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Relationship between Serum Sodium Level and Severity of Bronchiolitis in Children Hospitalized in Amirkola Children's Hospital, Iran

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ABSTRACT

Background and Objective: Despite the self-limiting nature of bronchiolitis, its severe forms require hospitalization. Electrolyte imbalance during bronchiolitis is common, however, the relationship between bronchiolitis severity and serum sodium (Na) levels has not been well studied. The purpose of this study was to investigate the relationship between serum Na level and bronchiolitis severity.

Methods: This cross-sectional study included hospitalized children with bronchiolitis at Amirkola Children's Hospital, Babol, Iran, from May 2020 to May 2021. Diarrhea, underlying disease, glucocorticoid intake, and intravenous fluid therapy before admission were considered exclusion criteria. The Bierman-Pierson scale was used to evaluate the severity of the disease, and hyponatremia was divided into mild, moderate, and severe groups. Variables were analyzed using Statistical Packages for Social Sciences (SPSS) 26. A value of $P<0.05$ was considered significant.

Findings: Sixty-one children (55.7% male) with a mean age of 5.19 ± 4.36 months were enrolled in the study, with most (50.8%) belonging to the mild form of the disease. The mean serum Na levels based on the severity of bronchiolitis were 136.22 (SD: 2.99), 133.76 (SD: 3.88), and 130.50 (SD: 11.45) in the mild, moderate, and severe groups, respectively. There was a statistically significant relationship between serum sodium level and severity of bronchiolitis (P-value = 0.013).

Conclusion: The results showed that higher severity of bronchiolitis was associated with an increased risk of hyponatremia. Therefore, periodic monitoring and correction of hyponatremia in children with bronchiolitis, especially at younger ages, is necessary to improve the outcome of the disease.

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Introduction

Bronchiolitis is the most common lower respiratory tract infection [1]. The condition makes up for 18% of hospitalizations in the USA [2], 15% of which require admission into the intensive care unit (ICU) [3]. Most patients experience mild-to-moderate symptoms and the disease is self-limiting, however, in the case of severe disease, the outcome could be very different and requires clinical assessment by a physician. Different scoring systems have been suggested, such as modified TAL, Respiratory Distress Assessment Instrument (RDAI), and Bierman-Pierson score which classifies the disease into mild, moderate, and severe categories [1]. Despite the significant burden associated with the disease, there exists a debate among clinicians about the management and prediction of the clinical course of bronchiolitis [4]. Electrolyte imbalance is an important problem during the treatment of bronchiolitis. In particular, hyponatremia is common in patients with respiratory infections [5]. Hyponatremia is associated with poor prognosis in adult patients with critical diseases. The underlying mechanism of hyponatremia in such cases could be the syndrome of inappropriate antidiuretic hormone (SIADH), which is common in respiratory infections, or fluid retention [4]. Unlike adults, there is limited evidence in children regarding the relationship between serum sodium (Na) and the clinical prognosis of the disease [3]. Viral bronchiolitis, especially due to respiratory syncytial viruses (RSVs) is common [6-10]. Additionally, rhinovirus, parainfluenza, human metapneumovirus, influenza, adenoviruses, and coronaviruses are less common causes of the condition [6, 11-13].

Bronchiolitis in children younger than 1-2 years of age presents with clinical findings such as fever, rhinorrhea, and respiratory distress that is marked by increased respiratory rate, chest wall retraction, wheezing, and crackle [14]. Diagnosis of the disease is often based on clinical presentation. Therapy is usually supportive and includes hydration and resolving hypoxemia until recovery [1].

While a limited number of studies have investigated the relationship between serum Na levels and mortality, duration of hospitalization, or bronchiolitis severity and its prognosis [2, 3], there is a lack of studies investigating the prevalence and severity of hyponatremia in pediatrics with bronchiolitis. The present work was conducted to explore the relation of serum Na levels with bronchiolitis severity and prognosis. Moreover, we utilized the Bierman-Pierson scoring system to quantify the bronchiolitis severity and its association with serum Na levels in pediatrics admitted to Amirkola Children's Hospital in Northern Iran. The results of the present study can be useful in improving the current treatment protocols.

Methods

Study design and participant

The population of this cross-sectional clinical study was all children hospitalized for bronchiolitis between May 2020 and May 2021 at Amirkola Children's Hospital, Babol, Iran. Patients were selected from those who met the inclusion criteria. The inclusion criteria for this study included age less than two years and a diagnosis of bronchiolitis by a pediatric pulmonologist. Exclusion criteria included diarrhea during the course of illness, chronic underlying diseases such as pulmonary, cardiac, renal, and metabolic problems, and use of glucocorticoids or fluid therapy before hospitalization.

Sample size and sampling method

A non-probabilistic and simple sampling was performed. Based on the sample size formula, 61 children were recruited for the study.

Data collection

This study was approved by the Ethics Committee of Babol University of Medical Sciences in northern Iran. First, all children suspected of having bronchiolitis were examined by a specialist in pediatric pulmonology. Bronchiolitis was identified by upper respiratory tract symptoms, such as rhinitis, fever, and cough, followed by dyspnea and wheezing with or without crackles in the child [15]. Using a

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nonprobabilistic simple random sampling method, 61 patients were enrolled in the study. Data extracted included clinical findings on admission such as respiratory rate, cyanosis, and use of accessory muscles in breathing, breath sounds, and serum Na levels along with demographic data (age, gender). The severity of bronchiolitis was determined using the Bierman-Pierson scoring scale [16] (Table 1).

In the present study, the severity of bronchiolitis was measured using the Bierman-Pierson instrument. The instrument measured the presence of wheezing, cyanosis, and the accessory muscle used to quantify the severity of bronchiolitis. The score for each of the above-mentioned parameters ranged from 0 to 3 points. The total score for each person ranged from 0 to 12 points, with higher scores indicating higher severity of disease. More specifically, a score between 1 and 5 indicates mild bronchiolitis, a score between 6 and 10 indicates moderate bronchiolitis and a score above 10 indicates severe bronchiolitis. To measure serum sodium levels, 2 milliliters of venous blood were taken from the patient at the beginning of hospitalization and sent to the laboratory at Amirkola Children's Hospital. Serum sodium level was measured with an electrolyte analyzer (Caretium, China) available in the laboratory and reported as Meq/liter. A serum level of 135 to 145 Meq/L was considered a normal serum level, and levels below 135 Meq/L were considered hyponatremia. Hyponatremia was classified into 3 subgroups: mild (Na level between 130 and 134 Meq/L), moderate (Na level between 125 and 129 Meq/L), and severe (Na level < 125 Meq/L) [17].

Statistical analysis

Collected data were entered into Statistical Packages for Social Scoencessciences (SPSS), V22, and used for statistical analysis. Descriptive analyses were reported as mean, SD, and percentage to describe the variables of the study. Chi-square, independent Student's t-test, and analysis of variance (ANOVA) were used as needed. A threshold of $p < 0.05$ was chosen for the significance test.

Table 1. Bierman-Pierson tool for the evaluation of bronchiolitis severity

Total score	RR (in< 6 months)	RR (in> 6 months)	Cyanosis	Use of accessory muscles	Wheezing or Rales
0	40<	30<	Absent	No	Absent
1	40-54	30-44	when crying	subcostal recession	During expiration
2	55-70	45-60	At rest	suprasternal recession	During inspiration and expiration
3	70>	60>	Generalized	Nasal flaring	Lack of vesicular respiratory sounds or presence of stridor

RR: respiratory rate (breath per minute)

Mild bronchiolitis: 1-5 points, Moderate bronchiolitis: 6-10 points, severe bronchiolitis: more than 10 points.

Results

This cross-sectional study was conducted on 61 children hospitalized for bronchiolitis. The mean age of the children was 5.19 ± 4.36 months, the mean serum Na level was 134.9 ± 3.95 Meq/L, and the mean hospitalization time was 6.21 ± 2.22 days. 55.7% and 44.3% of participants were male and female, respectively. Moreover, 82% of participants did not require admission to the ICU. One patient underwent mechanical ventilation. Overall, hyponatremia occurred in 29 patients (47.5%) (Table 2).

The severity of bronchiolitis was divided into three categories: mild, moderate, and severe, and the number of patients in each category was 31 (50.8%), 28 (45.9%), and 2 (3.3%), respectively. 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 bronchiolitis groups, respectively. The results of one-way ANOVA test showed that there was a statistically significant

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relationship between serum sodium level and severity of bronchiolitis (p-value= 0.013). A lower mean serum sodium level was observed in children with higher severity of bronchiolitis.

Table 3 represents a statistically significant relationship between serum Na levels in patients with mild and moderate bronchiolitis (p=0.037), indicating that the mean serum Na level is significantly lower in patients with moderate bronchiolitis compared with patients with mild bronchiolitis (133.76 vs. 136.22 mEq/L). To test the relationship between serum sodium level and hospitalization status in the pediatric ICU (PICU), the independent Student t test was used. The results showed no statistically significant relationship between serum Na level in children hospitalized in the ICU and other children.

Furthermore, no statistically significant relationship was found between the use of mechanical ventilation (in one patient) [Na: 136 Meq/L]) and the mean serum sodium level (134.89 ±3.98 Meq/L) (p-value=0.783). Pearson correlation analysis was used to measure the relationship between serum sodium level and length of hospital stay. The relationship between serum sodium level and length of hospital stay was not significant (p-value=0.446, r=-0.99).

To investigate the relationship between the serum Na level and the mean age of the studied children, Pearson correlation was used. A statistically significant relationship was observed between serum sodium level and the mean age of the children (p-value = 0.018). This indicated that in younger children, the reduction in serum sodium level was more severe (Pearson correlation r = -0.30). Finally, no statistically significant difference was found between the mean serum Na levels in boys compared with girls (p-value = 0.881, 134.82±4.07 for girls and 134.97±3.90 for boys).

Table 2. Clinical parameters of bronchiolitis patients

Parameter	Status	Prevalence (percentage)
Gender	Male	34 (55.7)
	Female	27 (44.3)
ICU admission	Yes	11 (18.0)
	No	50 (82.0)
Mechanical ventilation	Yes	1 (1.6)
	No	60 (98.4)
Serum Na level	Normal	32 (52.5)
	Mild hyponatremia	23 (37.7)
	Moderate hyponatremia	4 (6.6)
	Severe hyponatremia	2 (3.3)

Table 3. Comparison of mean serum Na levels in patients with moderate and severe bronchiolitis

Bronchiolitis Severity	Mean Difference	P-value	CI 95%	
			Lower	Upper
Moderate	2.46*	0.037*	0.123	4.80
Severe	5.72	0.098	-0.819	12.27

Discussion

The present study showed a statistically significant relationship between the serum Na level at admission and the severity of bronchiolitis in the studied children. The mean serum Na level on admission was found to be 134.9 ± 3.95 Meq/L, which was lower than the mean serum Na level in the study conducted by Gultekingil *et al.* (136 ± 2.0 mEq/L).

In addition, about half of the cases in our study had a serum Na level of less than 135 Meq/L, most of whom (37.7%) experienced a mild form of hyponatremia (Na level of 130-135 Meq/L). This was higher compared to the results of the study by Gultekingil et al. [18], who found 21.2% of children

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in their study had hyponatremia (serum Na level less than 135 Meq/L). In Gultekingil's study, the increase in the level of ADH hormone and the intravenous injection of hypotonic fluids were suggested as the main etiology of hyponatremia, and considering the lack of participation of patients receiving intravenous fluids in our study, it seems that the role of the increase in the level of ADH hormone in the occurrence of hyponatremia, in hospitalized patients due to bronchiolitis, is the more probable hypothesis. However, further study is suggested.

In the study conducted by Shein *et al.* [19], 36% of patients had hyponatremia at the beginning of hospitalization and 25.7% had hyponatremia during hospitalization. The mean serum sodium level in these patients was reported 133 Meq/L.

In the study conducted by Milani *et al.* [5], 57% of the patients had hyponatremia, of which 81.31%, 16.48%, and 1.09% had mild, moderate, and severe forms of the condition, respectively. Hyponatremia was significantly more common in infants younger than six months compared to infants older than six months. In the study conducted by Albinski *et al.* [20], the serum sodium level was less than 135 mmol/L in 21% of the patients admitted to the hospital and 33% of the patients admitted to the Pediatric ICU (PICU) due to acute bronchiolitis. Shibli and colleagues [21] found 45% of pediatric bronchiolitis under 2 had hyponatremia, and 80% of these cases had hyponatremia on admission. Overall, it seems if hyponatremia occurs during bronchiolitis, most of the patients will have a mild form of hyponatremia and consequently a good clinical outcome.

The significant relationship between serum Na levels and bronchiolitis severity was also corroborated in another study by Masarweh and colleagues [22]. In our study, the average duration of hospitalization was found 6.21±2.22 days, which is higher than the report by Masarweh et al. [22], in which the duration ranged from 2.5 to 3 days. This value was also higher compared to the average reported in the study conducted by Shein et al. [19], in which the duration was 2.5 days.

In our research, 18% of the patients were admitted to the ICU and 1.6% of the patients required mechanical ventilation, while in the research conducted by Masarweh *et al.* [22], 13% of the admitted patients needed ICU admission. In a paper by Ghazaly *et al.* [23], 13.5% of children with bronchiolitis required admission to the ICU. Further, Shibli *et al.* [21] found 13% of children in their study were admitted to the ICU, of which 61% required continuous positive air pressure (CPAP), 26% required mechanical ventilation, and 13% required oxygen only.

Although the relationship between ICU admission status and serum Na levels was not meaningful in our study, this was significant in the study by Shibli et al [21]. However, this comparison may not be valid due to differences in the study designs. We recorded baseline Na, while Shibli *et al.* recorded Na periodically. This is a valuable suggestion for upcoming works.

Mechanical ventilation was not related to serum Na levels, but, this was meaningful in the study by Shein et al. [19] who discussed patients with hyponatremia were more likely to receive mechanical ventilation. This difference may be explained by the early admission of patients in our work.

Age and serum Na levels showed an inverse and significant correlation in our work. This confirms similar results by Mazzoni et al. [24]. Considering the possible hypothesis of increased ADH level as the cause of hyponatremia, it seems that the relationship between the younger age of the child and the higher incidence of hyponatremia is secondary to the underdevelopment of the hormonal system. Therefore, conducting additional studies to investigate the relationship between the level of ADH and The incidence of hyponatremia is recommended in different age groups of children.

Limitations of the study

The limitation of this study was that the serum Na level of patients was measured only at the beginning of hospitalization. We recommend that future studies measure Na levels several times during hospitalization to more accurately assess hyponatremia.

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Conclusion

The results of the present study and their comparison with previous studies indicated a relatively significant incidence of hyponatremia in children with acute bronchiolitis, which in most cases occurred in a mild form that did not adversely affect the clinical outcome of the disease. However, as the severity of bronchiolitis increases, the likelihood of hyponatremia and its more severe forms may be higher. Clinicians should pay attention to the negative effects caused by disturbances in serum Na levels, especially neurological symptoms such as seizures. Our results warrant close monitoring for Na levels and taking timely therapeutic measures to correct it in pediatric bronchiolitis to improve disease outcomes, especially in younger children.

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Ethics statements

The present study was approved by the Ethics Committee of Babol University of Medical Sciences (IR.MUBABOL.REC.1399.024).

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Consent for publication

All authors agreed to publish the present study.

Data availability statement

Data may be available from the corresponding author upon reasonable request.

Authors' Contributions

S.K., I.M., H.S., M.K., M.H.A., and K.S. drafted the manuscript and conceptualized the study. K.S. prepared the final draft and critically appraised the manuscript. M.H.A. and K.S. performed statistical analyses. I.M., H.S., and M.K. helped with treating patients. S.K. and K.S. helped with data collection.

Conflict of interest

There was no conflict of interest.

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