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Multifactorial Model-Based Risk Assessment and Predictive Biomarker Analysis in Pediatric Severe Pneumonia

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Abstract: *Community-acquired pneumonia (CAP) remains a leading cause of mortality among children under 5 years of age in China, underscoring the critical need for early identification of severe cases and timely intervention; however, ideal predictive indicators for severe pediatric pneumonia are currently lacking. This study aimed to investigate the risk factors and predictive value of severe pneumonia in children, thereby providing a theoretical basis for early clinical diagnosis and prompt therapeutic intervention. A retrospective analysis was performed on clinical data from pediatric patients with CAP who were hospitalized in the Department of Pediatrics, Guangzhou Red Cross Hospital, between December 2023 and June 2024. Clinical characteristics were compared between study groups, risk factors for severe pneumonia were analyzed using multivariate logistic regression, and the predictive value of each indicator was evaluated via receiver operating characteristic (ROC) curve analysis. A total of 237 children with CAP were included, comprising 123 cases in the mild group (58 males and 65 females) with a median age of 5.0 years (interquartile range [IQR], 2.0–7.0 years) and 114 cases in the severe group (54 males and 60 females) with a median age of 6.0 years (IQR, 4.0–8.25 years). Compared with the mild group, the severe group exhibited significantly higher values for age, neutrophil percentage (NEUT%), absolute neutrophil count, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), interleukin-6 (IL-6), procalcitonin (PCT), C-reactive protein (CRP), and the rate of pulmonary consolidation, while platelet count (PLT), absolute lymphocyte count, absolute monocyte count, albumin (ALB), creatine kinase (CK), and creatine kinase-MB (CK-MB) were significantly lower (all P<0.05). Multivariate logistic regression analysis, after adjustment for confounding factors, identified absolute lymphocyte count, NLR, lactate dehydrogenase (LDH), and pulmonary consolidation as independent risk factors for severe pneumonia (all P<0.05). ROC curve analysis demonstrated that the individual diagnostic value of absolute lymphocyte count, NLR, LDH, or pulmonary consolidation for predicting severe pneumonia was limited, whereas their combined detection yielded good predictive performance (area under the curve [AUC] >0.8, P<0.05). All enrolled children achieved clinical cure and were discharged following treatment; notably, the severe group had significantly higher rates of oxygen therapy utilization, corticosteroid administration, immunoglobulin use, and fiberoptic bronchoscopic alveolar lavage, as well as a longer hospital stay, compared with the mild group (all P<0.01). Collectively, these findings indicate that absolute lymphocyte count, NLR, LDH, and pulmonary consolidation are independent risk factors for the development of severe pneumonia in children, capable of assessing the risk of severe disease in affected patients, with the highest predictive value observed when these indicators are detected in combination.*

Keywords: *Community-Acquired Pneumonia, Severe Pneumonia, Children, Risk Factors, Prediction*

1. Introduction

Community-acquired pneumonia (CAP) in children is defined as an acute pulmonary infection occurring outside the hospital or within 48 hours of hospital admission[1]. It constitutes a major cause of hospitalization among pediatric populations in developed countries and ranks as a leading contributor to childhood mortality in developing countries[2]. Notably, children exhibit immature development of multiple bodily systems, with their respiratory system possessing distinct anatomical and physiological features—including narrow airways, delicate mucosa, inadequate mucus gland secretion, reduced

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alveolar quantity, and impaired ciliary motility. These characteristics render children more vulnerable to pathogenic invasion, with disease progression often rapid, potentially evolving swiftly into severe pneumonia and culminating in various pulmonary and extra-pulmonary complications, or even death. Furthermore, some children may develop long-term sequelae post-recovery, which can significantly compromise their long-term quality of life while imposing substantial burdens on families and society at large. Therefore, the early identification of severe pneumonia followed by prompt and effective interventions is crucial for preventing disease progression, reducing complications, and mitigating sequelae. In the present study, we retrospectively analyzed the clinical data, laboratory indicators, etiological results, and imaging findings of 237 children diagnosed with community-acquired pneumonia to explore the risk factors and predictive value of severe pediatric pneumonia, aiming to provide a basis for the early clinical identification of severe pneumonia.

2. Methods

2.1 Study subjects

A retrospective analysis was performed on the clinical data of children with CAP admitted to the Pediatric Inpatient Department of Guangzhou Red Cross Hospital between December 2023 and June 2024. The inclusion criteria were as follows: (1) age ≤ 14 years; (2) fulfillment of the diagnostic criteria for CAP; (3) complete clinical data. The exclusion criteria included: (1) presence of underlying diseases, such as immunodeficiency, cardiovascular disorders, hematologic malignancies, hepatorenal diseases, genetic metabolic diseases, encephalitis, and epilepsy; (2) receipt of immunosuppressive therapy; (3) discharge, transfer, or death within 48 hours of admission. Subjects were stratified into mild and severe groups according to disease severity.

The diagnosis of CAP was established based on the presence of clinical symptoms (e.g., fever, cough, wheezing), physical signs (e.g., tachypnea, pulmonary wet rales), and radiological evidence of pulmonary lesions. Classification into mild or severe pneumonia was determined by evaluating the patient's general condition, level of consciousness, respiratory rate, presence of cyanosis, dyspnea or hypoxemia (oxygen saturation ≤ 92%), and occurrence of pulmonary or extra-pulmonary complications.

2.2 Data collection

Clinical data of the study participants were retrieved from the electronic medical record system, encompassing demographic information, laboratory parameters, respiratory pathogen detection results, imaging findings, and treatment details. Specifically, the collected data included:(1) Demographic and clinical variables: age, gender, and hospital stay duration. (2) Laboratory indicators: Peripheral venous blood samples were collected within 24 hours of admission for the following analyses: white blood cell count (WBC), platelet count (PLT), neutrophil percentage (NEUT%), red cell distribution width (RDW), absolute counts of neutrophils, lymphocytes, and monocytes, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), lactate dehydrogenase (LDH), alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin (ALB), creatine kinase (CK), creatine kinase-MB (CK-MB), interleukin-6 (IL-6), C-reactive protein (CRP), and procalcitonin (PCT). (3) Respiratory pathogen detection: Pharyngeal swab samples were collected within 24 hours of admission. Prior to sampling, the oral cavity was thoroughly cleansed, and pathogen analysis was performed using the targeted next-generation sequencing (tNGS) method. (4) Imaging findings: Pulmonary consolidation was documented based on chest X-ray and/or computed tomography (CT) results. (5) Treatment modalities: In addition to standard treatment, comprehensive interventions were administered according to disease severity, including oxygen therapy, corticosteroids, intravenous immunoglobulin, and fiberoptic bronchoscopic alveolar lavage.

2.3 Statistical analysis

Statistical analyses were performed using SPSS 29.0 software. For continuous variables, normally distributed data were expressed as mean ± standard deviation ($\bar{x} \pm s$) and compared using the independent-samples t-test; non-normally distributed data were presented as median and interquartile range [M (P25, P75)] and analyzed with the non-parametric Mann-Whitney U test. Categorical variables were expressed as counts (percentages) and compared using the χ^2 test. Multivariate logistic regression analysis was employed to identify independent risk factors for severe pneumonia. The

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receiver operating characteristic (ROC) curve was used to evaluate the predictive value of each factor. A two-tailed $P < 0.05$ was considered statistically significant.

3. Results

3.1 General Information

A total of 237 pediatric patients diagnosed with community-acquired pneumonia (CAP) were enrolled in this study and stratified into two groups: the mild group (n=123) and the severe group (n=114). Demographic profiling revealed that the mild group included 58 male subjects, with a median age of 5.0 years (interquartile range [IQR], 2.0–7.0 years), whereas the severe group comprised 54 male patients, with a median age of 6.0 years (IQR, 4.0–8.25 years). Statistical analysis indicated no significant difference in gender distribution between the two groups ($P>0.05$). Notably, children in the severe group exhibited a higher median age and a longer hospital stay, with both parameters showing statistically significant differences ($P<0.05$). Comprehensive demographic data are summarized in Table 1.

3.2 Laboratory Indicators

Compared with the mild group, the severe group displayed significantly higher levels of NEUT%, absolute neutrophil count, NLR, PLR, IL-6, PCT, and CRP (all $P<0.05$). Conversely, the severe group had significantly lower values of PLT, absolute lymphocyte count, absolute monocyte count, ALB, CK, and CK-MB compared to the mild group (all $P<0.05$). Detailed laboratory findings are presented in Table 1.

3.3 Respiratory Pathogen Detection

Statistically significant discrepancies were observed in the distribution of respiratory pathogens between the two groups ($P<0.05$). Specific pathogen detection data are tabulated in Table 2.

3.4 Imaging Examination

The proportion of patients with pulmonary consolidation was significantly higher in the severe group than in the mild group ($P<0.05$). Corresponding imaging data are provided in Table 2.

3.5 Treatment Outcomes

All children with CAP achieved clinical cure and were discharged successfully. The utilization rates of oxygen therapy, corticosteroids, immunoglobulin, and fiberoptic bronchoscopic alveolar lavage were significantly higher in the severe group compared to the mild group, with all differences reaching statistical significance ($P<0.01$). A comprehensive summary of treatment-related parameters is available in Table 3.

3.6 Multivariate Logistic Regression Analysis

After screening variables with statistical significance in univariate analysis, binary logistic regression was performed. Following adjustment for potential confounding factors, the results identified absolute lymphocyte count, NLR, LDH, and pulmonary consolidation as independent risk factors for severe pneumonia (all $P<0.05$). Relevant regression coefficients and odds ratios are displayed in Table 4.

3.7 Predictive Value of Factors for Severe Pneumonia

ROC curve analysis demonstrated that the individual diagnostic value of absolute lymphocyte count, NLR, LDH, and pulmonary consolidation for predicting severe pneumonia was limited. However, the combined detection of these indicators exhibited good predictive performance (area under the curve [AUC] >0.8, $P<0.05$). Detailed ROC parameters and corresponding plots are provided in Table 5 and Figure 1, respectively.

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Table 1 Comparisons of general conditions and laboratory indicators [($\bar{x}\pm s$), n(%),M(P25,P75)]

Information	Mild (n=123)	Severe (n=114)	χ^2/t/Z	P
Gender (male)	58 (47.2)	54 (47.4)	0.001	0.974
Age (years old)	5.0 (2.0, 7.0)	6.0 (4.0, 8.25)	-2.689	0.007
Length of stay (days)	7.15±1.7	10.2±3.05	-9.384	<0.001
WBC ($\times10^9$/L)	8.07 (6.06, 11.38)	8.12 (6.53, 10.80)	-0.134	0.894
PLT ($\times10^9$/L)	304 (239, 362)	257 (204, 327.75)	-2.986	0.003
NEUT%	56.5 (42.2, 66.0)	65.7 (57.0, 73.0)	-4.673	<0.001
RDW	0.127 (0.12, 0.13)	0.124 (0.12, 0.13)	-1.955	0.051
Neutrophil count ($\times10^9$/L)	4.15 (2.68, 6.62)	4.99 (3.41, 7.03)	-2.06	0.039
Lymphocyte count ($\times10^9$/L)	2.55 (1.77, 4.01)	1.96 (1.3, 2.67)	-4.349	<0.001
Monocyte count ($\times10^9$/L)	0.69 (0.51, 0.99)	0.63 (0.44, 0.8)	-2.264	0.024
NLR	1.79 (0.91, 2.68)	2.73 (1.66, 4.03)	-4.302	<0.001
PLR	111.14 (77.47, 140.79)	132.24 (92.31, 185.43)	-2.844	0.004
LMR	3.83 (2.65, 6.23)	3.38 (2.43, 5.11)	-1.949	0.051
LDH (U/L)	301.25 (266, 339.48)	314.2 (271.4, 370.9)	-1.653	0.098
ALT (U/L)	14.1 (11.03, 18.9)	13.6 (10.85, 17.8)	-0.444	0.675
AST (U/L)	32 (27, 40.9)	31.5 (25.85, 37.7)	-0.606	0.545
ALB (g/L)	41.8 (39.03, 44.1)	40.5 (37.6, 42.45)	-2.692	0.007
CK (U/L)	110.7 (79.73, 193.3)	101.4 (72.53, 144.03)	-2.353	0.019
CK-MB (U/L)	26.6 (21.53, 34.38)	21.4 (18.4, 29.53)	-4.067	<0.001
IL-6 (pg/ml)	13.18 (4.58, 23.52)	20.15 (11.21, 32.41)	-3.818	<0.001
PCT (ng/ml)	0.1 (0.06, 0.24)	0.13 (0.07, 0.28)	-2.629	0.009
CRP (mg/ml)	8.5 (2.5, 20.25)	16.62 (6.73, 35.56)	-3.461	<0.001

Table 2 Comparisons of pathogenetic and imaging findings [n(%)]

Information	Mild(n=123)	Severe (n=114)	χ^2	P
pathogen			14.879	0.005
negative	7 (5.7)	0 (0)		
bacteria	9 (7.3)	4 (3.5)		
viruses	27 (22)	14 (12.3)		
mycoplasma	30 (24.4)	42 (36.8)		
mixed infection	50 (40.7)	54 (47.4)		
pulmonary consolidation	14 (11.4)	68 (59.6)	60.913	<0.001

Table 3 Comparisons of treatment Outcomes [n(%)]

Information	Mild(n=123)	Severe (n=114)	χ^2	P
oxygen therapy	0 (0)	69 (60.5)	105.024	<0.001
corticosteroid	33 (26.8)	98 (86)	83.691	<0.001
immunoglobulin	5 (4.1)	38 (33.3)	34.126	<0.001
bronchoscope	0 (0)	30 (26.3)	37.059	<0.001

Table 4 Results of the Multivariate Logistic Regression Analysis

Factors	B	S.E	χ^2	P	OR	95 %CI
lymphocyte count	0.402	0.149	7.296	0.007	1.117	1.117-2.001
NLR	0.285	0.086	11.072	<0.001	1.124	1.124-1.573
LDH	0.013	0.003	16.888	<0.001	1.007	1.007-1.02
pulmonary consolidation	2.686	0.425	39.896	<0.001	6.378	6.378-33.787
Constant	-2.47	1.031	5.736	0.017		

Table 5 Predictive value of independent correlation factors

Independent factors	Cut-off value	Sensitivity (%)	Specificity (%)	Yoden Index	AUC(95%CI)	P
lymphocyte count	2.94	83.33	44.72	0.2805	0.664 (0.6-0.723)	<0.0001
NLR	2.11	64.91	62.6	0.2751	0.662 (0.598-0.722)	<0.0001
LDH	377.2	23.68	91.8	0.1549	0.566 (0.5-0.63)	0.0801
pulmonary consolidation	1	59.65	88.62	0.4827	0.741 (0.681-0.796)	<0.0001
Combined testing		85.44	78.33	0.6377	0.867 (0.815-0.909)	<0.0001

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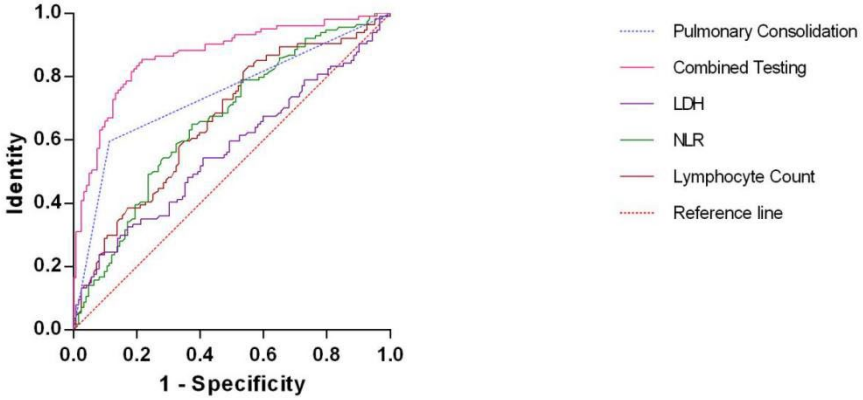

Figure 1 ROC curves of various factors for predicting severe pneumonia

4. Discussion

Pneumonia ranks among the most prevalent infectious diseases in pediatric populations. Severe pneumonia is characterized by prolonged clinical course, increased therapeutic difficulty, extended hospitalization, elevated medical costs, and potential long-term sequelae—all of which can significantly impact children's growth and development. Consequently, the timely identification of risk factors associated with severe pneumonia is paramount for improving the prognosis of high-risk children[3].

In recent years, research on the risk factors of severe pneumonia has expanded considerably[4], with a growing number of biomarkers being incorporated into the identification and prognostic assessment of pediatric severe pneumonia[5,6]. While traditional biomarkers possess well-established clinical significance and widespread utility, their specificity and sensitivity remain amenable to improvement. In contrast, novel biomarkers are challenging to popularize in primary healthcare settings due to their high detection costs and insufficient validation of clinical practicability. This current situation underscores the urgency of exploring biomarkers that are operationally straightforward, cost-effective, rapid, and minimally invasive—such markers would hold greater value for evaluating the severity and prognosis of severe pneumonia.

Through comparative analysis, the present study revealed that the NEUT%, neutrophil count, NLR, PLR, IL-6, PCT, CRP, and pulmonary consolidation rate were all significantly higher in the severe group compared to the mild group. In terms of therapeutic interventions, the rates of oxygen therapy, glucocorticoid administration, immunoglobulin use, and fiberoptic bronchoscopic alveolar lavage were also significantly elevated in the severe group. Collectively, these differences indicate that children with severe pneumonia exhibit a more intense systemic immune-inflammatory response, accompanied by more severe chest imaging abnormalities, increased treatment complexity, prolonged hospitalization, and substantial economic burden on families.

To further identify key determinants, logistic regression analysis confirmed that lymphocyte count, NLR, LDH, and pulmonary consolidation are independent risk factors for severe pneumonia in children. Mechanistically, upon pathogenic invasion, neutrophils initiate immune responses via chemotaxis and phagocytosis, exhibiting reactive proliferation. In contrast, lymphocytes—central to cellular immunity—display more pronounced quantitative reduction and functional impairment in severe cases[7], directly reflecting a state of immune dysregulation. Among these factors, NLR, with its advantages of convenient detection and low cost, has been validated as an effective biomarker across various diseases. Multiple studies support its role as an independent risk factor and diagnostic predictor for severe pneumonia[8]. LDH, released into the bloodstream during tissue inflammation or injury, correlates closely with the severity of severe pneumonia, emerging as a potential indicator for early diagnosis[9,10].

In diagnostic practice, chest imaging holds irreplaceable value[11]. Compared with traditional X-ray, chest CT more sensitively detects subtle pulmonary lesions, including pulmonary consolidation, atelectasis, and pleural effusion—characteristic changes directly linked to disease severity. Children with pulmonary consolidation typically experience prolonged fever duration, higher incidence of

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pulmonary and extrapulmonary complications, and significantly delayed resolution of pulmonary lesions[12]. Thus, timely chest imaging not only facilitates early diagnosis and precise management of severe pneumonia but also informs decisions regarding fiberoptic bronchoscopic alveolar lavage, ultimately promoting recovery and reducing the risk of sequelae.

To evaluate the predictive efficacy of indicators, ROC curve analysis in this study showed that lymphocyte count, NLR, LDH, and pulmonary consolidation alone had limited diagnostic efficacy in predicting severe pneumonia; however, their combined detection exhibited good predictive value (AUC>0.8, P<0.05). This finding underscores that a single indicator is insufficient for effective assessment of pediatric severe pneumonia, necessitating comprehensive evaluation with multiple indicators. Moreover, combining these indicators with imaging examinations can significantly enhance the accuracy of early diagnosis and prognostic judgment.

Notably, this study has limitations inherent to its single-center retrospective design: the short study period and limited sample size may be confounded by factors such as population characteristics, geographical distribution, and seasonal variations, introducing potential biases. Future research should therefore focus on multi-center, large-sample prospective cohort studies to further clarify and validate the risk factors of severe pneumonia, providing more robust theoretical support for clinical practice.

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