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Original Article

Predictors of Prolonged Hospitalization in Pediatric Respiratory Syncytial Virus Infections

ATEŞ et al. Predictors of Prolonged Pediatric RSV Hospitalization

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Introduction: Respiratory syncytial virus (RSV) is a leading cause of lower respiratory tract infections (LRTIs) in infants and young children. This study evaluated clinical and laboratory factors associated with prolonged hospitalization in pediatric RSV infection.
Methods: This retrospective study included children under 18 years of age hospitalized with LRTI and confirmed RSV infection at our center between 2023 and 2025. Demographic, clinical, and laboratory data were collected from hospital records. Patients were divided into two groups according to length of stay (LOS): ≤2 days and >2 days. Multivariate logistic regression analysis was performed using the backward stepwise method.
Results: A total of 185 RSV-infected children were analyzed. The median age was 2 months, and 51.9% were male. Patients with LOS >2 days had significantly higher rates of PICU admission, non-invasive ventilation, mechanical ventilation, and secondary bacterial infections. Laboratory findings showed higher lymphocyte counts and BUN levels in the prolonged-stay group, whereas MPV levels were lower. No mortality was observed. In the multivariate logistic regression analysis, PICU stay was associated with approximately 12-fold increased risk of hospitalization longer than 2 days.
Conclusion: Hospitalization longer than 2 days was associated with a more severe clinical course. In the multivariate logistic regression analysis, PICU stay was the main factor associated with hospitalization longer than 2 days. Lymphocyte count, MPV, and BUN may provide supportive clinical information; however, their independent prognostic value remains uncertain.
Keywords: Respiratory syncytial virus, prolonged hospitalization, respiratory support, mean platelet volume

INTRODUCTION

Respiratory syncytial virus (RSV) is among the most common etiologic agents of bronchiolitis and pneumonia, particularly in infants and older adults.[1] Lower respiratory tract infections (LRTIs) are a major cause of morbidity and mortality in children under 5 years of age, and RSV is one of the leading pathogens in this age group.[2,3] In temperate climates, RSV typically causes annual epidemics during autumn and winter, whereas in tropical regions circulation often increases during the rainy season and cases may occur year-round.[4,5] Globally, it was estimated that in 2019, RSV-associated acute LRTI occurred in 33.0 million children aged 0–60 months; these episodes resulted in 3.6 million hospitalizations, 26,300 in-hospital deaths, and a total of 101,400 deaths attributable to RSV.[6] In Türkiye, studies in children aged ≤2 years have shown high annual hospitalization incidences for lower respiratory tract infections and bronchiolitis, with a substantial disease burden and higher RSV positivity clusters specifically in the 0–3 months age group.[7] Accordingly, RSV remains an important respiratory pathogen in both national and global clinical practice.

Severe RSV infection may present with hypoxemia and bronchiolitis-associated respiratory failure, particularly in young infants and children with significant comorbidities; some cases require intensive care and invasive mechanical ventilation. A nationwide cohort study in Denmark reported that mechanical ventilation was required in 14.3 per 1000 RSV hospitalizations, primarily due to bronchiolitis-related respiratory failure in young infants and those with comorbidities, while extra-pulmonary complications were more prevalent among children without classic risk factors.[8]

In RSV infection, routine laboratory tests are not diagnostic; they are primarily used to support the clinical picture, monitor disease severity, and guide management when co-infection is suspected.

RT-PCR is the gold standard for diagnosis.[9] Regarding blood parameters, some studies have reported differences in CRP

and systemic inflammatory markers in RSV-positive cases; however, these parameters are meaningful for adjunct clinical assessment rather than confirmation of RSV infection.[10] In severe bronchiolitis, hyponatremia in association with increased ADH secretion/SIADH and AST/ALT elevations may be observed in severe RSV bronchiolitis.[11,12]
This study aimed to describe the clinico-laboratory characteristics of RSV-positive children, and to identify the factors associated with clinical outcomes, specifically length of hospital stay and disease severity.

MATERIALS AND METHODS

This retrospective observational study included 985 pediatric patients, followed in the pediatric infectious diseases ward and/or the pediatric intensive care unit (PICU) for acute LRTI and tested for RSV between January 1, 2022, and December 31, 2025, were screened via the hospital's electronic database. Patients aged <18 years, hospitalized for acute LRTI with confirmed RSV positivity in a respiratory specimen, were included.
Exclusion criteria were: suspected nosocomial RSV infection (symptom onset ≥48–72 hours after admission), conditions markedly affecting laboratory analyses (e.g., active malignancy, chemotherapy, severe immunosuppression, advanced chronic kidney or liver disease), and missing baseline laboratory or primary outcome data.
All data were obtained from the hospital information system. Recorded variables included demographics (age, sex), clinical outcomes (length of hospital and PICU stay, need for non-invasive and invasive ventilation, secondary bacterial infections), and laboratory parameters (WBC, neutrophils, lymphocytes, hemoglobin, platelets, MPV, Na, BUN, creatinine, AST, ALT, GGT, albumin, and CRP). The CRP/albumin ratio was calculated for the same time point.
RSV was detected using multiplex real-time RT-PCR on nasopharyngeal swabs or aspirates as part of routine clinical practice. Patients with two or more viral detections on the respiratory panel were excluded to avoid interpretive difficulty. Secondary bacterial infection was defined as a clinically suspected bacterial infection recorded during the hospitalization period and supported by microbiological evidence and/or compatible radiological and laboratory findings. Bacterial detection by PCR was considered clinically significant only when accompanied by compatible clinical findings such as persistent or recurrent fever, increased inflammatory markers, radiological evidence of pneumonia, positive blood culture, or an antibiotic treatment decision by the attending physician. Because of the retrospective design, the exact timing of secondary bacterial infection in relation to admission could not be consistently determined in all cases. Therefore, secondary bacterial infection was not included in the multivariable model as a baseline predictor.

To identify factors associated with prolonged hospitalization, the study population was dichotomized according to length of stay (LOS) as ≤2 days and >2 days. Because the median LOS of the cohort was 2 days, this cutoff was selected to identify patients hospitalized longer than the cohort median. This median-based cutoff is consistent with previous pediatric RSV/ALRI research in which longer LOS was defined as >2 days as the median.[13]
The study protocol was approved by the XXX ethics committee on April 14, 2026, with protocol number 2026/133.

Statistical analysis

Statistical Package for Social Science (SPSS) version 22 software was used for statistical analyses (IBM SPSS Statistics for Windows, Version 22.0, NY, USA). Descriptive statistics were presented as number and percentage for normally distributed categorical data, while continuous variables are presented as median (25th–75th percentile) for non-normally distributed data. Normality of distribution of continuous variables was evaluated by means of the Kolmogorov-Smirnov test. Between-group comparisons were performed using the Mann–Whitney U test for continuous variables and the chi-square test or Fisher's exact test for categorical variables. Statistical significance was defined as $p<0.05$. Multivariate logistic regression analysis was performed using the backward stepwise method to evaluate factors associated with hospitalization longer than 2 days. PICU stay, non-invasive ventilation, mechanical ventilation, lymphocyte count at diagnosis, BUN, and MPV were included in the initial model. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for the variables retained in the final model.

RESULTS

A total of 185 (18.8%) patients were diagnosed with RSV via multiplex real-time RT-PCR. Of these, 123 (66.5%) had a length of stay (LOS) of ≤2 days and 62 (33.5%) had a stay of >2 days (Table 1). The median age was 2 months (IQR: 2–7) in the ≤2-day group and 3 months (IQR: 2–6) in the >2-day group, with no significant difference ($p=0.915$). Male sex accounted for 54.5% (67/123) of the ≤2-day group and 46.8% (29/62) of the >2-day group ($p=0.323$).
The median LOS was 1 day (IQR: 1–2) in the ≤2-day group and 3 days (IQR: 3–7) in the >2-day group ($p<0.001$). PICU admission was required for 14.1% (26/185) of all patients, differing significantly between groups: 4.1% (5/123) in the ≤2-day group versus 33.9% (21/62) in the >2-day group ($p<0.001$). Non-invasive ventilation was required in 7.6% (14/185) of patients, with a higher requirement in the >2-day group (19.4% vs. 1.6%, $p<0.001$). Invasive mechanical ventilation was required in 2.2% (4/185) of patients, occurring exclusively in the >2-day group (6.5% vs. 0%, $p=0.012$). Secondary bacterial infections were detected in 33.5% (62/185) of the cohort, showing a significant difference between groups ($p<0.001$).
Complete blood count parameters (WBC, neutrophils, hemoglobin, and platelets) were comparable between groups, with the exception of lymphocytes and MPV. The median MPV was significantly higher in the ≤2-day group (10 [9–11] vs. 9 [9–10] fL, $p=0.039$). Conversely, the median lymphocyte count was lower in the ≤2-day group (2349 [1314–3842] vs. 2891 [2000–4600], $p=0.011$). Other laboratory parameters, including sodium, CRP, albumin, CRP/albumin ratio, AST, ALT, GGT, and creatinine, were statistically similar between groups, except for BUN. Median BUN was 4 mg/dL (4–8) in the

≤2-day group compared to 7 mg/dL (4–9) in the >2-day group (p=0.023).
In the logistic regression analysis performed using the backward stepwise method with PICU stay, non-invasive ventilation, mechanical ventilation, lymphocyte count at diagnosis, BUN, and MPV variables for hospitalization longer than 2 days, PICU stay increased the risk of hospitalization longer than 2 days by 12-fold in the significant final model (95% CI: 4.2–34.3) (Table 2).

DISCUSSION

In the present cohort, prolonged hospitalization due to RSV infection was associated with a more severe and clinically demanding disease course, suggesting a bidirectional relationship. Patients hospitalized for more than two days exhibited significantly higher rates of non-invasive and invasive mechanical ventilation, as well as a greater frequency of secondary bacterial infections. In addition, they had higher lymphocyte counts, lower MPV values, and higher BUN levels.
The close relationship between longer LOS and greater respiratory support requirements has been demonstrated in previous studies. In the prospective national BRICK study, the use of invasive mechanical ventilation rate was 61.1% in infants admitted to the PICU due to RSV, which shows the high burden of respiratory support in this population.[14] In a Hungarian study evaluating hospitalized children with severe acute respiratory infection, the median LOS was 5 days, and multivariable logistic regression analysis showed that receiving mechanical ventilation or oxygen support increased the likelihood of hospitalization lasting >4 days by 3.23-fold, pneumonia by 3.65-fold, and RSV etiology by 3.25-fold.[15] Similarly, in another study evaluating RSV-associated LRTI cases, "severe RSV" was defined as hospitalization for >7 days, ICU admission, need for non-invasive/invasive ventilation, or in-hospital mortality, and 40.16% of cases were reported to meet this definition.[16] In our study, hospitalization longer than 2 days was used as a median-based outcome to evaluate factors associated with a more severe clinical course in children with RSV infection.

The association between secondary bacterial infection and prolonged hospitalization is clinically plausible. However, because the timing of secondary bacterial infection could not be consistently determined, this association should be interpreted as a disease-course relationship rather than evidence of baseline prediction. Recent studies have similarly shown that bacterial infections accompanying RSV can increase both disease severity and length of hospitalization. In a multicenter prospective surveillance study from Portugal, potential pathogenic bacteria were detected in 20.4% of hospitalized RSV cases; in this group, PICU admission was more frequent, hospital stay was longer, and the risk of severe disease was reported to be increased by 13.2-fold.[17] In different series, bacterial coinfection was identified in 32.4% of children with RSV pneumonia and in 47.3% of hospitalized RSV-positive children. Pneumococcus was the most prevalent pathogen and children with bacterial coinfection were shown to have longer hospital stays and greater PICU requirement.[18] LOS remained one of the independent predictors of bacterial coinfection.[19] Díaz-Díaz et al. defined prolonged stay as longer than 3 days. They described nasopharyngeal coexistence of *Streptococcus pneumoniae* and/or *Haemophilus influenzae* as a more severe clinical course, particularly increasing the likelihood of oxygen requirement and prolonged hospitalization.[20]
In this study, prolonged hospitalization due to RSV infection was associated with higher lymphocyte counts. In contrast, the study by Matera et al involving 1,297 infants hospitalized for bronchiolitis reported that RSV positivity was more frequent in the lowest lymphocyte group, which was associated with higher clinical severity scores, greater oxygen requirements, longer hospital stays, and more frequent pediatric intensive care unit admissions.[21] In another study evaluating 325 children with RSV-associated bronchiolitis, each unit increase in lymphocyte percentage was shown to be associated with a lower likelihood of severe disease similar to our study.[22] Lymphocyte difference observed in our study is not merely an isolated laboratory variable but may represent for the immunological response resembling a more severe clinical course and longer hospitalization.
We observed lower MPV levels in patients with prolonged hospitalization, which may reflect platelet consumption or an altered platelet response during a more severe and sustained inflammatory process. However, MPV does not show a consistent trend across RTIs. While Doğan et al.[23] reported increased MPV associated with bronchiolitis severity in 179 cases, Feketea et al.[24] found lower MPV in non-influenza viral respiratory infections compared to influenza and healthy controls. To date, no study has specifically evaluated MPV in RSV. Therefore, although our findings align with some data from viral RTIs, further studies are needed before MPV can be considered an RSV-specific marker or a reliable indicator of disease severity.
We found higher BUN levels in the prolonged-stay group, which may likely reflect reduced oral intake, dehydration, and increased catabolic stress rather than intrinsic renal dysfunction, as creatinine levels did not differ between groups. This is indirectly supported by bronchiolitis literature, which identifies dehydration and poor feeding as predictors of escalated care, often accompanied by clinically significant fluid-electrolyte disturbances. However, specific evidence for BUN as an independent severity marker in RSV remains limited, and recent predictive studies failed to identify urea as an independent risk factor. Consequently, elevated BUN should be regarded as a supportive clinical finding rather than a definitive prognostic marker.[25,26,27]
Apart from the significant variables identified, most clinical and laboratory parameters did not differ between groups according to length of hospital stay. Patients with shorter and prolonged hospitalization were similar in terms of age, sex, hyponatremia, total WBC and neutrophil counts, hemoglobin, platelet count, sodium, CRP, albumin, AST, ALT, GGT, creatinine, and the CRP/albumin ratio. These findings suggest that LOS-related differences were limited to selected clinical

severity indicators and specific laboratory parameters, while the majority of baseline characteristics remained comparable between groups.

Although this study provides clinically relevant data on factors associated with prolonged RSV hospitalization, notably respiratory support requirements, secondary bacterial infections, and specific laboratory abnormalities, it has several limitations. First, the single-center retrospective design is inherently subject to selection bias and limited generalizability. Important clinical confounders such as prematurity, congenital heart disease, chronic lung disease, immunodeficiency, and other underlying medical conditions could not be consistently retrieved from the retrospective database. The absence of these variables may have resulted in residual confounding and limits causal interpretation of the observed associations. Clinical decisions, such as PICU transfers and ventilation initiation, were based on physician judgment rather than a standardized protocol, potentially introducing practice-based variability. Second, dichotomizing LOS (≤2 vs. >2 days) simplified the analysis but may have reduced data granularity and obscured dose-response relationships. Third, the lack of consistent data on ventilation duration and dynamic severity markers limited a more comprehensive characterization of disease burden. Finally, potential repeated admissions of the same patient may have influenced clinical outcome frequencies.

In conclusion, hospitalization longer than 2 days in this pediatric RSV cohort was associated with a more severe clinical course, including PICU admission and greater need for respiratory support. In the multivariate logistic regression analysis, PICU stay emerged as the main factor associated with hospitalization longer than 2 days. Secondary bacterial infections were more frequent in the prolonged-stay group; however, because their timing could not be consistently determined, this finding should be interpreted cautiously as part of the clinical disease course rather than as a baseline predictor. Selected laboratory parameters, including lymphocyte count, MPV, and BUN, may provide supportive clinical information; however, their independent prognostic value remains uncertain. Future prospective studies including major clinical confounders and validated LOS thresholds are needed to confirm these findings.

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Table 1. Characteristics of the patients according to the duration of hospitalization

	Hospitalization ≤2 days n=123 (66.5%)	**Hospitalization >2 days** n=62 (33.5%)	**p**
Age, months, mean (25-75 percentile)	2 (2-7)	3 (2-6)	0.915

Male gender, n(%)	67 (54.5)	29 (46.8)	0.323
PICU stay, n(%)	5 (4.1)	21 (33.9)	**<0.001**
Non-invasive ventilation, n(%)	2 (1.6)	12 (19.4)	**<0.001**
Mechanical ventilation, n(%)	0 (0)	4 (6.5)	**0.012**
Secondary bacterial infections, n(%)	0 (0)	62 (33.5)	**<0.001**
Hyponatremia (Serum Na<135 Meq/mL), n(%)	16 (13)	6 (9.7)	0.509
WBC, /mm^3, mean (25-75 percentile)	9536 (8353-11734)	10239 (8656-12000)	0.128
Neutrophils, /mm^3, mean (25-75 percentile)	5942 (4000-7245)	5967 (4200-6738)	0.578
Lymphocytes, /mm^3, mean (25-75 percentile)	2349 (1314-3842)	2891 (2000-4600)	**0.011**
Hemoglobin, gr/dL, mean (25-75 percentile)	11 (10-12)	11 (10-12)	0.556
Platelets, /mm^3, mean (25-75 percentile)	432000 (378000-481000)	395000 (365000-473000)	0.538
MPV, fL, mean (25-75 percentile)	10 (9-11)	9 (9-10)	**0.039**
Na, gr/dL, mean (25-75 percentile)	136 (136-137)	136 (136-138)	0.097
CRP, gr/dL, mean (25-75 percentile)	4 (1-8)	5 (1-12)	0.515
Albumin, gr/dL, mean (25-75 percentile)	39 (36-41)	38 (37-40)	0.849
AST, U/L, mean (25-75 percentile)	35 (27-46)	38 (28-50)	0.524
ALT, U/L, mean (25-75 percentile)	28 (22-34)	27.5 (22-36)	0.769
GGT, U/L, mean (25-75 percentile)	28 (21-39)	27.5 (20-41)	0.823
BUN, mg/dL, mean (25-75 percentile)	4 (4-8)	7 (4-9)	**0.023**
Creatinine, mg/dL, mean (25-75 percentile)	1 (1-1)	1 (1-1)	0.314
CRP/Albumin, mean (25-75 percentile)	0.10 (0.02-0.20)	0.12 (0.02-0.46)	0.551
PICU, pediatric intensive care unit; MPV, mean platelet volume			

Table 2. Multivariate Logistic Regression Analysis of R*isk Factors for Prolonged Hospitalization*			
Independent variable	Odds ratio	95% CI	p
PICU admission	12.047	4.236–34.263	<0.001
MPV	0.746	0.527–1.056	0.098
Backward stepwise logistic regression was performed. Nagelkerke R^2=0.219; Cox & Snell R^2=0.158; Hosmer–Lemeshow $\chi^2(4)$=6.712.			