(Original Article)

Risk Factors Associated with Pneumonia in Pediatric COVID-19 Patients

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Abstract

Background: While the COVID-19 pandemic has been extensively studied in adults, there is a lack of data on the clinical characteristics and outcomes of the disease in pediatric populations, particularly regarding the development of pneumonia.

Objective: To determine the risk factors for developing pneumonia in children under 15 years of age who were infected with COVID-19.

Materials and Methods: A retrospective case-control study was conducted at Bhumibol Adulyadej Hospital, Thailand, from April 1 to November 30, 2021. The study included children under 15 years old with RT-PCR-confirmed COVID-19 infection. The patients were divided into two groups: 145 cases with radiologically confirmed pneumonia and 145 controls without pneumonia. We analyzed and compared patient demographics, clinical symptoms, comorbidities, and RT-PCR cycle threshold (Ct) values between the two groups. Multivariate logistic regression was performed to determine the independent risk factors for pneumonia.

Results: A total of 290 pediatric patients were included in the analysis. The findings showed that an age of less than 3 years (OR 3.5; 95% CI 2.07–5.92) and the presence of fever (OR 4.23; 95% CI 2.33–7.86) were significant independent risk factors for the development of pneumonia. Other symptoms, including diarrhea and rash, were also associated with an increased risk of pneumonia.

Conclusion: Children under the age of three and those who present with a fever are at a significantly higher risk of developing pneumonia when infected with COVID-19. These findings highlight the need for close monitoring of these high-risk pediatric patients to facilitate early intervention and improve clinical outcomes.

Keywords: COVID-19, pneumonia, risk factors, pediatric patients

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ปัจจัยเสี่ยงของการเกิดโรคปอดอักเสบในผู้ป่วยเด็กที่ติดเชื้อโควิด 19

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บทคัดย่อ

ความเป็นมา: ข้อมูลเกี่ยวกับการติดเชื้อโควิด 19 ในกลุ่มผู้ป่วยเด็กยังมีจำกัด โดยเฉพาะอย่างยิ่งอาการแสดง และภาวะแทรกซ้อนที่รุนแรง เช่น โรคปอดอักเสบ ซึ่งแตกต่างจากการศึกษาในกลุ่มผู้ใหญ่ที่มีจำนวนมาก

วัตถุประสงค์: เพื่อศึกษาหาปัจจัยเสี่ยงที่ทำให้เกิดโรคปอดอักเสบจากเชื้อโควิด 19 ในผู้ป่วยเด็กที่มีอายุน้อยกว่า 15 ปี ที่เข้ารับการรักษาในโรงพยาบาล

ระเบียบวิธีวิจัย: การศึกษาย้อนหลังแบบมีกลุ่มควบคุมนี้ ทำการเก็บข้อมูลจากเวชระเบียนของผู้ป่วยเด็กอายุแรกเกิดถึง 15 ปี ที่ได้รับการวินิจฉัยยืนยันว่าติดเชื้อโควิด 19 ด้วยวิธี Real-time Polymerase Chain Reaction (RT-PCR) และเข้ารับการรักษาที่โรงพยาบาลภูมิพลอดุลยเดช ระหว่างวันที่ 1 เมษายน 2564 ถึง 30 พฤศจิกายน 2564 ผู้ป่วยถูกแบ่งออกเป็นสองกลุ่ม กลุ่มละ 145 ราย ได้แก่ กลุ่มที่มีภาวะปอดอักเสบ และกลุ่มที่ไม่มีภาวะปอดอักเสบ จากนั้นได้ทำการเปรียบเทียบปัจจัยต่าง ๆ เช่น อายุ, อาการและอาการแสดง, โรคประจำตัวร่วม และค่า Cycle Threshold (Ct)

ผลลัพธ์: จากผู้ป่วยเด็กที่ติดเชื้อโควิด 19 จำนวน 290 ราย พบว่าปัจจัยเสี่ยงที่มีนัยสำคัญต่อการเกิดโรคปอดอักเสบ ได้แก่ เด็กที่มีอายุต่ำกว่า 3 ปี มีความเสี่ยงที่จะเป็นโรคปอดอักเสบมากกว่าผู้ป่วยกลุ่มอายุอื่นถึง 3.5 เท่า (OR, 3.5; 95%CI 2.07-5.92), และการมีอาการไข้เพิ่มความเสี่ยงต่อการเกิดปอดอักเสบถึง 4.23 เท่า (OR, 4.23; 95%CI 2.33-7.86) นอกจากนี้ อาการถ่ายเหลวและผื่นผิวหนังยังเป็นปัจจัยเสี่ยงร่วมที่พบได้ในกลุ่มผู้ป่วยที่มีภาวะปอดอักเสบ

สรุป: ผลการศึกษาชี้ให้เห็นว่าผู้ป่วยเด็กที่ติดเชื้อโควิด 19 ที่มีอายุน้อยกว่า 3 ปี หรือมีอาการไข้ร่วมด้วย มีความเสี่ยงสูงต่อการพัฒนาไปสู่ภาวะปอดอักเสบอย่างมีนัยสำคัญ ข้อมูลนี้มีความสำคัญต่อการเฝ้าระวังและการดูแลรักษาผู้ป่วยเด็กในโรงพยาบาลเพื่อป้องกันภาวะแทรกซ้อนที่รุนแรง

คำสำคัญ: โควิด 19, ปอดอักเสบ, ปัจจัยเสี่ยง, ผู้ป่วยเด็ก

Introduction

The global COVID-19 pandemic, caused by the SARS-CoV-2 virus, has resulted in a devastating impact on public health worldwide. While the majority of severe illness and mortality have been concentrated in adult and elderly populations, pediatric cases, though often milder, can still lead to serious complications.[1] A significant portion of infected children may remain asymptomatic, but symptomatic cases commonly present with mild, nonspecific symptoms such as fever, cough, and gastrointestinal issues.[2] However, a subset of these patients may progress to severe disease, including pneumonia, acute respiratory failure, and multisystem inflammatory syndrome in children (MIS-C).[1]

Previous studies have identified various risk factors for severe COVID-19 in children, including age, gender, and underlying comorbidities like chronic renal disease, chronic pulmonary disease, congenital heart disease, and malignancy.[4,5] Additional risk factors identified for severe COVID-19 and mortality include obesity, diabetes, asthma, and an immunocompromised status.[5-7] This study aimed to contribute to this body of knowledge by specifically

identifying risk factors for the development of pneumonia in pediatric COVID-19 patients treated at a hospital in Thailand.

Materials and Methods

Study design and setting

This analytical retrospective case-control study was conducted between April 1 and November 30, 2021, at Bhumibol Adulyadej Hospital. The study protocol received approval from the hospital ethics committee (IRB no. 110/64).

Study population

All participants were children under 15 years of age diagnosed with COVID-19 infection confirmed by RT-PCR testing using ARIDIA (Biotech, Inc., CA, USA). Participants were categorized into two groups: those diagnosed with COVID-19 pneumonia comprised the case group, while those with COVID-19 infection without pneumonia served as controls. Pneumonia diagnosis was established by pediatricians based on clinical signs and radiological findings.

Data collection

The following variables were collected for both groups: age, sex, clinical manifestations, obesity (defined as BMI Z-score ≥2 standard deviations for same sex and age), comorbidities, and RT-PCR cycle threshold values. Risk factors for pneumonia development were systematically evaluated.

Statistical Analysis

Sample size estimation utilized the two-independent proportion formula. Baseline characteristics and clinical manifestations were compared between patients with and without COVID-19 pneumonia. Age, sex, clinical manifestations, obesity, comorbidities, and cycle threshold values were described as counts and percentages, compared using chi-square and Fisher's exact tests. Odds ratios with 95% confidence intervals (CI) were calculated for risk factors associated with COVID-19 pneumonia. Multivariate logistic regression models were performed to adjust for covariates correlated with pneumonia. Statistical analysis was conducted using SPSS version 27 (IBM Corporation, NY, USA).

Results

During the study period, 337 pediatric patients with RT-PCR-confirmed COVID-19 infection presented to Bhumibol Adulyadej Hospital. Forty-seven patients were excluded from the study due to insufficient data. A total of 290 patients were included: 145 patients with COVID-19 pneumonia formed the case group, while 145 patients without pneumonia served as controls.

The baseline characteristics of the two groups were compared. As shown in Table 1, the COVID-19 pneumonia group had a significantly higher proportion of children under three years of age compared to the no pneumonia group (46.9 % vs. 13.1 %, $p<0.001$). The prevalence of fever was also significantly higher in the pneumonia group (72.4% vs. 35.9%, $p<0.001$). Additionally, a higher percentage of patients with pneumonia presented with diarrhea (13.8 % vs. 6.2 %, $p=0.03$) and rash (9 % vs. 2.1 %, $p=0.01$).

No significant differences were found between the two groups regarding other clinical symptoms such as rhinorrhea, cough, sore throat, anosmia, conjunctivitis, and vomiting. Similarly, there were no significant differences in the prevalence of comorbidities like obesity, asthma, and allergic rhinitis, or in the RT-PCR cycle threshold values between the two groups.

Risk Factor Analysis

The multivariate logistic regression analysis revealed two independent risk variables for the

development of COVID-19 pneumonia. Age less than three years was identified as a significant risk factor, with an odds ratio (OR) of 3.50 (95% CI 2.07-5.92). Furthermore, fever was an independent risk factor, with an odds ratio (OR) of 4.23 (95% CI 2.33-7.86).

Table 1 Demographic data and characteristics of COVID-19 subjects with or without pneumonia

	Pneumonia*		p-value
	With (n=145)	Without (n=145)	
Age <3 years	68 (46.9)	19 (13.1)	<0.001p
Clinical manifestations			
Fever	105 (72.4)	52 (35.9)	<0.001p
Rhinorrhea	54 (37.2)	41 (28.3)	0.10p
Cough	98 (67.6)	88 (60.7)	0.22p
Sore throat	22 (15.2)	24 (16.6)	0.75p
Anosmia	3 (2.1)	9 (6.2)	0.77p
Diarrhea	20 (13.8)	9 (6.2)	0.03p
Conjunctivitis	3 (2.1)	0 (0.0)	0.25f
Vomiting	12 (8.3)	5 (3.4)	0.80p
Rash	13 (9)	3 (2.1)	0.01p
Co-morbidities			
Obesity	42 (29.0)	31 (21.4)	0.14p
Allergic rhinitis	5 (3.4)	1 (0.7)	0.21f
Asthma	1 (0.7)	1 (0.7)	1.00f
Cycle threshold** <20	92 (63.4)	98 (67.6)	0.46p

*n (%), p: Pearson Chi-Square, f: Fisher's Exact Test, **cycle threshold: cycle threshold values in RT-PCR

Table 2 Risk factors associated with COVID-19 pneumonia in pediatric patients (n=290)

	Crude OR*	p-value	Adjusted OR*	p-value
Age <3 years	5.86 (3.27, 10.45)	<0.001	3.50 (2.07, 5.92)	<0.001
Fever	4.70 (2.85, 7.72)	<0.001	4.23 (2.33, 7.86)	<0.001
Diarrhea	2.42 (1.06, 5.51)	0.03		
Rash	4.66 (1.30, 16.73)	0.02		

* OR= odds ratio (95%CI)

Discussion

In Thailand, by November 2021, children accounted for a significant portion of COVID-19 cases, though the crude mortality rate remained low.[1] While COVID-19 in children is typically mild, a small number of patients develop severe complications, including pneumonia, which has been identified as a key risk factor for ICU admission and mortality in this population.[8] Lung involvement is a critical determinant of poor outcomes, with extensive lung segment involvement correlating with higher disease severity and a poorer prognosis.[9]

Our study specifically focused on factors associated with pneumonia development in children with confirmed COVID-19. We found that age less than three years significantly increased the risk of COVID-19 pneumonia, consistent with similar findings in Mexico.[5] This heightened vulnerability in very young children can be attributed to their smaller airways, still-developing immune systems, and limited respiratory reserve, all of which make them more susceptible to respiratory complications.

Fever was another significant risk factor for COVID-19 pneumonia. This aligns with other studies that have identified fever as a predictor of severe COVID-19 pneumonia. The presence of a fever likely indicates a more robust inflammatory response and a higher viral load, which in turn leads to more extensive tissue damage and a greater likelihood of pulmonary complications.[10]

Interestingly, our study did not find a significant association between obesity or other comorbidities and the development of pneumonia. This contrasts with research in both pediatric and adult populations that has identified these factors as major risk factors for severe COVID-19.[11-13] This discrepancy may be due to the very low number of patients with underlying diseases who developed pneumonia in our study cohort.

Furthermore, we found no significant difference in RT-PCR cycle threshold (Ct) values between the pneumonia and no-pneumonia groups, despite some studies suggesting that lower Ct values (indicating a higher viral load) are associated with worse outcomes.[14]

Limitations and future directions

This study's retrospective, single-center design is a limitation, as the findings may not be generalizable to other healthcare settings or populations. The retrospective nature also prevents us from prospectively validating any risk stratification methods. Future multicenter, prospective studies are needed to confirm our findings and develop robust, validated risk prediction models for pediatric COVID-19 patients.

Conclusion

This study identifies children under three years of age and those presenting with fever as having significantly elevated probability of developing pneumonia when infected with COVID-19. These findings provide evidence-based guidance for risk stratification and clinical decision-making in pediatric COVID-19 management. Healthcare providers should implement heightened surveillance protocols for children meeting these risk criteria to optimize early identification and intervention for potential respiratory complications.

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