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Significance of Serum Sodium Level as Potential Severity Biomarker in Pediatric Acute Bronchiolitis

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KEYWORDS

Bronchiolitis, Hyponatremia, Wheeze, Anti diuretic hormone

ABSTRACT:

Introduction: Due to viral infection, specifically RSV, acute bronchiolitis, which is common in infants under two years old, increases in the winter. Most of the time, supportive treatment can alleviate moderate symptoms. Hospitalization is required in severe cases, particularly in high-risk newborns. Because of fluid therapy and high levels of antidiuretic hormone, hyponatremia—which is frequently observed in cases of severe bronchiolitis—may be a sign of a more serious illness. Preventing mortality in at-risk newborns requires early detection of extrapulmonary symptoms.

Aim: The purpose of this study is to determine whether there is any correlation, if any, between the severity of the illness and its prognosis in hospitalized children with acute bronchiolitis.

Material and Methods: This prospective observational study was carried out on children aged one month to two years who were admitted with acute bronchiolitis at a tertiary care hospital in eastern India.

Results: The study found that 19.2% of children with acute bronchiolitis developed hyponatremia, with most having mild (78.3%) or moderate (21.7%) cases. Initial severity on admission varied, with moderate bronchiolitis most common (71.7%). Significant differences in serum sodium levels were observed among severity groups, being higher in mild cases (141.60±4.48) compared to severe (135.11±6.52). Hyponatremic children had longer hospital stays (7.57±2.51 days) than normonatremic ones (6.00±2.2), correlating negatively with serum sodium levels (r= -0.57, p=0.003).

Conclusion: According to the study's findings, children with acute bronchiolitis—mostly mild to moderate in severity—have a significant prevalence of hyponatremia. Milder cases of bronchiolitis are correlated with higher initial serum sodium levels. Significantly, hyponatremia is linked to longer hospital stays, suggesting that it may serve as a marker for the severity of the illness and the length of hospital stay in these patients.

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Introduction

Approximately 15–17% of hospitalizations in children under the age of two are due to bronchiolitis, which is a major cause of hospital admission for newborns and early children globally [1]. The most straightforward and concise clinical case definition of acute bronchiolitis can be defined as respiratory distress in an infant under 2 years old, accompanied by cough, wheeze, or crackles on auscultation, with radiological hyperinflation and/or increased translucency but no conclusive evidence of consolidation [2]. The Indian subcontinent has outbreaks between September and March. Within the first two years of life, 90% of children acquire RSV, and during that initial illness, up to 40% of them develop lower respiratory tract infections [3]. Adenovirus, influenza, corona virus, human boca virus, human rhinovirus, human metapneumovirus, and parainfluenza viruses are some of the other viruses that can cause acute bronchiolitis. There are two strains of RSV: A and B. RSV A is linked to a more serious form of illness. It is feasible to reinfect during the same season using a different strain [4]. Cough, nasal stuffiness, post-tussive vomiting with feed intolerance, inconsolable crying, infrequently reduced awareness, and convulsions are the signs and symptoms of acute bronchiolitis.Most babies have a fever of less than 39 degrees Celsius, while 50% of them have a fever of more than 38.5 degrees Celsius. Tachypnea, chest in-drawing, nasal flaring, intercostal recession, hypoxemia (SPO2 < 90%), grunting, apnea, respiratory failure, and dehydration are among the warning indications that frequently call for therapy in a critical care setting[5]. A well-established and widely accepted clinical severity grading symptom for acute bronchiolitis was proposed by Golan-Tripto et al. in 2018 [6]. Another significant feature of this scoring system is that the score has been subgrouped, with an age-based cutoff of six months, in place of universalization. Another score system that is only based on clinical evidence is the Indian Academy of Paediatrics Standard Treatment Guidelines 2022 [7]. Although numerous studies have confirmed that hyponatremia, the most common electrolyte abnormality, has a strong correlation with the severity of any respiratory illness and that its presence significantly alters the prognosis of the illness, neither of them focuses on dyselectrolytemia as a potential biomarker of severity [8–10]. The most frequent electrolyte anomaly we see in pediatric critical care settings, especially in complex respiratory illnesses like pneumonia and empyema, is hyponatremia. This is no longer a mystery. Since there is no literature or research on the subject, the relationship between acute bronchiolitis and changes in serum sodium levels is frequently disregarded or discovered unintentionally [11,12]. Since Acute Bronchiolitis is one of the most common causes of pediatric respiratory morbidity, measuring blood sodium levels is crucial because it is a modifiable risk factor. This is the foundation of our investigation, which looks for any meaningful associations between the two.

Methodology

This was an inpatient hospital based prospective observational study conducted in a tertiary care pediatric center in eastern India over a span of one year. A total of 120 children of clinically diagnosed acute Bronchiolitis following an informed consent were enrolled into the study who were admitted in our paediatric Medicine ward in that span of time after excluding patients with concomitant congenital heart disease, chest wall deformities. Patients requiring invasive mechanical ventilation and patients with Preexisting risk factors for hyponatremia [diuretic therapy, cardiac diseases, renal Disease and hypothyroidism] were also excluded from the study. Most of the diagnosis were based on clinical judgement and in some cases they were consolidated by a chest skiagram done by using a portable X-ray machine Allengers-HF. At the time of admission, blood sample was collected in clotted vial and serum sodium Measured by blood Electrolyte analyzer machine (ST-200CLElectrolyte analyzer from SENSA CORE) . They were further classified as mild moderate or severe acute bronchiolitis on day 1, day 3, and day 5 of admission according to MODIFIED TAL SCORE [Table 1]. As per the serum sodium concentration they are classified into normonatremia, hyponatremia and hypernatremia. Final outcome in the form of discharge, death, leave against medical advice, and length of hospital stay were recorded. The relationship between serum sodium level and severity of Bronchiolitis and disease outcome were assessed.

Statistical analysis

The results are presented in frequencies, percentages and mean±SD. The Unpaired t-test was used to compare two means. The one way analysis of variance (ANOVA) test

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followed by Tukey's post hoc tests was used to compare more than two means. The Chi-square test was used to find the associations among categorical variables. The Pearson correlation coefficient was calculated. The p-value<0.05 was considered significant. All the analysis was carried out On SPSS 16.0 version (Chicago, Inc., USA).

Ethics

The study was approved by the Institutional Ethics Committee (BCR/ME/PR/ 2149C). The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1964, as revised in 2013. Informed patient consent was obtained from the patients prior to enrollment in the study.

Results

Among 120 children more than half of children were <6 months of age (55.8%) followed by 6-12 (26.7%) and >12 months (17.5%). The mean age of children was 6.54±5.57 months. As per our study this disease showed a male predilection, where more than half of children were males (64.2%). When looked at perinatal history, 44.2% had low birth weight at delivery (<2.5 kg) whereas 55.8% children had a birth weight more than 2.5 kg and 56.7% patients were delivered at term. The incidence of Hyponatremia and normonatremia was 19.2% and 78.3% respectively. The mean serum sodium level was obtained as138.90±5.74. The 23 children who were found to be hyponatremic were further subgrouped, 18 children (78.3%) being mildly hyponatremic and 5 children (21?7%) being moderately hyponatremic. As per Modified TAL scoring when the severity of Acute Bronchiolitis was assessed it was found that at Day 1, the disease was of moderate severity in majority of the patients (71.7%) whereas this was severe in only 7.5% cases. As the disease progressed the patients became clinically better with an increase in milder severity percentage at Day 3 and Day 5 as 87.5% and 99.1% respectively. Overall the duration of hospital stay was <7 days among more than half of children (64.2%) followed by ≥7 days (35.8%). The mean duration of hospital stay was 6.37±2.30 days. IThe one way analysis of variance showed that there was significant (p=0.006) difference in serum sodium level at day 1 among severity of bronchiolitis. The pairwise comparisons showed that serum sodium level was significantly (p<0.05) higher among mild acute bronchiolitis children (141.60±4.48) than severe (135.11±6.52) at day 1. The serum sodium level was significantly (p=0.01) higher among mild acute bronchiolitis children (139.01±5.64) compared to moderate (133.73±6.66) at day 3. In addition to this it was also observed that the length of hospital stay was higher among children with Hyponatremia (7.57±2.51 days) compared to normonatremia (6.00±2.20 days). When the length of hospital stay which is an indirect indicator of security is compared with the levels of hyponatremia it was found that the length of hospital stay was significantly higher among children with moderate Hyponatremia (10.20±4.14 days) compared to mild hyponetremia (6.83±1.24 days) with a p-value of 0.005. There was significant negative correlation obtained among length of hospital stay with serum sodium level (r= -0.57, p=0.003)[Figure – 1]. And similarly another strong negative correlation was found between the length of hospital stay and level of hyponatremia (r= -0.44, p=0.005) [Figure – 2]. When the levels of hyponatremia were compared between other clinico epidemiological parameters like age, gender, birth weight, gestational maturity all came out to be statistically insignificant. Similarly apart from the serum sodium level, all the other clinico epidemiological parameters were also statistically insignificant when compared to the severity scoring.

Discussion

Acute Bronchiolitis is one of the leading causes of respiratory morbidity which predominantly affects the paediatric age group below 2 years which usually runs an uncomplicated course but in some cases patient may progress to respiratory failure leading to admission to a critical care unit. In our study a total of 120 children were included, the mean age being 6.54±5.57 months with a male to female ratio of 1.7:1. In an Indian study by Singh et al. it was observed among the bronchiolitis patients majority belonging to age group of 2 months to 1 years (75%) with a male to female ratio more than 2:1 [13]. Similarly in the study by Turkmenoglu et al. the mean age group of affected patients were 5.5 ± 4.6 months [14] . This study observed that more than half of children had birth weight ≥2.5 kgs (55.8%). The mean birth weight was 2.37±0.64 kgs. More than half of children were term (56.7%) in the present study.

This study found that the incidence of Hyponatremia,Normonatremia and Hypernatremia was

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19.2% ,78.35 and 2.5% respectively. The mean serum sodium level was 138.90±5.74. In this study, mild and moderate hypotremia among children with hyponatremia was 78.3% and 21.7% respectively. The categorisation of hyponatremia is followed as per standard range division of serum sodium level [15]. It has been demonstrated that hyponatremia in children affected by acute bronchiolitis is associated with seizures and potential severe complications [16]. Turkmenoglu et al. [14] and Luu et al. [11] had demonstrated almost similar percentage of prevalence of hyponatremia in their study as 17.4% and wr.e% respectively. Our study did not point out any cases of severe hyponatremia. However in the studies by Singh et al. [13] and by Jain et al. [16] some cases of severe hyponatremia has been demonstrated in patients with acute bronchiolitis although the percentage being minimal as 6% and 3% respectively. There has been some contrasting data in some studies which boasts a higher percentage of prevalence of hyponatremia as evidenced by the study of Sarkar et al [17] and Patil et al [18]. However the high percentage burden may be due to fact that the studies encompassed all the cases of lower respiratory tract infection rather than proper acute bronchiolitis.

It is now known that the syndrome of inappropriate anti diuretic hormone secretion (SIADH) occurs frequently in several pulmonary conditions including acute bronchiolitis which may lead to hyponatremia [2]. Normally ADH is secreted by the posterior pituitary gland in response to high plasma osmolality. However, in various clinical condition including fever, hypoxia, hypercarbia, pain nonosmotic stimulation of ADH secretion can lead to hyponatremia. In acute bronchiolitis the stimulus of ADH release is likely to be nonosmotic in nature; in particular, lung hyperinflation and pulmonary infiltrates may stimulate ADH secretion by causing a false perception of hypovolemia by intrathoracic receptors [19] . Therefore, if IV fluid is administered, judicious and careful calculation of the fluid intake is advised to reverse hypervolemia in acute bronchiolitis [20]. In the present study, moderate acute bronchiolitis was among majority of children on day 1 of admission (71.7%) followed by mild (20.8%) and severe (7.5%). Mild acute bronchiolitis became among majority of children on day 3 of admission (87.5%) and day 5 (99.1%). This study also observed that the duration of hospital stay was <7 days among more than half of children (64.2%) followed by ≥7 days (35.8%).In this study, the one way analysis of variance showed that there was significant ($p=0.006$) difference in serum sodium level on day 1 of admission among severity of acute bronchiolitis. The pairwise comparisons showed that serum sodium level was significantly ($p<0.05$) higher among mild acute bronchiolitis children (141.60±4.48) than severe (135.11±6.52) on day 1 of admission. The serum sodium level was significantly ($p=0.01$) higher among mild acutebronchiolitis children (139.01±5.64) compared to moderate (133.73±6.66) on day 3 of admission. Khanbabaie et al [12] showed that the mean serum Na level was 136.22±2.99, 133.76±3.88, and 130.50±11.45 in the mild, moderate and severe acute bronchiolitis groups, respectively. The results of one-way ANOVA test showed that there was a statistically significant relationship between serum sodium level and severity of acute bronchiolitis (p-value= 0.013). A lower mean serum sodium level was observed in children with higher severity of acute bronchiolitis. A statistically significant relationship was found between serum sodium levels in patients with mild and moderate acute bronchiolitis ($p = 0.037$), indicating that the mean serum sodium level is significantly lower in patients with moderate acute bronchiolitis compared with patients with mild acute bronchiolitis (133.76 vs. 136.22 mEq/L). The literature suggests that in acute bronchiolitis mild hyponatremia is associated with worse outcomes, such as higher need for intubation, longer hospitalization and increased mortality. Neurogenic pulmonary edema might be a further under-recognized complication of these cases [21].

The current study showed that the length of hospital stay was higher among children with Hyponatremia (7.57±2.51 days) compared to Hypernatremia (6.00±0.00 days). Khatab et al (2020)51 showed that there was a highly significant statistical difference regarding length of stay in hospital ($P = 0.001$) between with and without Hyponatremia. This study revealed that the length of hospital stay was significantly higher among children with moderate Hyponatremia (10.20±4.14 days) compared to mild hyponatremia (6.83±1.24 days). A similar statistically significant observation was also obtained from other various studies like Sarkar et al [13] , Singh et al (2019)[17] . This study found that there was significant negative correlation of length of hospital stay with serum sodium level ($r= -0.57$, $p=0.003$) and serum

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sodium level among hyponatremia children (r= -0.44, p=0.005).

In this study, the incidence of hyponatremia was highest among children of age <6 months (25%) and was lowest among >12 months of age (4.8%). However, the association of incidence hyponatremia with age was insignificant (p>0.05). Jain et al [16] showed that hyponatremia was found to be more common among 1 to 5 years age group as compared to ≥ 2months to 12 months and > 5 to 12 years age groups.There are very few studies which had reported on the age related association of hyponatremia. Wrotek et al [22] found that the age group of more than 4 years has greater chance of hyponatremia and severe infection. Park et al [23] found that increasing age is an independent risk factor for the development of hyponatremia. But again all of them are based on either pneumonia or lower respiratory tract infection. The difference of results obtained in our study may be due to the classical age group of bronchiolitis i.e. below 2 years were taken into consideration. This study showed that the incidence of hyponatremia was higher among male children (23%) than females (14%). However, the association of incidence hyponatremia with gender was insignificant (p>0.05). A similar finding was observed by Sarkar et al [17] which also consolidated the fact that sex of the child had no correlation with hyponatremia. The other correlation between incidence of hyponatremia and birth weight and birth gestational age was also not statistically significant.

Modified Tal Scoring is a simple and validated scoring system for evaluation of infants with acute bronchiolitis and application of this clinical tool at day 1 is a fair predictor of oxygen requirements at day 2 and probability of length of hospital stay beyond 72 hours [6]. Our study also highlights the potential of serum sodium level as a adjunctive severity biomarker as the clinical parameters may not be sufficient in every case and we are more inclined to routine blood gas analysis in a patient with respiratory distress, so the availability of laboratory value of serum sodium is easily available. The other clinico epidemiological parameters included in this study such as age, sex, birth weight, maturity doesn't hold any statistical significance when it comes to measurement of severity. In some studies a history of prematurity with low birth weight, an excess birth weight more than 4 kg, age less than 3 months has been found to be independent risk factors with higher chances of complications but no such significance was obtained from our study[24, 25]. A larger sample size with a multicentric data may be needed to corroborate such observations.

Conclusion

Acute Bronchiolitis is a disease which often runs an uncomplicated course still possess the highest burden of respiratory comorbidity. A clinical tool like Modified Tal Score can assess the outcome which can be very well adjuncted by Serum sodium concentration testing for prognostication. Although Normonatremia is prevalent in the study but Hyponatremia has significantly altered the disease course in terms of severity reflected by the scoring system and the length of hospital stay. This study establishes Serum sodium concentration as potential biomarker of the disease severity which warrants a routine estimation of such in each and every cases of Acute Bronchiolitis at day 1.

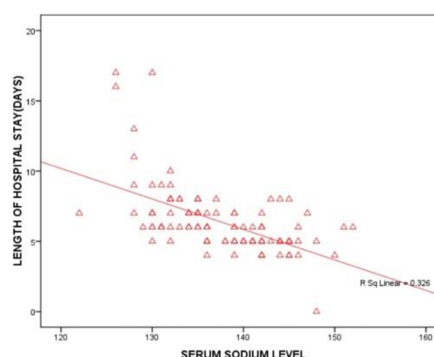

Figure 1 : Scatter diagram showing Correlation of length of hospital stay with Serum Sodium level

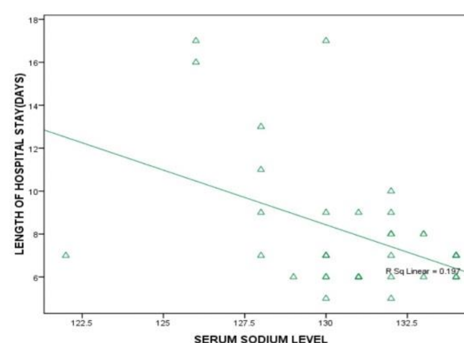

Figure 2 : Scatter diagram showing Correlation of length of hospital stay with Serum Sodium level among Hyponatremia children

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Score	Respiratory rate/ min <6 mths	Respiratory rate/min ≥6 mths	Wheezing	Cyanosis	Accessory muscle use
0	≤40	≤30	None	None	None
1	41–55	31–45	End expiratory with stethoscope	Peri-oral with crying	+
2	56–70	46–60	Inspiration and expiration with stethoscope	Peri-oral at rest	++
3	>70	>60	Audible without stethoscope	Generalised at rest	+++
Respiratory distress category				Total score	
Mild				0–3	
Moderate				4–8	
Severe				9–12	

Table 1 : Modified TAL Scoring

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