

## Original Research Article

# Incidence of hyponatremia and its utility as an indicator of morbidity in children hospitalised with community acquired pneumonia

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**Received:** 27 November 2019

**Revised:** 21 December 2019

**Accepted:** 27 January 2020

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## ABSTRACT

**Background:** The aims of the study were to determine the incidence of hyponatremia associated with pneumonia and to assess its utility as an indicator of morbidity in children hospitalized with community acquired pneumonia between 2 months and 5 years of age.

**Methods:** This was a prospective study of children aged 2 months to 5 years hospitalized with community acquired pneumonia. 120 children aged 2 months to 5 years with symptoms of lower respiratory tract infection and had radiological evidence of pneumonia were recruited into the study. Children with chronic diseases, previously treated with intravenous fluids and those with chronic drug intake were excluded from study.

**Results:** Of the 120 children, 40.8% (49/120) had hyponatremia at admission. The relationship of hyponatremia to different clinical and laboratory parameters was analyzed. Sixty-one percent (31/51) of children under 1 year and 26% (18/69) of children between 1 to 5 years of age had hyponatremia ( $P = 0.001$ ). Hyponatremia was seen more commonly in children with severe pneumonia, with initial high temperature ( $P = 0.001$ ), with tachycardia ( $P = 0.001$ ), leukocytosis ( $P = 0.001$ ), increased neutrophils ( $P = 0.001$ ) and reactive thrombocytosis ( $P < 0.001$ ) and in children who had hemodynamic instability on admission ( $P < 0.001$ ). All 11 (9.2%) children who required mechanical ventilation had hyponatremia ( $P < 0.001$ ). Consolidation was significantly associated with hyponatremia ( $P < 0.001$ ). Hyponatremia also showed a significant association with prolonged hospital stay ( $P < 0.001$ ).

**Conclusion:** The incidence of hyponatremia in children hospitalised with pneumonia is 40.8%. This study concludes that the hyponatremia shows a significant association with the morbidity of the disease like requirement of intensive care and mechanical ventilation, hemodynamic instability and prolonged hospital stay. Hence the presence of hyponatremia at admission can be used as an indicator of morbidity.

**Keywords:** Community acquired pneumonia, Hyponatremia, Morbidity indicator, Prolonged hospital stay

## INTRODUCTION

Pneumonia is the leading infectious killer of children claiming more lives than any other diseases. Around 15% of under 5 mortality is attributed to pneumonia. The burden is more common in the developing nations.

Pneumonia caused the death of around 935,000 children under the age of 5 years globally in 2013.<sup>1</sup> India and Nigeria were the two countries which contributed to majority of cases.<sup>2</sup> Pneumonia can present in many ways and can also lead to many complications. Hyponatremia (HN) is a common electrolyte disturbance occurring in children hospitalized with pneumonia. The basic

pathophysiology is thought to be due to stress induced release of anti-diuretic hormone (ADH). This inappropriate production of ADH results in water retention and hence euvoletic hyponatremia leading to the Syndrome of inappropriate antidiuretic hormone (SIADH) secretion.<sup>3</sup> But hyponatremia is a frequently overlooked complication and little importance is paid to it. The range of symptoms of hyponatremia are headache, vomiting, lethargy, seizures, coma and apnoea. The symptoms are related to both serum sodium levels and rate of decline. The diagnosis of SIADH occurring in pneumonia can be confirmed by measuring serum electrolytes, serum osmolality, urine sodium and urine osmolality. The main treatment in SIADH is fluid restriction.<sup>4,5</sup>

The aims of the study were to determine the incidence of hyponatremia associated with pneumonia and to assess its utility as an indicator of morbidity in children hospitalized with community acquired pneumonia between 2 months and 5 years of age.

## METHODS

This prospective observational study was conducted at Institute of Child Health and Hospital for Children, Madras Medical College from February 2015 to August 2015. The protocol was approved by Institutional Ethics Committee. 120 children who met the inclusion criteria were recruited into the study after obtaining informed written consent from parents by convenience sampling method. Children aged 2 months to 5 years with symptoms of lower respiratory tract infection (fever, increased respiratory rate, chest retraction) and radiological evidence of pneumonia were included in the study. Children with chronic diseases, previously treated with intravenous fluids and those with chronic drug intake were excluded from study. The clinical severity of disease was classified into mild to moderate and severe according to British Thoracic Society (BTS).<sup>6</sup> The baseline demographic characteristics and clinical characteristics were obtained from all the children at the time of admission after detailed history taking and clinical examination. Temperature of the children was measured at the axilla using a digital thermometer. Oxygen saturation was measured using Nelcor pulse oximeter. Routine blood investigations like full blood count, renal function tests, serum electrolytes, random blood sugar, C reactive protein (CRP), blood culture etc. were drawn from the patient and sent without any delay on the day of admission before commencing any treatment. Full blood counts were analyzed using an auto analyzer. The blood samples were analyzed using Erba Manihier EM 200 auto analyzer at the biochemistry laboratory. Serum sodium and potassium were measured by Ion selective electrode method. Serum creatinine was measured using Jaffe's kinetic method and serum urea by enzymatic method (Glutamate dehydrogenase). Random blood sugar was measured by glucose oxidase peroxidase method. Urine spot sodium was measured by ion

selective electrode (ISE) method. Urine osmolality was measured using freezing point depression method. All the investigations were collected, and the values were documented. The results of total white cell count and neutrophil percentage were interpreted based on the reference ranges shown in Table 1.

**Table 1: Normal WBC count and neutrophils.**

Age of the child	Total count	Neutrophil (%)
2 months-5months	6000-18000	30
6months-5years	6000-15000	45

**Table 2: Platelet count.**

Normal	1.5lakhs - 4.5lakhs
Thrombocytopenia	Less than 1.5lakhs
Reactive Thrombocytosis	Greater than 5lakhs

**Table 3: Renal function test.**

Normal serum urea	11- 39 mg/dl
Normal serum creatinine	0.3- 0.7 mg/dl

**Table 4: Radiological criteria<sup>18-20</sup>.**

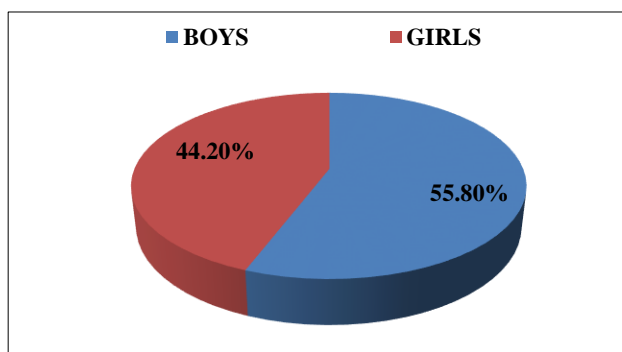
Radiological finding	Definition
Pneumonitis	Small ill-defined non homogenous linear or reticular opacities.
Bronchopneumonia	Patchy areas of non-homogenous white opacity which is multifocal and bilateral
Consolidation	Homogenous white opacity obscuring the vessels with or without air bronchograms
Empyema	Homogenous white opacity of the pleural space with compression of the underlying lung segment (and diagnostic pleural aspirate showing pus)

Platelet counts were reported as normal or abnormal based of the reference ranges as shown in table 2. Serum urea and creatinine values were interpreted based on the reference ranges shown in Table 3. The chest x-ray reports were obtained from a single radiologist after blinding the test results and the study definitions which were used are given in Table 4. Hyponatremia was graded as mild (131 to 134 mmol/L), moderate (126 to 130 mmol/L) and severe ( $\leq 125$  mmol/L) according to Ellison and Berl.<sup>5</sup> Estimated serum osmolality was calculated for all the patients in the study using serum sodium, urea and blood glucose {Osmolality =  $2 \times \text{Na}^+$  (mmol/L) + Urea(mg/dL)/6 + Glucose(mg/dL)/18}. The estimated serum osmolality was considered normal when the values were between 280 to 290 mOsm/Kg and

decreased when the value was less than 280 mOsm/Kg. In hyponatremic children additional investigations such as urine spot sodium and spot urine osmolality were sent. Urine spot sodium was considered elevated when the value was above 30 mEq/L. In patients with hyponatremia urine osmolality above 100mOsm/Kg was considered elevated. Fluid volumes were restricted to 2/3<sup>rd</sup> of maintenance requirements for all children with hyponatremia. In hyponatremic children serum sodium values were repeated on day 4 after admission. To assess the relationships between the various parameters and hyponatremia, univariate analyses were performed. All the data obtained were categorized into qualitative variables. The data was analyzed using SPSS Software version 20.0. The primary outcome was expressed as proportion. Chi Square test was used to determine the association between outcome variable and dependent variable. P value <0.05 was considered significant.

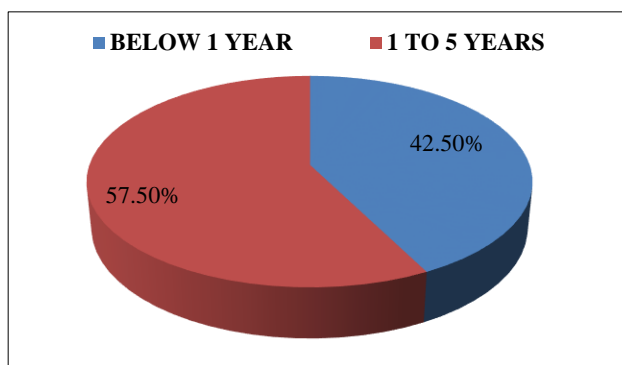
## RESULTS

A total of 120 children were recruited into the study which included 67 (55.8%) boys and 53 (44.2%) girls as shown in Figure 1.



**Figure 1: Sex distribution in the study population.**

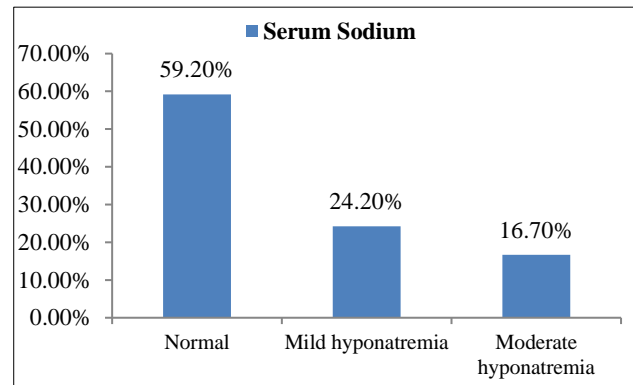
Among them 42.5% (51/120) of children were less than 1 year and 57.5% (69/120) were between 1 to 5 years of age as shown in Figure 2.



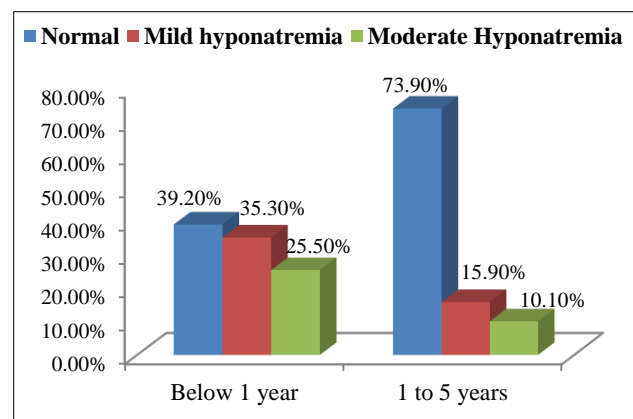
**Figure 2: Age distribution in the study population.**

The incidence of HN at the time of admission was found to be 40.8% (49/120). The degree of HN was mild in

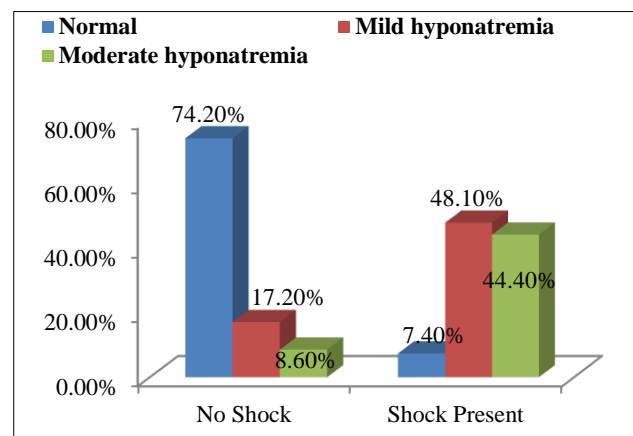
24.2% (29/120) and moderate in 16.7% (20/120) of children as shown in Figure 3. None of the patients had severe HN. The relationship of HN to different clinical parameters (such as age, sex, BTS class, admission temperature, admission heart rate, shock, requirement for mechanical ventilation, length of hospital stay, outcome) and laboratory parameters (initial total white blood cell count, neutrophil count, platelet count, blood culture, CRP, chest x-ray) were analyzed.



**Figure 3: Grades of hyponatremia in the study population.**



**Figure 4: Comparison of serum sodium level with age.**



**Figure 5: Comparison of serum sodium level with shock.**

**Table 5: Comparison of serum sodium with different study parameters.**

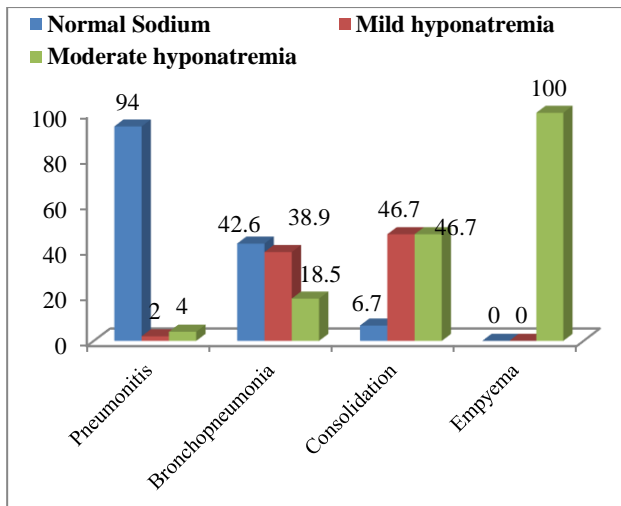
Study parameter		Mild HN	Moderate HN	Normal sodium	p value
Age	Below 1 year	18	13	20	0.001
	1 to 5 years	11	07	51	
Sex	Boy	19	07	41	0.094
	Girl	10	13	30	
BTS class	Mild- moderate	05	03	68	<0.001
	Severe	24	17	03	
Temperature	<38.5°C	05	02	63	<0.001
	>38.5 °C	24	18	08	
Heart rate	Normal	05	0	58	<0.001
	Tachycardia	24	20	13	
Hemodynamic instability	Absent	16	08	69	<0.001
	Present	13	12	02	
Mechanical ventilation	No	24	14	71	<0.001
	Yes	05	06	0	
Total count	Normal	02	0	51	<0.001
	Increased	27	20	20	
Neutrophil count	Normal	02	0	51	<0.001
	Increased	27	20	20	
Platelet count	Decreased	02	01	02	<0.001
	Normal	15	07	69	
	Increased	12	12	0	
Blood culture	No growth	28	18	71	0.038
	Growth	01	02	0	
Qualitative CRP	Negative	0	0	06	0.113
	Positive	29	20	65	
Chest x-ray	Pneumonitis	01	02	47	<0.001
	Bronchopneumonia	21	10	23	
	Consolidation	07	07	01	
	Empyema	0	01	0	
Length of stay (days)	Up to 7	02	0	67	<0.001
	8 to 14	25	12	04	
	Above 14	01	05	0	
Outcome	Death	01	03	0	0.004
	Improved	28	17	71	

Figure 4 shows that 61% (31/51) of children under 1 year had hyponatremia compared to 26% (18/69) between 1 to 5 years of age ( $p = 0.001$ ). There was no significant sex related difference in distribution of hyponatremia ( $P = 0.094$ ).

Hyponatremia was more common in children who had severe pneumonia according to BTS class at admission ( $P < 0.001$ ) and in those who had high initial temperature ( $P < 0.001$ ), tachycardia ( $P < 0.001$ ) and hemodynamic instability on arrival ( $P < 0.001$ ). Among the children with hemodynamic instability 48.1% (13/27) had mild hyponatremia and 44.4% (12/27) had moderate hyponatremia as shown in Figure 5.

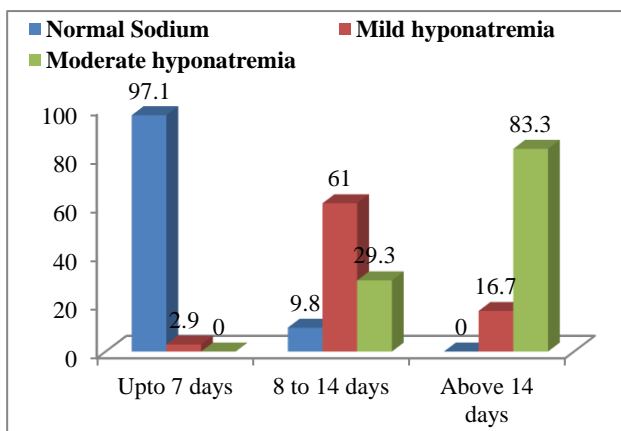
Hyponatremia was significantly associated with leukocytosis ( $P < 0.001$ ), high neutrophils ( $P < 0.001$ ) and

reactive thrombocytosis ( $P < 0.001$ ). Eleven (9.2%) children required mechanical ventilation and all of them had hyponatremia which was mild in 45.5% (5/11) and moderate in 54.5% (6/11) which is statistically significant ( $P < 0.001$ ). Only 3 (2.5%) children showed growth in blood culture (2-MRSA; 1-E.coli). All the children with positive blood culture had hyponatremia ( $P = 0.038$ ). No association was found between qualitative CRP and hyponatremia ( $P = 0.113$ ) (Table 5). Figure 6 shows that among the 45% (54/120) of children with bronchopneumonia, 38.9% (21/54) had mild hyponatremia and 18.5% (10/54) had moderate hyponatremia. Of the 15 children with consolidation, only 1(6.7%) child was found to be normonatremic, 46.7% (7/15) had mild hyponatremia and 46.7% (7/15) had moderate hyponatremia. Out of the 120 children 50 (41.7%) children had pneumonitis.



**Figure 6: Comparison of serum sodium level with radiological findings.**

Among them only 3 (6%) had hyponatremia. Only 1 child had empyema and had moderate hyponatremia. Hyponatremia was significantly associated with consolidation ( $P < 0.001$ ) and prolonged hospital stay ( $P < 0.001$ ) (Figure 7). Of the 120 children enrolled in the study 4 (3.3%) children died and all of them had hyponatremia [mild in 1 and moderate in 3,  $P = 0.04$ ]. All the above results are summated in Table 5.



**Figure 7: Comparison of serum sodium level with length of hospital stay.**

Estimated serum osmolality was found to be low in all patients with hyponatremia. The serum urea and creatinine levels were normal in all patients. Urine spot sodium and urine osmolality were increased in 45 (91.8%) patients with hyponatremia.

## DISCUSSION

The study sample is representative of children with CAP admitted in a tertiary care center in South India. The study confirms that hyponatremia is a common finding (40.8%) in children admitted with CAP. The incidence of

hyponatremia in this study is comparable with the results of previous studies by Massimiliano et al (45.4%), Wrotek et al (33.3%) and Sakellaropoulou et al (35.2%).<sup>7-9</sup> However, the majority had only mild hyponatremia. The fact that none of the patients had severe hyponatremia could be due to release of Atrial natriuretic peptide (ANP) in these children. ANP helps in maintaining water and electrolyte balance through its diuretic and natriuretic effects as described by Haviv et al.<sup>10</sup> This study showed that hyponatremia is significantly associated with initial high temperature, tachycardia and elevation of non-specific inflammatory markers. All these results are in concordance with the results of the previous studies.<sup>11-17</sup> Hyponatremia was seen more in children with bronchopneumonia and with consolidation. The more frequent association of hyponatremia with consolidation in this study supports the study by Glatstein et al.<sup>11</sup>

Most of the children with hyponatremia had low estimated serum osmolality, high urine sodium and high urine osmolality indicating that it is euvoletic hypotonic hyponatremia. By conventional criteria all these patients may be labelled as having SIADH since most of the features fit into the diagnostic criteria.<sup>4,17</sup> Thus stress induced release of ADH causing salt loss and water retention might be the reason for hyponatremia. However further studies are needed to unravel the cause of hyponatremia in acute infections. Repeat serum sodium measurements done on 4th day of hospitalization were found to be normal in almost all subjects with hyponatremia suggesting that fluid restriction by itself can correct hyponatremia.

Four children included in the study died. All the four children were found to be hyponatremic. This deserves a special mention, but studies need to be done in large numbers of patients to establish a significant association with mortality. All the children who required mechanical ventilation were found to be hyponatremic, as well. Hence this study showed that hyponatremia showed a significant association with morbidity associated with CAP like requirement of mechanical ventilation and intensive care admission, hemodynamic instability and prolonged hospital stay.

## CONCLUSION

The study concludes that hyponatremia is a common finding in children hospitalised with community acquired pneumonia with an incidence of 40.8% in this study. This study highlights the fact that hyponatremia at admission is associated significantly with severity (BTS classification, initial high temperature, serum nonspecific inflammatory markers) and morbidity (requirement of intensive care and mechanical ventilation, hemodynamic instability and prolonged hospital stay). Hence hyponatremia at admission can be utilized as an indicator of morbidity associated with CAP. This study also stresses the importance of measuring serum electrolytes in children admitted with pneumonia.



*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Natarajan T, Sadique TNS, Shanmugham K. Incidence of hyponatremia and its utility as an indicator of morbidity in children hospitalised with community acquired pneumonia. *Int J Contemp Pediatr* 2020;7:616-21.