

Predictive Value of Traditional and Novel Composite Inflammatory Indicators for Severe and Refractory *Mycoplasma pneumoniae* Pneumonia in Children

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Objective: This study aimed to comprehensively evaluate the predictive efficacy of traditional single inflammatory indicators and novel composite inflammatory indicators (CLR, LMR, NLR, NPR, PIV, PLR, SII, SIRI) for severe *Mycoplasma pneumoniae* pneumonia (SMPP) and refractory MPP (RMPP) in children.

Methods: This study retrospectively enrolled 1791 children with MPP and collected their case data. A phased modeling strategy (univariate analysis, LASSO regression, multivariate logistic regression) was employed to construct prediction models. Model performance was evaluated using area under the curve (AUC) from receiver operating characteristic (ROC) curves, calibration curves with the Hosmer-Lemeshow test, bootstrap resampling with 1000 repetitions, and decision curve analysis (DCA).

Results: The cohort included 512 SMPP, 269 RMPP, and 1180 general MPP cases; mentiontly, 170 children met both SMPP and RMPP criteria. The SMPP prediction model identified nine independent risk factors (Hb, PLT, D-D, FIB, LMR, NPR, SII, duration of cough and fever), achieving an AUC of 0.803. The RMPP model identified seven factors (Hb, CRP, FIB, LMR, NPR, duration of cough and fever) with an AUC of 0.889. The calibration curves, Hosmer-Lemeshow test, bootstrap internal validation, and DCA curve together confirmed the robustness and clinical applicability of the models.

Conclusion: This multi-parameter integration strategy enables precise MPP risk stratification, holding significant implications for clinical treatment planning and antibiotic selection.

Keywords: composite inflammatory indicators, refractory *Mycoplasma pneumoniae* pneumonia, risk prediction model, *Mycoplasma pneumoniae* pneumonia, severe *Mycoplasma pneumoniae* pneumonia

Introduction

Mycoplasma pneumoniae pneumonia (MPP), an inflammatory disease of the lower respiratory tract caused by *Mycoplasma pneumoniae* (MP) infection, mainly manifests clinically as persistent high fever, paroxysmal irritating dry cough, and dyspnea.¹ Epidemiological analysis reveals that due to factors like environmental changes, the incidence of MPP has significantly increased, accounting for about 40% of community-acquired pneumonia in children and presenting features of a growing infection proportion among young children and increasingly severe symptoms.² Although MPP is generally regarded as a self-limiting disease, approximately 10% to 40% of children with MPP may progress to severe MPP (SMPP) or refractory MPP (RMPP).²⁻⁴ SMPP often occurs around one week after the onset of the disease and serves as frequently complicated by extensive pulmonary consolidation, pleural effusion, and extra-pulmonary complications, including liver injury, encephalitis, hemolytic anemia, and thrombosis.³ RMPP manifests as a poor response to macrolide antibiotic treatment and a protracted disease course, which can lead to irreversible sequelae such as bronchiolitis obliterans and bronchiectasis.⁴ Given the potential progression of MPP to more severe forms with serious complications, early identification of high risk children is crucial for optimizing the timing of intervention.

The pathogenesis of MPP has not been fully elucidated, but current studies suggest that the inflammatory response may play a crucial role in the course of MPP.^{1,2} Clinically, peripheral blood inflammatory markers are important tools for monitoring this inflammatory process: classic indicators such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen (FIB) and procalcitonin (PCT) can quantify the intensity of inflammation, while blood routine parameters like lymphocyte count (LYMP), monocytes count (MONO), neutrophil count (NEUT), platelet count (PLT) and white blood cells count (WBC) reflect the balance status of immune cells. Although traditional single inflammatory indicators are widely used in clinical practice, their effectiveness in predicting diseases is limited by insufficient biological specificity. In recent years, composite inflammatory indicators proposed by researchers, such as CRP-to-lymphocyte ratio (CLR), lymphocyte-to-monocyte ratio (LMR), Neutrophil-lymphocyte ratio (NLR), neutrophil-to-platelet ratio (NPR), pan-immune-inflammation value (PIV), platelet-lymphocyte ratio (PLR), systemic inflammation index (SII) and systemic inflammatory response index (SIRI), can capture the characteristics of inflammation more sensitively by integrating multi-dimensional immune parameters.^{5,6} Notably, such a multiple parameters combination strategy has shown advantages in the prediction models of immune and inflammatory related diseases. Moreover, with the widespread application of artificial intelligence methods in medical prediction models, feature selection and model optimization strategies based on machine learning provide new approaches for integrating multi-dimensional indicators to achieve precise risk stratification.^{7,8}

However, most current studies have focused on the analysis of traditional single inflammatory indicators, and there have been few systematic studies on the relationships between the above eight composite inflammatory indicators (CLR, LMR, NLR, NPR, PIV, PLR, SII, SIRI) and SMPP or RMPP. Based on this, this study aimed to comprehensively and systematically evaluate the predictive efficacy of traditional single inflammatory indicators and novel composite inflammatory indicators for childhood SMPP and RMPP, and construct a risk prediction model accordingly.

Methods

Study Subjects

This study retrospectively included and systematically analyzed the clinical data of 1791 children with MPP admitted to the Department of Pediatrics at the Affiliated Hospital of Qingdao University from January 2023 to December 2024. The diagnosis of MPP refers to the diagnostic criteria of the National Health Commission of China.^{3,9} Specifically, in addition to clinical symptoms and imaging findings, patients should test positive in at least one of the following laboratory examinations: (1) positive for MP-DNA or MP-RNA; (2) the titer of MP antibodies in a single-serum sample was $\geq 1:160$ (using the PA method); or there was a four-fold or greater increase in the titer of MP antibodies in paired-serum samples during the course of the disease. The inclusion criteria for MPP included: (1) confirmed cases of children no more than 14 years old; (2) complete clinical and laboratory data. The presence of any of the following criteria indicated a patient with SMPP:^{3,9} (1) persistent high-grade fever (above 39°C) for ≥ 5 days or fever for ≥ 7 days without a trend of defervescence; (2) accompanied by respiratory symptoms such as wheezing, shortness of breath, dyspnea, chest pain, or hemoptysis; (3) extrapulmonary complications; (4) finger pulse oxygen saturation $\leq 93\%$ at rest while breathing room air; (5) one of the following imaging manifestations can be observed. Involvement of $\geq 2/3$ of a single lung lobe with homogeneous consolidation, or high-density consolidation in two or more lung lobes; diffuse bronchiolitis in one whole lung or bronchiolitis manifestations in $\geq 4/5$ of bilateral lung lobes; (6) progressive deterioration of clinical symptoms, with the imaging showing that the lesion area has progressed by more than 50% within 24–48 hours; (7) significantly elevated CRP, lactate dehydrogenase (LDH), or D-dimer (D-D). The inclusion criteria for RMPP were as follows:⁴ In children with MPP, after receiving standardized treatment with macrolide antibiotics for ≥ 7 days, those who still have persistent fever and clinical/imaging deterioration.

Exclusion criteria: (1) incomplete clinical data; (2) having entered the convalescent phase upon admission; (3) co-infection with other pathogens; (4) a history of respiratory tract infection and the use of macrolide antibiotics within 2 months before the onset of the disease; (5) co-existence of serious underlying diseases (such as congenital heart disease, chronic organ diseases, hematological diseases); (6) history of major surgery, trauma and blood transfusion in recent 3 months; (7) presence of abnormal immune function (including immunodeficiency or use of immunomodulators within 3 months). This study was approved by the Medical Ethics Committee of the Affiliated Hospital of Qingdao University (Approval Number: QYFYWZLL29996), and given its retrospective design and the complete anonymization of the data, the requirement for informed consent was waived.

according to the principles of the Declaration of Helsinki. This study was conducted and is reported in accordance with the Reporting of studies Conducted using Observational Routinely-collected Data (RECORD) guideline.

Data Collection

Case data of the children with MPP were collected, including: (1) general clinical characteristics, including age, gender, underlying diseases, length of hospital stay, co-infection status, disease progression and outcome; (2) physical examination results, such as respiratory rate, heart rate and breath sounds; (3) laboratory indicators: CRP, D-D, ESR, FIB, hemoglobin (Hb), LDH, LYMP, MONO, NEUT, PCT, PLT, red blood cell count (RBC) and WBC; (4) imaging examination results. All laboratory tests were completed within 24 hours after admission. Based on the laboratory data, CLR, LMR, NLR, NPR, PIV, PLR, SII and SIRI were calculated.^{5,6}

Statistical Analysis

General Data Analysis

Using SPSS 26.0 to analyse clinical data. Having conducted the Shapiro–Wilk normality test on measurement data, represent data with a normal distribution as mean $\pm$ standard deviation, and use the *t*-test for comparisons between groups. Non-normal data was expressed as median (interquartile range) [M (P25, P75)], and was employed by the Mann–Whitney *U*-test for comparisons between groups. Presenting count data as frequency (%), and utilizing the χ^2 -test or Fisher's exact test for comparisons between groups. Using R 4.4.2 to completely analyse correlation. Statistical significance was defined as a two-tailed $P < 0.05$ for all analyses.

Construction of the Prediction Model

This study adopted a phased screening strategy to construct a prediction model. First, variables were initially screened through univariate analysis ($P < 0.05$). Then, collinear features were compressed via LASSO regression (the λ value was optimized by ten-fold cross-validation), and variables with non-zero coefficients were selected to be included in the multivariate logistic regression to identify independent risk factors. Finally, a nomogram was constructed based on the R software to achieve individualized prediction.

Model Validation and Evaluation

The receiver operating characteristic (ROC) curve and AUC quantified the model's discriminative ability. Bootstrap resampling with 1000 repetitions conducted internal validation. Calibration curves integrated with the Hosmer–Lemeshow test assessed model accuracy, while decision curve analysis (DCA) evaluated clinical utility.

Results

Study Population

This study enrolled 1791 children with MPP, including 512 cases in the SMPP group and 269 in the RMPP group; the remaining 1180 children who did not meet the inclusion criteria for these two groups were classified into the general MPP (GMPP) group. Mentionly, 170 children included in the study met both the diagnostic criteria for SMPP and RMPP. The comparison results of the baseline characteristics of the three groups of children and all candidate predictors (including traditional indicators and eight novel composite inflammatory indicators) are presented in [Table 1](#).

SMPP Prediction Model

Model Construction

Fifteen variables with $P < 0.05$ in the univariate analysis were included in the LASSO regression; through ten-fold cross-validation ($\lambda = 0.020$), 14 variables with non-zero regression coefficients were selected; subsequently, a multivariate logistic regression analysis served as conducted ([Figure 1A, B](#), and [Table 2](#)). Based on the results of the multivariate logistic regression analysis, Hb, PLT, D-D, FIB, LMR, NPR, SII, duration of cough, and duration of fever were finally included as independent risk factors for SMPP ($P < 0.05$). To further evaluate the multicollinearity among variables, the variance inflation factors (VIFs) were calculated. All VIF values ranged from 1.02 to 2.10, which were far lower than the

Table 1 Comparison of Baseline Characteristics Among the Three Groups

Variables	GMPP (n = 1180)	SMPP (n = 512)	RMPP (n = 269)	P1	P2
Age (years)	6.00 (4.00, 8.00)	6.00 (5.00, 8.00)	6.00 (5.00, 8.00)	0.098	0.651
Weight (kg)	23.00 (19.00, 30.00)	25.00 (19.00, 29.00)	24.50 (20.00, 29.50)	0.066	0.122
Sex				0.744	0.439
Male	566 (47.97%)	250 (48.83%)	122 (45.35%)		
Female	614 (52.03%)	262 (51.17%)	147 (54.65%)		
WBC (10 ⁹ /L)	7.79 (5.60, 9.67)	7.55 (5.86, 10.15)	7.93 (6.36, 9.77)	0.961	0.256
NEUT (10 ⁹ /L)	3.73 (2.51, 5.05)	3.73 (2.54, 4.65)	3.93 (2.45, 4.87)	0.787	0.987
LYMP (10 ⁹ /L)	1.98 (1.50, 2.96)	2.04 (1.60, 2.49)	1.94 (1.60, 2.47)	0.840	0.295
MONO (10 ⁹ /L)	0.51 (0.36, 0.72)	0.52 (0.38, 0.73)	0.57 (0.44, 0.87)	0.113	<0.001
RBC (10 ¹² /L)	4.43 (4.14, 4.73)	4.39 (4.14, 4.60)	4.32 (4.07, 4.55)	0.003	<0.001
Hb (g/L)	126.00 (119.00, 131.00)	124.00 (121.00, 127.00)	119.00 (109.00, 123.00)	<0.001	<0.001
PLT (10 ⁹ /L)	337.50 (279.00, 384.00)	270.50 (178.00, 349.25)	350.00 (187.00, 408.00)	<0.001	0.878
ESR (mm/h)	19.20 (12.90, 29.90)	23.00 (13.00, 32.80)	24.90 (10.90, 33.10)	0.078	0.170
D-D (ng/mL)	450.00 (350.00, 610.00)	515.00 (330.00, 820.00)	540.00 (240.00, 780.00)	<0.001	0.734
LDH (U/L)	273.85 (239.07, 329.00)	282.50 (217.00, 353.25)	264.00 (194.00, 330.00)	0.640	<0.001
CRP (mg/L)	6.28 (2.04, 15.03)	7.87 (3.93, 19.68)	8.00 (5.62, 21.44)	<0.001	<0.001
FIB (g/L)	3.75 (3.30, 4.38)	3.83 (3.39, 4.83)	4.63 (3.58, 7.06)	<0.001	<0.001
PCT (ng/mL)	0.01 (0.01, 0.10)	0.02 (0.01, 0.04)	0.02 (0.01, 0.04)	0.794	0.274
CLR	2.79 (0.79, 7.95)	3.86 (1.36, 10.71)	3.84 (2.77, 12.12)	<0.001	<0.001
LMR	4.02 (3.04, 5.57)	3.92 (2.58, 5.71)	3.34 (2.17, 4.82)	0.017	<0.001
NLR	1.61 (1.02, 2.58)	1.91 (1.15, 2.61)	1.85 (1.16, 2.63)	0.087	0.159
NPR	1.17 (0.71, 1.56)	1.34 (0.99, 1.97)	1.21 (0.77, 1.82)	<0.001	0.014
PIV	254.80 (162.18, 469.43)	249.97 (121.65, 411.85)	293.39 (184.85, 520.88)	0.014	0.026
PLR	162.53 (115.93, 224.10)	124.95 (87.03, 176.17)	156.67 (102.58, 220.12)	<0.001	0.059
SII	544.39 (331.21, 887.84)	466.86 (276.46, 720.72)	480.09 (306.96, 860.10)	<0.001	0.152
SIRI	0.78 (0.48, 1.42)	1.00 (0.56, 1.61)	1.03 (0.60, 1.83)	0.002	<0.001
Duration of cough (days)	12.00 (9.00, 14.00)	14.00 (12.00, 21.00)	16.00 (13.00, 21.00)	<0.001	<0.001
Duration of fever (days)	7.00 (5.00, 9.00)	8.00 (7.00, 10.00)	10.00 (8.00, 12.00)	<0.001	<0.001

Notes: P1: Comparison between the GMPP group and the SMPP group; P2: Comparison between the GMPP group and the RMPP group.

generally recognized critical value of 10, indicating that collinearity would not affect the model’s stability. Based on this, a nomogram model for predicting the risk of SMPP was constructed (Figure 2).

Model Evaluation

The AUC of the model was 0.803 (95% CI: 0.778–0.827), and the AUC after bootstrap validation was 0.796 (95% CI: 0.763–0.829), indicating that the model had good discriminatory ability (Figure 3A). The calibration curve showed that the predicted probability was close to the actual probability; the Hosmer-Lemeshow test suggested that the model had a high goodness-of-fit ($P = 0.060$) (Figure 3B). The DCA curve showed that this predictive model could bring clinical benefits to patients within a wide range of threshold probabilities (Figure 3C).

RMPP Prediction Model

Model Construction

LASSO regression screened out 13 characteristic variables (Figure 1C and D). Multivariate logistic regression analysis further identified 7 independent risk factors, which were Hb, CRP, FIB, LMR, NPR, duration of cough, and duration of fever ($P < 0.05$, Table 3). A nomogram model served as constructed based on the above 7 independent risk factors (all VIF < 1.18, Figure 4).

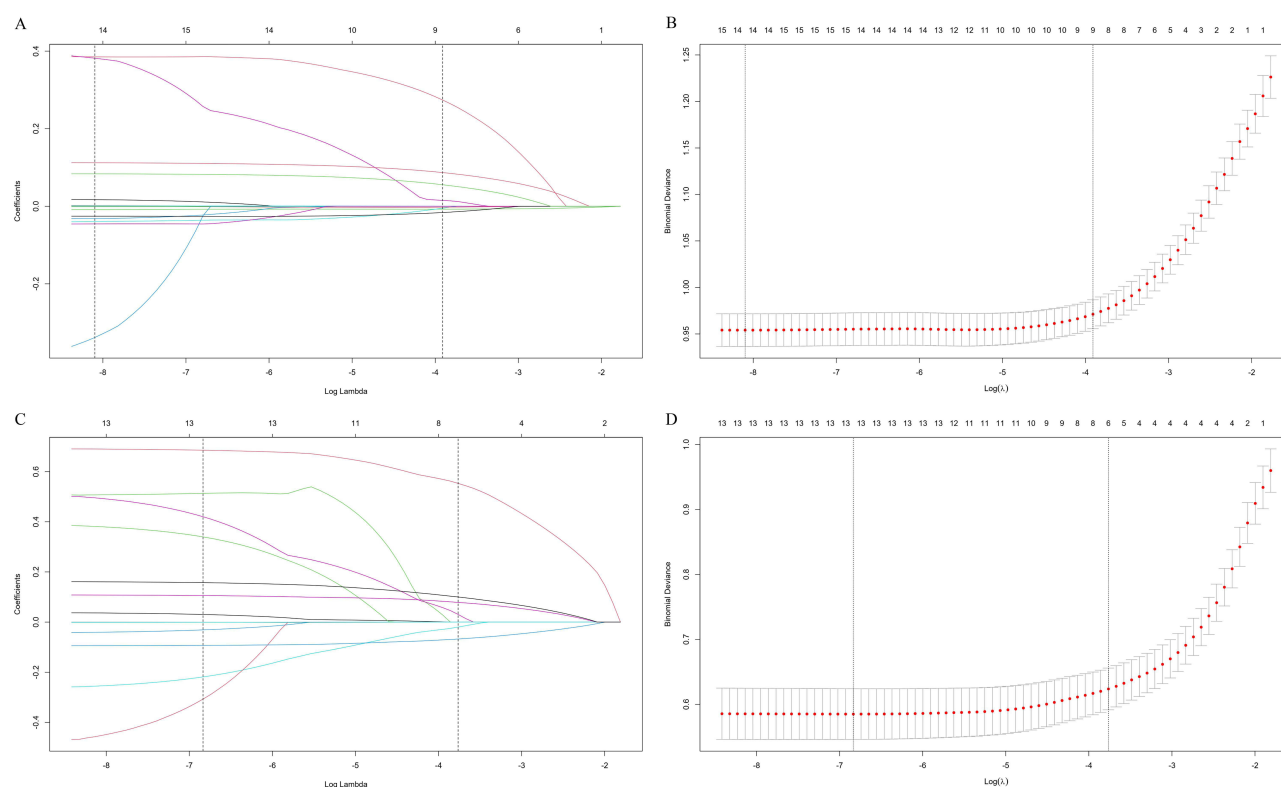


Figure 1 Variable selection trajectory of LASSO regression: (A) LASSO coefficient curve of the SMPP; (B) cross-validation plot of the SMPP; (C) LASSO coefficient curve of the RMPP; (D) cross-validation plot of the RMPP.

Model Evaluation

The AUC of the model was 0.889 (95% CI: 0.867–0.911), and the AUC after bootstrap validation was 0.884 (95% CI: 0.850–0.913), indicating good discriminatory ability (Figure 3D). The calibration curve and the Hosmer-Lemeshow test ($P = 0.375$) confirmed that the model had good calibration (Figure 3E). The DCA curve showed that the model had significant clinical utility in predicting RMPP (Figure 3F).

Table 2 Multivariate Logistic Regression Analysis of SMPP

Variables	β	S.E	Z	P	Adjusted OR (95% CI)
RBC	-0.05	0.14	-0.33	0.743	0.96 (0.73–1.26)
Hb	-0.03	0.01	-3.28	0.001	0.97 (0.96–0.99)
PLT	-0.01	0.00	-6.20	<0.001	0.99 (0.99–0.99)
D-D	0.01	0.00	2.51	0.012	1.01 (1.01–1.01)
CRP	0.02	0.01	1.43	0.153	1.02 (0.99–1.04)
FIB	0.39	0.06	6.39	<0.001	1.47 (1.31–1.66)
CLR	-0.03	0.02	-1.62	0.106	0.97 (0.93–1.01)
LMR	-0.04	0.02	-2.03	0.043	0.96 (0.92–0.99)
NPR	0.41	0.15	2.75	0.006	1.50 (1.12–2.01)
PIV	0.00	0.00	1.71	0.088	1.00 (1.00–1.00)
SII	-0.01	0.00	-3.44	<0.001	0.99 (0.99–0.99)
SIRI	-0.44	0.29	-1.53	0.126	0.64 (0.37–1.13)
Duration of cough	0.11	0.01	8.54	<0.001	1.12 (1.09–1.15)
Duration of fever	0.08	0.02	4.98	<0.001	1.09 (1.05–1.12)

Abbreviations: β , Beta Coefficient; S.E, Standard Error; Z, Z-statistic; P, P-value; Adjusted OR, Adjusted Odds Ratio; CI, Confidence Interval.

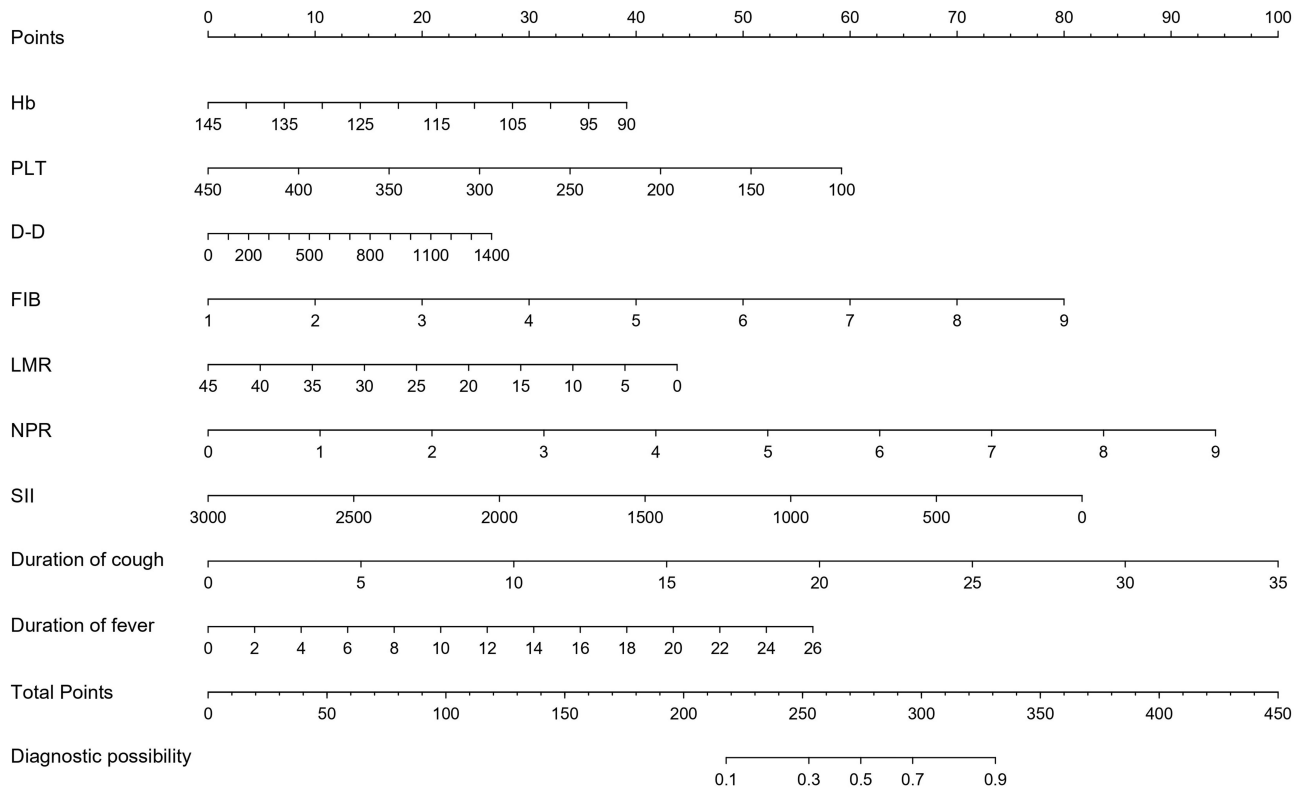


Figure 2 Nomogram for predicting the risk of SMPP.

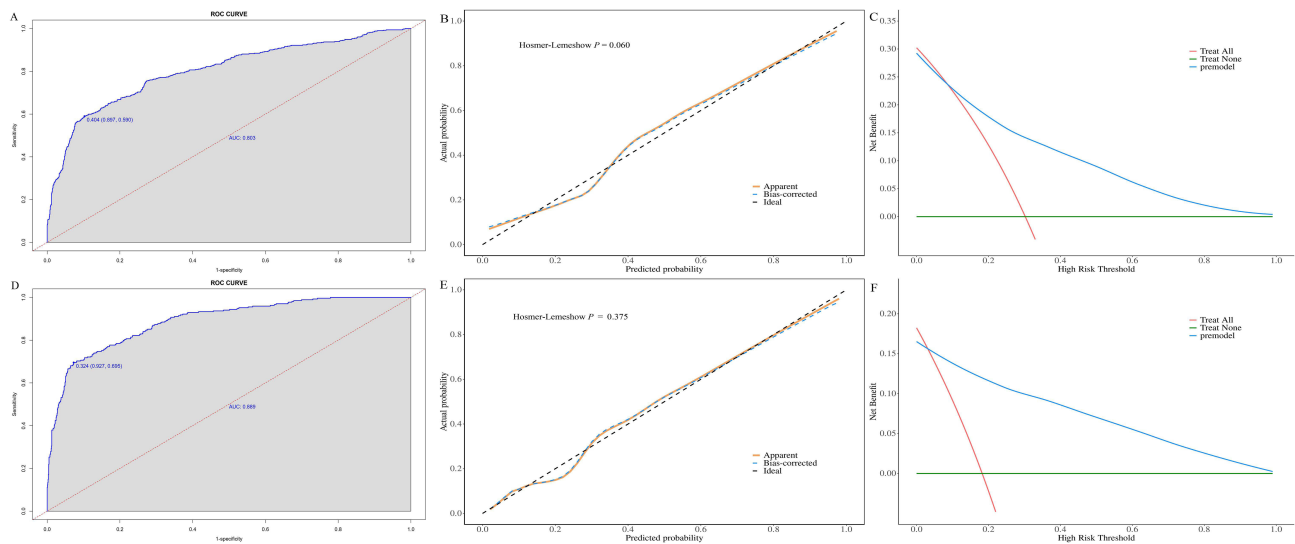


Figure 3 Model evaluation: (A) ROC curve of SMPP; (B) calibration curve of SMPP; (C) DCA curve of SMPP; (D) ROC curve of RMPP; (E) calibration curve of RMPP; (F) DCA curve of RMPP.

Discussion

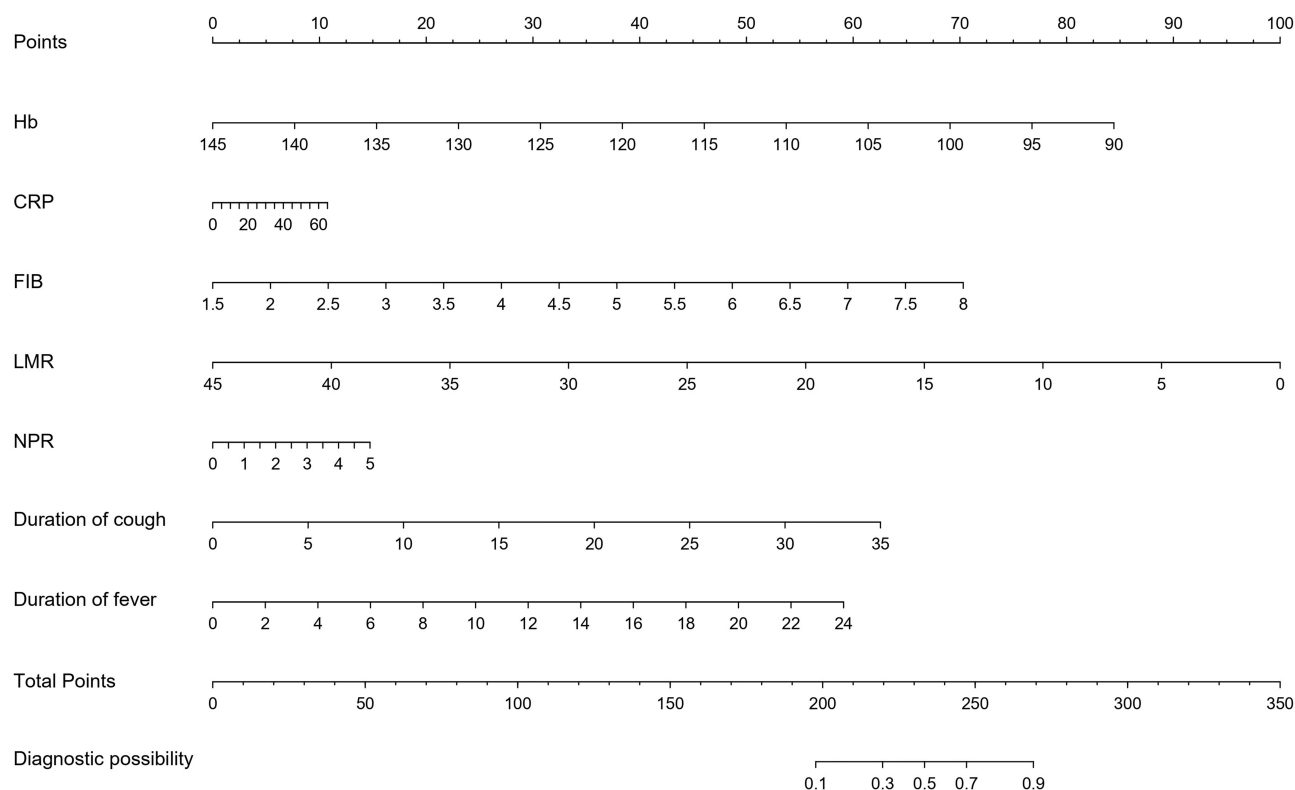
Although MPP often shows a self-limited course, some children may progress to SMPP or RMPP, leading to serious complications or sequelae; therefore, constructing a dynamic prediction model for the progress of MPP in children so that early identifying high-risk children, and providing timely intervention is of great significance for improving the prognosis of children with MPP. This study broke through the traditional research framework of single biomarkers and, for the first

Table 3 Multivariate Logistic Regression Analysis of RMPP

Variables	β	S.E	Z	P	Adjusted OR (95% CI)
MONO	0.50	0.41	1.22	0.224	1.66 (0.73–3.73)
RBC	0.40	0.22	1.82	0.069	1.49 (0.97–2.29)
Hb	−0.09	0.01	−8.91	<0.001	0.91 (0.89–0.93)
LDH	−0.00	0.00	−0.90	0.367	1.00 (1.00–1.00)
CRP	0.04	0.02	2.40	0.017	1.04 (1.01–1.07)
FIB	0.69	0.08	8.82	<0.001	2.00 (1.71–2.33)
CLR	−0.04	0.03	−1.67	0.095	0.96 (0.91–1.01)
LMR	−0.27	0.08	−3.60	<0.001	0.76 (0.66–0.88)
NPR	0.53	0.22	2.42	0.016	1.70 (1.11–2.61)
PIV	−0.00	0.00	−0.23	0.816	1.00 (1.00–1.00)
SIRI	−0.53	0.47	−1.12	0.264	0.59 (0.23–1.49)
Duration of cough	0.11	0.02	6.15	<0.001	1.11 (1.08–1.15)
Duration of fever	0.16	0.02	6.55	<0.001	1.18 (1.12–1.23)

Abbreviations: β , Beta Coefficient; S.E, Standard Error; Z, Z-statistic; P, P-value; Adjusted OR, Adjusted Odds Ratio; CI, Confidence Interval.

time, systematically evaluated the predictive efficacy of traditional inflammatory indicators and eight composite inflammatory indicators for SMPP and RMPP in children, which successfully constructed a stratified prediction model integrating multi-dimensional parameters that significantly improved the predictive efficacy. The study adopted a phased modeling strategy in which candidate variables were first screened through univariate analysis, then LASSO regression was used to eliminate multicollinearity and retain key predictors, and finally nine independent risk factors for SMPP and seven independent risk factors for RMPP were respectively determined via multivariate logistic regression. The validation results showed that the AUCs of the prediction models for SMPP and RMPP reached 0.803 and 0.889

**Figure 4** Nomogram for predicting the risk of RMPP.

respectively, and the calibration curves, Hosmer-Lemeshow test, bootstrap internal validation, and DCA curve together confirmed the robustness and clinical applicability of the models. This multi-dimensional analysis strategy provides a brand-new perspective for the precise classification of MPP, and is of prime importance for the formulation of clinical treatment plans and the selection of antibiotics during the diagnosis and treatment of the disease.

Although the specific pathogenesis of SMPP and RMPP has not been fully elucidated, their underlying mechanisms may be the combined effects of the host's excessive inflammatory response to MP infection, coagulation dysfunction, and immune imbalance. In the model constructed in this study, six indicators, including a decrease in Hb, an increase in NPR, a prolonged duration of fever and cough, an increase in FIB, and a decrease in LMR, jointly revealed the common pathological mechanisms of SMPP and RMPP. Among them, a decrease in Hb, a prolonged duration of cough and fever, and an increase in NPR indicate the occurrence of an excessive inflammatory response. Some studies have shown that MP infection activates the TLR2/4 pathway of alveolar macrophages, leading to the release of pro-inflammatory factors such as IL-6 and IL-8, and triggering a "cytokine storm".¹⁰ In addition, the elevation of NPR may be the result of the combined effects of the formation of neutrophil-platelet aggregates and platelet activation, suggesting the occurrence of platelet adhesion, release of inflammatory mediators, and activation of coagulation.^{11,12} In terms of coagulation indicators, an elevated FIB level indicates coagulation dysfunction.¹³ In terms of immune indicators, a decreased LMR indicates excessive activation of monocytes-macrophages and a reduction in lymphocytes, which may be related to lymphocyte apoptosis or migration. To sum up, the above-mentioned key indicators screened by the prediction model constructed in this study provide direct clinical evidence to support the existence of a common "triple-hit" pathophysiological mechanism (excessive inflammatory response, coagulation dysfunction, and immune imbalance) between SMPP and RMPP. However, in clinical practice, there are differences in the phenotypic characteristics and outcomes between SMPP and RMPP, suggesting that there may also be unique driving factors for each of them.

For SMPP, the significantly elevated D-D, decreased PLT, and reduced SII independently included in the model are prominent features that distinguish it from RMPP. D-D, as the terminal product of cross-linked fibrinogen degradation, with its elevated level indicating the widespread and active formation and dissolution of fibrin in the body, serves as the direct evidence of microthrombus formation and tissue damage.¹⁴ PLT, which plays a crucial role in the pathogenesis of inflammation-induced coagulation activation, may lead to thrombocytopenia in severe cases due to increased consumption, reduced production, and immune destruction in microthrombi, and this phenomenon is also consistent with the predictive value of decreased PLT in the model. Combined with elevated FIB, these indicators collectively illustrate a more pronounced tendency towards disseminated intravascular coagulation and microcirculatory disturbances in SMPP, which pathophysiological state may also underlie the key mechanism for its earlier and more frequent development of extensive pulmonary consolidation, pleural effusion, and even extrapulmonary thrombotic complications (such as cerebral infarction). Notably, although an elevated SII usually indicates aggravated inflammation, a slight decrease in SII in the model of this study may reflect PLT consumption rather than alleviated inflammation. In contrast, the most prominent characteristic of the RMPP model is the persistent elevation of CRP. As a key acute-phase reactant, a persistently high level of CRP indicates uncontrolled pathogen activity and/or dysregulated innate immunity, which directly explains the poor efficacy under the standardized treatment with macrolides. The underlying mechanism may involve the impaired function of macrophages in clearing intracellular MP and the Treg-mediated inhibition of inflammation resolution.¹⁵ The identification of these unique indicators provides important biological clues for understanding the different clinical courses and complication risks of SMPP and RMPP.

The prediction models of SMPP and RMPP constructed in this study have significant clinical implications. By integrating routine laboratory indicators, composite inflammatory indicators, and clinical features such as the duration of fever and cough, the model can achieve rapid and non-invasive risk stratification at the early stage of admission. Individualized risk assessment based on the nomogram can provide a direct basis for real-time triage and treatment decisions in pediatric wards: For children at high risk of SMPP, it is recommended to increase the level of nursing care, strengthen the monitoring of coagulation function and extrapulmonary complications, and initiate anti-inflammatory or anticoagulant adjuvant therapy at an early stage; for children at high risk of RMPP, it indicates that attention should be paid to macrolide resistance, and a timely switch to second-line antibiotics should be made to avoid protracted illness. In addition, this study systematically evaluated the value of multiple composite inflammatory indicators in predicting SMPP/RMPP in children for the first time, and confirmed the independent effects of LMR, NPR, and SII. However, the study has some limitations: the retrospective single-center design may introduce selection bias and limit the extrapolation of the results; some potential confounding factors, such as differences

in pre-admission treatment among children, regional differences in MP resistance, and physiological differences in inflammatory indicators across different age groups, have not been fully incorporated into the analysis; only the baseline data at admission were used, lacking the evaluation of the dynamic changes of the indicators. In the future, multicenter prospective studies should be conducted to integrate treatment history, regional drug-resistance data, dynamic monitoring indicators, and age-stratified parameters, so as to further enhance the generalization ability and clinical application value of the model.

Conclusion

This study has confirmed that novel composite inflammatory indicators such as LMR, NPR, and SII can significantly enhance the early prediction ability for SMPP and RMPP in children. The risk prediction model constructed by integrating routine indicators has achieved a preliminary discrimination of disease severity and treatment response. This research fills the knowledge gap in the field of MPP risk prediction, provides a clinical tool for shifting from single-indicator assessment to multi-dimensional integration, and offers new strategies for early intervention and individualized treatment.

Abbreviations

AUC, areas under the curve; CLR, CRP-to-lymphocyte ratio; CRP, C-reactive protein; DCA, decision curve analysis; ESR, erythrocyte sedimentation rate; FIB, fibrinogen; GMPP, general MPP; Hb, hemoglobin; KD, Kawasaki disease; LMR, lymphocyte-to-monocyte ratio; LYMP, lymphocyte count; MONO, monocytes count; MP, Mycoplasma pneumoniae; MPP, Mycoplasma pneumoniae pneumonia; NEUT, neutrophil count; NLR, Neutrophil-lymphocyte ratio; NPR, neutrophil-to-platelet ratio; PCT, procalcitonin; PIV, pan-immune-inflammation value; PLR, platelet-lymphocyte ratio; PLT, platelet count; RBC, red blood cell count; RMPP, refractory MPP; ROC, receiver operating characteristic; SII, systemic inflammation index; SIRI, systemic inflammatory response index; SMPP, severe MPP; TLR2/4, Toll-like receptor 2/4; WBC, white blood cells.

Data Sharing Statement

The datasets generated and analyzed during the current study are not publicly available due to patient privacy restrictions but are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

This study was approved by the Medical Ethics Committee of the Affiliated Hospital of Qingdao University (Approval Number: QYFYWZLL29996). Given its retrospective design and the complete anonymization of the data, the requirement for informed consent was waived by the same ethics committee in accordance with the principles of the Declaration of Helsinki.

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Author Contributions

Guo Zhen Fan: Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Writing-original draft; Yu Hui Zhu: Data Curation, Investigation, Software, Validation, Visualization, Writing-original draft; Li Xin Hu: Data Curation, Investigation, Software, Validation, Visualization, Writing-original draft; Zheng Hai Qu: Conceptualization, Data curation, Resources, Supervision, Writing-review & editing; Yin Bo Liu: Conceptualization, Formal analysis, Investigation, Supervision, Validation, Project administration, Writing-review & editing. All authors took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

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