

Hyponatremia as a Predictor for Bronchiolitis Severity in Children Admitted to Intensive Care Unit: A Prospective Cohort Study

Prashant Gaurav¹, Sonu Kumar²

¹Senior Resident, Dept of Paediatrics BMIMS Pawapuri

²Senior Resident, Dept of Paediatrics BMIMS Pawapuri

Received: 10-03-2023 / Revised: 16-04-2023 / Accepted: 07-05-2023

Corresponding author: Sonu Kumar

Conflict of interest: Nil

Abstract

Background and Objective: Bronchiolitis is self-limiting in most children, and hyponatremia is one of the well-known complications of bronchiolitis and its presence at the time of admission is known to have an impact on the adverse outcome. To the best of our knowledge there has been no study has been done in the past in the Indian setting on the relationship between hyponatremia and the severity of bronchiolitis in children.

Methods: The study was a prospective cohort study that was conducted for a time period of Two years on sixty children with diagnosis of bronchiolitis in admitted in PICU was based on NICE clinical criteria These two groups were compared for the outcome variables. Outcomes were use of mechanical ventilation and ICU length of stay (LOS). To examine the association of sodium status with outcomes, we fit logistic and linear regression models with propensity score adjustment.

Conclusion: Our findings confirm in bronchiolitis children there is no significant association between the development of hyponatremia and severity of bronchiolitis. Further studies needed to validate about hyponatremia as a prognostic factor.

Keywords: Hyponatremia, Paediatric Community Acquired Pneumonia.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

One of the most common diseases that occur in children are the respiratory diseases [1]. Infections of the respiratory tract are perhaps the most common human ailments. Acute Respiratory Infections (ARI) has quite high morbidity and mortality in children in developing countries [1]. On an average, children below 5 years of age suffer about 5 episodes of ARIs annually regardless of, where they live, or what their economic situation is. ARI is responsible for about 30-50 percent of visits to health facilities

and for about 20-40 percent of hospital admissions. Despite being the cause of significant morbidity and mortality, LRTIs are often mistreated and underestimated. The acute infections of the respiratory tract are that occur commonly are bronchitis, bronchiolitis and pneumonias in the increasing severity of the disease. [2] Acute bronchiolitis usually occurs following exposure to a patient with minor respiratory symptoms within the previous week. Infant first develops a mild upper respiratory tract infection with sneezing and rhinorrhea. This is followed by

decreased appetite and moderate grade fever. After a few days respiratory distress ensues. In most cases the cause of bronchiolitis in infants and children is viral lower respiratory tract infection. [1] Most children with bronchiolitis, irrespective of the disease severity, get better without any sequelae. [1] The disease most often lasts for a period of 7-10 days, but in a small number the affected child remains ill for weeks. There are reports that some of the children following an episode of bronchiolitis and recovery from acute bronchiolitis have an augmented occurrence of repeated wheezing episodes. [3] The occurrence of bronchiolitis is suspected when the child between 1 and 2 years of age has a first episode of wheezing who has no physical findings of a viral respiratory infection and has no other explanation for the wheezing, such as pneumonia or atopy [3,4,5] Bronchiolitis usually affect children less than two years of age with a peak incidence between two and six months of age. [3,5,6]. Various researchers have documented that the respiratory syncytial virus infection is responsible for 30-70% cases of bronchiolitis in children [6,7,8]. Management of bronchiolitis is often frustrating for physicians and caregivers because 'nothing seems to work' in most cases. [4] There is lack of robust evidence for almost all the interventions that are usually tried including inhaled epinephrine, bronchodilators, steroids, anticholinergics, antibiotics, surfactant and chest physiotherapy. Some experts have questioned whether bronchiolitis can be treated at all, and current research data is far from adequate to draw definite conclusions. Even though the disease is self-limiting in most children, there are various risk factors that make them prone for recurrent diseases like congenital heart disease, neuromuscular disorders, immunodeficiency and chronic lung disease and these group of children are most likely to be vulnerable to the complications of bronchiolitis. [7-9].

Hyponatremia (serum sodium level of less than 135 mmol/l) is the most common electrolyte abnormality seen in the intensive care unit and is associated with increased morbidity and mortality. Critically ill children with bronchiolitis are at risk of developing hyponatremia, due to impaired renal free water excretion and exogenous sources of excess free water intake. Hyponatremia in lower respiratory infections is one of the well-known complications of bronchiolitis and its presence at the time of admission is known to have an impact on the adverse outcome [10-12].

Objectives

To study the association of hyponatremia and bronchiolitis severity and its clinical outcome.

Material and Methods

The study was a prospective cohort study that was conducted for a time period of Two Years, on sixty children between the ages 2 months to 2 years chosen by convenient sampling method who were admitted to paediatric intensive care unit a diagnosis of bronchiolitis who met a predefined criterion.

Inclusion criteria

All children diagnosed with bronchiolitis and were admitting to the PICU based on clinical criteria

Age group of 2 months to 2 years

Within 18hrs of hospitalization

Exclusion criteria

Referral cases treated outside the participating hospital.

Hypernatremia (serum sodium >145 mEq/l).

Bronchiolitis associated with known comorbidities like congenital heart disease, neuromuscular disorders and chronic lung disease.

The representative of those children who

were who were admitted to paediatric intensive care unit with a diagnosis of bronchiolitis who met a pre-defined criteria were briefed of the study and given the patient information sheet Those who were willing to participate in the study were chosen and a written informed consent was taken from legal representative of the child. The base line demographics and clinical characteristics of patients were obtained at the time of admission based on pre-structured proforma. These bronchiolitis children were screened for the serum sodium status within 18hrs of admission for which 3ml serum sample was collected at admission and sent for estimation of serum electrolytes. Based on sodium level patients were classified into 2 groups for comparison in the study based on the first measured serum sodium concentration on the day of hospitalization.

Normonatremic with a serum sodium of

135–145 mEq/L and

Hyponatremic with a serum sodium of < 135 mEq/L

These two groups were compared for the outcome variables like

Length of stay in ICU

Length of stay in hospital

Oxygen requirement

High flow requirement

Collected Data was analysed by frequency, percentage, mean, standard deviation. Comparison of the variables was done by ANOVA, T-test, chi-square test and Wilcoxon-Mann-Whitney tests were used for analysis. P value < 0.05 was considered as significant.

Results

Demographic data

| Age | Hyponatremia | Normonatremia | Total | Percentage |
|--------------|--------------|---------------|---------|------------|
| 6 -12 months | 7 | 22 | 29 | 48.33% |
| <6 month | 12 | 14 | 26 | 43.33% |
| >12 months | 2 | 3 | 5 | 8.33% |
| TOTAL | 21 | 39 | 60 | 100.00% |
| Percentage | 35.00% | 65.00% | 100.00% | P=0.834 |

In the present study we had 26 cases accounting for 43.33%, 29 cases accounting for 48.33%, and 5 cases accounting for 8.33% of the age groups, <6 months, 6 -12 months and >12 months respectively. Hyponatremia is seen more in the age group of <6 months. The two groups have the p value more than 0.05 indicating no difference between them.

| Chi-Square Tests | | Value | P |
|------------------|--------------------|-------|-------|
| Male | Pearson Chi-Square | 4.233 | 0.120 |
| Female | Pearson Chi-Square | 0.196 | 0.906 |

In the present study on evaluating the gender between the study groups we found that we had 22 females with 4 cases (50%), 3 cases (37.5%), 1 case (12.5 %) between ages <6 month, 6 -12 months and >12 months respectively in the hyponatremia group and 7 cases (50.0%), 6 cases (42.9%), 1 case (7.10%)

between ages <6 month, 6 -12 months and >12 months respectively in the normonatremia group. The overall male to female ratio was 1.9:1. In all age groups males were higher in both the study groups. The two groups had a p value more than 0.05 indicating no difference between them.

| Chi-Square Tests | | | |
|------------------|--------------------|-------|------|
| group | | Value | p |
| Hyponatremia | Pearson Chi-Square | 4.421 | .110 |
| Normonatremia | Pearson Chi-Square | 1.140 | .566 |

In the present study of the 21 cases with hyponatremia, 2 were preterm gestational deliveries and 39 cases with Normonatremia, 9 were Preterm gestational deliveries. period of gestation showed no effect in hyponatremia group. The two groups had a p value more than 0.05 indicating no difference between them.

Duration of ICU stay

| ICU stay | | Group | | Total |
|--------------------|----------------------|--------------|---------------|--------|
| | | Hyponatremia | Normonatremia | |
| <2 days | < 6-month Count % | 9 | 9 | 18 |
| | | 69.2% | 36.0% | 47.4% |
| | 6-12 Count months % | 3 | 14 | 17 |
| | | 23.1% | 56.0% | 44.7% |
| >12 months Count % | 1 | 2 | 3 | |
| | 7.7% | 8.0% | 7.9% | |
| Total | Count % | 13 | 25 | 38 |
| | | 100.0% | 100.0% | 100.0% |
| 2 - 4 days | < 6-month Count % | 3 | 3 | 6 |
| | | 42.9% | 25.0% | 31.6% |
| | 6 -12 Count months % | 3 | 8 | 11 |
| | | 42.9% | 66.7% | 57.9% |
| | >12 months Count % | 1 | 1 | 2 |
| | | 14.3% | 8.3% | 10.5% |
| Total | Count % | 7 | 12 | 19 |
| | | 100.0% | 100.0% | 100.0% |
| >4days | < 6-month Count % | 0 | 2 | 2 |
| | | 0.0% | 100.0% | 66.7% |
| | 6-12 Count months % | 1 | 0 | 1 |
| | | 100.0% | 0.0% | 33.3% |
| Total | Count % | 1 | 2 | 3 |
| | | 100.0% | 100.0% | 100.0% |

In the present study on evaluating the duration of ICU stay between the study groups we found that we had overall 38 cases needed ICU for less than 2 days, 19 cases between 2-4 days and 3 cases needed more than 4 days of ICU care. In the hyponatremia group 9 cases (69.2%), 3 cases (23.1%), 1 case (7.7%) between ages

<6 month, 6 -12 months and >12 months respectively needed less than 2 days in ICU as compared to 9 cases (36.0%),14 cases (56.0%), 2 cases (8.0%) between ages <6 month, 6 -12 months and >12 months respectively in the normonatremia group. 3 cases (25.0%), 8 cases (66.7%), 1 case (8.3%)

| Mortality | Hyponatremia | Normonatremia |
|-----------|--------------|---------------|
| No | 60 | 60 |
| Yes | 0 | 0 |

In the present study we had anemia in 7 cases (50.0%), 6 cases (42.9%), 1 case (7.1%) in the Hyponatremia group and 11 cases (36.7%), 17 cases (56.7%), 2 cases (6.7%) in the normonatremia group in age groups <6 month, 6-12 months and >12 months respectively. In hyponatremia group anemia is seen in below 1 yr age group. The two groups had a p value more than 0.05 indicating no difference between them.

Discussion

Bronchiolitis is a common childhood illness, and its most common etiologic agent is respiratory syncytial virus. Hospitalization is required in approximately 1% of affected children, primarily because of dehydration, inadequate oral intake, or respiratory insufficiency. Between 10-15% of hospitalized children will require intensive care due to impending respiratory failure. Complications of severe and rapidly evolving hyponatremia include central nervous system dysfunction, seizures, coma, permanent brain damage, brain edema, brainstem herniation, and death [13]. Sound pathophysiologic reasoning is required in managing hyponatremia, so far as specific treatment differs in various clinical scenarios. The determination of whether hyponatremia is of depletion, dilutional, or of mixed origin can generally be made by history, physical examination especially the presence or absence of dehydration, and commonly available laboratory measurements. In our study out of 21 cases of hyponatremia 12 cases (57.1%) were in the age group of less than 6 months, 7 cases (33.3%) were in the age group of 6-12 months, 2 cases (9.52%) were in the age group of > 12 months. In our study hyponatremia is seen more in the age group of < 6 months. These results were similar to study conducted by Gregorio P. Milan et al [4]. Gregorio P. Milan [4] reported the cumulative prevalence of hyponatremia in bronchiolitis is 28% in 160 infants

≥ 1 month and ≤ 24 months of age with bronchiolitis. Of 160 consecutive infants enrolled, hyponatremia was observed in 91 (57%) patients and occurred more commonly in infants ≤ 6 months than in older infant ($P < 0.005$). Ricky Luu, et al the mean age was 10.7 ± 6.7 months. In the hyponatremia group the mean age was 11.2 months which is higher than our study. Kohei Hasegawa et al the mean age of hyponatremia group was 3 months which is similar to our study. In the present study we had one child of hyponatremia with mechanical ventilation requirement (22 hrs). Out of 21 cases with hyponatremia, 13 cases (61.9%) had ICU length of stay < 2 days, 7 cases (33.33%) had ICU length of stay 2-4 days, 1 case (4.76%) had ICU length of stay >4 days. Out of 39 cases of normonatremia, 25 cases (64.1%) had ICU length of stay < 2 days, 12 cases (30.76%) had ICU length of stay 2 - 4 days, 3 cases (15.78%) had ICU length of stay >4 days. Kohei Hasegawa et al also showed that those with hyponatremia had higher risks of mechanical ventilation use in hyponatremia (58%) compared to normonatremia group (40%) and longer ICU stay in hyponatremia group (3 days) compared to normonatremia (6 days). These results are not similar in our study. Luu R et al stated that in children hospitalized with bronchiolitis in the hyponatremia group vs normonatremia group, the total mortality (13% versus 0%; $P = 0.011$), ventilator time (8.41 ± 2 days vs 4.11 ± 2 days; $P = 0.001$), duration of stay in the PICU (10.63 ± 2.5 days vs 5.82 ± 2.09 days; $P = 0.007$), and noninvasive ventilator support (65% vs 24%; $P = 0.007$) were significantly different. Hyponatremia is an independent predictor of prognosis and morbidity as those with hyponatremia needed longer ICU stay and mechanical ventilation use. Hussain et al [14] stated that anemia (predominantly iron deficiency anemia) was significantly found in acute lower respiratory tract infections (ALTRI) patients, and these

patients were found to be 4.6 times more susceptible to ALRTI. Early and accurate diagnosis of anemia in children suffering from various ailments in particular to ALRTI. In both the groups of bronchiolitis children anemia is seen predominantly in below 1 yr age group. The two groups had a p value more than 0.05 indicating no statistical difference between them. [15]

Conclusion

According to my study hyponatremia seen in more commonly seen age groups < 6 months age, predominantly in males (1.9:1), with no effect from gestational age or mode of delivery, seen in low-birth-weight babies predominantly, with no effect seen with past h/o NICU admission, commonly seen in rainy season. Oxygen requirement, prolonged stay in hospital/ICU and with anemia seen predominantly in < 1yr age. High flow requirement and mechanical ventilation requirement seen in one case each in normonatremia and hyponatremia respectively. This is probably due to limited sample size.

References

1. Casas M, den Dekker HT, Kruithof CJ, Reiss IK, Vrijheid M, Sunyer J, de Jongste JC, Jaddoe VW, Duijts L. The effect of early growth patterns and lung function on the development of childhood asthma: a population-based study. *Thorax*. 2018 Jul 31; thorax nl-2017.
2. Lieberthal AS, Bauchner H, Hall CB, Johnson DW, Kotagal U, Light MJ, Mason W, Meissner HC, Phelan KJ, Zorc JJ. Diagnosis and management of bronchiolitis. *Pediatrics*. 2006 Oct 1;118(4):1774-1793.
3. Weiss ST, Tager IB, Muñoz A, Speizer FE. The relationship of respiratory infections in early childhood to the occurrence of increased levels of bronchial responsiveness and atopy. *American Review of Respiratory Disease*. 1985 Apr;131(4):573-578.
4. Milani GP, Rocchi A, Teatini T, Bianchetti MG, Amelio G, Mirra N, Grava A, Agostoni C, Fossali EF. Hyponatremia in infants with new onset moderate- severe bronchiolitis: A cross-sectional study. *Respiratory medicine*. 2017 Dec 31; 133:48-50.
5. Verma N, Lodha R, Kabra SK. Recent advances in management of bronchiolitis. *Indian pediatrics*. 2013 Oct 1;50(10):939-949.
6. Homaira N, Luby SP, Petri WA, Vainionpaa R, Rahman M, Hossain K, Snider CB, Rahman M, Alamgir AS, Zesmin F, Alam M. Incidence of respiratory virus-associated pneumonia in urban poor young children of Dhaka, Bangladesh, 2009–2011. *PloS one*. 2012 Feb 22;7(2):e32056.
7. Leung AK, Kellner JD, Davies HD. Respiratory syncytial virus bronchiolitis. *Journal of the National Medical association*. 2005 Dec;97(12): 1708.
8. Willson DF, Landrigan CP, Horn SD, Smout RJ. Complications in infants hospitalized for bronchiolitis or respiratory syncytial virus pneumonia. *The Journal of pediatrics*. 2003 Nov 1;143(5):142-149.
9. Deterding RR. Infants and young children with children's interstitial lung disease. *Pediatric allergy, immunology, and pulmonology*. 2010 Mar 5;23(1):25-31.
10. Don M, Valerio G, Korppi M, Canciani M. Hyponatremia in pediatric community-acquired pneumonia. *Pediatric nephrology*. 2008 Dec 1;23 (12):2247-2253.
11. Wrotek A, Jackowska T. Hyponatremia in children hospitalized due to pneumonia. *Adv Exp Med Biol*. 2013; 788:103–108
12. Meissner HC Uncertainty in the management of viral lower respiratory tract disease. *Pediatrics*. 2001;10810 00- 1003.
13. Coates BM, Camarda LE, Goodman DM. Wheezing, Bronchiolitis, and

- Bronchitis. In: Kliegman, RM, Stanton BF, St Geme III JW, Schor NF, editors. Nelson Textbook of Pediatrics. 20th Edition. Philadelphia: Elsevier; 2016; 2:2044-49
13. Malik, K Kumar. Hyponatremia — an Unusual Presentation of Respiratory Syncytial Virus Infection. The Internet Journal of Pediatrics and Neonatology. 2012; 14 ;1.
14. Sheikh Quyoom Hussain, Mohd Ashraf, Juveria Gull Wani, Javid Ahmed. Low Hemoglobin Level a Risk Factor for Acute Lower Respiratory Tract Infections (ALRTI) in Children. Journal of Clinical and Diagnostic Research. 2014 Apr, Vol- 8(4): PC01-PC03.
15. Pyar K. P., Su K. K., Wunna K., Aung, Z. N. H., Maung N. L., Kyaw A. P., Hlaing S. W., Tun T. H., Htun S. M., Aung N. M., Than A. M., Mon M. K., Min W., Myint T. T., Ya K. Z., Win T., Shan M. A., Thu S. P., Aung Y. L., Aung Z. P., Kyaw M. T., Maung K. T., & Aung H. L. Initial presenting symptoms and severity of SARS-CoV-2 Wild type, the Delta variant and the Omicron variant infected cases in early fourth wave of epidemics in Myanmar. Journal of Medical Research and Health Sciences, 2022; 5(1): 1765–1769.