

## Original Research Article

# Study of hyponatremia as a prognostic marker in lower respiratory tract infections in children

Mandira Sarkar<sup>1</sup>, Pramila Ramawat<sup>2</sup>, Vandana Varma<sup>3</sup> & Shachi Jain Taran<sup>4</sup>

<sup>1</sup> Postgraduate Resident, <sup>2</sup> Assistant Professor, Department of Pediatrics, <sup>3</sup> Associate Professor, Department of Biochemistry, <sup>4</sup> Associate Professor, Department of Pediatrics, Mahatma Gandhi Memorial Medical College & M.Y Hospital, Indore, Madhya Pradesh, India

Corresponding Author: Dr. Shachi Jain Taran

## Abstract

**Background:** Lower respiratory tract infection(LRTI) is a single largest cause of death in children worldwide. Hyponatremia is the most common electrolyte disturbance in admitted patients of LRTI. This study may help in prognostication of disease in terms of course, complication and possible outcome in these patients.

**Objective:** To estimate prevalence of hyponatremia in hospitalized patients of LRTI and to identify demographic, clinical and laboratory factors, complications and outcome associated with hyponatremia in patients with LRTI.

**Materials and Methods:** Children between 1 month to 18 years with LRTI admitted in department of pediatrics in a tertiary care centre in central India, as per inclusion and exclusion criteria were enrolled and their detailed clinical history, physical examination, routine investigations and serum sodium levels, complication, treatment were recorded.

**Results:** Out of 150 patients of LRTI admitted, hyponatremia was present in 43 cases (27%). Mild and moderate hyponatremia were present in 19.3% and 9.3% patients respectively. Hyponatremia was found to be more common in 1 to 5 years. Mean duration of hospital stay was longer in hyponatremic children. 69.8% of patients with hyponatremia on admission were found to have SIADH which was statistically significant. Mortality in patients with hyponatremia was 18.6%, which was significantly higher as compared to eunatremic patients where mortality was only 1.9%.

**Conclusion:** Hyponatremia is a common association among hospitalized children with LRTI. Serum sodium level at the time of admission can be used for timely identification and intervention of at risk LRTI patients and may help in reduction of morbidity and mortality.

**Keywords:** Hyponatremia, Pneumonia, SIADH, LRTI, Sodium

## 1. INTRODUCTION

LRTI is an infection of respiratory tract beneath the larynx, include Pneumonia, Wheeze associated LRTI (WALRI), Bronchiolitis and Empyema. <sup>[1]</sup> Pneumonia is the single largest infectious cause of death in children worldwide. It is a common illness affecting children, especially in developing countries accounting for approximately one fifth of childhood deaths. <sup>[2]</sup>

As per WHO data 2019, Pneumonia killed 7,40,180 children under the age of 5, accounting for 14 % of all deaths of children <sup>[2]</sup>.10-15 % of hospitalized children require intensive care

due to imminent respiratory failure and severe respiratory distress. These children are critically ill and often have complications like electrolyte abnormalities, pleural effusion, empyema, pericardial effusion, meningitis. Hyponatremia is the most common electrolyte irregularity seen in the intensive care unit (ICU), with an occurrence as high as 30% in some reports.<sup>[3]</sup> But hyponatremia is a frequently overlooked complication and little importance is paid to it.

As there are paucity of studies regarding association of hyponatremia with lower respiratory tract infection in children and serum sodium level may help to predict the course, complication and possible outcome in these patients. Hence, present study was planned to assess the prevalence of hyponatremia and its role for prognostication in admitted patients of lower respiratory tract infections (LRTIs).

Timely intervention and identification of at risk children will lead to better and prompt management of these critically ill patients and LRTI related morbidity and mortality can be reduced.

## 2. MATERIALS AND METHODS

Prospective analytical and single centred study conducted over 1 year in the department of Pediatrics at a tertiary care centre in central India after approval from Institutional Ethics Committee. All children whose parents agreed to give written informed confirmed consent and assent above 1 month till 18 years of age with clinical or radiological signs of LRTI requiring hospitalization were included in our study. Children who are on drug therapy which can cause hyponatremia such as diuretics, congestive cardiac failure (CCF), renal disease, acute gastroenteritis and dehydration and those who left against medical advice (LAMA) before final outcome were excluded from the study.

Patients were diagnosed with LRTI based on clinical and radiological findings. Patient was managed according to unit protocol. Routine investigations like complete blood count, serum electrolytes, C reactive protein was drawn from patient and sent on the day of admission before starting any treatment. Serum sodium was measured by ion selective electrode method. Hyponatremia was graded as mild (131- 134 mg/dl), moderate (126 -130 mg/dl), severe ( $\leq 125$  mg/dl). Estimated serum osmolality was calculated for all patients and in hyponatremic patients with low serum osmolality additional investigations like urine spot sodium and urine osmolality were sent. Patients with hyponatremia with low serum osmolality ( $< 280$  mOsm/kg), high urine osmolality ( $> 100$  mOsm/kg) and high urinary sodium ( $> 30$  mEq/L) were diagnosed as SIADH. All relevant clinical details, laboratory findings, interventions, duration of hospital stay and outcome were recorded in preformed proforma.

## STATISTICAL ANALYSIS

Descriptive statistics was applied to obtain the frequency distribution. Pearson's Chi-square test was applied to determine the association between two different variables. Comparison of mean values of any numeric parameters for any two groups was done using student 't' test for two sample mean. The p-value of  $<0.05$  was considered significant. The data was analysed by statistical software SPSS 25.

## 3. RESULTS AND OBSERVATIONS

The study population contained 107 (71.3%) children with normal sodium levels at admission while mild hyponatremia and moderate hyponatremia was seen in 29 (19.3%) and 14 (9.3 %) children respectively. No patients were found to have severe hyponatremia. The prevalence

of hyponatremia was found to be 28.6%. Among patients with anemia, higher total leukocyte count and higher CRP, hyponatremia was found to be more associated ( $p < 0.05$ ) (Table 1). Children with hyponatremia on admission had significantly higher mechanical ventilation and inotrope requirement as compared to eunatremic patients. Duration of PICU and hospital stay was longer in hyponatremic patients as compared to eunatremic patients (Table 2). Among 43 hyponatremic patients, 18.6% were expired which was significantly ( $p < 0.05$ ) higher in comparison to eunatremic group, wherein 1.9% patients expired (Table 3). Amongst 43 cases of hyponatremia, 30 (69.8%) patients were found to have SIADH. In our study SIADH was significantly higher in patients with moderate hyponatremia on admission as compared to mild hyponatremia. ( $p < 0.05$ ) (Table 4).

TABLE 1: ASSOCIATION OF DEMOGRAPHIC AND LABORATORY PARAMETERS WITH SERUM SODIUM

Parameters		S.Na		Total N = 150 (%)	p Value
		Hyponatremia N = 43 (%)	Eunatremia N = 107 (%)		
Age	1-12 months	7 (16.3%)	75 (70.1%)	82 (54.7%)	0.001
	1-5 years	27 (62.8%)	13 (12.1%)	40 (26.7%)	
	>5 years	9 (20.9%)	19 (17.8%)	28 (18.7%)	
Sex	F	20 (46.5%)	52 (48.6%)	72 (48%)	0.817
	M	23 (53.5%)	55 (51.4%)	78 (52%)	
Hemoglobin	Normal	7 (16.3%)	90 (84.1%)	97 (64.7%)	0.000
	Decreased	36 (83.7%)	17 (15.9%)	53 (35.3%)	
Total Leucocyte Count	Normal	1 (2.3%)	64 (59.8%)	65 (43.3%)	<0.001
	Raised	42 (97.7%)	43 (40.2%)	85 (56.7%)	
Platelets	Decreased	8 (18.6%)	8 (7.5%)	16 (10.7%)	0.000
	Normal	10 (23.3%)	96 (89.7%)	106 (70.7%)	
	Raised	25 (58.1%)	3 (2.8%)	28 (18.7%)	
C Reactive Protein	Normal	7 (16.3%)	99 (92.5%)	106 (70.7%)	< 0.001
	Raised	36 (83.7%)	8 (7.5%)	44 (29.3%)	

TABLE 2. ASSOCIATION OF INTERVENTIONS AND COMPLICATIONS WITH SERUM SODIUM LEVELS

Charateristics		Sodium Level		Total ( N = 150 )	p value
		Hyponatremia ( N = 43 )	Eunatremia ( N = 107 )		
Mechanical	N	32 ( 74.4%)	96 ( 89.7%)	128 (85.3%)	0.001
	Y	11 (25.6%)	11 (10.3%)	22 (14.7%)	

ventilation					
Inotrope	N	35 ( 81.4%)	103 (96.3%)	138 (92%)	0.002
	Y	8 ( 18.6%)	4 ( 3.7%)	12 (8.0%)	
Total hospital stay	≤ 7 Days	29 (67.4%)	92 (86.0%)	121 (80.7%)	0.009
	> 7 Days	14 (32.6%)	15 (14.0%)	29 (19.3%)	
PICU stay	< 2 Days	15 (34.9%)	60 (56.1%)	75 (50%)	0.019
	> 2 Days	28 (65.1%)	47 (43.9%)	75 (50%)	

TABLE 3: ASSOCIATION OF OUTCOME AND SERUM SODIUM LEVELS

Outcome	S.Na		Total N=150	p value
	Hyponatremia (N= 43)	Eunatremia N= 107		
Death	8 (18.6%)	2 (1.9%)	10 (6.7%)	0.000
Discharge	35 (81.4%)	105 (98.1%)	140 (93.3%)	

TABLE 4: ASSOCIATION OF SIADH WITH SEVERITY OF HYPONATREMIA

Cause of hyponatremia	Hyponatremia		Total	p Value
	Mild	Moderate		
No SIADH	13 (44.8%)	0 (0.0%)	13 (30.2%)	0.005
SIADH	16 (55.2%)	14 (100%)	30 (69.8%)	

#### 4. DISCUSSION

In our study hyponatremia was found in 43 ( 28.6%) cases. This was similar to *Attri et al's* analysis in which hyponatremia was present in 33% of children who were hospitalized due to LRTI <sup>[4]</sup> and *Mandal et al* where hyponatremia was seen in 21% <sup>[5]</sup> . This was comparable to few other studies like *Singhi et al* <sup>[6]</sup> done in India where the hyponatremia was found to be 27%.

Out of all cases of hyponatremia, 29 (19.3%) cases had mild hyponatremia and 14 (9.3%) cases had moderate hyponatremia, no cases of severe hyponatremia were seen in our study group. A study done by *Channawar et al* <sup>[7]</sup>, states that out of 54 diagnosed hyponatremia cases, 10 cases (18.5%) had moderate hyponatremia and 3 cases (5.5%) had severe hyponatremia . Another study done by *Sakellaropoulou A et al* <sup>[8]</sup> found that out of 54 patients, 33.3% of patients had mild and 1.9% had moderate hyponatremia. Our findings resonated with the previous studies like *Mandal et al* <sup>[5]</sup> and *Hasegawa et al* <sup>[9]</sup> which also reported majority of the cases with mild hyponatremia. In our study severe hyponatremia were not seen could be attributed by the fact that it was based on small sample size and not representative of entire population.

In our study it was found that age group of 1 - 5 years carried a significantly increased risk of hyponatremia in relation to other age groups. There are very few studies which had reported on the age related association of hyponatremia. *Wrotek et al's* found that the age group of more than 4 years has greater chance of hyponatremia and severe infection

<sup>[10]</sup>. *Park et al.* found that increasing age is an independent risk factor for the development of hyponatremia <sup>[11]</sup>. The difference of results obtained in our study may be due to classification of age group taken into consideration. In *Wrotek et al's* <sup>[10]</sup> study the children were divided into two age groups: under and over the age of four, while in the current study children were divided into three age groups. The study population contained 52% males and 48% females. Sex of the child had no correlation with hyponatremia. This was shown by other study done by *Don M et al* <sup>[12]</sup> in sex distribution of pneumonia.

Among the laboratory parameters studied by us like CRP, WBC count and platelet count taken as surrogate markers for severity of illness, were significantly higher in hyponatremic group. *Don et al* <sup>[12]</sup> also found higher WBC count, neutrophil percentage, thrombocytosis and serum CRP in hyponatremic patients on admission, indicating that increasing inflammation may be associated with the severity of hyponatremia. *Kanai et al* <sup>[13]</sup> also reported that during admission severity of fever and CRP levels both are early features of pneumonia.

Patients of hyponatremia had longer duration of hospital stay. In our study, children with hyponatremia on admission had longer hospitalization times. An association was observed between degree of hyponatremia and duration of hospitalization. This was similar to *Nair et al* <sup>[14]</sup>, which found hyponatremia to be associated with more severe presentation on admission and extended hospital stays. In our study out of 22 cases which needed mechanical ventilation 50% cases were hyponatremic on admission. This was in line with study conducted by *Lamichhane et al* <sup>[15]</sup> showed that out of 6 cases who needed mechanical ventilation all of them had hyponatremia.

In our study children admitted with LRTI with hyponatremia on admission were having significantly longer duration of PICU stay ( $4.37 \pm 2.4$  days) as compared to eunatremic patients ( $2.93 \pm 1.88$  days). Mean hospital stay ( $7.37 \pm 4.33$  days) in hyponatremic group as compared to ( $5.36 \pm 2.77$  days) in children with normal serum sodium levels. *Nair et al* <sup>[14]</sup> found hyponatremia to be associated with more severe illness and extended hospital stays. This was in line with *Patil et al* <sup>[16]</sup> wherein mean duration of hospital stay of patients with hyponatremia in pneumonia was  $9.54 \pm 2.63$  days, however in patients without hyponatremia was  $6.43 \pm 1.16$  days. Association of hyponatremia with duration of stay was significant, the result is consistent with our study.

Mortality in hyponatremic group was found to be 18.6% as compared to eunatremic group where mortality was only 1.9%. Mortality was significantly high ( $p < 0.05$ ) in patients with hyponatremia on admission as compared to normal serum sodium levels. It was 19.25 times higher in *Mandal et al* <sup>[5]</sup>, 3.5 times higher in the study by *Singhi and Dhawan* <sup>[17]</sup>, 7 times higher in study by *Tierney WM et al* <sup>[18]</sup>.

Most of the children with hyponatremia had decreased serum osmolality, high urine osmolality and high urine sodium indicating euvoletic hyponatremia and were conventionally labelled as having SIADH. In the current study SIADH was found in one fifth of children admitted with LRTI comprising about 20%. SIADH was major cause of hyponatremia in our study comprising of 69.8% of all patients with hyponatremia. This was in line with *Jain et al* <sup>[19]</sup> wherein SIADH was found in 72.2% of all hyponatremic children admitted with LRTI. It has been proposed that fever resets the hypothalamic thermostat and osmostat (for ADH secretion) in children. The new osmostat increases the secretion of ADH, causing fluid retention and decreased osmolality in the body, thereby leading to hyponatremia. Based on current study results and study done by *Park et al* <sup>[11]</sup>, it is demonstrated that SIADH may be the result of inflammation wherein proinflammatory

cytokines such as IL-1 $\beta$  and IL-6 form the primary mediators causing increased ADH secretion and SIADH.

There is still an enigma whether hyponatremia in most patients is simply a powerful marker of severity of underlying disease or a direct contributor to the adverse outcome observed. But whatever it may be, hyponatremia is a compelling marker of adverse outcome. Various studies have concluded that fluid therapy in pneumonia should be individualized and not generalized. Those having hyponatremia with hyperosmolality need liberal fluids while those with hyposmolality need fluid restriction.

### **LIMITATION**

Limiting factors for our study was small sample size, cases were taken from single centre, serum sodium was taken only on admission and serial sodium monitoring could not be done. Since our study centre was a tertiary referral centre, many sick babies were referred to the hospital from various hospitals and their pre admission fluid therapy was unknown.

### **5. CONCLUSION**

Hyponatremia is quite common among those children hospitalized with LRTI. Initial measurement of serum is recommended in all hospitalized LRTI patients and patients showing hyponatremia on admission should get special attention as it is a strong indicator of higher mortality and morbidity. Regular follow up of serum sodium level during period of hospital stay should be considered to pick up the high risk cases at an early stage. Whether early treatment of hyponatremia improves outcome is not clear and need further study that can enlighten upon the amount of fluid restriction essential to improve outcome without causing complications.

### **6. REFERENCES**

1. Park K. Acute respiratory infections. In: Park's text book of preventive and social medicine, 20th ed. Jabalapur: M/s Banarasidas Bhanot Publishers; 2009. p.151-9.
2. World Health Organization. Pneumonia Factsheet. Geneva: WHO; <http://www.who.int/news-room/factsheets/detail/pneumonia>
3. Upadhyay A, Jaber BL, Madias NE. Incidence and prevalence of hyponatremia, American Journal of Medicine. 2006;119(7):30-5.
4. Attri HK, Singh T, Vandana, Sehgal G, Kumar K. Impact of Hyponatremia on Clinical Presentation and Management in Pediatric Patients with lower Respiratory Infections.
5. Mandal PP, Garg M, Choudhary IP. To study the association and significance of hyponatremia in pneumonia in paediatric patients treated in hospital setting. Age (months). 2018;18:18-6.
6. Singhi S, Dhawan A. Frequency and significance of electrolyte abnormalities in pneumonia. Indian pediatrics. 1992 Jun 1;29(6):735-40.
7. Channawar, Kanchan S., et al. "Correlation of hyponatraemia in children with lower respiratory tract infection--an institutional observational study." *Journal of Evolution of Medical and Dental Sciences*, vol. 5, no. 88, 3 Nov. 2016, pp. 6533+.
8. Sakellaropoulou A, Hatzistilianou M, Eboriadou M, Athanasiadou-Piperopoulou F. Clinical research Hyponatraemia in cases of children with pneumonia. Archives of Medical Science. 2010;6(4):578-583. doi:10.5114/aoms.2010.14471.
9. Hasegawa K, Stevenson MD, Mansbach JM, Schroeder AR, Sullivan AF, Espinola JA, Piedra PA, Camargo Jr CA. Association between hyponatremia and higher bronchiolitis

- severity among children in the ICU with bronchiolitis. *Hospital pediatrics*. 2015 Jul;5(7):385-9.
10. Wrotek A, Jackowska T. Hyponatremia in children hospitalized due to pneumonia. In *Neurobiology of Respiration 2013* (pp. 103-108). Springer, Dordrecht.
  11. Park SW, Shin SM, Jeong M, Cho DH, Lee KH, Eisenhut M, Kronbichler A, Moritz M, Il Shin J. Hyponatremia in children with respiratory infections: a cross-sectional analysis of a cohort of 3938 patients. *Scientific reports*. 2018 Nov 7;8(1):1-9.
  12. Don M, Valerio G, Korppi M, Canciani M. Hyponatremia in pediatric community-acquired pneumonia. *Pediatric nephrology*. 2008 Dec;23(12):2247-53.
  13. Kanai H, Sato Y, Ichihashi K. Hyponatremia in patients with respiratory syncytial virus bronchiolitis. *Pediatric Health Med Ther*. 2012 Jun 29;3(3):39-43.
  14. Nair V, Niederman MS, Masani N, Fishbane S. Hyponatremia in community-acquired pneumonia. *American journal of nephrology*. 2007;27(2):184-90.
  15. Lamichhane M, Shrestha L, Bajracharya L, Bagale A. Hyponatremia As A Predictor Of Adverse Outcome In Children With Severe Lower Respiratory Tract Infection In Tribhuvan University Teaching Hospital (Tuth), Nepal.
  16. Kanai H, Sato Y, Ichihashi K. Hyponatremia in patients with respiratory syncytial virus bronchiolitis. *Pediatric Health Med Ther*. 2012 Jun 29;3(3):39-43.
  17. Patil J. Hyponatremia in pneumonia in children: hospital based cross sectional study. *Journal of drug discovery and therapeutics*. 2015;3(30):17-22
  18. Tierney WM, Martin DK, Greenlee MC, Zerbe RL, McDonald CJ. The prognosis of hyponatremia at hospital admission. *Journal of general internal medicine*. 1986 Nov;1(6):380-5.
  19. Jain S, Kumar V, Kapoor S, Bhalke S, Gupta S. Assessment of serum sodium levels in patients of lower respiratory tract infections (LRTI) in children at tertiary care center