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Clinical Characteristics and Disease Severity Analysis of Mycoplasma pneumoniae Pneumonia in Guangxi ChildrenCarrying Drug-Resistant Genes: A Retrospective Clinical Study

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Abstract

Objective: To investigate the clinical characteristics of Mycoplasma pneumoniae pneumonia (MPP) in children from Guangxi carrying drug-resistant genes and to identify risk factors for predicting severe cases.
Methods: A total of 621 pediatric patients with drug-resistant gene-positive MPP who were hospitalized in the Department of Pediatrics, Maternal and Child Health Hospital of Guangxi Zhuang Autonomous Region, between December 2022 and June 2024 were retrospectively enrolled. According to diagnostic criteria, the patients were divided into mild and severe groups. Clinical data from the two groups were compared to analyze the correlation between clinical features and disease severity in MPP children carrying drug-resistant genes.

Result：A total of 621 cases were included, among which 321 were male (51.7%) and 300 were female (48.3%). The cases were divided into two groups: mild cases (535 cases, 86.2%) and severe cases (86 cases, 13.8%), without specific collection based on the month of onset. Among the MPP patients carrying drug-resistant genes, the age of the severe cases was younger than that of the mild cases, with a statistically significant difference ($P < 0.001$), but there was no statistically significant difference in gender between the two groups ($P > 0.05$). The severe cases were more likely to have extrapulmonary rash and wheezing than the mild cases, with a statistically significant difference ($P < 0.05$). The WBC count, PLT count, LDH and D-Dimer levels were higher in the severe cases than in the mild cases, with statistically significant differences ($P < 0.05$). There were no statistically significant differences in the types of changes in imaging and bronchoscopy between the two groups ($P > 0.05$). The results of binary Logistic regression analysis showed that age, extrapulmonary rash, wheezing and LDH were independent influencing factors for the occurrence of severe cases in patients with positive drug-resistant genes ($P < 0.05$).

Conclusion: The younger the age, the more likely children with MPP carrying drug-resistant genes are to progress to severe cases. Laboratory results such as WBC count, PLT count, LDH, and D-Dimer can be used as predictive indices for severe MPP. Age, extrapulmonary rash, wheezing, and LDH are independent risk factors for severe cases, which can predict disease progression to a certain extent and provide a scientific theoretical basis for timely and effective intervention.

Clinical trial number: not applicable.

Introduction

Mycoplasma pneumoniae pneumonia (MPP) is usually a benign and self-limiting disease. Mycoplasma pneumoniae (MP) is a common pathogen causing community-acquired pneumonia in children. In the past, macrolide antibiotics were the first-line treatment for Mycoplasma pneumoniae in clinical practice and achieved ideal results. However, in recent years, with the extensive use of these drugs, the resistance rate of macrolide antibiotics has been increasing. Despite the early use of appropriate antibiotics in cases of Mycoplasma pneumoniae infection, persistent fever and worsening symptoms

may still occur, leading to serious complications. With the development of science and technology, the wide application of pathogen-targeted sequencing and other technologies, the detection results of macrolide resistance genes have been widely known to medical staff. This study aims to analyze the clinical characteristics of children with Mycoplasma pneumoniae pneumonia carrying resistance genes (macrolide-resistant Mycoplasma pneumoniae pneumonia, MRMP), explore the related factors of severe Mycoplasma pneumoniae pneumonia, provide early warning plans for clinical treatment, and intervene and treat early to reduce the sequelae of severe Mycoplasma pneumoniae pneumonia, providing scientific theoretical basis.

Materials and Methods

Research Subjects

878 children with mycoplasma pneumonia were selected from those hospitalized in the Pediatrics Department of Guangxi Zhuang Autonomous Region Maternal and Child Health Hospital from December 2022 to June 2024. 621 cases (70.7%) of children with mycoplasma pneumonia were identified who carried drug-resistant genes; among them, 321 cases (51.7%) were male and 300 cases (48.3%) were female; according to the diagnostic criteria, they were divided into two groups: mild and severe, with 535 cases (86.2%) in the mild group and 86 cases (13.8%) in the severe group.

Diagnosis and Inclusion Criteria

Inclusion Criteria: (1) Select children aged ≤ 14 years. (2) Meet the diagnostic criteria for mycoplasma pneumoniae pneumonia as agreed upon by experts [1]. (3) Positive MP-DNA detected by PCR in throat swabs or BALF. (4) Complete clinical data of the patients. (5) Able to tolerate and cooperate with the operation of the video electronic flexible endoscopy. (6) Parents of the patients understand and express their support and cooperation for the treatment.

Exclusion criteria: (1) Before enrollment, had underlying lung diseases such as bronchopulmonary dysplasia, tuberculosis, or obliterative bronchiolitis; (2) Had congenital immune dysfunction disorders and received corticosteroid and/or human immunoglobulin treatment before admission; (3) Had major diseases in other systems that affected the experimental results (cardiovascular complications including heart failure; neurological involvement including epilepsy, intracranial hemorrhage, and encephalitis; digestive system complications including liver failure, gastritis); (4) Had contraindications for visual electronic flexible bronchoscopy; (5) Had poor compliance and did not cooperate with treatment.

Grouping

The positive group of macrolide resistance genes (23SrRNA V region A2063G, A2617G, A2067G, and A2064G mutation genes) was grouped according to the type of disease.

Severe group

The enrolled cases were defined as those with one of the following symptoms of MPP [2, 3] (1) An increased respiratory rate under normal air conditions: < 60 breaths/min for infants under 2 months; 50 breaths/min for infants aged 2 months to 5 years; 40 breaths/min for children aged 1 to 5 years; 30 breaths/min for those over 5 years; excluding the influence of factors such as fever and crying; (2) Difficulty breathing and cyanosis, intermittent apnea, respiratory grunting; (3) Involvement of multiple lung lobes or ≥ 2/3 of the lung lobes; (4) Extrapulmonary complications; (5) Pleural effusion; (6) Under normal air conditions, arterial blood oxygen saturation (SaO2) ≤ 0.92 (sea level) [4].

Mild case group

All the enrolled cases except those of severe type

Research Methods

Patients who meet the criteria for the study subjects are admitted to the hospital. Medical history collection and physical examination are conducted. Sputum or BALF is used for detecting the drug resistance genes of Mycoplasma pneumoniae. On the first day of admission, blood routine, CRP, LDH, NLR, PLR, SII, SIRI, lung CT and other examinations are completed. By comparing the clinical symptoms, types of lung imaging [5, 6], laboratory tests, the therapeutic effect of macrolide drugs, and the mucosal changes under bronchoscopy in each group, the current drug resistance status of MPP is discovered and the factors related to the clinical severity are analyzed.

Detection of MP-DNA using throat swabs or BALF: Collect throat swabs or BALF from the research subjects. Extract the nucleic acid using an automatic nucleic acid extraction instrument (Jiangsu Shoushi SSNP-9600A). Use the pneumococcal mycoplasma nucleic acid detection kit (Guangzhou Da'an Genomics Co., Ltd.; PCR fluorescent probe method) for MP-DNA detection. The specific PCR amplification detection conditions are as follows: 2 minutes at 93℃, 45 seconds at 93℃ → 60 seconds at 55℃ → 30 cycles, 30 seconds at 93℃ → 45 seconds at 55℃ → 30 cycles. The fluorescence collection point is selected within 45 seconds at 55℃. Operate strictly according to the instrument and reagent instructions.

Statistical Methods5 Statistical Methods

The statistical analysis and charting of the data were conducted using IBM SPSS 25.0 software, R 4.3.3 and MedCalc software. Quantitative data were tested for normality using the Shapiro-Wilk test based on sample size. Data that met the normal distribution were described using (mean ± standard deviation), and comparisons between groups were conducted using the two independent samples t-test; data that did not meet the normal distribution were described using Median (P25, P75), and comparisons between groups were conducted using the two independent samples rank sum test. Qualitative data were described using [n(%)], and comparisons between groups were conducted using the chi-square test. When T < 1, the Fisher exact probability method was used. Multivariate analysis was performed using the binary Logistic regression model, with variable selection based on difference comparison and LASSO

regression. Then, collinearity diagnosis was conducted for the included independent variables in the multivariate analysis, and VIF > 10 indicated severe collinearity and was not suitable for inclusion. Hosmer-Lemeshow test was used to evaluate the goodness of fit of the binary Logistic regression model, and the receiver operating characteristic curve (ROC) was used to analyze the predictive efficacy of single variables and multiple variables jointly predicting the occurrence of severe illness in patients with positive drug resistance genes. All statistics were considered statistically significant when $P < 0.05$.

Results

Comparison of Age and Gender Data

There was a statistically significant difference in age between the severe group and the mild group ($P < 0.05$). The patients in the severe group were younger than those in the mild group, but there was no statistically significant difference in gender between the two groups ($P > 0.05$). (See Table 1)

Table 1
Comparison of Demographic Data Between Mild and Severe Groups Among Patients Positive for Drug-Resistance Genes[n = 621]

Severity Level	**Number of Cases**	**Age(years)**	**Gender,n(%)**	
		M(P25, P75)	□	□
Mild Group	535	6.00(3.69, 7.48)	278(52.0)	257(48.0)
Severe Group	86	4.67(2.67, 6.96)	43(50.0)	43(50.0)
Z/X^2 Value		-6.024	0.114	
P Value		< 0.001	0.735	

Comparison of Clinical Characteristics

The proportion of patients in the severe group with extrapulmonary rashes and wheezing was higher than that in the mild group, and the difference was statistically significant ($P < 0.05$). (See Table 2)

Table 2
Comparison of Clinical Characteristics Between Mild and Severe Groups Among Patients Positive for Drug-Resistance Genes[n = 621]

Severity Level	**Mild Group n = 535**	**Severe Group n = 86**	X^2 **Value**	**P Value**
Fever≥7Days n(%)	235(43.9)	37(43.0)	0.024	0.876
Extrapulmonary Rash n(%)	3(0.6)	5(5.8)	12.213	< 0.001
Crackle n(%)	387(78.2)	67(91.8)	7.334	0.007
Wheezing n(%)	50(9.3)	35(40.7)	61.644	< 0.001

Comparison of Blood Cell Classification and Blood Biochemical Indicators

The WBC count, PLT count, LDH and D-D levels of patients in the severe group were higher than those in the mild group, and the differences were statistically significant (P < 0.05). (See Table 3)

Table 3
Comparison of Blood Cell Classification and Biochemical Indicators Between Mild and Severe Groups [n = 621]

Severity Level	Mild Group n = 535	Severe Group n = 86	Z Value	P Value
WBC Count (×10⁹/L) M(P25, P75)	7.80(6.30, 9.80)	8.20(6.78, 11.13)	-2.690	0.030
Neutrophil Count (×10⁹/L) M(P25, P75)	4.41(3.30, 5.73)	4.68(3.45, 6.49)	-1.551	0.121
Lymphocyte Count (×10⁹/L) M(P25, P75)	2.23(1.72, 3.15)	2.56(1.68, 4.24)	-1.508	0.131
PLT Count (×10⁹/L) M(P25, P75)	308.00(247.00, 388.00)	367.00(283.00, 454.75)	-3.668	< 0.001
M Count (×10⁹/L) M(P25, P75)	0.60(0.45, 0.82)	0.55(0.40, 0.84)	-1.380	0.167
NLR M(P25, P75)	1.93(1.26, 2.83)	1.83(0.94, 3.28)	-0.032	0.974
PLR M(P25, P75)	131.22(99.16, 180.34)	126.89(91.31, 194.30)	-0.119	0.905
SII M(P25, P75)	597.83(385.00, 894.41)	608.32(346.06, 1124.31)	-1.348	0.178
SIRI M(P25, P75)	1.15(0.71, 1.80)	0.95(0.50, 2.15)	-0.996	0.319.0
CRP M(P25, P75)	9.14(5.12, 21.48)	8.65(3.68, 19.10)	-1.256	0.209
LDH M(P25, P75)	301.00(268.00, 342.00)	334.50(298.00, 400.00)	-4.555	< 0.001
D-D M(P25, P75)	480.00(340.00, 660.00)	510.00(390.00, 812.50)	-2.172	0.030

Comparison of Imaging Patterns

No statistically significant differences in imaging pattern distributions were observed between the mild and severe groups (P > 0.05), suggesting that imaging features alone may not serve as reliable indicators for distinguishing disease severity. Detailed data are presented in Table 4.

Table 4
Comparison of Imaging Patterns Between Mild and Severe Groups Among Patients Positive for Drug-Resistance Genes [n = 621]

Severity Level	Mild Group n = 535	Severe Group n = 86	X^2 Value	P Value
Consolidation Type n(%)	328(61.3)	46(53.5)	1.891	0.169
Bronchiolar Type n(%)	189(35.3)	38(44.2)	2.507	0.113
Mixed Type n(%)	25(4.7)	7(8.1)	1.182	0.277
Pleural Effusion n(%)	35(6.5)	2(2.3)	2.351	0.125
Hilar Lymphadenopathy n(%)	65(12.1)	7(8.1)	1.162	0.281
Necrotic Type n(%)	3(0.6)	0(0.0)	a	1.000

Comparison of Histopathological Changes Between Mild and Severe Groups

No statistically significant differences were observed in the types of histopathological changes between the mild and severe groups (P > 0.05) (see Table 5).

Table 5
Comparison of microscopic changes between the mild and severe subgroups with positive drug resistance genes[n = 621]

Severity Level	Mild Group n = 535	Severe Group n = 86	X^2 Value	P Value
Mucosal Hyperemia/Edema n(%)	410(76.6)	60(69.8)	1.899	0.168
Longitudinal Mucosal Folds n(%)	240(44.9)	37(43.0)	0.101	0.750
Follicular Hyperplasia n(%)	27(5.0)	2(2.3)	1.232	0.267
Mucosal Erosion/Necrosis with Inflammatory Stenosis n(%)	9(1.7)	0(0.0)	0.526	0.468
Plastic Bronchial Casts n(%)	3(0.6)	0(0.0)	a	1.000
Circular Mucosal Folds n(%)	2(0.4)	1(1.2)	a	0.361
Moderate-to-Large Sputum Volume n(%)	156(29.2)	26(30.2)	0.041	0.839
Small Sputum Volume n(%)	268(50.1)	34(39.5)	3.306	0.069
Note: Fisher's exact test was applied (no χ^2 statistic available).				

Comparison of Medication and Bronchoscopy Treatments Between Mild and Severe Groups

The mild group had a lower proportion of patients receiving levofloxacin and intravenous immunoglobulin (IVIG) compared to the severe group, but required more frequent bronchoscopy interventions ($P < 0.05$ for all comparisons) (see Table 6).

Table 6
Comparison of Treatment Modalities Between Mild and Severe Groups Among Patients Positive for Drug-Resistance Genes[n = 621]

Severity Level	Mild Group n = 535	Severe Group n = 86	X^2 Value	P Value
Macrolides n(%)	493(92.1)	79(91.9)	0.009	0.926
Doxycycline n(%)	56(10.5)	8(9.3)	0.109	0.742
Levofloxacin n(%)	1(0.2)	7(8.1)	30.86	< 0.001
Intravenous Immunoglobulin (IVIG) n(%)	4(0.7)	7(8.1)	19.212	< 0.001
Anticoagulant Therapy n(%)	34(6.4)	9(10.5)	1.942	0.163
Bronchoscopy Procedures n(%)	1.00(1.00, 1.00)	1.00(0.00, 1.00)	-2.016	0.044
Repeated Bronchoscopy n(%)	15(2.8)	3(3.5)	0.00003	0.996

Multivariate Analysis of Drug Resistance Gene Positive Mild and Severe Cases

LASSO Regression

Taking "Y = 0" as mild cases and "Y = 1" as severe cases, 7 variables with P < 0.05 from the analysis of differences in demographic, admission clinical characteristics, and admission imaging types were included in the LASSO regression for analysis: age, extrapulmonary rash, wheezing, WBC count, PLT count, LDH, and D-D. The assignment is shown in Table 7.

The LASSO regression results are shown in Fig. 1. The coefficients of the independent variables initially included in the model were gradually compressed, and finally some of the coefficients of the independent variables were compressed to 0, thereby avoiding overfitting of the model. A 10-fold cross-validation was selected to screen the potential independent influencing factors for the occurrence of severe cases in patients with positive drug resistance genes. The results showed that the variables corresponding to the non-zero coefficients under the optimal parameters were age, extrapulmonary rash, wheezing, PLT count, LDH, and D-D, a total of 6 variables.

Table 7
Variable Assignment for LASSO Regression Analysis

Variable	Factor	Assignment
Age	X1	Continuous variable (raw value, no coding required)
Extrapulmonary rash	X2	0 = Absent; 1 = Present
Wheezing	X3	0 = Absent; 1 = Present
WBC count	X4	Continuous variable (raw value, no coding required)
PLT count	X5	Continuous variable (raw value, no coding required)
LDH	X6	Continuous variable (raw value, no coding required)
D-Dimer	X7	Continuous variable (raw value, no coding required)
Disease severity	Y	0 = Mild; 1 = Severe

Logistic Regression

The six variables selected by LASSO regression were subjected to collinearity diagnosis. The results showed that the VIF of all independent variables was less than 10, as shown in Table 8, indicating no severe collinearity and suggesting that they could be included in the binary Logistic regression model for analysis. The Omnibus test of model coefficients X2 = 107.847, P < 0.001, indicated that the model was valid. The Hosmer-Lemeshow test X2 = 5.885, P = 0.660 > 0.05, suggested good model fit.

The binary Logistic regression analysis results showed that age, extrapulmonary rash, wheezing, and LDH were independent influencing factors for the occurrence of severe disease in patients with positive drug resistance genes (P < 0.05). The higher the age, the lower the risk proportion of severe disease in patients with positive drug resistance genes (OR = 0.793, 95% CI: 0.706–0.890, P < 0.001), and the higher the LDH, the higher the risk proportion of severe disease in patients with positive drug resistance genes (OR = 1.004, 95% CI: 1.002–1.007, P = 0.001). The proportion of severe disease in patients with positive drug resistance genes who had extrapulmonary rash was 11.874 times that of those without (OR = 11.874, 95% CI: 2.341–60.217, P = 0.003). The proportion of severe disease in patients with positive drug resistance genes who had wheezing was 5.657 times that of those without (OR = 5.569, 95% CI: 3.201–9.997, P < 0.001). See Table 9 for details.

Table 8
Collinearity Diagnosis of Independent Variables

Variable	Collinearity statistics	
	Tolerance	VIF (Variance Inflation Factor)
Age	0.852	1.173
Extrapulmonary rash	0.996	1.004
Crackles (wet rales)	0.979	1.021
PLT count	0.919	1.089
LDH	0.687	1.455
D-D	0.732	1.366

Table 9
Binary Logistic Regression Analysis: Factors Influencing the Occurrence of Severe Disease in Patients with Drug-Resistant Gene Positivity

Variable	Regression Coefficient	Standard Error	Wald X2	OR Value	95% CI for OR	*P* Value
Age	-0.233	0.059	15.534	0.793	0.706, 0.890	< 0.001
Extrapulmonary Rash						
No (Reference)	-	-	-	1.000	1.000, 1.000	-
Yes	2.474	0.828	8.921	11.874	2.341, 60.217	0.003
Wheezing						
No (Reference)	-	-	-	1.000	1.000, 1.000	-
Yes	1.733	0.290	35.586	5.657	3.201, 9.997	< 0.001
PLT	0.001	0.001	1.723	1.001	0.999, 1.004	0.189
LDH	0.004	0.001	10.295	1.004	1.002, 1.007	0.001
DD	0.000143	0.000094	2.287	1.000143	0.999958, 1.000328	0.130

OR: Odds Ratio; 95% CI: 95% Confidence Interval; PLT count: Platelet Count; LDH: Lactate Dehydrogenase; D-D: D-DimerOR: Odds Ratio; 95% CI: 95% Confidence Interval; PLT count: Platelet Count; LDH: Lactate Dehydrogenase; D-D: D-Dimer

Predictive Efficacy Evaluation

Receiver Operating Characteristic (ROC) analysis was conducted to evaluate the predictive efficacy of age, extrapulmonary rash, wheezing, and lactate dehydrogenase (LDH) for the occurrence of severe disease in patients with drug-resistant gene positivity. The results are presented in Table 10 and Fig. 2.

The analysis revealed that age, wheezing, and LDH were significant predictors of severe disease ($P < 0.05$), with Area Under the Curve (AUC) values of 0.702, 0.657, and 0.653, respectively. Notably, the combined predictive model incorporating all three variables demonstrated a higher AUC of 0.794, which was significantly greater than the AUCs of individual predictors ($P < 0.05$).

Table 10
Comparative Efficacy of Single and Combined Predictors for Severe Disease in Patients with Drug-Resistant Gene Positivity

Variable	AUC	Standard Error	95% CI for AUC	*P* Value
Age	0.702	0.031	0.664 ~ 0.738	< 0.001
Extrapulmonary Rash	0.526	0.035	0.486 ~ 0.566	0.449
Wheezing	0.657	0.036	0.618 ~ 0.694	< 0.001
LDH	0.653	0.033	0.614 ~ 0.690	< 0.001
Combined prediction	0.794	0.028	0.760 ~ 0.825	< 0.001
Note: AUC: Area Under the Curve; 95% CI: 95% Confidence Interval				

Discussion

Mycoplasma pneumoniae (MP) is currently the smallest prokaryotic microorganism capable of independent survival without a host cell. It is also recognized as one of the smallest pathogenic bacteria of significant clinical importance in childhood respiratory tract infection-related diseases [7]. MP serves as a crucial pathogen in childhood respiratory infections, accounting for 20%–40% of community-acquired pneumonia cases in children, with an even higher incidence in older children and during epidemic seasons. MP infections exhibit a certain degree of self-limitation, with most cases being mild and having a favorable prognosis. However, some infected individuals may progress to pneumonia, often presenting with respiratory symptoms such as fever, cough, and dyspnea. In severe cases, extrapulmonary complications may occur. Macrolide antibiotics are the first-line treatment for MP infections, with clinical symptoms typically improving within 48–72 hours after medication administration.

Since the first report of a macrolide-resistant Mycoplasma pneumoniae (MRMP) strain in Japan in 1968, numerous countries worldwide have successively reported cases of MRMP, with varying incidence rates across different regions [8, 9]. Infections with MRMP often respond poorly to macrolide antibiotics, leading to uncontrolled clinical symptoms and laboratory findings, such as prolonged fever and hospitalization, extended antibiotic treatment duration, increased cough, and worsening chest imaging

results. Some early clinical symptoms and laboratory tests can predict the occurrence of severe cases of MRMP.

This study analyzed the clinical data of hospitalized children with MRMP in our hospital and found no significant difference in the incidence of severe cases between genders. However, younger age was associated with a higher likelihood of developing severe cases following MRMP infection. Binary logistic regression analysis revealed that age was an independent risk factor influencing the occurrence of severe cases in patients with positive drug-resistant genes ($P < 0.05$). The risk of severe cases in patients with positive drug-resistant genes decreased with increasing age. This finding deviates significantly from the risk factors for MP susceptibility in children. A prospective study conducted in Uganda [10] showed that females and children aged > 12 months were more susceptible to MP infection, possibly related to the characteristics of child growth and development and the timing of immune system maturation. Younger children have immature organ development, an underdeveloped immune system, poor respiratory barrier function, and weak pathogen clearance ability, making them more prone to developing severe cases upon MRMP infection.

Children infected with macrolide-resistant Mycoplasma pneumoniae (MRMP) often exhibit prolonged fever and other symptoms, leading to extended hospital stays, increased frequency of corticosteroid use, and so on. Furthermore, there is an elevated risk of disease progression, severe pneumonia, and pulmonary and/or extrapulmonary complications. This study found that patients in the severe group had a higher incidence of extrapulmonary rashes, wheezing, hypoxemia, and the need for mechanical ventilation compared to those in the mild group. Additionally, laboratory test results indicated that the severe group had significantly higher levels of white blood cell (WBC) count, platelet (PLT) count, lactate dehydrogenase (LDH), and D-dimer (D-D) than the mild group, which is consistent with the findings of Huang W et al. [11]. Therefore, D-D, along with WBC, C-reactive protein (CRP), and LDH, can be used in combination to assess disease severity [12, 13].

Binary logistic regression analysis and receiver operating characteristic (ROC) curve analysis revealed that higher LDH levels were associated with an increased risk of severe cases in patients with positive drug-resistant genes. Patients with positive drug-resistant genes who had extrapulmonary rashes were 11.874 times more likely to develop severe cases compared to those without rashes, while those with wheezing were 5.657 times more likely. Thus, extrapulmonary rashes, wheezing, and LDH are independent risk factors influencing the occurrence of severe cases in patients with positive drug-resistant genes ($P < 0.05$). The simultaneous presence of these three factors further increases the likelihood of severe cases.

A foreign study [14] proposed that patients with mucocutaneous diseases following MP infection had a longer duration of fever in the early stage and were at a higher risk of requiring oxygen therapy and developing sequelae. Meanwhile, Fan F et al. [15] also suggested that interleukin-6 (IL-6) levels and LDH activity are good predictors of refractory Mycoplasma pneumoniae pneumonia (RMPP). However, some studies [12, 13, 16, 17] have indicated that elevated D-dimer levels may be an independent risk factor for

RMPP, which differs from the findings of this study. This discrepancy may be attributed to differences in sample size, laboratory techniques, and other factors.

Mycoplasma pneumoniae (MP), as an atypical pathogen, primarily exerts its pathogenic effects by adhering to respiratory epithelial cells and releasing virulence factors such as community-acquired respiratory distress syndrome toxin (CARDS Tx), triggering intense local and systemic inflammatory immune responses. Resistance genes (e.g., mutations in the 23S rRNA gene) affect the binding of macrolide antibiotics to ribosomes but do not directly enhance the pathogen's ability to produce toxins or damage tissues. Instead, strains carrying resistance genes may primarily contribute to prolonged inflammation by "persisting" rather than causing more severe immediate tissue destruction.

Furthermore, the imaging manifestations of MP infection (e.g., centrilobular nodules, bronchial wall thickening, consolidation) and bronchoscopic findings (e.g., mucosal hyperemia, increased secretions, luminal narrowing) are primarily related to the degree of pathogen invasion of the airway mucosa, the intensity of the host immune response (e.g., neutrophil infiltration, cytokine release), and the duration of infection, rather than being directly associated with resistance genes themselves. Therefore, regardless of whether patients have mild or severe disease, as long as the infecting strains have similar colonization and invasion capabilities, the imaging and bronchoscopic pathological changes may not differ significantly.

This study summarized and compared the imaging and bronchoscopic findings between mild and severe cases and found no significant differences in imaging patterns between the two groups. This finding is similar to the conclusion of a nationwide retrospective observational study by Gavaud A et al. [18] in France, which suggested that radiological findings alone cannot rule out MP infection. However, some existing clinical studies have proposed that early imaging examinations are helpful for the early diagnosis of severe Mycoplasma pneumoniae pneumonia (SMPP) [19]. The reason may be that the severity of SMPP primarily depends on the host's exaggerated immune-inflammatory response (e.g., cytokine storm) rather than direct tissue necrosis caused by the pathogen. Both mild and severe patients may undergo similar initial infection and inflammatory processes, but in severe cases, dysregulated immune responses lead to uncontrolled inflammation in terms of intensity and duration, resulting in more severe clinical symptoms (e.g., high fever, dyspnea). However, these differences may manifest as quantitative variations in imaging (e.g., larger areas of consolidation) rather than qualitative differences (e.g., similar patterns of bronchopneumonia, ground-glass opacities, and consolidation).

In terms of treatment, this study found significant differences ($P < 0.05$) between the mild and severe patient groups regarding medication and bronchoscopic interventions. Specifically, patients in the mild group were less likely to receive levofloxacin and intravenous immunoglobulin (IVIG) compared to those in the severe group, but they underwent bronchoscopic procedures more frequently. These findings underscore the importance of developing individualized treatment strategies based on the severity of the illness.

Bronchoscopy is an invasive procedure primarily used to clear mucus plugs and necrotic debris from the airways, thereby improving airway patency. It is particularly suitable for patients with significant local airway obstruction but relatively mild overall disease. Patients with mild illness generally have better overall conditions and can tolerate bronchoscopy more effectively. In contrast, the core treatment for severe patients focuses on controlling systemic infection and correcting respiratory dysfunction (e.g., oxygen therapy, mechanical ventilation support). Bronchoscopy serves more as an "adjunctive measure" in severe cases, reserved for situations involving severe airway obstruction, and is less frequently performed due to the patients' lower tolerance for invasive procedures.

Consequently, the severe group received more pharmacological treatments (e.g., levofloxacin, IVIG) than the mild group. Levofloxacin is typically considered a second-line treatment option and is used when conventional therapies fail to achieve satisfactory results. Studies [8] have shown that even without levofloxacin, mild patients with macrolide-resistant Mycoplasma pneumoniae (MRMP) pneumonia can achieve favorable outcomes through other treatment modalities. For MRMP pneumonia patients, the levofloxacin treatment group demonstrated significantly shorter fever duration and hospital stay compared to the macrolide treatment group. Severe patients often exhibit more pronounced immune dysfunction due to the severity of their infection, necessitating IVIG administration to supplement antibodies and modulate immune function. According to guidelines [8], IVIG is primarily recommended for severe cases with extrapulmonary complications, such as central nervous system involvement, severe mucocutaneous lesions, hematological manifestations, severe Mycoplasma pneumoniae pneumonia (MPP) complicated by adenovirus infection, or evidence of excessive inflammatory response or severe lung injury. This recommendation aligns with the observed difference in IVIG usage between the mild and severe groups in this study.

In conclusion, early identification and intervention for mild and severe cases of refractory Mycoplasma pneumoniae pneumonia (RMPP) in children, along with the provision of appropriate treatment plans, hold significant importance in reducing hospital stays, alleviating economic burdens, and minimizing the occurrence of complications. Meanwhile, the notable differences in treatment strategies between mild and severe RMPP patients profoundly reflect the precise weighing of risks and benefits by clinicians based on the severity of the illness. For severe cases, the focus of treatment lies in systemic control to achieve rapid and stable outcomes, whereas for mild cases, local intervention with precision and minimal invasiveness is prioritized. Recognizing and understanding this strategic differentiation is crucial for optimizing individualized treatment plans for RMPP. However, our study still has some limitations. The primary constraint is that all samples were sourced from a single center, which necessitates cautious interpretation of the results due to potential selection bias.

Declarations

Ethical Approval and Informed Consent

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki, and approved by the Ethics Committee of Guangxi Zhuang Autonomous Region Maternal and Child Health

Hospital. For this retrospective study, individual informed consent was waived by the ethics committee because all clinical data were anonymized, and no additional invasive interventions or potential risks were imposed on the participants.

Declaration of Conflicting Interests

The authors declare no potential conflicts of interest with respect to the research, authorship, and publication of this article.

Data availability statement

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Funding Declaration

No funding was received for conducting this study.

Author Contribution

R.M. drafted the manuscript. J.C. analyzed clinical data ,created tables and drafted the manuscript. G.L., L.H. and Y.Q. collected clinical case information.W.W. and P.L. collected and analyzed imaging findings. H.H. performed data analysis and revised the manuscript. All authors read and approved the final manuscript.

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Figures

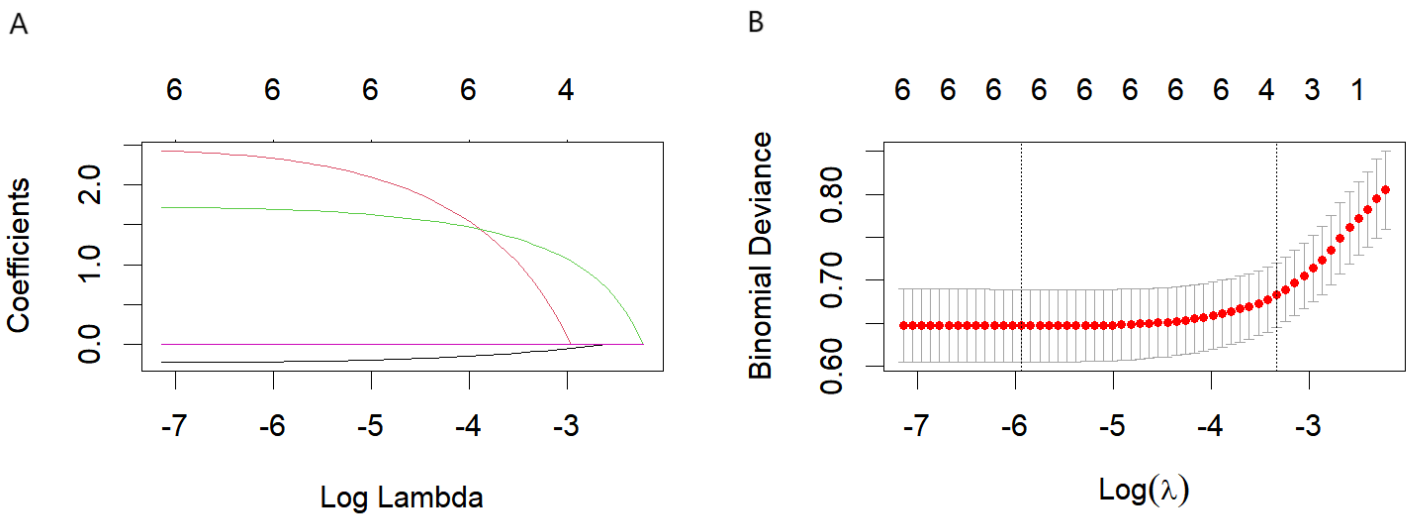


Figure 1

Factors influencing the occurrence of severe cases with positive drug resistance genes identified by LASSO regression

(A) Dynamic process diagram of variable selection by LASSO regression model; (B) Process of variable selection in LASSO regression model through 10-fold cross-validation method

Note: As the penalty coefficient λ is reduced to 0, 6 variables are finally selected, thereby achieving variable screening

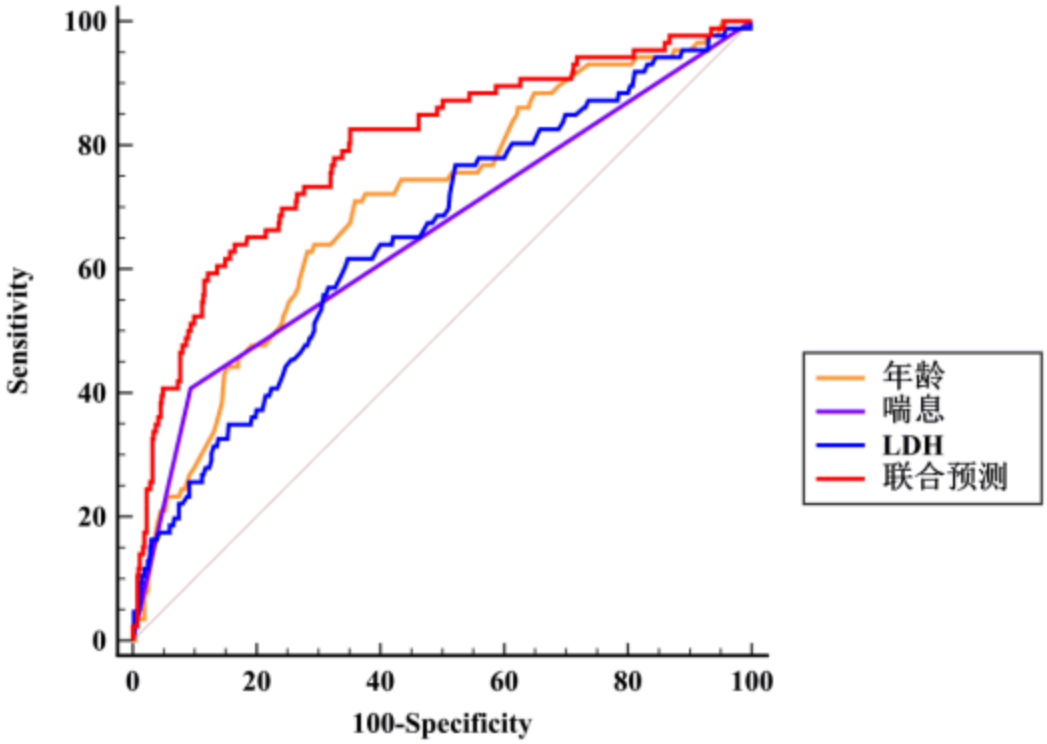


Figure 2

ROC curve analysis of the area under the curve (AUC) for predicting the occurrence of severe illness in patients with positive drug resistance genes based on age, wheezing, single LDH, and combined LDH.