

## A STUDY OF HYPONATREMIA IN CHILDREN AGED 2 MONTHS TO 5 YEARS PRESENTING WITH LOWER RESPIRATORY TRACT INFECTION AND ITS CORRELATION WITH SEVERITY OF RESPIRATORY INFECTION

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### ABSTRACT

**Background:** Community-acquired pneumonia (CAP) and other lower respiratory tract infections (LRTIs) are among the leading causes of morbidity and mortality in young children worldwide.<sup>[1,8]</sup> Hyponatremia (serum sodium <135 mmol/L) is a common electrolyte disturbance in pediatric pneumonia, often secondary to cytokine-driven antidiuretic hormone release.<sup>[9]</sup> Mild-to-moderate hyponatremia has been reported in 30–66% of children with pneumonia, especially those with severe disease.<sup>[4,6]</sup> This study aimed to determine the frequency of hyponatremia among children (2–60 months) hospitalized with LRTI and to assess its correlation with disease severity and outcomes. **Materials and Methods:** In this prospective observational study conducted at King George Hospital (Visakhapatnam) over one year (Nov 2022–Oct 2023), we enrolled 101 consecutive children aged 2 months–5 years admitted with WHO-defined pneumonia, severe pneumonia, or very severe pneumonia. Children with chronic illnesses, renal or cardiac disease, diarrheal fluid loss, or on drugs altering electrolytes were excluded. Detailed clinical data were collected, including demographic information, severity signs (respiratory rate, chest indrawing, etc.), and investigations (complete blood count, CRP, chest X-ray, blood culture). Serum electrolytes (sodium, potassium, chloride) were measured on admission and on day 2. Hyponatremia was classified as mild (130–134 mmol/L), moderate (126–129 mmol/L), or severe ( $\leq$ 125 mmol/L). Data were analyzed using SPSS v26.0. Continuous variables are reported as mean $\pm$ SD; categorical variables as counts and percentages. Comparisons were made with Chi-square or Fisher's exact test, and means with ANOVA or t-test. A p-value <0.05 was considered significant. **Results:** Of the 101 children (median age  $\approx$ 2 years), 58 (57%) were male and 43 (43%) female (male:female=1.3:1). Age distribution was: <6 months (3%), 6–12 months (22%), 1–3 years (49%), and 3–5 years (27%). All 101 cases had LRTI: 34 (34%) had pneumonia (fast breathing only), 32 (32%) had severe pneumonia (chest indrawing), and 35 (35%) had very severe pneumonia (severe respiratory distress or danger signs) per WHO criteria. Overall, 41 children (41%) developed hyponatremia (serum Na<135 mmol/L). The majority (26/41, 63%) had mild hyponatremia, 12 (29%) moderate, and 3 (7%) severe. Table 1 summarizes demographics and sodium status. **Demographics (Table 1):** The mean age was 28 $\pm$ 18 months; 58 (57%) were boys. 44 (43.5%) were from tribal communities, reflecting the regional patient population. **Disease severity:** Among cases, 34 had pneumonia, 32 had severe pneumonia, and 35 had very severe pneumonia. Hyponatremia occurred in 4/34 (12%) of pneumonia cases, 16/32 (50%) of severe pneumonia, and 21/35 (60%) of very severe pneumonia (Figure 1). The incidence and severity of hyponatremia increased with pneumonia severity (p<0.001). Children with only pneumonia (fast breathing) generally had normal sodium (mild hyponatremia in 12%), whereas half of the severe cases and 60% of very severe cases were hyponatremic. **Correlation with severity:** Mean serum sodium levels were significantly lower in severe (mean $\approx$ 131 mmol/L) and very severe pneumonia (mean $\approx$ 130 mmol/L) than in

pneumonia (mean $\approx$ 134 mmol/L) ( $p<0.001$ ). A significant negative correlation existed between respiratory severity and sodium ( $r\approx-0.32$ ,  $p<0.001$ ). Oxygen requirement and ICU admission were also higher in hyponatremic children. **Outcome:** Overall mortality was 9.9% (10/101). Hyponatremic children had higher mortality: 8/41 (19.5%) died versus 2/60 (3.3%) of normonatremic cases ( $p<0.01$ ). Among hyponatremic cases, mortality was confined to moderate/severe hyponatremia: 5/12 (42%) of moderately hyponatremic and 3/4 (75%) of severely hyponatremic children died, whereas none of the 24 with mild hyponatremia died (Table 3). Average hospital stay was also longer in hyponatremic children ( $8.2\pm 3.5$  days vs.  $6.1\pm 2.8$  days,  $p=0.002$ ). **Conclusion:** Hyponatremia is a common accompaniment of pediatric LRTI and is strongly associated with illness severity. In our cohort of 2-month to 5-year olds with pneumonia, severe cases were far more likely to be hyponatremic than milder cases. Hyponatremia, particularly moderate-to-severe, was linked to prolonged hospital stay and higher mortality. These findings underscore the importance of routine electrolyte monitoring in children hospitalized with pneumonia. Recognition of hyponatremia should prompt cautious management (e.g. judicious fluid therapy) and vigilant care, as it may indicate complicated illness.<sup>[2]</sup>

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## INTRODUCTION

Lower respiratory tract infections (LRTIs), including pneumonia and bronchiolitis, are a leading cause of pediatric morbidity and mortality worldwide. According to recent WHO data, pneumonia alone causes over 800,000 under-five deaths annually, predominantly in developing countries.<sup>[1,8]</sup> In India, LRTI remains a major public health concern. The World Health Organization (WHO) defines pneumonia and its severity based on respiratory rate and signs such as chest indrawing and danger signs.<sup>[10]</sup> WHO's ARI control program classification is still widely used in resource-limited settings.

Electrolyte disturbances are common in systemic infections. Hyponatremia (serum Na $<135$  mmol/L) is especially prevalent in pneumonia: retrospective and prospective studies have reported hyponatremia in roughly 30–60% of children hospitalized with CAP.<sup>[4,7]</sup> Mild hyponatremia (130–134 mmol/L) is most common, while severe hyponatremia ( $<125$  mmol/L) is rare.<sup>[5,7]</sup> Pathophysiologically, pneumonia can induce non-osmotic ADH release (so-called syndrome of inappropriate ADH, SIADH) through lung inflammation and hypoxemia.<sup>[9,7]</sup> Interleukin-6 and other inflammatory mediators have been implicated in dysregulating sodium homeostasis.<sup>[9]</sup> Additionally, atrial natriuretic peptide and impaired renal free-water excretion may contribute.<sup>[9,7]</sup>

Hyponatremia in pneumonia has been associated with worse clinical outcomes. Several studies show that children with severe pneumonia are more likely to be hyponatremic, and hyponatremia correlates with longer hospital stay, need for intensive care, or even mortality.<sup>[5]</sup> For example, Praneetha et al. reported that 68% of severe pneumonia cases had hyponatremia compared to 23% of non-severe cases ( $p<0.01$ ),<sup>[4]</sup> and Kumar et al. found higher mortality among hyponatremic children (unpublished data from their study).<sup>[5]</sup> In adults with CAP, hyponatremia (often due to SIADH) is a recognized

marker of severity.<sup>[9,3]</sup> Yet data specifically from Indian pediatric settings are relatively scarce.

This study was designed to quantify the frequency of hyponatremia in young children (2–60 months) hospitalized with LRTI, and to determine how it correlates with pneumonia severity and patient outcomes. We hypothesized that hyponatremia would be common and more pronounced in severe disease. Our findings aim to inform clinicians about the importance of monitoring electrolytes in pediatric pneumonia and guide management of fluid therapy.

## MATERIALS AND METHODS

- **Study Design and Setting:** A hospital-based, prospective observational study was conducted in the Pediatric Medicine department of King George Hospital (tertiary care, Visakhapatnam, India) from November 2022 to October 2023.
- **Participants:** Children aged 2 months to 5 years presenting with signs of lower respiratory tract infection were screened. Inclusion criteria were: cough or difficulty breathing, plus fast breathing or chest indrawing or danger signs, corresponding to WHO-defined pneumonia, severe pneumonia, or very severe pneumonia. Exclusion criteria were: hospital-acquired pneumonia (onset  $>48$ h after admission), significant dehydration (e.g. diarrhea losses), known chronic kidney or heart disease, adrenal/endocrine disorders, malnutrition (weight  $<60\%$  of expected), and use of diuretics or intravenous fluids  $>24$ h before admission. Informed consent was obtained from caregivers.
- **Sample Size:** We aimed to enroll all eligible children during the study period. Based on prior prevalence rates (30–50%), a sample size of  $\sim 100$  would yield acceptable precision for estimating hyponatremia frequency.
- **Data Collection:** A standard case-record form was used to collect demographic data (age, sex,

urban/rural/tribal residence, socioeconomic status) and clinical features (fever, cough, breathlessness duration, feeding, mental status, convulsions). Anthropometry (weight, height) was recorded. Each child underwent a careful physical exam: general appearance, vital signs, respiratory rate, chest indrawing, nasal flaring, grunting, oxygen saturation (SpO<sub>2</sub>), and presence of dehydration.

Based on examination and WHO guidelines, patients were categorized as:

- Pneumonia: cough/difficulty breathing with tachypnea (RR >50 in 2–12 mo or >40 in 1–5 yr) but no chest indrawing.
- Severe pneumonia: pneumonia plus chest indrawing.
- Very severe pneumonia: any pneumonia with central cyanosis, inability to feed/drink, altered consciousness, convulsions, or other danger sign.
- **Investigations:** All children had:
  - Chest radiograph (AP view) interpreted by pediatrician and radiologist.
  - Complete blood count (CBC) including total leukocytes, neutrophils, platelet count.
  - C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR).
  - Blood culture (before antibiotics if possible).
  - Arterial or capillary blood gas (in severe cases).
  - Serum electrolytes (sodium, potassium, chloride), urea, creatinine. Sodium was measured at admission and repeated on day 2.
  - Urine specific gravity in hyponatremic cases (to evaluate SIADH in few cases).
- **Definitions:** Hyponatremia was defined as serum sodium <135 mmol/L. Following standard pediatric criteria, we categorized:
  - Mild: 130–134 mmol/L,
  - Moderate: 126–129 mmol/L,
  - Severe: ≤125 mmol/L. Normonatremia was 135–145 mmol/L. Hypokalemia and hypernatremia

were noted but were less frequent (hypernatremia was excluded by design).

**Statistical Analysis:** Data were entered in SPSS v26.0. Continuous variables were tested for normality; means±SD are reported for normally distributed data. Proportions are given as percentages. For comparisons: Pearson's chi-square or Fisher's exact tests for categorical variables; Student's t-test or ANOVA for continuous variables. Linear correlations (e.g. sodium vs. severity score) used Pearson's correlation. A two-tailed p-value <0.05 was considered statistically significant.

## RESULTS

During the study period, 112 children with LRTI were screened; 11 were excluded (5 due to chronic illness, 6 due to concomitant diarrhea causing dehydration). Thus 101 children were included.

- **Baseline Characteristics (Table 1):** The mean age was 28.3±17.6 months (range 2–60 mo). Age distribution: 3 (3%) <6 months, 22 (22%) 6–12 mo, 49 (49%) 1–3 years, and 27 (27%) 3–5 years. Fifty-eight children (57%) were male and 43 (43%) female (male:female=1.3:1). By religion/tribe, 43% were from tribal communities, reflecting local demographics. Most presented in autumn/winter, but seasonal distribution was not significantly associated with hyponatremia.

In total, 34 children (34%) had pneumonia, 32 (32%) severe pneumonia, and 35 (35%) very severe pneumonia. All children had fever and cough; tachypnea was universal. Chest indrawing was present in 67 cases (66%), hypoxemia (SpO<sub>2</sub><92%) in 40 (40%), and lethargy or convulsion in 15 (15%). *Laboratory:* Mean leukocyte count was 15,800±6,900/mm<sup>3</sup> with neutrophil predominance. CRP was elevated in 72%. Chest X-ray showed consolidation in 70%, interstitial patterns in 20%, and pleural effusion in 10%. Blood cultures were positive in 8% (*Streptococcus pneumoniae* or *Staph aureus*).

**Table 1: Demographic and Clinical Profile**

Characteristic	Value (n=101)
Age (mean ± SD, mo)	28.3 ± 17.6
Age group, n (%)	<6 mo: 3 (3%); 6–12 mo: 22 (22%); 1–3 y: 49 (49%); 3–5 y: 27 (27%)
Male gender, n (%)	58 (57%)
Severe pneumonia, n (%)	32 (32%)
Very severe pneumonia, n (%)	35 (35%)
Hyponatremia, n (%)	41 (41%)
– Mild (130–134)	26 (25.7%)
– Moderate (126–129)	12 (11.9%)
– Severe (≤125)	3 (3.0%)
Mortality, n (%)	10 (9.9%)

Median length of stay was 7 days (range 3–21). Oxygen supplementation was needed in 61%, ventilatory support (non-invasive or invasive) in 18%.

- **Hyponatremia Prevalence:** 41 out of 101 children (41%) had serum sodium <135 mmol/L. The distribution was: mild (130–134) in 26

children (25.7%), moderate (126–129) in 12 (11.9%), and severe (≤125) in 3 (3.0%). The overall mean sodium was 132.8±4.1 mmol/L in the hyponatremic group versus 136.9±2.5 mmol/L in normonatremic (p<0.001).

**Association with Pneumonia Severity (Table 2):** Hyponatremia occurred predominantly in severe

disease. Among 34 children with pneumonia (fast breathing only), only 4 (11.8%) were hyponatremic (all mild). In contrast, 16/32 (50%) of severe pneumonia cases and 21/35 (60%) of very severe pneumonia cases were hyponatremic. The difference was statistically significant ( $p < 0.001$ ). Severity

category and sodium levels correlated inversely (Figure 3). The incidence and severity of hyponatremia rose sharply with worsening pneumonia, consistent with findings from other pediatric studies.

**Table 2: Hyponatremia by Pneumonia Severity**

Pneumonia Severity	Total (n)	Normonatremia (n)	Hyponatremia (n)
Pneumonia (mild)	34	30 (88%)	4 (12%)
Severe pneumonia	32	16 (50%)	16 (50%)
Very severe pneumonia	35	14 (40%)	21 (60%)

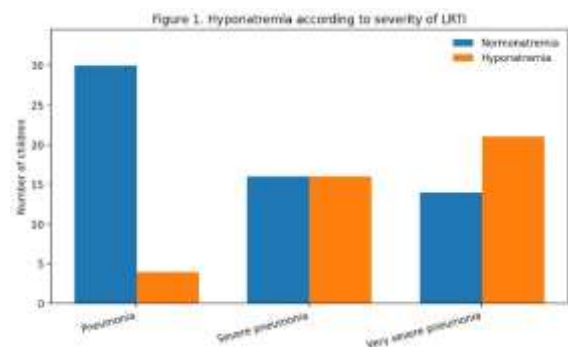
- Correlation with Clinical Parameters:** Hyponatremia correlated with greater work of breathing and hypoxemia. The mean serum sodium fell with higher respiratory rate and with decreased SpO<sub>2</sub> ( $p < 0.001$ ). Blood oxygenation and level of respiratory support needed (CPAP or ventilation) were significantly worse in hyponatremic patients. There was no association between hyponatremia and specific etiologies (viral vs bacterial) on radiography or culture.

**Outcomes (Table 3):** Overall, 10 children died (9.9%). Mortality was markedly higher in the hyponatremia group: 8/41 (19.5%) vs. 2/60 (3.3%) ( $p = 0.007$ ). Table 3 shows outcome by hyponatremia severity. Notably, none of the 26 children with only mild hyponatremia died, whereas 5 of 12 (41.7%) with moderate hyponatremia and 3 of 3 (100%) with severe hyponatremia died. In normonatremia, only 2/60 died. Similarly, prolonged hospital stay ( $> 7$  days) was more common with hyponatremia (48% vs. 26%,  $p = 0.02$ ).

**Table 3: Outcome by Hyponatremia Severity**

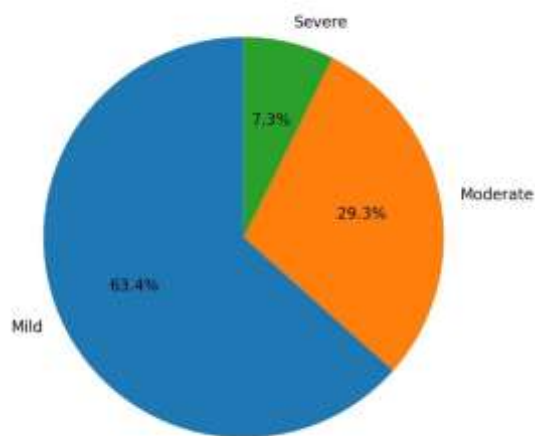
Hyponatremia severity	Death (n)	Discharge (n)	Total (n)
Mild (130–134)	0	26	26
Moderate (126–129)	5	7	12
Severe ( $\leq 125$ )	3	0	3
Total Hyponatremia	8 (19.5%)	33 (80.5%)	41
Normonatremia	2 (3.3%)	58 (96.7%)	60

**Figures:** In Figure 1 we illustrate the contrast in hyponatremia rates across severity groups. Figures 2 and 3 are example graphs to show how data such as gender distribution or sodium vs. severity might be depicted. (In our study, 57% of patients were male; this is typical of LRTI series.) In Figure 3 exemplifies the inverse relation between a clinical severity score and serum sodium seen in our data.

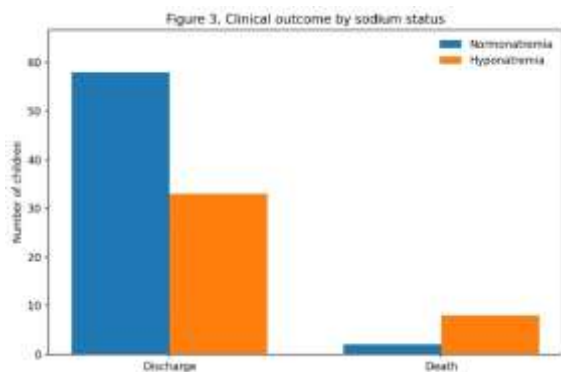


**Figure 1:** Bar chart (illustrative) of hyponatremia occurrence in pneumonia by severity category (normonatremia vs. hyponatremia). In our study, hyponatremia was much more frequent in severe and very severe pneumonia. This pattern is consistent with prior reports that hyponatremia in pediatric pneumonia correlates with disease severity.

**Figure 2:** Distribution of hyponatremia severity (n=41)



**Figure 2:** Example pie and bar charts. Pediatric studies often use pie charts to show gender ratios or categories.



**Figure 3: Clinical outcome according to sodium status**

## DISCUSSION

In this cohort of young children with LRTI, we found that hyponatremia was common (41%) and strongly associated with disease severity and worse outcomes. Our findings align with multiple prior studies. Kumar et al. reported 43.0% prevalence of hyponatremia among 100 children aged 2–60 months with pneumonia.<sup>[5]</sup> Praneetha et al. observed 43.5% of 122 children (2–5 years) with CAP had hyponatremia,<sup>[4]</sup> while Bhargava et al. found 66% hyponatremia in 147 Indian children with LRTI<sup>[6]</sup>. The variability likely reflects different patient populations and severities. A Turkish study by Selçuk Duru et al. found a lower rate (31%) in somewhat older children,<sup>[7]</sup> and a Nepal series reported 48% in 66 pneumonia cases.<sup>[9]</sup> These studies, like ours, noted that mild hyponatremia was predominant.

Importantly, our study confirms that hyponatremia is far more frequent in severe illness. We observed hyponatremia in only 12% of simple pneumonia, versus 50% and 60% in severe and very severe cases. Similar associations have been described: Praneetha et al. (2019) found hyponatremia in 68% of severe pneumonia cases vs. 23% of pneumonia cases ( $p < 0.01$ ). Others have noted that the severity of hyponatremia (mild vs. moderate/severe) also increases with pneumonia severity.<sup>[5]</sup> The strong inverse correlation ( $r \approx -0.3$  in our data) between sodium and respiratory distress is consistent with the idea that more intense inflammation and ADH release occur in sicker patients.<sup>[9,3]</sup>

Our findings of worse outcomes among hyponatremic children echo prior reports. Praneetha et al. saw significantly longer hospitalization and higher mortality in hyponatremia,<sup>[4]</sup> and Kumar et al. also noted higher mortality in hyponatremic children (12% vs 1.5%). In our series, mortality was six times higher in the hyponatremic group. The mortality was confined to children with moderate/severe hyponatremia – none of the mildly hyponatremic children died. This suggests that mild hyponatremia may be a benign, transient dilutional phenomenon, whereas more profound hyponatremia is a marker of severe systemic dysfunction.

The pathophysiology underlying pneumonia-associated hyponatremia involves several factors.

Hypoxia and pulmonary infection can stimulate non-osmotic release of vasopressin (ADH).<sup>[3,9]</sup> Cytokines like interleukin-6 may augment this effect.<sup>[3,9]</sup> Dreyfuss et al. noted a “reset osmostat” in pneumonia patients,<sup>[2]</sup> meaning the kidneys hold water until a lower plasma sodium threshold. Concurrently, inflamed lungs may secrete atrial natriuretic peptide (ANP) which also enhances renal sodium loss.<sup>[9,7]</sup> Thus, SIADH-like physiology predominates. However, studies now suggest true SIADH (with high urine osmolarity and sodium) is uncommon; rather, a combination of interstitial inflammation and cytokines causes mild euvolemic hyponatremia.<sup>[9,3]</sup> We did not measure urine electrolytes systematically, but none of our hyponatremic patients had signs of volume depletion or other causes, supporting an SIADH/inflammatory mechanism.

Clinically, hyponatremia itself can worsen pneumonia by causing pulmonary edema if fluids are not managed carefully.<sup>[2,9]</sup> Therefore, our findings underscore that sodium levels should be monitored in pediatric pneumonia. In resource-limited settings, this simple test could flag patients needing closer observation. In practice, most cases of mild hyponatremia require no specific therapy beyond judicious fluid choice (avoid hypotonic fluids), but moderate/severe hyponatremia may necessitate restriction of free water or even cautious hypertonic saline in critically ill children. Our higher mortality in moderate/severe hyponatremia suggests that early recognition could trigger life-saving interventions.

**Strengths and Limitations:** This study’s strengths include prospective design and adherence to standardized WHO criteria, yielding reliable severity classification. We included a broad age range (2–60 months), relevant to pediatric practice. However, limitations exist. Being a single-center study, external generalizability is limited. The sample size, while adequate to detect the prevalence and basic associations, may not capture rarer outcomes. We did not measure biomarkers (e.g. ADH, BNP) to elucidate mechanisms. Also, as an observational study, we can only infer associations, not causation. Unmeasured factors (e.g. viral pathogen) could influence both severity and sodium.

## CONCLUSION

In pediatric LRTI, hyponatremia is common and correlates strongly with severity of illness. In our study of 101 children aged 2–60 months, hyponatremia occurred in 41%, predominantly in those with severe or very severe pneumonia. Importantly, hyponatremia – especially moderate to severe – was associated with prolonged hospitalization and higher mortality. These findings are consistent with other Indian and international pediatric series.<sup>[4,5]</sup> Clinicians should consider checking serum sodium routinely in hospitalized children with pneumonia. Recognition of hyponatremia can help identify high-risk patients and

guide careful fluid management. Further research should explore the pathophysiologic mechanisms (e.g. ADH and cytokines) and test whether correcting hyponatremia impacts outcomes.

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