to increased vascular permeability and fluid retention [23].

Hyponatremia and length of hospital stay and outcome

The current study found that prolonged hospital stay (> 7 days) was significantly more common in hyponatremic children with CAP compared to another group (62.2% vs. 42.6%, $p = 0.04$). Moreover, the mortality rate was significantly higher in the hyponatremic group with CAP than the normonatremic group (15.6% vs. 3.3%, $p=0.02$). The association between hyponatremia and mortality has been previously established in pediatric studies. A similar study reported that patients with hyponatremia had a higher chance of staying in the hospital for more than 7 days (48% vs. 26%). The risk of death was also significantly higher in those with hyponatremia (13%) compared to those without it (1.5%) ($P < 0.001$). A study by Karki *et al.* found that hyponatremia at admission was significantly associated with longer hospital stays and higher mortality rates [24].

Similarly, Singhi *et al.* examined electrolyte abnormalities in pneumonia and reported that all four children who died had a serum sodium level of ≤ 125 mmol/L, which persisted until death. A study by Dhawan *et al.* found that hyponatremia was linked to a 60% longer hospital stay, twice the risk of complications, and a 3.5 times higher mortality rate compared to normonatremia [25]. Pande V *et al.* described electrolyte

imbalances were common in children with severe pneumonia (59%), with hyponatremia being the most prevalent. Nearly all ICU-admitted cases had dyselectrolytemia, and 24% faced fatal outcomes [26]. However, Sakellaropoulou *et al.* found an inverse relationship between the severity of hyponatremia and the length of hospital stay. The possible explanation could be that hyponatremia in children with pneumonia exacerbates severe complications, including cerebral oedema, hypoxia-related neuronal injury (causing seizures, coma, and death), hypovolemia and shock, as well as electrolyte imbalances may result in arrhythmias and cardiac arrest. These factors contribute to increased morbidity and mortality. This emphasizes the prognostic importance of hyponatremia in CAP and suggests that monitoring and correcting sodium levels could be crucial in managing critically ill children with pneumonia. The presence of hyponatremia showed a significant correlation with disease severity, requirement for ventilation, and prolonged hospital stay.

CONCLUSION

The present study highlights that hyponatremia is a common finding in children with Community-Acquired Pneumonia (CAP). This study also highlights the significant association of hyponatremia with severe pneumonia, increased need for ventilation, prolonged hospital stays, and higher mortality in children with CAP. Routine assessment of serum sodium levels in pediatric pneumonia cases may help in the early identification of high-risk patients and improve clinical decision-making. Awareness among healthcare providers is crucial for early detection and management, which may improve outcomes and reduce complications. Further research is needed to explore whether early correction of hyponatremia in CAP could lead to better clinical outcomes.

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