



Impact of Hyponatremia on Clinical Presentation and Management in Pediatric Patients with lower Respiratory Infections

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Abstract

Objectives: The purpose of this study was to characterize the impact of hyponatremia on clinical presentation and management in pediatric patients suffering from lower respiratory infection within 2 hours of admission in ICU and to investigate whether there is link between hyponatremia and the severity and outcome of LRIs.

Methods: 100 pediatric patients of age group 2 months to 5 years suffering from lower respiratory infections were recruited in the study. Clinical presentation and chest X ray were recorded. Serum sodium levels were assessed to diagnose Hyponatremia (s. sodium < 135 mEq/L). Appropriate fluid therapy was administered to each patient and impact of hyponatremia over isonatremia was evaluated in patients.

Results: 75 were in the age group of 2 months to 1 year and 25 were in the age group of 1 to 5 years. 63 children had normal sodium levels (Isonatremia) and 33 children had hyponatremia at the time of admission. Association of clinical symptoms and signs in isonatremic versus hyponatremic patients were not found significant statistically in both age groups ($p > 0.05$). It was evident from these observation that abnormal x ray findings were more common in the hyponatremic cases ($p = 0.008$) than the isonatremic cases ($p < 0.001$). Association of requirement of i/v fluids in hyponatremic versus isonatremic patients was found to be significant statistically in both age groups (p value 0.000).

Conclusion: Thus it is concluded that, presence of hyponatremia in LRI's increases the morbidity of these patients as radiographic findings were more common. Therefore, fluid therapy is required more in Hyponatremic patients.

Introduction

Lower respiratory infections (LRI's), are infections below the level of larynx. These infections including pneumonia, empyema, bronchitis, bronchiolitis and wheeze associated

with lower respiratory infections (WALRI) continue to threaten the health of children worldwide, especially in developing countries. Lower respiratory infection is one of the most serious illness especially in less than 5 year of age

requiring hospitalization and contributes to 30% deaths yearly worldwide mainly due to pneumonia as the leading cause.¹ Hyponatremia is a common electrolyte disturbance occurring in children hospitalized with pneumonia, but it is frequently an overlooked complication and most of the time not given much importance. Most of the cases of hyponatremia occur as a response to stress which causes increased Antidiuretic hormone (ADH) release which in turn causes water retention.²

Fluids and electrolytes are the main components in the maintenance of body homeostasis. The most important among electrolytes is sodium which is the major cation of the extracellular fluids. Hyponatremia (serum sodium <135 meq/l) is the most common electrolyte abnormality seen in intensive care unit (ICU) with an incidence as high as 30% in some reports.^{3,4} Hyponatremia do occurs in many acute inflammatory disease like respiratory tract infections, meningitis, febrile convulsions and Kawasaki disease in children.^{5,6}

In childhood lower respiratory infections like pneumonia and bronchiolitis are the most common diseases which are at particular risk of developing hyponatremia.^{7,8} Hyponatremia associated with pediatric pneumonia is most commonly due to the syndrome of inappropriate secretion of antidiuretic hormone (SIADH).⁹ Acute hyponatremia in lower respiratory infections in children can lead to an immediate danger to the central nervous system. The rapid shift of fluids associated with this condition frequently result in brain oedema. Administration of hypotonic maintenance fluid may worsen this condition (oedema).¹⁰

Although hyponatremia is one of the most common electrolyte abnormality in children with LRI between 2mnths to 5 years of age, but there are lack of researches evidenced on this aspect. Moreover, due to its serious complications it is important to explore the impact of hyponatremia on clinical presentation and fluid therapy in patients with lower respiratory infections to facilitate early recovery and reduced morbidity and mortality in pediatric patients. Therefore, the

purpose of this study was to characterize the impact of hyponatremia on clinical presentation and management in pediatric patients suffering from lower respiratory infection within 2 hours of admission in ICU and to investigate whether there is link between hyponatremia and the severity and outcome of LRIs.

Materials and Methods

The present study was conducted in the department of pediatrics, Bebe Nanki Children ward of Government Medical College, Amritsar, Punjab from January 2017 to January 2018. The study group consisted of 100 pediatric patients of the age group of 2 months to 5 years which are admitted in the Department of Pediatrics with lower respiratory infections as defined by the modified WHO-British Thoracic Society (BTS)¹¹ guidelines and confirmed radiologically.

The study protocol for all procedures was approved by the Institutional Review Board for Ethical Clearance of Government Medical college, Amritsar, Punjab and was performed in accordance with the Code of Ethics of the World Medical Association according to the Declaration of Helsinki of 1975, as revised in 2000. All patients parents were asked to sign a written consent form prior to commencement of the study.

Inclusion Criteria

1. Children between age of 2 months to 5 years.
2. These children will have clinical diagnosis of lower respiratory infections at the time of admission as per modified WHO-BTS guidelines.
3. Patients whose parents have signed the informed consent.

Exclusion Criteria

1. Infants <2 months of age and > 5 years of age.
2. Children with associated gastroenteritis, renal disorders, CNS infection, congestive heart failure and adrenocortical disorders.

- Those on drugs which can cause electrolyte imbalance such as diuretics, anticonvulsants.

Investigation

Two venous samples were collected at the time of admission. The first urine sample was also collected. One venous sample was used for the estimation of serum sodium and serum potassium. The second serum sample and urine sample was refrigerated and were used for the work up for the diagnosis of SIADH, in those patients who had serum sodium value <135mEq/L. In these patients blood urea, serum creatinine, blood glucose, urinary sodium, urinary urea, urinary creatinine, urine osmolality & serum osmolality were estimated. Blood urea and creatinine also helped to rule out any renal dysfunction. X-ray chest were taken in all cases to confirm the diagnosis of lower respiratory infections. The patients' clinical data including age, sex, duration of hospital stay, Record of Fluid therapy and the final outcome (discharge or death) were recorded in all the cases. Diagnosis criteria for hyponatremia:

Normal Serum Sodium was taken as 135-145mEq/L. Serum Sodium concentration of <135mEq/L was taken as hyponatremia.

Serum Sodium concentration of 131-134mEq/L was taken as mild hyponatremia, 126-130mEq/L was taken as moderate hyponatremia and \leq 125mEq/L was taken as severe hyponatremia.

Diagnosis criteria for SIADH

- Hyponatremia together with decreased effective serum osmolality <280mOsm/kg.
- Spontaneous urinary osmolality >100mOsm/kg.
- Spot urinary sodium concentration of >40mEq/L
- Normal renal functions (blood urea and serum creatinine)^{12,13}

Statistical Analysis

Data were tabulated and examined using the Statistical Package for Social Sciences Version 20.0 (IBM SPSS Statistics for Mac, Armonk, NY: IBM Corp, USA). Descriptive statistical analysis had been carried out in the present study. Results

on continuous measurements are presented as Mean \pm SD. Categorical data has been presented as frequency distribution. The statistical power calculation was based on the assumption that the data were normally distributed. P-value of <0.05 was considered as significant.

Results

This observational study was carried out over a time period of one year from January 2017 to January 2018 which included pediatric patients of 2 months to 5 years. 75 patients (75%) were in the age group of 2 months to 1 year and 25 (25%) were in the age group of 1 to 5 years i.e the number of children were higher in the younger age group of 2 months to 1 year than the age group of 1-5 years. (Table 1) results revealed that there were 70 (70%) male children and 30(30%) female children in the study. Table 2 showed male predominance in the total study, as well as in 2-12 months age group. There is slightly higher predominance of females in the 1-5 year age group. Results depicted that 33 (33%) children were found to have hyponatremia. Hyponatremia looks to be a more common observation in 1-5 year age group. Difference of serum sodium levels in two age groups was not significant statistically. (p value 0.933) (Table 3)

Difference of clinical symptoms was not found to be statistically significant in hyponatremic patients (p=0.655) as well as in isonatremic patients (p=0.459) in both age groups. Similarly difference of clinical symptoms in isonatremic versus hyponatremic patients was not significant statistically in both age groups. (p value 0.807) (Table 4) Difference of clinical signs was not significant statistically in hyponatremic group. (p value 0.980) as well as in isonatremic group (p value 0.679) in both age group. Similarly difference of clinical signs in hyponatremic versus isonatremic patients was not significant statistically in both age groups. (p value 0.983) (Table 5) It was evident from these observation that abnormal x ray findings were more common in the hyponatremic cases (p=0.008) than the

isonatremic cases ($p < 0.001$). In both age groups this difference was statistically significant ($p < 0.001$) (Table 6) Difference of requirement of

i/v fluids in hyponatremic versus isonatremic patients was significant statistically in both age groups (p value 0.000).(Table 7)

Table No -1: Age Wise Distribution of Study Cases

Age groups	Number	Percent
2-12 months	75	75%
1-5 year	25	25%
Total	100	100

Table 2: Sex Wise Distribution of Study Cases

SEX	Age groups				Total (n=100)	
	2-12 month (n=75)		1-5 year (n=25)		No.	%age
	No.	%age	No	%age		
Male	58	77.00	12	48.00	70	70.00
Female	17	23.00	13	52.00	30	30.00
Total	75		25		100	

Table 3: Distribution of study Cases according to Serum Sodium Levels at the time of Admission

Serum sodium levels	AGE				Total (n=100)	
	2-12 (months) (n=75)		1-5 (years) (n=25)		No. of cases	%age
	No. of cases	%age	No. of cases	%age		
Normal (137.15 ± 2.84 mEq/L)	48	64.00	15	60.00	63	63.00
Hyponatremia (130.34 ± 3.47 mEq/L)	24	32.00	9	36.00	33	33.00
Hypernatremia (147.50 ± 1.11 mEq/L)	3	4.00	1	4.00	4	4.00
Total	75	100.00	25	100.00	100	100.00

Table 4: Hyponatremic Versus Isonatremic Cases in Different Clinical Symptoms

Symptoms	Hyponatremia (n=33)				Isonatremic (n=67)				Total (n=100)
	2-12 (months) n=24		1-5 (years) n=9		2-12 (months) n=51		1-5 (years) n=16		
	No	%	No	%	No	%	No	%	
Cough	24	100.0	9	100.0	43	84.0	16	100.0	92
Fever	22	92.0	9	100.0	22	43.0	16	100.0	69
Running Nose	21	87.5	3	33.0	22	43.0	14	87.5	60
Poor oral intake	24	100.0	7	78.0	32	63.0	12	75.0	75
Difficulty in breathing	24	100.0	7	78.0	26	51.0	14	87.5	71
P value	0.655				0.459				0.807

Table 5: Hyponatremic Versus Isonatremic Cases in Different Clinical Signs

Clinical Signs	Hyponatremia (n=33)				Isonatremia (n=67)				Total (n=100)
	2-12 (months) n=24		1-5 (years) n=9		2-12 (months) n=51		1-5 (years) n=16		
	No	%	No	%	No	%	No	%	
Tachypnea	24	100.0	9	100.0	16	31.0	16	100.0	65
Tachycardia	24	100.0	8	89.0	17	33.0	10	62.5	59
Chestreractions	24	100.0	7	78.0	19	37.0	11	68.7	61
Use of accessory muscles	9	37.5	3	33.0	5	10.0	3	19.0	20
P value	0.980				0.679				0.983

Table 6: Hyponatremic versus Isonatremic Cases Chest X-Ray Findings

Chest x-ray	Hyponatremia (n=33)				Isonatremia (n=67)				Total
	2-12 (months) (n=24)		1-5 (years) (n=9)		2-12 (months) (n=51)		1-5 (years) (n=16)		
	No	%	No	%	No	%	No	%	
Consolidation	6	25.00	4	44.44	7	13.73	14	87.50	31
Increased bronchovascular marking	7	29.17	0	0.00	13	25.50	0	0.00	20
Hyperinflation	7	29.17	0	0.00	19	37.25	2	12.50	28
Empyema	2	8.33	5	55.56	0	0.00	0	0.00	7
Normal X-Ray	2	8.33	0	0.00	12	23.52	0	0.00	14
P value	0.008				0.000				0.000

Table 7: Hyponatremic Versus Isonatremic Cases Receiving Parental Fluids/Oral Feeds

Oral feed / i/v fluid	Hyponatremia (n=33)				Isonatremia (n=67)				Total (n=100)
	2-12 (months) n=24		1-5 (years) n=9		2-12 (months) n=51		1-5 (years) n=16		
	No	%	No	%	No	%	No	%	
Oral Feed	1	4.0	1	11.0	14	27.5	10	62.5	26
I/V Fluid	23	96.0	8	89.0	37	72.5	6	37.5	74
Total	24	100.0	9	100.0	51	100.0	16	100.0	100
P value	0.457				0.011				0.000

Discussion

The present study was conducted by enrolling 100 pediatric patients in the age group of 2 months to 5 years admitted with LRI's. Age criterion was selected on the basis of modified WHO-BTS guidelines and on the basis of evidence from various studies that have concluded higher incidence rate of LRI's in children aged 0-5 years. Chhina AS et al.¹⁴ reported 2 months to 1 year as common age group in their study(n=172) in 2015in Department of Pediatrics, KIMS Bangalore.

There were 70% male children and 30% female children. Although, age and sex had no correlation with hyponatremia in our study comparable to study by Don M et al,¹⁵ in age and gender. . This gender bias may be due to the reason that male children are brought early to the hospital for treatment than females due to comparatively more preference for male children in our country & other developing countries. This may also be due to the reason that females have two X-chromosomes, thus less vulnerability to infections although no studies are available to confirm this hypothesis.

Hyponatremia was present in 33% of children admitted with LRI's which is comparable to few

other studies done in India where the frequency ranged from 27-31%.^{16,17} Chaitra et al¹, conducted in 2015 in 91 children suffering from LRTI admitted to PICU at KIMS, Bangalore, the incidence of hyponatremia in pneumonia patients was 26%.Hyponatraemia in association with LRI's may occur due to many reasons, such as salt deficit, or surplus of water. Other contributory factors may be primary illness, impaired water excretion, improper release of vasopressin, use of hypotonic fluids, redistribution of sodium and water, sick cell syndrome, and numerous drugs .¹⁸ When all the parameters like symptoms, signs & chest x-ray findings were compared in hyponatremic versus isonatremic groups statistically, it was found that all the parameters were significantly more common as well as of longer duration in the hyponatremic group as compared to isonatremic group. The present study stated that on admission hyponatremic group had higher-body temperature, longer duration of cough, running nose & poor oral intake in hyponatremic group (HN) as compared to isonatremic group (IN). the results stated by present study is in accordance with Channawar et al¹⁹ where it was concluded that body temperature at the time of admission and duration of fever &

cough were significantly higher and of longer duration in hyponatremic group than in one without hyponatremia. Thus symptoms were more common in hyponatremic patients in both age groups as shown by their percentage of occurrence but this difference was not found to be statistically significant ($p=0.807$).

When all clinical signs were compared in hyponatremic versus isonatremic groups in different age groups it was found that occurrence of clinical signs of respiratory distress were more common in hyponatremic group (HN) as compared to isonatremic group (IN). The present study depicted that clinical signs were more common in hyponatremic group when compared with isonatremic group in both age groups although this difference was not significant statistically ($p=0.983$). These results were consistent with study by Sakellaropoulou et al¹⁸ conducted at Department of Pediatrics, Medical School, Aristotle University of Thessaloniki from January 2008 to May 2009 in 54 children, where they had concluded that symptoms and signs indicative of severe pneumonia were two to three times more frequent and the mean duration of tachypnoea, chest wall retractions was about 50% longer in children with hyponatremia.

The present study revealed that when chest x-ray findings were compared in hyponatremic and isonatremic patients in both age groups abnormal X-ray findings were significantly more common in hyponatremic group than in isonatremic group in both age groups ($p<0.001$). These findings were found to be in contrast with results showed by Don M et al²⁰ which failed to find any association of x-ray finding of consolidation to hyponatremia. On comparison of requirement of rehydration fluid in two age groups it was found that children of 2-12 month age group needed i/v fluid significantly more commonly than of 1-5 years age group ($p=0.018$). When this requirement of rehydration fluids was compared in hyponatremic versus isonatremic patients it was found that requirement of i/v fluid in hyponatremic patients was significantly more common than isonatremic

patients in both age groups ($p<0.001$). Although no study is available for comparison but as dehydration can occur in bronchiolitis & WALRI patients due to low intake, vomiting in some cases or respiratory losses due to tachypnoea, this aspect should be carefully taken care.

There are many contributing factors towards the pathogenesis of SIADH in cases of LRI's. Firstly, the stress induced release of ADH causing salt loss and water retention might be reason for hyponatremia.²¹ In addition, severe infections are associated with release of inflammatory mediators like interleukin 6, which stimulates ADH production. Inflammatory markers also stimulates thermoregulatory center resulting in reset of the thermostat hence the high temperature.^{22,23} Moreover, Don M et al.¹⁵ well explained the concept of fever stimulating non-osmotic release of ADH.

Conclusion

It can be concluded that, hyponatremia is a significantly common association among hospitalized children with LRI's in the age group of 2 months to 5 years and it is mainly due to syndrome of inappropriate antidiuretic hormone secretion (SIADH). Although being common, there are lack of researches evidenced on this aspect and is often overlooked by the clinician. Moreover, due to its serious complications it is important to explore the impact of hyponatremia on clinical presentation and fluid therapy in patients with lower respiratory infections to facilitate early recovery and reduced morbidity and mortality in pediatric patients. So, such hospitalized children suffering from LRI's should be evaluated not only clinically but also for serum levels of sodium at the time of admission. Careful fluid management especially in the form of fluid restriction therapy in addition to the specific treatment of the underlying cause can prove very useful in lowering the morbidity and complications in these children.

References

1. Chaitra KM. Hyponatremia in lower respiratory tract infections. *International Journal of Contemporary Pediatrics*. 2016;3(2):381-4.
2. Lussyk HO, Friedstein H. Water retention in pneumonia. *American Journal of Diseases of Children*. 1920;19(5):337-43.
3. Upadhyay A, Jaber BL, Madias NE. Incidence and prevalence of hyponatremia. *The American Journal of Medicine*. 2006;119(7):S30-5.
4. Eisenhut M. Extrapulmonary manifestations of severe respiratory syncytial virus infection—a systematic review. *Critical Care*. 2006;10(4): R107.
5. Sharples PM, Seckl JR, Human D, Lightman SL, Dunger DB. Plasma and cerebrospinal fluid arginine vasopressin in patients with and without fever. *Archives of Disease in Childhood*. 1992;67(8):998-1002.
6. Watanabe T, Abe Y, Sato S, Uehara Y, Ikeno K, Abe T. Hyponatremia in Kawasaki disease. *Pediatric Nephrology*. 2006;21(6):778-81.
7. Van Steensel-Moll HA, Hazelzet JA, van der Voort E, Neijens HJ, Hackeng WH. Excessive secretion of antidiuretic hormone in infections with respiratory syncytial virus. *Archives of Disease in Childhood*. 1990; 65(11):1237-9
8. Szabo FK, Lomenick JP. Syndrome of inappropriate antidiuretic hormone secretion in an infant with respiratory syncytial virus bronchiolitis. *Clinical Pediatrics*. 2008;47(8):840-2.
9. Nair V, Niederman MS, Masani N, Fishbane S. Hyponatremia in community-acquired pneumonia. *American Journal of Nephrology*. 2007;27(2):184-90.
10. Greenbaum LA. Hypervitaminosis D. In: Kliegman RM, Stanton BF, Geme JW, Schor NF, Behrman RE (eds). *Nelson Textbook of Pediatrics*.
11. Principi N, Esposito S. Management of severe community-acquired pneumonia of children in developing and developed countries. *Thorax*. 2011;66(9):815-22.
12. Sorensen JB, Andersen MK, Hansen HH. Syndrome of inappropriate secretion of antidiuretic hormone (SIADH) in malignant disease. *Journal of Internal Medicine*. 1995;238(2):97-110.
13. Gross P. Clinical management of SIADH. *Therapeutic advances in Endocrinology and Metabolism*. 2012;3(2):61-73.
14. Chhina AS, Iyer CR, Gornale VK, Katwe N, Sushma S, Harsha PJ. Clinical profile of acute lower respiratory tract infections in children between 2 months to 5 years. *J Evidence Based Med Healthcare*. 2015;2(35):5426-31.
15. Don M, Valerio G, Korppi M, Canciani M. Hyponatremia in pediatric community-acquired pneumonia. *Pediatric nephrology*. 2008 Dec 1;23(12):2247-53.
16. Singhi S, Dhawan A. Frequency and significance of electrolyte abnormalities in pneumonia. *Indian Pediatrics*. 1992;29(6):735-40.
17. Dhawan A, Narang A, Singhi S. Hyponatraemia and the inappropriate ADH syndrome in pneumonia. *Annals of Tropical Paediatrics*. 1992;12(4):455-62.
18. Sakellaropoulou A, Hatzistilianou M, Eboriadou M, Athanasiadou-Piperopoulou F. Hyponatraemia in cases of children with pneumonia. *Archives of medical science: AMS*. 2010;6(4):578.
19. Channawar KS, Deshmukh N, Prasad VS. Correlation of hyponatraemia in children with lower respiratory tract infection—an institutional observational study. *Journal of Evolution of Medical and Dental Sciences*. 2016;5(88):6533-6.
20. Don M, Valerio G, Korppi M, Canciani M. Hyponatremia in pediatric community-acquired pneumonia. *Pediatric Nephrology*. 2008;23(12): 2247-53.

21. Rahul V, Jose O. Prevalence of Hyponatremia in Children with Pneumonia-Cross-Sectional Study. *Journal of Dental and Medical Sciences* 2017; 16(3):46-50.
22. Rudan I, Boschi-Pinto C, Biloglav Z, Mulholland K, Campbell H. Epidemiology and etiology of childhood pneumonia. *Bulletin of the World Health Organization*. 2008;86:408-16B.
23. Unicef W. Pneumonia: the forgotten killer of children. UNICEF/WHO. 2006;140.