

Original Research Article

Hyponatremia in children with severe pneumonia and its effect on overall outcome

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ABSTRACT

Background: Severe pneumonia is often associated with dyselectrolytemia, most commonly hyponatremia and the level of sodium significantly correlates to the overall outcome of the patient. The present study was conducted to identify the incidence of hyponatremia in children with Severe Pneumonia and to identify its association with Syndrome of Inappropriate secretion of Anti Diuretic Hormone (SIADH) and the effect on morbidity, mortality and duration of hospital stay.

Methods: This study was conducted on 102 children between the age group of 6 months to 5 years admitted to the Upgraded Department of Pediatrics, Patna Medical College and Hospital with clinically and radiologically confirmed severe pneumonia from March 2017 to September 2018.

Results: There were 33(32.4%) cases of hyponatremia out of which 26(25.5%), 5(4.9%) and 2(1.9%) had mild, moderate and severe hyponatremia respectively. 19(57.6%) cases of hyponatremia were due to SIADH out of which the duration of hospital stay was prolonged in 10(52.6%) cases, 10(52.6%) cases developed complications and 7(36.8%) patients died. The mortality of patients with hyponatremia was significantly higher ($p < 0.05$) in the group with SIADH when compared to those without SIADH. The average duration of stay in hospital also was significantly higher ($p < 0.05$) for the group with hyponatremia i.e. 8.2 ± 4.5 days when compared to the group with normnatremia i.e. 7.3 ± 1.7 days.

Conclusions: Hyponatremia is commonly associated with Severe Pneumonia. Hyponatremia is usually mild and results in prolonged hospital stay, increased complications and mortality especially when associated with SIADH.

Keywords: Hyponatremia, Severe Pneumonia, Syndrome of inappropriate secretion of anti-diuretic hormone

INTRODUCTION

Globally, pneumonia is the leading cause of death among children younger than 5 years. The advances made in the field of medicine with better antibiotics and immunization has reduced the incidence of lower respiratory tract infection in the developed world. However, pneumonia is currently the leading cause of death in children younger than 5 years in developing countries, accounting for approximately 20% of childhood deaths.¹ India being developing country

pneumonia remains a significant cause of morbidity and mortality. The report, titled "Fighting for Breath", by non-profit organization Save the Children said that in 2015, 1,78, 717 children below the age of five died in India because of pneumonia - this means that every hour, 20 children died of the disease in the country that year.²

Electrolyte disturbances especially hyponatremia (serum sodium < 135 mEq/L) have been described in a wide variety of acute infections including pneumonia. Other abnormalities like hypernatremia (serum sodium > 145

mEq/L), hypokalemia (serum potassium <3.5 mEq/L and hyperkalemia (serum potassium >6 mEq/L) are other infrequent electrolyte disorders seen in Pneumonia.³

Hyponatremia is associated with worsened outcomes in patients with pneumonia and indicates a poor prognosis.^{4,5} According to the study conducted by Singhi and Dhawan, it resulted in longer hospital stay, two fold increase in complications and 3.5 times higher mortality than those with normonatremia.⁴

Water retention due to impaired renal water excretion secondary to SIADH has been described in several pulmonary conditions including lower respiratory tract infection in children.⁶ Hence, the current study was undertaken to identify the incidence of hyponatremia and its possible effect on the clinical course and outcome of severe pneumonia in children between 6 months to 5 years.

METHODS

A prospective study was conducted for a period of 19 months from March 2017 to September 2018 on 102 children between 6 months to 5 years admitted to the Upgraded Department of Pediatrics, Patna Medical College and Hospital with clinically and radiologically confirmed severe pneumonia. Severe pneumonia was defined according to modified World Health Organization (WHO) guidelines.⁷

Children with tachypnea (Infants 6 months to 1 year)

Respiratory rate >50 breaths/min and Children 1 to 5 years: Respiratory rate >40 breaths/min) and anyone or more of the following criteria were included in the study.

Infants 6 months to 1 year

Chest Retraction, Nasal Flaring, Cyanosis, Intermittent Apnea, Grunting, Not Feeding, Capillary Refill Time >2s, Oxygen Saturation <92%.

Children 1 to 5 years

Chest Retraction, Nasal Flaring, Cyanosis, Grunting, Capillary Refill time >2s, Oxygen Saturation <92%

Chest X-ray

Findings on chest X-ray suggestive of pneumonia are: Lobar consolidation, Alveolar infiltrates, Interstitial infiltrates, Hyperinflation.

Findings suggestive of complications of Pneumonia are

Pleural Effusion/empyema (blunting of costo-phrenic angle), pneumothorax (seen as hyperlucency), hydropneumothorax (seen as air fluid level in a hemi-thorax).

USG chest

Findings suggestive of pneumonia in USG are hypoechoic areas with blurred margins suggestive of consolidation.

At the time of enrollment an informed written consent was obtained from the parents/guardians. Detailed history was elicited from them with relevance to the case. Thorough General Examination was done with special attention to measuring the Respiratory Rate, Oxygen Saturation (by pulse oximetry) and presence of Cyanosis. Detailed clinical examination of the respiratory system was done with special focus on presence of nasal flaring, grunting, chest retractions (subcostal, xiphisternal, intercostals and suprasternal), rhonchi, crepitations, bronchial breathing and use of accessory muscles. Evaluation of the cardiovascular, gastrointestinal and central nervous system was also done.

All children were screened for hyponatremia on day 1 of admission by taking venous samples and measuring serum levels of sodium. In those cases where hyponatremia was detected further evaluation was done to determine the cause, including renal function tests (Blood Urea and Serum Creatinine levels) to rule out renal dysfunction. Urine Sodium, Serum Osmolality and Urine Osmolality were measured for all cases of hyponatremia. Hyponatremia was defined as serum sodium <135 mEq/L and was further classified as mild, moderate and severe. The severity of Hyponatremia was determined by the reports of Ellison and Berl.⁸ Serum concentration of 131-135 mEq/L means mild hyponatremia, 126-130 mEq/L means moderate hyponatremia, and ≤125 mEq/L means severe hyponatremia. SIADH was defined as plasma osmolality <275 mOsm/kg, urine osmolality >100 mOsm/kg and urine Na >20 mEq/L.

Inclusion criteria

- Children between 6 months and 5 years with radiologically and clinically confirmed Pneumonia.

Exclusion criteria

- Infants <6 months of age.
- Children >5 years of age.
- Children with renal disorders.
- Children with associated CNS infections.
- Children with gastroenteritis.
- Children on drugs which can cause electrolyte imbalance such as diuretics, anticonvulsants, etc.

Statistical analysis

Data was entered on an Excel spread sheet and then analyzed using SPSS 23 version. Collected data was analyzed by frequencies, percentage, mean, standard

deviation and by Chi-Square test. The significance level was set at 0.05 and confidence intervals were set at 95% level.

RESULTS

A total of 102 children aged 6 months to 5 years with clinically and radiologically confirmed Severe Pneumonia were enrolled in the study.

Out of 102 cases, 73(71.6%) were male and 29(28.4%) were female. The male to female ratio was 2.5:1 (Table 1).

Table 1: Sex distribution of children with severe pneumonia.

Sex	No. of patients	Percentage (%)
Male	73	71.6
Female	29	28.4
Total	102	100.0

Majority of the patients, 66(64.7%) were in the age group of 6 months to 11 months, while 36(35.2%) patients were in the age group of 1 year to 5 years. The mean age of patients was 1.3±0.4 years (Table 2).

Table 2: Age distribution of children with severe pneumonia.

Age	No. of males	No of females	Total
6 months - 11 months	47 (46.1%)	19 (18.6%)	66(64.7%)
1 year - 5 years	26 (25.5%)	10(9.8%)	36(35.3%)
Total	73	29	102

Table 3: Complications seen in children with severe pneumonia.

Complications	Number of patients	Percentage (%)
Pleural effusion	9	8.8
Pneumothorax	12	11.8
Hydropneumothorax	3	2.9
Empyema	4	3.9
Total	28	27.5

Complications developed in 27.5% of the patients (Table 3). Majority (25.5%) cases of hyponatremia had mild hyponatremia. Moderate hyponatremia and severe hyponatremia were seen in 5(4.9%) and 2(1.9%) cases respectively. Hypernatremia was seen in 3 cases only. Rest 66 cases had normonatremia. The mean serum sodium concentration was 131.3±3.7mmol/L in hyponatremic patients and 140.4±2.9mmol/L in normonatremic patients (Table 4).

It was observed that 57.6% of hyponatremia were due to SIADH (Figure 1).

Table 4: Serum sodium level in children with severe pneumonia.

Serum sodium level	Number of patients	Percentage (%)
Normonatremia (136-145meq/l)	66	64.7
Mild hyponatremia (131-135meq/l)	26	25.5
Moderate hyponatremia (126-130meq/l)	5	4.9
Severe hyponatremia (<126meq/l)	2	1.9
Hypernatremia (>145meq/l)	3	2.9

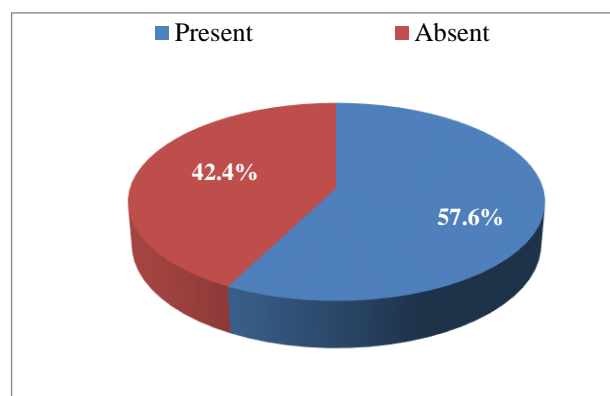


Figure 1: Percentage of patients admitted with severe pneumonia having hyponatremia due to SIADH.

Outcome of the 19 cases of hyponatremia due to SIADH shows that the duration of hospital stay was more than 7 days in 10(52.6%) cases. 10(52.6%) cases developed complications. 10(52.6%) patients were successfully discharged, 7(36.8%) patients died and 2 patients dropped out of the study (Table 5). 21.2% cases of hyponatremia due to SIADH had died. The mortality of patients with hyponatremia was found to be significantly higher (p=0.03) in the group with SIADH when compared to those without SIADH (Table 6).

The duration of hospital stay was significantly higher in the children with hyponatremia (p=0.0005) compared to those children without hyponatremia (p=0.01). Average duration of the hospital stay in the present study in severe pneumonia with normonatremia was 7.3±1.7 days (range of 5-9 days) while that with hyponatremia was 8.2±4.5 days (range of 1-14 days) including those cases who died (Table 7).

DISCUSSION

Table 1 shows that majority of the patients were male (71.6%). This is supported by the study conducted by Dhairya Lakhani and Prasad Muley in 2011 where they found that males were more commonly affected, as compared to females.⁹ In a study conducted by Joseph et

al, in December 2015, 74.8 % of the patients enrolled were males. Another study conducted by Eduardo Jorge da Fonseca Lima et al, (2016) concluded that male gender constituted a protective factor. The role of sex as a risk factor for Community Acquired Pneumonia (CAP) remains unclear, and no consensus has been reached in the literature. Males are more likely to develop lower

respiratory tract infections. The greater resistance found in females maybe explained by their enhanced Th1 immune response. Another contributing factor to the increased prevalence of pneumonia in males that has been seen in this study could be the gender bias prevalent in the study population where males receive preferential treatment over females.

Table 5: Outcome of patients with hyponatremia due to SIADH in children with severe pneumonia.

N= 19	Hospital stay \geq 7days	Complications	Successfully discharged	Dropouts	No of cases who died
Present	10	10	10	2	7
Absent	9	9	9	19	12

Table 6: Mortality in patients with hyponatremia with SIADH in children with severe pneumonia.

	SIADH	No SIADH	Total
Died	7(21.2%)	1(3.03%)	8
Alive	12	13	25
Total	19	14	33

*The chi-square statistic = 4.242. The p-value = 0.039436 i.e. significant at p <0.05

Table 7: Duration of hospital stay in children with hyponatremia versus those children without hyponatremia.

Characteristics	Hyponatremia N=33	p value	Normonatremia N=69	p value
Duration of hospital stay in days	8.2±4.5	0.0005	7.3±1.7	0.01

From Table 2, Author can see that the patients were divided into two groups. The 1st group included cases within the age of 6 months to 11 months and they constituted 64.7% of the study population. The 2nd group included cases within the age of 1 year to 5 years and they constituted 35.2% of the study population. Thus, in this study severe pneumonia was found to be more common in the first group which included the infants. Age has been associated with a greater incidence of respiratory infections in the pediatric population, with infants being more vulnerable to CAP. The most reasonable explanation is that later part of infancy is the transitional phase of immune physiology where maternal antibodies start to wane, and children are weaned off breast feeding, and complementary feeding is started. Table 3 shows that in this study, complications were seen in 28 out of 102 patients. The complications observed were pleural effusion in 9(8.8%), pneumothorax in 12(11.8%), empyema 4(3.9%) and hydropneumothorax in 3(2.9%) cases. In a study conducted by Rabia A. Ahmed, MD, Thomas J. Marrie, MD, Jane Q. Huang, MSc, in 2006 on patients of CAP a diagnosis of empyema was made in 47 patients (1.3%) by the attending physician; 24 patients (0.7%) met criteria for definite cases. The in-hospital mortality rate for patients with definite empyema was 4.2%.¹⁰

From Table 4 we can see that in this study, hyponatremia was seen in 32.4% and hypernatremia were seen in a small number of children i.e. 2.9%. This was similar to the result obtained by the study conducted by Singhi and Dhawan et

al, in 1989 where hyponatremia was seen in 27% and hypernatremia in 3.7%.⁴ Till date only few studies exist which concern with the correlation of hyponatremia and pneumonia in children. It was first described by Stormont and Waterhouse in 1962.¹¹ Over the past 35 years only case reports and a few relevant studies on the association between hyponatremia and pneumonia have been published, of which only very few concern children.^{4,5,12,13}

Hyponatremia, occurring in more than one-fourth of patients with CAP, is associated with greater disease severity and worsened outcomes.¹⁴ Recent single-center cohort study found the incidence of hyponatremia at hospital admission among CAP patients to be 28%.¹⁵ In this study out of the 33 cases of hyponatremia 25.5% had mild hyponatremia, 4.9% had moderate hyponatremia and 1.9% had severe hyponatremia. This findings are close to the study conducted by Afroditi Sakellaropoulou et al, in 2008 on 54 patients where 33.33% of children had mild hyponatremia and 1 child (1.90%) had moderate hyponatremia.¹⁶ The results of a study done by Nair V., Niederman M.S., Masani N., Fishbane S. et al, in 2007 showed that hyponatremia was present at hospital admission in 27.9% of patients. The magnitude was generally mild and only 4.1% of patients had serum sodium <130 mEq/l.¹⁵ In the study by Wrotek A. et al, hyponatremia was observed in 33.3 % patients.¹⁷ Figure 1 shows that 57.6% of hyponatremia were due to SIADH. The renal function tests and hydration status were normal in all this patient. In the

remaining 14 cases, the cause of hyponatremia couldn't be found. In the study conducted by Singhi and Dhawan in 1989, out of the 71 hyponatremic children, 48(68%) had dilutional hyponatremia secondary to SIADH. According to studies, SIADH occurs in about one third of children hospitalized for pneumonia and was associated with poorer outcome.⁴

Table 5 shows the outcome of the 19 cases who developed hyponatremia due to SIADH. In this study author found that in 52.6% duration of hospital stay was prolonged, 52.6% developed complications, 52.6% patients were successfully discharged and 7(36.8%) patients died.

Table 6 shows that 21.2% cases died who had hyponatremia due to SIADH. The mortality of patients with hyponatremia was significantly higher ($p=0.03$) in the group with SIADH versus those having hyponatremia without SIADH. This shows that the presence of SIADH has negative effect on the duration of hospital stay, development of complications and mortality in patients with severe pneumonia. This is in agreement to the study conducted by Dhawan and Narang et al. They found that SIADH occurs in about one third of children hospitalized for pneumonia and was associated with a more severe disease and a poorer outcome.⁶

From Table 7 author can see that the average duration of stay in hospital was significantly higher for the groups with hyponatremia i.e. 8.2 ± 4.5 days (range of 1-14 days, $p=0.0005$) as compared to the group with normonatremia i.e. 7.3 ± 1.7 days (range of 5-9 days, $p=0.001$). This is similar to the the study conducted by Singhi and Dhawan et al, where they found that in hyponatremic children the duration of hospitalization was prolonged by 60%. Wrotek A. et al, concluded in their study that hyponatremia is a frequent finding in CAP which is associated with the disease severity and found that duration of hospitalization was longer in hyponatremic children when compared with non-hyponatremic children.¹⁷ However Muller M. et al, in 2018 in their study showed that hyponatremia on admission is not associated with length of hospitalisation.¹⁸ Singhi and Dhawan et al, found that in hyponatremic children not only was the duration of hospitalization prolonged, but also the occurrence of complication was about two-fold and the mortality was about 3.5 times higher as compared to normonatremic patients. The mean length of hospital stay was significantly prolonged in children who had coexisting hyponatremia with hypokalemia.⁴

Hyponatremia is common among hospitalized patients with pneumonia and is associated with worsened clinical and economic outcomes and indicates a poor prognosis including death and longer hospitalization.¹⁸⁻²⁰ In the study conducted by Afroditi Sakellaropoulou et al, children with hyponatremia at admission had longer hospitalization times and a prolonged duration of fever, although their final outcome was favourable, including cases that developed pleural effusion.¹⁶ In a recent study done by Muller M. et al,

in 2018 they concluded that mild hyponatremia ($<130\text{mmol/L}$) predicts poor outcome in patients admitted with pneumonia and that it is an independent risk factor for hospital mortality and ICU admission.¹⁸

CONCLUSION

In this study author found that 32.3% of patients with severe pneumonia had hyponatremia out of which majority had mild hyponatremia. Hyponatremia was due to SIADH in 57.6 % cases. The duration of hospital stay was significantly higher statistically in those children who had hyponatremia ($p=0.0005$). Complications developed in 10.8% cases with hyponatremia. Hospital stay was prolonged, and complications and mortality were significantly higher ($p=0.03$) in cases of hyponatremia due to SIADH. Based on this study author found that hyponatremia is fairly a common association with Severe Pneumonia. Hyponatremia is usually mild, and majority of the cases are due to SIADH. Hyponatremia results in prolonged hospital stay, increased complications and mortality especially when associated with SIADH.

Thus, author conclude that estimation of serum sodium, plasma and urine osmolality with urinary sodium level is necessary to manage a case of Severe Pneumonia on account of the deleterious effect that hyponatremia has on the overall outcome. There is much need to continue research on explaining the pathophysiology of electrolyte imbalance in pneumonia.

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