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Risk Factors of Long PICU Stay for Term-Born Bronchiolitis Patients Less than 3 Years Old

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Abstract

BACKGROUND/AIMS: Bronchiolitis, which is caused by a virus, is the most common lower respiratory infection in children aged <3 years. Several prenatal and postnatal risk factors affect the need for escalated care. To standardize the assessment of these patients, scoring systems based on clinical findings and respiratory examinations have been developed. Our primary aim was to determine the risk factors for longer pediatric intensive care unit (PICU) stays in term-born bronchiolitis patients who needed intensive care before 3-years of age. Our secondary aim was to evaluate the efficacy of the Pediatric Respiratory Severity Score (PRESS) scoring system.

MATERIALS AND METHODS: A prospective observational study was performed on pediatric patients aged ≤3-years who had been admitted to three tertiary-level PICUs in Ankara, during the epidemic season with clinical diagnoses of bronchiolitis. Those patients who were born preterm or who had congenital heart diseases were excluded. PRESS was used to define the clinical severity of bronchiolitis at admission.

RESULTS: Fifty three of the 79 (67.01%) were male and the median age was 6-months. Correlation analysis showed that Pediatric Risk of Mortality III Score (r=0.37), prenatal smoke exposure (r=0.34) and previous hospitalization (r=0.28) were significantly associated with the length of PICU stay. Multiple regression analysis showed that only prenatal smoke exposure was related with longer PICU stays (R-sq: 0.321). PRESS severity levels had no statistically significant effect on PICU or hospital stays.

CONCLUSION: Prenatal smoke exposure is the only independent risk factor for longer stays in intensive care units for term-born bronchiolitis patients under 3 years of age.

Keywords: Bronchiolitis, pediatric intensive care, prenatal smoke exposure, risk factors

INTRODUCTION

The symptoms of bronchiolitis and respiratory distress are triggered by acute inflammation, edema, necrosis of epithelial cells lining the small airways, increased mucus production, and/or bronchospasm. Viral diseases are the leading cause of bronchiolitis.[1]

Previous studies have aimed to evaluate the role of prenatal, perinatal and postnatal conditions in determining the risks of hospitalization for bronchiolitis[2,3] or clinical findings at admission and the need for escalated care.[4] In addition, studies have identified the demographics and epidemiological characteristics of previously healthy term infants who were hospitalized in pediatric intensive care unit (PICUs) because of severe bronchiolitis.[5] However, few studies have yet described the prenatal, perinatal, postnatal factors associated with PICU admission and their outcomes.[6]

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The diagnosis of acute respiratory diseases and hospital admission due to bronchiolitis are based on clinical observations and laboratory investigations.[7] For these purposes and to standardize the assessments of hospitalizations, several scoring systems based on physical findings and respiratory examination have been developed.[8] The Pediatric Respiratory Severity Score (PRESS) is one of them and it has five components including respiratory rate, wheezing, accessory muscle use, SpO_2, and feeding difficulties.[9] Also PRESS scores are a severity assessment used to categorize patients with respiratory infections into 3 groups: mild (0-1), moderate (2-3), or severe (4-5) based on these five parameters. This scoring system can be a useful and applicable bedside scoring method to assess and triage bronchiolitis patients. However, there is no data on whether it can be used to estimate PICU admission or length of hospital stay for severe patients.

Objectives: Our main objective was to analyze prenatal and postnatal risk factors for longer PICU and hospital stays for term-born bronchiolitis patients less than 3 years of age who applied to our hospital during winter. Our secondary objective was to determine reasons for higher PRESS scores and to evaluate if PRESS scoring could be used to estimate PICU durations for bronchiolitis patients.

MATERIALS AND METHODS

Study design and aspects to be covered: This was a prospective observational study, performed on pediatric patients aged ≤3 years, who were admitted to three tertiary level PICUs in Ankara, Türkiye during one epidemic season (between December, 2017 and April, 2018) with clinical diagnoses of bronchiolitis. The PICU physician decides whether the patient has bronchiolitis in light of their clinic, X-ray, and laboratory parameters. Intensive care unit (ICU) admission criteria were an increased work of breathing despite medical treatment, SO_2 <92 despite oxygen treatment or cyanosis. Those patients who were born preterm (before 37 completed weeks of gestation) or those who had congenital heart diseases were excluded from this study.

A questionnaire investigating the smoking status of the parents, the number of people living in the home, the number of siblings of school age and the living habitat of the family members was conducted. Recent studies have shown that any level of smoking exposure (one or more cigarettes per day) is likely to be associated with progressive and lasting lung damage,[10] so we accepted any level of cigarette smoking of the mother to be sufficient for prenatal smoke exposure and any level of smoking in the household adequate for passive smoke exposure. We collected data on nursery/school attendance for the patients. The PRESS was used to define the clinical severity of bronchiolitis at admission. Besides age, gender and any chronic diseases of the subjects, symptoms at admission were also recorded. Also, initial vital signs, Pediatric Risk of Mortality (PRISM) III Score,[11] blood gas and white cell count, and C-reactive protein at admission were recorded. Respiratory syncytial virus (RSV) and influenza Polymerase Chain Reaction test results were recorded if they were present. Treatment modalities such as high-frequency oxygen (HFO), non-invasive ventilation (NIV) and invasive ventilation were recorded on a daily basis. All patients who needed HFO received 2 Lt/kg air flow and weaning from HFO was performed by decreasing the oxygen concentration. The patients stopped HFO when their oxygen concentration was 30-40% without tachypnea. Those patients who had a saturation over 92% without respiratory distress, ventilatory support, positive inotropes or any organ failure were discharged from the PICU by the attending doctor and were followed up until discharge from the hospital.

Ethical considerations: Ethical approval was obtained from Dr. Sami Ulus Research Hospital Review Board (approval number: E22/03-294, date: 02.03.2022). With the admission of the subject to PICUs, written approval including informed consent about this study was obtained from the family.

Statistical Analysis

Data were expressed as descriptive statistics, percentages or medians as appropriate. We started our empirical analysis by reporting descriptive statistics (Table 1 and the accompanying discussion). Table 2 presents pairwise correlations between all the variables in the analyses. We also report the significant cases of correlation. In the next step, we employed multivariate analysis in order to check for confounding factors. In this observational study (i.e., not experimental), the patients' attributes were not under the control of the researcher. Hence, unlike experimental risk factors, they were not necessarily balanced among the samples. These unbalanced attributes can lead to a bias in the findings if not accounted for. Multivariate analysis allowed us to check for these potential biases. The dependent variables are continuous variables, so we performed Poisson regression analysis and negative binomial regression analysis. We also corrected the standard errors for heteroscedasticity. The analyses were performed using Stata/SE 15.1.

RESULTS

During four months, we recorded 86 patients in our study, however, 2 patients were excluded because of their history of prematurity and one

Table 1. Descriptive analysis

Parameters	Factor	Number of patients	Number (%)	Median (min.-max.)
Age	Months	79		6 (1-36)
PRISM III	Score	79		6 (0-28)
CRP	Mg/dL	79		3 (0.1-97)
PICU stay	Days	79		5 (1-38)
Hospital stay	Days	79		9 (3-64)
Sex	Male	79	53 (67.01)	
PRESS	Severe	79	29 (36.71)	
Risk factors				
	Age less than 6 months	79	45 (56.96)	
	Passive cigarette smoke exposure	79	43 (54.43)	
	Previous hospitalization	79	28 (35.44)	
	School age sibling	79	20 (25.31)	
	Prenatal smoke exposure	79	14 (17.72)	
	RSV positivity	64	27 (42.19)	
	Influenza positivity	63	5 (7.94)	
	Attending nursery	79	2 (2.53)	
	Household over five people	79	15 (18.00)	

PRISM III: Pediatric Risk of Mortality III, CRP: C-reactive protein, PICU: Pediatric intensive care unit, PRESS: Pediatric Respiratory Severity Score, min.: Minimum, max.: Maximum.

patient was excluded because of congenital heart disease. Two patients were excluded because they were over 36 months old. Among the rest, two other patients had missing information on their risk factors. The remaining 79 patients were included. 53 of these 79 (67.01%) were male. Their median age was 6 months and 45 of the 79 (56.96%) patients were equal to or less than 6 months old (Table 1). Their median ICU stay was 5 (2-38) days and their median hospital stay was 9 (3-64) days (Table 1).

Ten patients were intubated (12.05%), nine of these ten patients received NIV treatment either before or after intubation, 66 (83.54%) patients were treated with NIV, 51 (64.56%) of them were treated only with HFO therapy, 6 (7.59%) of them were treated only with continuous positive air pressure with or without pressure support (CPAP ± PS), 9 (11.39%) patients were treated with a combination of CPAP ± PS and HFO therapy. The mean duration for NIV ventilation was 4.75 days [standard deviation (SD): 4.26 days]. Three (3.79%) patients needed neither NIV nor invasive ventilation. We found no correlation between these ventilation support therapies and the risk factors.

All cases in our study had either moderate or severe PRESS severity scores. Although severe cases were hospitalized in the PICU for longer (mean: 9.03, SD: 9.42 days) than moderate cases (mean: 6.60, SD: 7.22 days), this difference was not statistically significant (p=0.189). A similar statistically insignificant relationship was detected for the length of hospital stay (mean: 10.67 vs. 14.58 days, p=0.118).

Univariate analysis showed that PRISM III scores, prenatal smoke exposure and previous hospitalizations were associated significantly with the lengths of PICU and hospital stays (Table 2). Also, there were significant correlations among the explanatory variables such as higher PRISM III scores and higher PRESS scores (correlation r=0.25), passive cigarette smoke exposure and PRISM III scores (r=0.34), passive cigarette smoke exposure and prenatal smoke exposure (r=0.42), previous hospitalization, PRISM III and PRESS scores (r=0.27). Older age was also found to be correlated with higher PRESS scores.

Multiple regression analysis showed that only prenatal smoke exposure was related with longer PICU and hospital stays (Table 3). According to the PRESS scores, severity levels had no statistically significant effect on the lengths of PICU or hospital stays.

Table 2. Pairwise correlations between risk factors, PRESS score and PICU stay duration

Factors	PICU stay	PRISM III	PRESS score	CRP	Age	Male	Passive exposure	Prenatal exposure	School age sibling	Attending nursery	Previous hospitalization
PRISM III	**0.37***										
PRESS score	0.09	**0.25***									
CRP (mg/dL)	0.15	0.11	-0.10								
Age (months)	0.20	0.07	**0.36***	-0.02							
Male	0.04	0.05	**-0.26***	0.10	-0.07						
Passive cigarette smoke exposure	0.08	**0.34***	-0.10	0.15	-0.20	-0.15					
Prenatal smoke exposure	**0.34***	**0.26***	0.15	-0.12	0.04	**-0.24***	**0.42***				
School age sibling	-0.08	0.02	0.19	0.09	-0.02	-0.03	-0.05	-0.04			
Attending nursery	-0.07	-0.04	-0.04	-0.05	-0.15	0.11	-0.01	-0.07	-0.09		
Previous hospitalization	**0.28***	**0.27***	**0.27***	-0.05	0.12	-0.04	0.20	0.21	-0.07	-0.12	
Household over five people	0.16	-0.01	-0.03	-0.06	-0.10	-0.00	**0.25***	**0.28***	-0.13	0.13	0.18

Number of patients: 79, *p<0.05, PICU: Pediatric intensive care unit, PRESS: Pediatric Respiratory Severity Score, CRP: C-reactive protein.

Table 3. Poisson regression analysis of risk factors affecting PICU and hospital stay

	PICU stay				Hospital stay			
	Beta	95% CI		p-value	Beta	95% CI		p-value
PRISM III	0.042	-0.002	0.086	0.063	0.038	-0.003	0.079	0.07
PRESS score severity	0.289	-0.098	0.676	0.144	0.272	-0.115	0.66	0.169
Age younger than six months	0.082	-0.273	0.436	0.652	0.012	-0.282	0.305	0.938
Male	0.269	-0.116	0.654	0.171	0.233	-0.152	0.619	0.235
Passive cigarette smoke exposure	-0.528	-0.981	-0.074	0.023	-0.373	-0.715	-0.031	0.033
Prenatal smoke exposure	**0.816**	**0.325**	**1.306**	**0.001**	**0.528**	**0.057**	**0.998**	**0.028**
School age sibling	-0.21	-0.692	0.272	0.393	-0.292	-0.681	0.098	0.142
Attending nursery	-0.323	-1.28	0.634	0.508	-0.049	-0.742	0.644	0.89
Previous hospitalization	0.309	-0.207	0.826	0.24	0.258	-0.14	0.656	0.204
Household over five people	0.319	-0.174	0.813	0.205	0.32	-0.068	0.708	0.106
No of patients	79				79			
Pseudo R-sq	**0.263**				**0.246**			

p-value <0.05 is accepted as statistically significant, PICU: Pediatric intensive care unit, PRISM III: Pediatric Risk of Mortality III, PRESS: Pediatric Respiratory Severity Score, CI: Confidence interval, R-sq: R-squared.

DISCUSSION

Prenatal smoke exposure is associated with the development of bronchiolitis in term, non-low birth weight infants without a history of cardiac or pulmonary illness.[12] With a similar patient group, we showed that prenatal smoke exposure also correlates with longer PICU stays. Our multivariable model estimates 86% longer PICU stays for a children under 3 years of age with prenatal smoke exposure history if all other parameters are equal. Stevenson et al.[13] showed that maternal cigarette smoking during pregnancy increased the probability of requiring an ICU hospitalization in children hospitalized with bronchiolitis. The same study revealed that children exposed to prenatal smoking alone had a higher risk for PICU admission than those children who had been exposed to passive smoking as well. Our study showed that these patients not only had a higher chance for PICU admission when they had bronchiolitis, but also they would stay for longer in the PICU. All of these clearly show that exposure to prenatal smoking may cause permanent damage to the babies' lungs and predispose them to serious lung infections for the rest of their lives.

A meta-analysis showed that children exposed to passive smoking by any household member had a higher risk of developing bronchiolitis throughout their first two years of life.[14] However, in our study, the coefficient estimate for passive cigarette smoke exposure was unexpectedly negative. Our in-depth analysis shows that this counterintuitive finding was the result of the significant correlation between passive cigarette smoke exposure and prenatal smoke exposure (correlation coefficient: 0.42). When we included passive cigarette smoke exposure in the empirical model without accounting for prenatal smoke exposure, the coefficient estimate for passive cigarette smoke exposure was positive.[1]

Age was associated with higher PRESS scores in our study (correlation coefficient: 0.36). In a previous study including patients with premature-birth, low birthweight and congenital heart diseases, a lower age was found to be a significant risk factor for both intensive care and respiratory support.[15] However, similar to Sala et al.[12], a younger age was not associated with invasive ventilation, longer PICU stay or hospital stay in our study.

In some studies, crowded living environments, defined as 5 or more people living in the household, were associated with increased RSV related bronchiolitis hospitalization.[2,16] However, in the FLIP-2 study, crowded households were not determined to be risk factors for bronchiolitis hospitalization.[17] In our study, households over 5 people were associated with higher rates of prenatal smoke exposure and passive smoke exposure (correlation coefficient: 0.28 and 0.26 respectively). The multivariate model did not show any relationship between crowded households and the length of PICU stay.

Only 2 children were attending nursery/school before hospitalization. In our sample, only 5 (out of 79) patients were older than 24 months. Most of the nurseries in Türkiye for very young children are private and not affordable for the parents of our patients. Therefore, our data was not sufficient to analyze the effects of nursery attendance on the length of bronchiolitis patients' hospital stay.

This study was carried out during the viral infection epidemic season. It has been shown that exposure to RSV was a risk factor for higher rates of hospitalization.[18] We did not test every patient for viral infections. Therefore, we did not include RSV or influenza in the main multivariate analysis. Multivariable analysis including the RSV variable showed that the coefficient estimates of this smaller sample for the main variables of interest were very similar to Table 3 and RSV or influenza positivity were not associated with longer PICU stays.[1]

Our secondary aim was to evaluate the relationship between the risk factors and the PRESS scores and to find out if the PRESS scoring system is useful in estimating the length of PICU stay. Thokngaen and Karoonboonyanan[19] showed that PRESS severity scoring could be helpful in evaluating patients' intensive care needs. We found that the PRESS score was positively correlated with the PRISM 3 scores, age, and previous hospitalizations and negatively correlated with male gender. However, we demonstrated that there was no correlation with higher PRESS scores and longer PICU or hospital stays.

Study Limitations

The number of patients was our most obvious limitation. If we had had more patients, we might have had the chance to comment on the effects of risk factors and/or PRESS scores on respiratory treatment modalities. More patients are needed in future studies in order to understand which patients are at higher risk of invasive ventilation or longer PICU stays. Another obvious limitation in our study was that the patients' family history of asthma and wheezing child were not taken into consideration. Last but not least, all of the patients should have been tested for seasonal viruses and these viral infections should have been included in the regression analysis.

CONCLUSION

In our study, prenatal smoke exposure was the only independent risk factor for longer stays in the intensive care unit and hospital for term-born bronchiolitis patients less than 3 years old who had been hospitalized in a PICU during winter. In contrast with the literature, in our study group, a younger age was not related with longer PICU stays. We also showed that the PRESS scoring system was not useful in estimating the length of PICU or hospital stay.

MAIN POINTS

- Bronchiolitis is a common respiratory infection in children under 3 years of age caused by a virus.
- This study was conducted to determine the risk factors for longer stays in intensive care for term-born bronchiolitis patients under the age of 3 years and to evaluate the efficacy of the PRESS scoring system.
- This study found that prenatal smoke exposure was the only independent risk factor for longer stays in intensive care for term-born bronchiolitis patients under 3 years of age.

ETHICS

Ethics Committee Approval: Ethical approval was obtained from Dr. Sami Ulus Research Hospital Review Board (approval number: E22/03-294, date: 02.03.2022).

Informed Consent: Written approval including informed consent about this study was obtained from the family.

Authorship Contributions

Surgical and Medical Practices: H.T., S.E., S.K., E.A., Concept: H.T., S.E., S.K., E.A., Design: H.T., S.E., S.K., E.A., Data Collection and/or Processing: H.T., S.E., S.K., E.A., Analysis and/or Interpretation: H.T., S.E., S.K., E.A., Literature Search: H.T., S.E., S.K., E.A., Writing: H.T., S.E., S.K., E.A.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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