Submitted: 12 December, 2024 Accepted: 08 February, 2025 Published: 08 January, 2026 DOI:10.22514/sv.2026.003

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ORIGINAL RESEARCH

Lactate levels as predictors of hospitalization in infants with acute bronchiolitis: a multicenter retrospective study

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Abstract

Background: Acute bronchiolitis (AB) is a common lower respiratory tract disease in infants and a major cause of emergency department visits and hospitalizations. Reliable biomarkers to predict hospitalization are needed because clear prognostic criteria are lacking. This study aimed to evaluate the predictive value of lactate levels for hospitalization in infants with AB. **Methods**: This retrospective observational study was conducted across three emergency medical centers in Korea from January 2020 to December 2022. A total of 234 infants diagnosed with AB were included. Demographic characteristics, vital signs, and laboratory results, including lactate levels, were collected and compared between discharged and hospitalized patients. Multivariable logistic regression and receiver operating characteristic (ROC) curve analyses were performed to identify significant predictors of hospitalization. **Results**: Lactate levels were significantly higher in the hospitalized group compared with the discharged group (2.00 *vs.* 1.70 mmol/L, $p = 0.003$). In multivariable analysis, lactate was identified as an independent predictor of hospitalization (odds ratio 1.718; 95% confidence interval 1.059–2.787). The ROC curve for lactate demonstrated an area under the curve of 0.628, indicating limited discriminative ability. **Conclusions**: Elevated lactate levels are associated with hospitalization in infants with AB; however, their predictive performance is modest. Larger, prospective studies are required to validate the clinical utility of lactate as a biomarker for risk stratification and decision-making in AB patients.

Keywords

Acute bronchiolitis; Infant; Lactate measurement

1. Introduction

Acute bronchiolitis (AB) is a prevalent lower respiratory tract illness globally and is a primary reason for hospitalization, particularly in infants under 12 months of age [1, 2]. It also significantly contributes to emergency department (ED) visits. The decision to hospitalize a patient with acute bronchiolitis is often challenging [3].

Traditionally, the decision to admit patients with AB was based on clinical history and physical examination [4]. Previous studies have, however, highlighted the limitations in the accuracy of these decisions [4]. With 5–10% of hospitalized patients with AB requiring intensive care unit (ICU) admission, making an accurate management decision is critical [2]. Nevertheless, beyond the presence of comorbidities such as congenital diseases or premature birth, clear criteria for predicting prognosis are lacking [1]. Therefore, there is a need for objective guidelines to manage patients with AB.

The criteria for hospitalization and management of patients with AB vary across institutions [3]. Identifying reliable and objective biomarkers is crucial for effective AB patient management [5]. Consequently, this study sought to determine whether laboratory test results can predict hospitalization needs.

2. Materials and methods

2.1 Settings

We performed a retrospective observational analysis involving infants diagnosed with AB who presented to the EDs of three medical centers between January 2020 and December 2022. We diagnosed AB based on various clinical features observed in patients with lower respiratory tract infections, including respiratory distress, diffuse crackles, and inflammatory wheezing [6]. The three EDs—situated in Gyeonggi, Chungcheong, and Seoul—each accommodate an annual patient volume of about 60,000, 60,000, and 40,000 individuals, respectively. From the medical records, we retrieved information on patient demographics (age and sex), clinical vital indicators, and laboratory test values.

2.2 Data sources

Patients whose vital signs were stable and showed prompt clinical recovery after basic supportive care in the ED generally did not undergo laboratory testing, unless the supervising emergency physician deemed it necessary. Collected laboratory information included White blood cell (WBC) counts, C-reactive protein (CRP) levels, lactate values, and findings from arterial blood gas tests, including pH, partial pressures of oxygen and carbon dioxide, bicarbonate, and base excess. Lactate levels were measured immediately upon the patient's visit to the ED using the GEM Premier 3500 analyzer (Werfen, Bedford, MA, USA). Whether laboratory testing was performed or not depended on the clinical judgment of the ED physician. Approval for this study was granted by the Institutional Review Board (IRB) of Soonchunhyang University Cheonan Hospital, and it was conducted under an IRB-approved exemption from obtaining informed consent (IRB File No. 2023–03-016).

Patients with a diagnosis of AB who were transferred to another facility or who returned to the ED within 24 hours after discharge were not included in the analysis. Patients with congenital diseases, such as chronic lung disease and hemodynamically important congenital heart disease, with immunodeficiency and neuromuscular disorders, and those born prematurely (<36 weeks gestational age), were also excluded [7].

2.3 Data analysis

The discharge group was defined as patients discharged following their initial ED visit, while the hospitalization group consisted of patients who were admitted during their first visit to the ED. We analyzed differences in baseline characteristics and laboratory findings between the two groups. Continuous and categorical variables are presented as median (interquartile range) or mean (standard deviation) and as frequency (percentages), respectively. Continuous variables were compared using the Student *t* test and Mann-Whitney U test, and categorical variables were analyzed using Pearson χ^2 and Fisher exact test. Univariable logistic regression tests, including for age, vital signs, WBC, lactate levels, pH, and partial pressure of carbon dioxide (pCO_2), were conducted to identify predictive variables for revisits, *i.e.*, those with *p* values less than 0.1. Using the Youden index, the optimal thresholds identified for age, systolic and diastolic blood pressure, heart rate, respiratory rate, body temperature, WBC, lactate levels, pH, and pCO_2 were 4.5 months, 87.5 mmHg, 50 mmHg, 133/min, 49.5/min, 37.05 ℃, 10,295/μL, 2.15 mmol/L, 7.345, and 45.15, respectively. Following the univariable logistic regression, variables with *p* values less than 0.1, including gender, age, pulse rate, lactate levels, and pCO_2, were selected for multivariable logistic regression analysis. Receiver operator curve (ROC) analysis was employed to assess the accuracy of independent laboratory data in predicting admissions. A *p* value of < 0.05 was considered statistically significant. All analyses were performed using SPSS version 27.0 (SPSS Inc., Chicago, IL, USA).

3. Results

A total of 353 infants received a diagnosis of AB over the study timeframe. After excluding 100 who revisited within 24 hours, 10 who were transferred to other hospitals, and 9 born prematurely, 234 infants were eligible for evaluation. Among them, 72 were managed as outpatients and 162 were hospitalized. No cases required ICU-level care or ventilatory support, and all hospitalized participants were discharged following noninvasive conservative management. Table 1 provides an overview of patient background characteristics in addition to the laboratory measurements collected. Of the total 234 patients, 100 were male (42.74%). In the discharge group, 25 patients (34.72%) were male, while in the hospitalization group, 75 patients (46.30%) were male; however, there was no significant difference in sex distribution between the two groups. The hospitalization group was significantly younger than the discharge group (7 *vs.* 4 months, $p = 0.002$) and had higher pulse rates (142.5 *vs.* 134/min, $p < 0.001$). When comparing laboratory results, the hospitalization group revealed higher lactate levels (2.00 *vs.* 1.70 mmol/L, $p = 0.003$), lower pH values (7.37 *vs.* 7.38, $p = 0.036$), and higher pCO_2 (41.00 *vs.* 38.00 mmHg, $p = 0.050$) than the discharge group.

In the univariable regression, gender, age, pulse rate, lactate, and pCO_2 showed *p* values below 0.1; therefore, these variables were included in the subsequent multivariable analysis. This analysis pinpointed lactate levels as a variable significantly associated with predicting admission (odds ratio, 1.718; 95% confidence interval (CI), 1.059–2.787) (Table 2).

We evaluated the predictive capability of lactate levels through ROC analysis, which resulted in an area under the curve (AUC) of 0.628 (95% CI, 0.568–0.680). An optimal threshold of 2.15 was derived from the analysis. At for this value, sensitivity reached 46.23% (95% CI, 36.49–56.18) and specificity was 79.41% (95% CI, 67.88–88.26). The corresponding positive predictive value and negative predictive value were 77.78% (95% CI, 65.54–87.28) and 48.65% (95% CI, 39.05–58.32) (Fig. 1).

4. Discussion

In this study, no significant differences were observed in vital signs between the hospitalization and discharge groups, except for an elevated heart rate in the hospitalization group. Furthermore, regression analysis revealed no significant correlations between any of the vital signs and hospitalization. Additionally, none of the patients required admission to the ICU or respiratory support, suggesting that the study included relatively mild cases. Therefore, lactate measurement may assist in determining the need for hospitalization in patients with mild symptoms and normal vital signs. Additionally, another study that analyzed the same population as this study revealed that lactate levels above 2.15 mmol/L were significantly correlated with predicting ED revisits within 24 hours post-discharge. Based on these results, it can be anticipated that measuring lactate levels in infants under 12 months of age presenting to the ED with acute bronchiolitis could aid in determining patient disposition.

Particularly in patients with AB, there is a high poten-

TABLE 1. Baseline characteristics and laboratory results of the study population.

	Total n = 234	Discharge group n = 72	Hospitalization group n = 162	*p*-value
Gender (%)				
Male	100 (42.74)	25 (34.72)	75 (46.30)	0.099
Female	134 (57.26)	47 (65.28)	87 (53.70)	
Age (mon)	5.00 (2.00–10.00)	7.00 (3.00–12.00)	4.00 (1.00–9.00)	0.002
Systolic blood pressure (mmHg)	90.00 (80.00–90.00)	90.00 (80.00–90.00)	90.00 (80.00–90.00)	0.114
Diastolic blood pressure (mmHg)	50.00 (50.00–60.00)	50.00 (50.00–60.00)	50.00 (50.00–60.00)	0.574
Pulse rate (/min)	140.00 (130.00–152.00)	134.00 (125.00–148.00)	142.50 (134.00–157.75)	<0.001
Respiratory rate (/min)	38.00 (30.00–48.00)	38.00 (30.00–46.00)	38.00 (30.00–48.00)	0.648
Body Temperature (°C)	37.40 (37.10–38.00)	37.30 (36.80–38.10)	37.40 (37.10–38.00)	0.210
WBC count (/μL)	11,030.00 (8560.00–14,240.00)	10,360.00 (7810.00–13,790.00)	11,345.00 (8842.50–14,610.00)	0.091
CRP (mg/dL)	1.22 (0.27–6.06)	2.03 (0.29–6.89)	0.98 (0.23–5.40)	0.202
Lactate (mmol/L)	1.85 (1.40–2.60)	1.70 (1.30–2.10)	2.00 (1.60–2.73)	0.003
pH	7.37 ± 0.05	7.38 ± 0.05	7.36 ± 0.05	0.036
pO_2 (mmHg)	50.00 (40.00–61.00)	50.50 (40.25–60.00)	50.00 (38.50–63.00)	0.878
pCO_2 (mmHg)	40.00 (35.00–47.00)	38.00 (35.00–44.00)	41.00 (35.00–48.00)	0.050
Bicarbonate (mmol/L)	23.10 (21.50–24.80)	23.05 (21.80–24.65)	23.30 (21.30–24.83)	0.958
Base Excess (mmol/L)	−1.68 ± 3.31	−1.80 ± 2.78	−1.63 ± 3.54	0.700

Data are presented as mean ± SD; variables not meeting normality criteria are presented as median (interquartile range). WBC: white blood cell; CRP: C-reactive protein; pO_2: partial pressure of oxygen; pCO_2: partial pressure of carbon dioxide.

tial for rapid deterioration over a short period, and frequent ED revisits are common. Consequently, identifying low-risk patients is crucial to ensure appropriate care and prevent unnecessary admissions. AB, especially during its seasonal outbreaks, consumes significant resources due to the need for respiratory support and monitoring. Thus, early identification of severe cases can enhance management quality, including hospitalization decisions [8, 9]. Rapid prognosis prediction and decision-making through lactate measurement could help prevent overcrowding in EDs.

Previous research has investigated the use of inflammatory and cardiac biomarkers in aiding decision-making for patients with AB. Inflammatory markers, like CRP and procalcitonin, have been found effective in differentiating bacterial causes of AB and forecasting the necessity for advanced respiratory support [1, 10]. However, in this study, CRP did not demonstrate a significant difference between the hospitalization and discharge groups.

Previous studies have demonstrated that cardiac biomarkers, such as N-terminal pro Brain Natriuretic Peptide (NT-proBNP), are correlated with predicting the severity of AB [11–13]. While other markers, such as immunoglobulin E and fractional exhaled nitric oxide, contribute to understanding the pathology of AB, and biomarkers like anticyclic citrullinated peptide (anti-CCP) antibody are more specific to the severity of respiratory diseases, data on these biomarkers were not collected in this study [14–16].

While some studies have suggested that cardiac markers could aid in predicting disease severity and the need for respiratory support, this study did not analyze those markers [1, 11]. To date, no recommendations have been made to base decisions for AB patients solely on laboratory results [7, 17]. Furthermore, to our knowledge, no prior studies have examined predictive markers for hospitalization in AB patients evaluated in the ED.

A scoring scale for predicting prognosis in AB patients has been developed, based on factors such as vital signs, wheezing, chest wall retraction, cyanosis, and oxygen saturation [18–24]. However, none of these scales has proven significantly superior to others, and in contrast to other respiratory diseases, such as asthma, no notable advancements in objective prognostic prediction have been achieved [25, 26]. In this study, vital signs and oxygen saturation were not helpful in predicting hospitalization. Caution is needed when interpreting these results, as respiratory rates vary by age group, and the severity of the patient population may differ.

Lactate, a metabolic product of cells undergoing glycolysis under anaerobic conditions, has long been considered a useless metabolic waste product [27]. Hypoxia, inflammation, viral infections, and tumor microenvironment are known to stimulate lactate production [28]. In pediatric patients, lactate measurement in the ED has proven helpful in predicting prognosis in cases of severe head trauma, sepsis, and diabetic ketoacidosis [29–33]. However, elevated lactate levels in children should be interpreted with caution as increases may result from epinephrine-dependent beta-2 adrenergic receptor

TABLE 2. Univariable and multivariable logistic regression for factors associated with admission.

	Odds ratio (95% CI)	*p*-Value
Univariable Analysis		
Gender		
• Male	1.621 (0.912–2.881)	0.099
• Female	ref.	
Age ≥4.5 mon	0.903 (0.843–0.966)	0.003
SBP ≥87.5 mmHg	0.962 (0.920–1.006)	0.191
DBP ≥50 mmHg	0.984 (0.943–1.026)	0.443
Pulse rate ≥133/min	1.032 (1.014–1.051)	0.001
Respiratory rate ≥49.5/min	1.010 (0.984–1.037)	0.465
Body temperature ≥37.05 °C	1.070 (0.733–1.560)	0.727
WBC count ≥10,295/μL	1.000 (1.000–1.000)	0.167
Lactate ≥2.150 mmol/L	1.804 (1.177–2.766)	0.007
pH ≥7.345	0.003 (0.000–0.709)	0.137
pCO_2 ≥45.15 mmHg	1.030 (0.997–1.065)	0.077
Multivariable Analysis		
Gender		
• Male	1.914 (0.965–3.793)	0.063
• Female	ref.	
Age ≥4.5 mon	1.000 (0.908–1.101)	0.996
Pulse rate ≥133/min	1.023 (1.001–1.045)	0.139
Lactate ≥2.150 mmol/L	1.718 (1.059–2.787)	0.028
pCO_2 ≥45.15 mmHg	1.032 (0.988–1.077)	0.157

CI: confidence interval; SBP: systolic blood pressure; DBP: diastolic blood pressure; WBC: white blood cell; pCO_2: partial pressure of carbon dioxide.

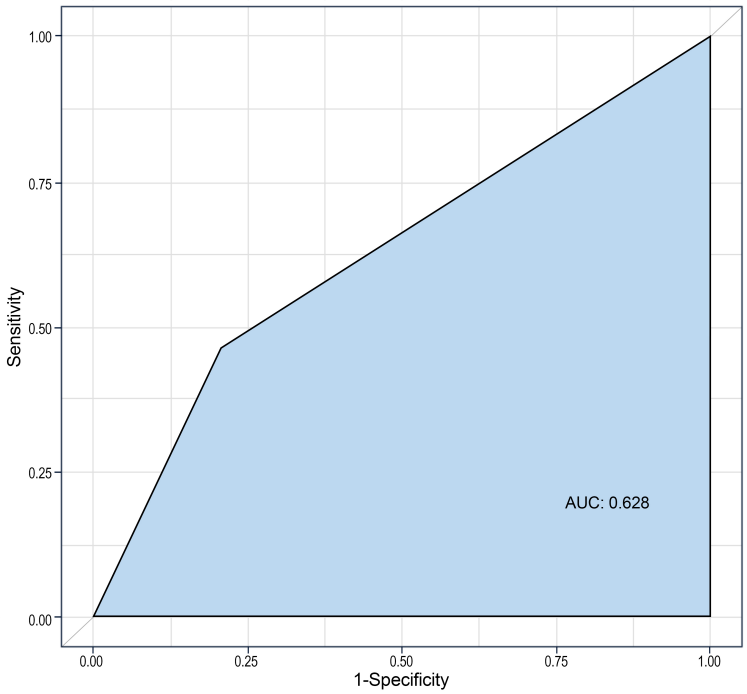

FIGURE 1. The receiver operating curve illustrating the predictive performance of lactate for hospital admission in infants with acute bronchiolitis. AUC: area under the curve.

stimulation during acute stress, as seen in infants with AB and other conditions [34, 35]. Additionally, in this study, the AUC was 0.628, suggesting that while lactate levels have potential, their predictive accuracy for hospitalization in patients with AB is limited. This indicates that lactate measurement alone may not be sufficiently reliable as a standalone indicator for clinical decision-making.

This study has several limitations, including its retrospective nature and a small sample size. Although we attempted to mitigate this limitation through a multicenter study, the number of patients presenting to the ED with respiratory symptoms declined during the COVID-19 pandemic, posing a challenge [36]. And sample size of this study was not equal between the discharged and hospitalized groups (72 *vs.* 162 patients, respectively). This imbalance may affect the generalizability of our findings. Secondly, compared with previous studies, the proportion of critically ill patients based on vital signs was relatively low. While this may appear as a limitation, it could also be considered a strength since the study focuses on decision-making for patients with normal vital signs. Thirdly, the study did not include analysis of cardiac enzymes and more specific inflammatory markers like anti-CCP antibody, which have previously been shown to be significant in predicting the prognosis of AB. Moreover, the omission of an analysis of vital signs by age group is another limitation. Finally, the study did not compare or incorporate existing scoring scales, which could also be seen as a limitation.

5. Conclusions

This study demonstrated that lactate levels could serve as a useful biomarker for predicting hospitalization in infants with AB, though their predictive accuracy remains limited. The retrospective nature of the study and the small sample size suggest that larger, prospective studies are necessary to validate these findings. Given the potential for rapid deterioration in AB patients, the identification of low-risk individuals is crucial for optimizing resource allocation and enhancing patient outcomes.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

AUTHOR CONTRIBUTIONS

DL—contributed to the concept and design of study. DL, JK—contributed to the collection, analysis and interpretation of data; contributed to the drafting of the manuscript. Both authors have read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study protocol was approved by the Soonchunhyang University Institutional Review Board (IRB No. 2023-03-016). The IRB approved a request to waive the documentation of informed consent.

ACKNOWLEDGMENT

Not applicable.

FUNDING

This research received no external funding.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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How to cite this article: Jihye Kim, Dongwook Lee. Lactate levels as predictors of hospitalization in infants with acute bronchiolitis: a multicenter retrospective study. Signa Vitae. 2026; 22(1): 52-57. doi: 10.22514/sv.2026.003.