RESEARCH ARTICLE
DOI: 10.4274/cjms.2024.2023-72

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

Tekgüç et al. Risk Factor for Long PICU Stay in Bronchiolitis Patients

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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 were developed. Our primary aim was to determine the risk factors for longer pediatric intensive care unit (PICU) stay in term-born bronchiolitis patients who needed intensive care before 3-years old. 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, admitted to three tertiary-level PICU's in Ankara, during epidemic season with clinical diagnosis of bronchiolitis. Patients who were born preterm and who have congenital heart diseases, were excluded. The PRESS was used to define clinical severity of Bronchiolitis at admission.

RESULTS: 53 of 79 (67.01%) were male and the median age was 6-months. Correlation analysis showed that PRISM-3 score (r:0.37), prenatal smoke exposure (r:0.34) and previous hospitalization (r:0.28) were associated significantly with longevity of PICU stay. Multiple regression analysis showed that only prenatal smoke exposure was related with longer PICU stay (R-sq:0.321). PRESS severity levels have no statistically important effect on PICU or hospital stay.

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

To cite this article: Tekgüç H, Emeksiz S, Kesici S, Azapağası E. Risk Factors of Long PICU Stay for Term-Born Bronchiolitis Patients Less Than 3 Years Old. Cyprus J Med Sci

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19.07.2023
24.01.2024

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 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 risk 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 PICU because of severe bronchiolitis (5). However, few studies have yet described the prenatal, perinatal, postnatal factors associated with PICU admission and outcomes (6).

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 assessment of hospitalization, several scoring systems based on physical findings and respiratory examination were developed (8). The Pediatric Respiratory Severity Score (PRESS) is one of them and has five components including respiratory rate, wheezing, accessory muscle use, SpO2, and feeding difficulties (9). Also PRESS scores are a severity assessment to categorize patients with respiratory infections into 3 groups: mild (0 - 1), moderate (2 - 3), and severe (4 - 5) based on these five parameters: This can be a useful and applicable bedside scoring method to assess and triage bronchiolitis patients. However, there is no data if it can be used to estimate PICU or hospital stay for severe patients.

Objectives: Our main objective is analyzing prenatal and postnatal risk factors for longer PICU and hospital stay for term-born bronchiolitis patients less than 3 years old who applied to hospital during Winter. Our secondary objective is to detect reasons for higher PRESS score and to evaluate if PRESS scoring could be used to estimate PICU duration for bronchiolitis patients.

MATERIALS AND METHODS

Study design and aspects to be covered: This is a prospective observational study, performed on pediatric patients aged ≤ 3 years, admitted to three tertiary level pediatric intensive care units in Ankara, Turkey during one epidemic season (between December 2017 and April 2018) with clinical diagnosis of bronchiolitis. The PICU attending physician decides whether the patient has bronchiolitis in the light of the clinic, X-ray, and laboratory parameters. ICU admission criteria were increased work of breathing despite medical treatment or $SO_2 < 92$ despite Oxygen treatment or cyanosis. Patients who were born preterm (before 37 completed weeks of gestation) and who have congenital heart diseases, were excluded from the study.

A questionnaire including questions about the smoking status of parents, number of people living at home, number of siblings at school age and living habitats of family members, was conducted. Recent studies show that any level of smoking (one or more cigarettes per day)

exposure is likely to be associated with progressive and lasting lung damage (10), so we accepted any level of cigarette smoking of mother to be sufficient for prenatal smoke exposure and any level of smoking in the household adequate for passive smoke exposure. We collect data on nursery/school attendance for the patient. The Pediatric Respiratory Severity Score (PRESS) was used to define clinical severity of Bronchiolitis at admission. Besides age, gender and chronic diseases of the subject, symptoms at the admission have been recorded. Also initial vital signs, Pediatric Risk of Mortality (PRISM) 3 score (11), blood gas and white cell count, C-Reactive Protein (CRP) at admission were recorded. Respiratory Syncytial Virus (RSV) and Influenza Polymerase Chain Reaction (PCR) test results were recorded if they existed. Treatment modalities like high-frequency oxygen (HFO), non-invasive ventilation (NIV) and invasive ventilation were daily recorded. All patients who needed HFO, received 2lt/kg air flow and weaning from HFO performed by decreasing Oxygen concentration. Patients were separated from HFO when Oxygen concentration was 30-40% without having tachypnea. Patients who had saturation over 92%, without respiratory distress, ventilatory support, positive inotropes and any organ failure were discharged from the PICU by attending doctor and were followed until discharge from hospital.

Ethical Considerations

Ethical approval was obtained from XXX Review Board (Protocol Number: E22/03-294). With the admission of the subject to PICU, written approval including informed consent about study, was obtained from the family.

Statistical Analysis

Data were expressed as descriptive statistics as percentages or median as appropriate. We start empirical analysis by reporting descriptive statistics (see Table 1 and accompanying discussion). Table 2 presents pairwise correlations between all the variables in analyses. We also report the significant cases of correlation. In the next step, we employ multivariate analysis to control for confounding factors. In this observational study (i.e., not an experiment) patients' attributes are not controlled by the researcher. Hence, unlike an experimental risk factor, it is not necessarily balanced among the sample. These unbalanced attributes can bias the findings if not accounted for. Multivariate analysis allows us to control for these potential biases. The dependent variables are continuous variables, so we perform poisson regression analysis and negative binomial regression analysis. We also correct the standard errors for heteroscedasticity. 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 history of prematurity and one 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 have missing information on risk factors, the remaining 79 patients were included. 53 of 79 (67.01 %) were male. Median age was 6 months and 45 of 79 (56.96%) patients were equal or less than 6 months old (Table 1). Median ICU stay was 5 (2-38) days and median hospital stay was 9 (3-64) days (Table 1),

10 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 combination of CPAP ±PS and HFO therapy. Mean duration for NIV ventilation was 4.75 days (SD: 4.26days). Three (3.79%) patients needed neither NIV nor invasive ventilation. We found no correlation between ventilation support therapies and risk factors. All cases in our study had either moderate or severe PRESS severity scoring. Although severe cases were hospitalized in the PICU 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).

Similar statistically insignificant relation was detected for the length of hospital stay (Mean= 10.67 vs 14.58 days, p=0.118).

Univariate analysis showed that PRISM 3 score, prenatal smoke exposure and previous hospitalization were associated significantly with longevity of PICU and Hospital Stay (Table 2). Also, there are significant correlations among explanatory variables such as higher PRISM 3 score and higher PRESS score (correlation r=0.25), passive cigarette smoke exposure and PRISM 3 score (r=0.34), passive cigarette smoke exposure and prenatal smoke exposure (r=0.42), previous hospitalization, PRISM 3 and PRESS score (r=0.27). Older age was found correlated with higher PRESS scores.

Multiple regression analysis showed that only prenatal smoke exposure was related with longer PICU and Hospital stay (Table 3). According to PRESS scores, severity levels have no statistically important effect on PICU or Hospital stay.

DISCUSSION

Prenatal smoke exposure is associated with the development of bronchiolitis in the 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 is correlated with longer PICU stay too. Our multivariable model estimates 86% longer PICU stay for a kid under age 3 with prenatal smoke exposure story if all other parameters were equal. Stevenson et al showed that maternal cigarette smoking during pregnancy increases the probability of requiring an ICU hospitalization in children hospitalized with bronchiolitis(13). Same study proved that children only exposed to prenatal smoking had higher risk for PICU admission than kids who had been exposed to passive smoking too. Our study showed that these patients not only have a higher chance for PICU admission when they have bronchiolitis but also, they will stay 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 his life.

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 is unexpectedly negative. Our in-depth analysis shows that this counterintuitive finding is the result of significant correlation between passive cigarette smoke exposure and prenatal smoke exposure (correlation coefficient: 0.42). If we include passive cigarette smoke exposure to the empirical model without controlling for prenatal smoke exposure, the coefficient estimate for passive cigarette smoke exposure is positive.[1]

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

In some studies crowded living environment, defined as 5 or more people living in the household, was associated with increased RSV related bronchiolitis hospitalization(2,16), on the contrary in the FLIP-2 study crowded household was not demonstrated as a risk factor 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 didn't show any relation between crowded households and longevity of PICU stay.

Only 2 kids 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 Turkey for very young

children are private and likely out of reach for parents of patients. Therefore, our data was not sufficient to analyze the effect of nursery attendance on the length of bronchiolitis patients' hospital stay.

The study was investigated during the viral infection epidemic season. It has been shown that exposure to RSV season was a risk factor for higher rates of hospitalization (18). We didn't test every patient for viral infections. Therefore, we didn't include RSV and influenza into the main multivariate analysis. Multivariable analysis including the RSV variable showed that the coefficient estimates of this smaller sample for main variables of interest were very similar to Table 3 and RSV or influenza positivity had not been associated with longer PICU stay[2].

Our secondary aim was to evaluate the relationship between risk factors and PRESS scoring and to find out if the PRESS scoring system is useful to estimate longevity of PICU stay. Thokngaen et al. showed that PRESS severity scoring could be helpful to evaluate patients' intensive care needs (19). We found that PRESS score was positively correlated with PRISM 3 score, age, previous hospitalization and negatively correlated with male gender. However, we demonstrated that there was no correlation with higher PRESS score and longer PICU or hospital stay.

Study Limitations

The number of patients was our most obvious limitation, if we had had more patients, we might have the chance to comment on the effects of risk factors and/or PRESS score on respiratory treatment modalities. More patients are needed in future studies, to understand which patients are under the risk of invasive ventilation or longer picu stay. Another obvious limitation in our study is that the patients' family history of asthma and wheezing child was not taken. Last but not least all patients should have been tested for seasonal virus and viral infections should have been included in regression analysis.

CONCLUSION

In our study, prenatal smoke exposure is the only independent risk factor for longer stay in intensive care and hospital for term-born bronchiolitis patients less than 3 years old, hospitalized in the PICU during winter. In contrast with literature in our study group, young age is not related with longer PICU stay. We also showed the PRESS scoring system is not useful to estimate longevity of PICU or hospital stay.

MAIN POINTS

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

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Table 1. Descriptive analysis				
Parameters	**Factor**	**Number of patients**	**Number (%)**	**Median (min-max)**
Age	Months	79		6 (1-36)
PRISM 3	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)	

Table 2. Pairwise correlations between risk factors, PRESS score and PICU stay duration											
Factors	**PICU stay**	**PRISM 3**	**PRESS score**	**CRP**	**Age**	**Male**	**Passive exposure**	**Prenatal exposure**	**School age sibling**	**Attending nursery**	**Previous hospitalization**
PRISM 3	**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	0.16	-0.01	-0.03	-0.06	-0.10	-0.00	**0.25***	**0.28***	-0.13	0.13	0.18

people											
Number of patients: 79 *: p<0.05											

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 3	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 meaningful.								