Original Article

Exploring high-risk factors for the prediction of severe mycoplasma pneumonia in children

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Background: As one of the most common causes of community-acquired pneumonia in children, the prevalence of mycoplasma pneumonia (MPP) has long been underestimated. This study aimed to analyze children's severe MPP (SMPP) by examining laboratory characteristics and identifying high-risk factors.

Methods: Clinical data from 447 hospitalized children with MPP were retrospectively analyzed. Patients were categorized into ordinary MPP and SMPP groups. Initial laboratory results on admission were compared between groups, and risk factors for SMPP were assessed using receiver operating characteristic (ROC) and logistic regression analyses.

Results: Children with SMPP exhibited significantly higher levels of neutrophils, neutrophil/lymphocyte ratio (NLR), C-reactive protein (CRP), interleukin-6 (IL-6), erythrocyte sedimentation rate (ESR), and lactate dehydrogenase (LDH), along with lower lymphocyte, albumin (ALB), and prealbumin (PAB) levels compared to the ordinary MPP group (all $P<0.05$). SMPP children also had a higher incidence of multiple pathogens ($P<0.05$). ROC analysis identified cutoff values for ESR, LDH, IL-6, CRP, neutrophil percentage, and NLR, with corresponding areas under the curve (AUCs) indicating their predictive values for SMPP. A combined analysis of these factors yielded an AUC of 0.732 ($P<0.05$). Multivariate logistic regression confirmed ESR >35.50 mm/h, LDH >360.50 U/L, IL-6 >20.28 pg/mL, and CRP >9.74 mg/L as independent high-risk factors for SMPP ($P<0.05$).

Conclusions: ESR, LDH, IL-6, CRP, neutrophil percentage, and NLR are valuable predictors for early identification of SMPP in children. These findings provide essential insights for clinical management aimed at assessing and intervening in prognosis.

Keywords: Children; severe mycoplasma pneumoniae pneumonia; laboratory examination; risk factors

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Introduction

Mycoplasma pneumoniae (MPP) remains one of the most common causes of community-acquired pneumonia (CAP) in children, accounting for 10% to 40% of hospitalized children with CAP (1-3). Due to the fact that children or young adults barely show related symptoms and seek medical care, the prevalence of MP in these individuals has been largely underestimated (4). Severe mycoplasma pneumonia (SMPP) cases in children may be accompanied with pleural effusion, pulmonary atelectasis, pneumothorax, and even necrotizing pneumonia, as well as multiple systemic complications. Even worse situation is that a small proportion of critically ill children may develop respiratory failure or even die (3). In this regard, effective identification of the risk factors of SMPP and early intervention can

help improve the prognosis and decrease the incidence among children. However, the precise diagnosis turns to be difficult or even controversial, because of the non-specific clinical and radiological characteristics as well as the lack of precise diagnostic methods. In this study, we investigated the risk factors of SMPP by comprehensively evaluating the blood parameters, inflammatory response markers, blood biochemistry and other laboratory indicators using receiver operating characteristic (ROC) analysis and multifunctional logistic regression analysis. The combined results are expected to provide a basis for the early identification and prevention of SMPP. We present this article in accordance with the TRIPOD reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-24-293/rc).

Methods

Patients

Clinical data of 447 hospitalized children diagnosed with MPP in the Department of Pediatrics of the Sixth People's Hospital Affiliated to the School of Medicine of Shanghai Jiaotong University, during the period from June 2020 to May 2023, were enrolled for retrospective analysis. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Ethics Committee of Shanghai Sixth People's Hospital [No. 2023-046-(1)] and informed consent was taken from all the patients' parents. Inclusion criteria followed the relevant diagnostic criteria of the Expert Consensus on Diagnosis and Treatment of Childhood Mycoplasma pneumoniae (2015 version) (3). Exclusion criteria included: (I) children with medical history of cardiovascular, respiratory, neurological and hematologic underlying diseases; (II) children with allergic diseases, autoimmune diseases and immunodeficiency diseases; (III) children who had recently used hormones or immunosuppressants; (IV) children with incomplete clinical data.

Highlight box

Key findings

- Erythrocyte sedimentation rate, lactate dehydrogenase, interleukin-6, C-reactive protein, neutrophil percentage, and neutrophil/lymphocyte ratio are valuable predictors for early identification of severe mycoplasma pneumonia (SMPP) in children.

What is known and what is new?

- SMPP cases in children are accompanied with multiple systemic complications.
- Due to the non-specific clinical and radiological characteristics as well as the lack of precise diagnostic methods, the precise diagnosis of SMPP turns to be difficult or even controversial.

What is the implication, and what should change now?

- These findings provide essential insights for clinical management aimed at assessing and intervening in prognosis, further exploration on the early predictors of SMPP in children is needed.

Methodology and data collection

Clinical data comprised general information (gender, age) and results of the first test on the day of admission of relevant laboratory tests. The laboratory items are listed as follows: (I) blood routine examination: white blood cell (WBC) count, neutrophil percentage, lymphocyte percentage, neutrophil/lymphocyte ratio (NLR), hemoglobin (Hb), red blood cell distribution width (RDW), platelet (PLT) count, platelet distribution width (PDW), and mean platelet volume (MPV), and inflammation reaction markers: C-reactive protein (CRP), interleukin-6 (IL-6), procalcitonin (PCT), serum amyloid A (SAA), erythrocyte sedimentation rate (ESR). (II) Blood biochemistry test: albumin (ALB), prealbumin (PAB), lactate dehydrogenase (LDH), triglyceride (TG), and creatine kinase isoenzyme (CK-MB). (III) Other pathogenetic tests: cytomegalovirus, Epstein-Barr virus (EBV), coxsackievirus, herpes simplex virus, influenza A/B virus, etc. The blood routine indexes were detected by SYSMEX XN-9000 automatic hematology analyzer, CRP was detected by Promen-200, IL-6 and PCT were detected by Roche Cobas e602 automatic chemiluminescence analyzer, and SAA was detected by EXPEN65 specific protein analyzer. The related indexes of blood biochemistry test were detected by Hitachi Labospect 008AS blood biochemistry analyzer. All of the above laboratory tests were performed by our laboratory staff.

MPP was documented as follows: single MP antibody (doxycycline) titer ≥1:160 or a >4-fold change in 2 serum MP antibody titers combined with MP nucleic acid testing. With reference to the diagnostic criteria related to severe pneumonia in the Diagnostic and Treatment Criteria for Community-Acquired Pneumonia in Children (2019 edition) (5), all the hospitalized children were divided into the ordinary MPP group and the SMPP group, according to the severity of the disease and changes. Specifically, SMPP was defined if one of the following manifestations

Table 1 Gender and average age of the children in the two groups

Characteristic	Ordinary MPP	SMPP	$t/\chi^2/Z$	P
Number	260	187	–	–
Gender			1.377	0.24
Male	123 (47.31)	78 (41.71)		
Female	127 (52.69)	109 (58.29)		
Age (years)	5.81±2.72	6.28±2.97	−1.828	−0.068

Data are presented as mean ± standard deviation, number or n (%). MPP, mycoplasma pneumonia; SMPP, severe mycoplasma pneumonia.

was at presence: (I) poor general condition; (II) markedly increased respiration: respiratory rate (RR) >70 beats/min in infants, RR >50 beats/min in older children; (III) impaired consciousness; (IV) intermittent apnea and respiratory distress (groaning, flaring of nostrils, and triple concavity sign); (V) extent of pulmonary infiltration with multilobar involvement or ≥2/3 of the lungs involvement; (VI) pleural effusion, pneumothorax, pulmonary atelectasis, lung necrosis, lung abscess; (VII) pulse oximetry ≤0.92; (VIII) accompanied by extrapulmonary complications.

The criteria for the determination of combination of multiple pathogens were as follows: positive antibodies to 2 or more pathogens (influenza A/B virus, cytomegalovirus, EBV, coxsackievirus, herpes simplex virus, etc.), and positive or positive cultures for the pathogens or positive tests for the DNA/RNA of the pathogens in the blood, sputum or throat swab or positive serological IgM, were defined as positive for multiple pathogens, and vice versa for the other pathogens.

Statistical analysis

SPSS25.0 software was applied for statistical analysis. Measurement information conforming to normal distribution was expressed as mean ± standard deviation, and *t*-test of two independent samples was conducted for the comparison between groups; abnormally distributed measurement information was expressed as median (P25, P75), and rank sum test was used for the comparison between groups. Count data were expressed as the number of cases or the percentage, and comparisons between groups were carried out using the χ^2 test. The predictive ability of the indicators with statistically significant differences was analyzed by plotting the ROC curve. Multifactor logistic regression was used to analyze each risk factor. Differences were considered significant when P<0.05.

Results

A total of 447 cases were included in this study with age ranging from 0.5 to 14 years (average age: 6.01±2.72 years), among which 260 (58.17%) children were diagnosed with normal MP and the other 187 (41.83%) ones were diagnosed with SMPP.

Comparison of the general conditions of children in the two groups

As shown in *Table 1*, the gender of the involved children in the two groups shows no significant difference (P>0.05). Although the average age of SMPP children was higher than that of the ordinary MPP group, the difference turned out to be not significant (P>0.05). That is to say, neither gender nor average age of the involved children would exert impact on the test results.

Comparison of peripheral blood routine related indexes between the two groups of children

Compared with that of the ordinary MPP group (*Table 2*), the peripheral blood neutrophil percentage and NLR of the children in SMPP group were higher, while the lymphocyte percentage was lower, and both of the differences were significant (P<0.05). A comparison of WBC count, Hb, erythrocyte distribution width (PDW), PLT count, PDW, and MVP between the two groups of children showed that the difference was not significant (P>0.05).

Comparison of inflammation-related indexes between the two groups of children

As shown in *Table 3*, CRP, IL-6 and ESR of SMPP children were higher than those of the ordinary MPP group, and the differences were all significant (P<0.05), while the differences of PCT and SAA in the two groups were not significant (P>0.05). ALB and PAB of children with SMPP were lower than those of the ordinary MPP group, while LDH was higher than that of the MPP group, and the differences were significant (P<0.05). Comparatively, the differences of TG and CK-MB between the two groups were not significant (P>0.05).

Table 2 Comparison of related indexes of peripheral blood routine between the two groups

Variable	Ordinary MPP	SMPP	t/Z	P
WBC (×10^9/L)	6.98±2.76	7.07±2.67	−0.346	0.73
N (%)	57.00 (43.98, 63.70)	57.80 (46.60, 63.90)	−4.325	<0.001
L (%)	32.45 (24.46, 41.85)	31.8 (24.50, 40.70)	−4.611	<0.001
NLR	2.01±1.54	2.58±1.76	−3.697	<0.001
Hb (g/L)	124.38±16.20	122.10±15.19	1.506	0.13
RDW (%)	12.40 (12.00, 12.90)	12.40 (11.90, 13.00)	−0.399	0.69
PLT (×10^9/L)	274.35±89.05	272.07±90.71	0.265	0.79
PDW (%)	10.50 (9.60, 10.60)	10.5 (9.60, 12.10)	−0.407	0.68
MPV (fl)	9.92±1.28	9.97±1.27	0.134	0.67

Data are presented as median (interquartile range) or mean ± standard deviation. WBC, white blood cell count; N (%), neutrophil percentage; L (%), lymphocyte percentage; NLR, neutrophil/lymphocyte ratio; Hb, hemoglobin; RDW, red blood cell distribution width; PLT, platelet count; PDW, platelet distribution width; MPV, mean platelet volume; MPP, mycoplasma pneumonia; SMPP, severe mycoplasma pneumonia.

Table 3 Comparison of inflammation-related indicators and blood biochemistry-related between the two groups

Variable	Ordinary MPP	SMPP	t/Z	P
CRP (mg/L)	8.61 (6.40, 14.26)	12.69 (8.05, 24.46)	−5.370	<0.001
IL-6 (pg/mL)	11.18 (5.11, 19.17)	18.91 (9.18, 30.45)	−5.676	<0.001
ESR (mm/h)	31.28±17.30	40.46±19.36	0.093	<0.001
PCT (ng/mL)	0.30±0.18	0.33±0.21	−1.736	0.08
SAA (mg/L)	107.90 (51.48, 137.95)	114.20 (60.20, 160.10)	−1.486	0.14
ALB (g/L)	45.00 (43.00, 47.00)	44 (41.70, 46.00)	−3.001	0.003
PAB (mg/L)	132.13±44.13	118.75±39.46	3.302	0.001
LDH (U/L)	277.00 (243.00, 319.75)	299.00 (262.00, 368.00)	−4.187	<0.001
TG (mmol/L)	0.75±0.30	0.78±0.29	−0.855	0.39
CK-MB (U/L)	20.66±8.45	19.97±9.04	0.825	0.41

Data are presented as median (interquartile range) or mean ± standard deviation. CRP, C-reactive protein; IL-6, interleukin-6; ESR, erythrocyte sedimentation rate; PCT, procalcitonin; SAA, serum amyloid A; ALB, albumin; PAB, prealbumin; LDH, lactate dehydrogenase; TG, triglyceride; CK-MB, creatine kinase isoenzyme; MPP, mycoplasma pneumonia; SMPP, severe mycoplasma pneumonia.

ROC curve analysis of risk factors for the prediction of SMPP occurrence

ROC curve analysis of the variables with statistically significant differences in one-way comparisons was carried out to predict the occurrence of SMPP (*Table 4* and *Figure 1*). The results showed that the cut-off values of ESR, LDH, IL-6, CRP, percentage of neutrophils, and NLR for the prediction of the occurrence of SMPP in children were 35.50 mm/h, 360.50 U/L, 20.28 pg/mL, 9.74 mg/L, 62.65%, and 2.05, respectively; while the area under the curve (AUC) was 0.639, 0.617, 0.657, 0.647, 0.618, and 0.625 (P<0.05), respectively. The combined effects of ESR, LDH, IL-6, CRP, percentage of neutrophils, and NLR on the prediction of SMPP was higher, with an AUC value of 0.732 (P<0.05).

Risk factor analysis for the occurrence of SMPP

As indicated by ROC curve analysis, ESR, LDH, IL-6,

Table 4 Results of ROC curve analysis of risk factors for the prediction of SMPP occurrence

Variable	Cut-off	AUC	95% CI	P	Sensitivity (%)	Specificity (%)
ESR (mm/h)	35.50	0.639	0.587 to 0.691	<0.001	59.40	66.40
LDH (U/L)	360.50	0.617	0.564 to 0.671	<0.001	26.70	93.10
IL-6 (pg/mL)	20.28	0.657	0.606 to 0.709	<0.001	47.10	78.80
CRP (mg/L)	9.74	0.647	0.596 to 0.699	<0.001	65.80	57.50
N (%)	62.65	0.618	0.566 to 0.671	<0.001	47.10	70.70
NLR	2.05	0.625	0.573 to 0.677	<0.001	57.20	64.50
ESR + LDH + IL-6 + N + CRP+ NLR	–	0.732	0.686 to 0.778	<0.001	51.30	82.20

ROC, receiver operating characteristic; SMPP, severe mycoplasma pneumonia; AUC, area under the curve; CI, confidence interval; ESR, erythrocyte sedimentation rate; LDH, lactate dehydrogenase; IL-6, interleukin-6; CRP, C-reactive protein; N (%), neutrophils percentage; NLR, neutrophil/lymphocyte ratio.

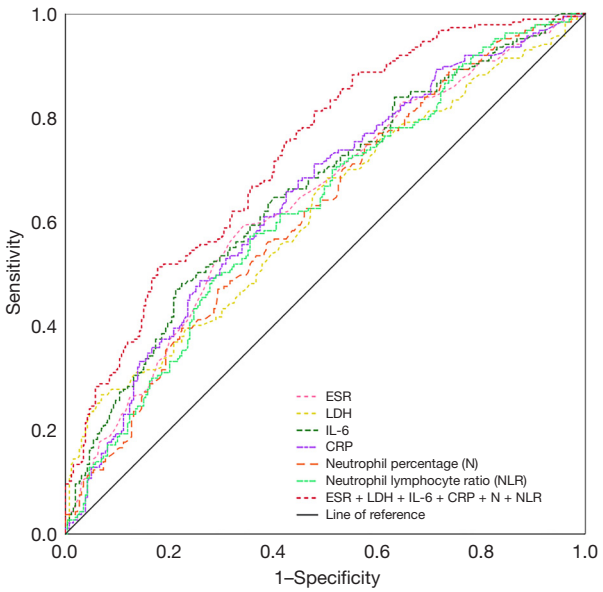

Figure 1 ROC curves of ESR, LDH, neutrophil (N) percentage, IL-6, and combined multiple pathogens for the prediction of SMPP occurrence. ESR, erythrocyte sedimentation rate; LDH, lactate dehydrogenase; IL-6, interleukin-6; CRP, C-reactive protein; N, neutrophils; NLR, neutrophil/lymphocyte ratio; ROC, receiver operating characteristic.

CRP, neutrophil percentage and NLR were predictive of the occurrence of SMPP in children, they were therefore included in the multifactorial logistic regression analysis. A value of 1 was assigned if these factors were higher than 35.50 mm/h, 360.50 U/L, 20.28 pg/mL, 9.74 mg/L, 62.65%, 2.05, respectively; otherwise a value of 0 was assigned. Combining multiple pathogens with clinical SMPP, therefore, combining multiple pathogens was also included, and combining multiple pathogens was assigned a value of 1, otherwise a value of 0. As shown in *Table 5*, ESR >35.50 mm/h, LDH >360.50 U/L, IL-6 >20.28 pg/mL, and CRP >9.74 mg/L were independent risk factors for the occurrence of SMPP in children (P<0.05).

Discussion

Mycoplasma pneumoniae (MP) is a prokaryotic cell-type microorganism without a cell wall. The pathogenic mechanism of MP infection is quite complex, coming with potential damage to the respiratory epithelium caused by the pathogen itself and the involvement of multiple aspects of immune factors of the organism, including intrinsic and adaptive immunity, which leads to clinical manifestations in the respiratory system and other systems (6-8). Recent reports have indicated increasingly higher number of SMPP cases, a high proportion of which is characterized by complications. Among these cases, a small proportion of children are unfortunately falling into critical illness and develop rapidly, which can even lead to death. Along with the in-depth research on the pathogenesis of MPP, extensive tests are being applied to the diagnosis of SMPP.

Blood parameters are traditional non-specific inflammatory markers, among which NLR, RDW, PDW and MVP are considered to closely correlate with MPP. Specifically, changes in RDW are correlated with elevated inflammatory markers, which, to some extent, can be correlated with immuno-inflammatory diseases, severe pneumonia in respiratory diseases, etc. RDW level has been recently reported to be correlated with the severity of

Table 5 Analysis of risk factors for SMPP development

Risk factor	Beta value	Standard error	Wald value	P	OR	95% CI
ESR (mm/h)	0.731	0.225	10.590	0.001	2.078	1.338 to 3.228
LDH (U/L)	1.601	0.333	23.058	<0.001	4.959	2.580 to 9.534
IL-6 (pg/mL)	0.888	0.242	13.464	<0.001	2.431	1.513 to 3.907
CRP (mg/L)	0.739	0.231	10.234	0.001	2.094	1.331 to 3.292

SMPP, severe mycoplasma pneumonia; OR, odds ratio; CI, confidence interval; ESR, erythrocyte sedimentation rate; LDH, lactate dehydrogenase; IL-6, interleukin-6; CRP, C-reactive protein.

MPP (9). MP infection can cause changes in PLT count, PDW and other indicators, while the elevated levels of platelet parameters PLT count and platelet pressure volume can be used to determine the changes in the disease of MPP; it has also been found that MP infection can lead to thrombocytopenia (10). In this work, although the Hb and PLT count levels of children in the SMPP group were lower than those in the ordinary MPP group, and the levels of RDW, PDW and MVP were higher. The differences of these factors were found statistically not significant (P>0.05) and therefore can be barely related to the severity of the MPP disease. MP infection can cause damage to the epithelial lining of the airway mucosa, impair clearance of mucus cilia, and tolerate bacterial and other pathogens. It is important to note that SMPP children are situated in a high-stress state and may have elevated levels of leukocytes and neutrophils, which serve as key cellular components of the human host defense system against infections; and the NLR reflects the systemic inflammatory state and immune response of the organism (11). In this work, we found that the peripheral blood WBC level of children in the SMPP group was higher than that of the ordinary MPP group, but the difference was not significant (P>0.05). However, the neutrophil percentage and NLR level were higher than that of the ordinary MPP group, and the lymphocyte percentage level was lower than that of the MPP group. Both of the differences were significant (P<0.05). This suggests that peripheral blood neutrophil percentage, lymphocyte percentage and NLR level can reflect the inflammatory state and severity of the disease in children with MPP, which can also be correlated with the occurrence of SMPP, keeping good consistency with the national reports (11-13).

Inflammatory response markers correlate pediatric severe mycoplasma pneumoniae pneumonia, and the commonly used ones in clinic are IL-6, CRP, PCT, SAA, ESR, etc. It is well acknowledged that IL-6 can promote the secretion of protective antibodies and enhance the production of other inflammatory factors to aggravate inflammatory injury, which has also been found to be efficient in promoting the synthesis of CRP, of which its serum level is positively correlated with the severity of the disease (8). It is documented that the level of IL-6 in bronchoalveolar lavage fluid (BALF) of the SMPP children is significantly higher than that of the ordinary MPP children (14,15). CRP is an acute phase protein synthesized by hepatocytes under the influence of IL-6 and IL-1, which can well reflect the infection status. Typically, CRP is significantly elevated in patients with SMPP, and it is correlated with the degree of lung tissue damage (16-18). ESR is also an important and effective marker of inflammatory infection and disease activity, which increases with disease activity to a more pronounced degree than CRP, and can monitor the degree of inflammatory response in children with MMPP (19). Clinically, a markedly elevated ESR level can be an early warning of the occurrence of SMPP (8). In this work, we found that the levels of CRP, IL-6 and ESR were higher in the SMPP group than in the ordinary MPP group, and the differences were all significant (P<0.05), suggesting that there was a stronger inflammatory response in SMPP children and the levels of CRP, IL-6, and ESR were related to the occurrence of SMPP. PCT is a calcitonin precursor substance with no hormonal activity, and it is highly specific for infections; while SAA is an acute-phase response protein produced by hepatocytes and then secreted into the serum, both of which are inflammatory markers of early infection. Studies have indicated that both PCT and SAA are significantly elevated in children with SMPP, reflecting the severity of the MPP condition (20-23). In this work, we did not find any differences in the levels of PCT and SAA between the two groups (P>0.05), due in large part to the differences in the changes of PCT and SAA levels in different types of infectious diseases, as well as the fact that the cases combined with other pathogens were not excluded from this work (8,24-26).

LDH is an enzyme that catalyzes the oxidation of pyruvate to lactate, and is present in the cytoplasm of almost all cells. Serum levels of LDH reflect the degree of cell membrane damage and can be used to monitor cell and tissue injury. LDH was found to be elevated in SMPP and refractory mycoplasma pneumonia (RMPP) (8,18). ALB and PAB are both acute negative time-phase reactive proteins. Relative to that of ALB, the average lifespan of PAB is shorter, which can more accurately reflect the inflammatory state and nutritional status of the body, and therefore, can be correlated with the severity of SMPP (14). In this work, the levels of ALB and PAB in the SMPP group were lower than those in the ordinary MPP group ($P<0.05$), which was considered to be related to the impaired synthesis of PAB in hepatocytes and overconsumption of PAB in critically ill children due to insufficient intake, accelerated metabolism, and abnormalities in the internal environment (9,27). The levels of LDH in children with SMPP were higher than those in the ordinary MPP group ($P<0.05$), which suggests that there is more serious lung tissue inflammation and injury in children with SMPP.

Children with SMPP are often co-infected with other pathogens. As stated before, two or more pathogens (cytomegalovirus, EBV, coxsackievirus, herpes simplex virus, influenza A/B virus, etc.) with positive antibodies or positive culture of the pathogen or positive DNA/RNA test of the pathogen, were defined as multiple pathogen positivity in this work. The results showed that the incidence of combined multiple pathogens in the SMPP group was higher than that in the ordinary MPP group ($P<0.05$), suggesting that the combination of multiple pathogens was associated with the occurrence of SMPP.

It was also found that ESR, LDH, IL-6, CRP, neutrophil percentage, and NLR were significantly elevated in children in the SMPP group. ROC curve analysis showed that their cut-off values for the prediction of SMPP occurrence in children were 35.50 mm/h, 360.50 U/L, 20.28 pg/mL, 9.74 mg/L, 62.25%, and 2.05, with AUCs of 0.639, 0.617, 0.657, 0.647, 0.618, and 0.625, respectively, which are in close proximity to those of national studies (13,18), suggesting that ESR, LDH, IL-6, CRP, percentage of neutrophils, and NLR can be used as an early predictor of the occurrence of SMPP, but the sensitivity of LDH, IL-6 and neutrophil percentage was not high. The AUC combining ESR, LDH, IL-6, CRP, neutrophil percentage, and NLR for the prediction of SMPP occurrence in children was determined to be 0.732, accompanied with a sensitivity of 51.30% and a specificity of 82.20%, suggesting a higher combined predictive efficacy. Further multifactorial logistic regression analysis showed that ESR >35.50 mm/h, LDH >360.50 U/L, IL-6 >20.28 pg/mL, and CRP >9.74 mg/L were the independent high-risk factors for the occurrence of SMPP in children ($P<0.05$). It is noteworthy that the children with these high-risk factors should be paid close attention to in the clinical treatment to prevent further deterioration.

Despite of the progress on the evaluation of high-risk factors which can potentially predict SMPP development in children, it is noteworthy that the current work falls into a single-center retrospective study, coming with limited sample size and age span, which may attenuate the sensitivity of some of the factors, such as LDH, IL-6 and neutrophil. In this regard, multicenter and large-sample studies are needed in the future. On the other hand, different infectious diseases can cause differences in the changes of some other factors, such as PCT and SAA levels. Such complicated variation can lead to the difficulty in evaluating potentially significant difference of these factors between the ordinary MPP and SMPP groups, which is expected to be further explored in near future by excluding the cases combined with other accompanied pathogens.

Conclusions

In summary, ESR, LDH, IL-6, CRP, neutrophil percentage, and NLR are significant in the early prediction of SMPP development in children, and the combined prediction efficacy is even higher. Specifically, ESR >35.50 mm/h, LDH >360.50 U/L, IL-6 >20.28 pg/mL, and CRP >9.74 mg/L are independent high-risk factors for SMPP development in children. Exploring the risk factors and early predictors of SMPP in children can help to evaluate the disease, actively intervene and improve the prognosis.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-24-293/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Ethics Committee of Shanghai Sixth People's Hospital [No. 2023-046-(1)] and informed consent was taken from all the patients' parents.

References

1. Oumei H, Xuefeng W, Jianping L, et al. Etiology of community-acquired pneumonia in 1500 hospitalized children. J Med Virol 2018;90:421-8.
2. Lee E, Kim CH, Lee YJ, et al. Annual and seasonal patterns in etiologies of pediatric community-acquired pneumonia due to respiratory viruses and Mycoplasma pneumoniae requiring hospitalization in South Korea. BMC Infect Dis 2020;20:132.
3. Respiratory Group of the Chinese Medical Association Pediatrics. Expert consensus on the diagnosis and treatment of Mycoplasma pneumoniae pneumonia in children (2015 edition). Chinese Journal of Practical Pediatrics 2015;30:1304-8.
4. Bajantri B, Venkatram S, Diaz-Fuentes G. Mycoplasma pneumoniae: A Potentially Severe Infection. J Clin Med Res 2018;10:535-44.
5. National Health Commission of the People's Republic of China. Community-acquired pneumonia diagnosis and treatment standard for children (2019 edition). Chinese Journal of Clinical Infectious Diseases 2019;12:6-13.
6. He J, Liu M, Ye Z, et al. Insights into the pathogenesis of Mycoplasma pneumoniae (Review). Mol Med Rep 2016;14:4030-6.
7. Chaudhry R, Ghosh A, Chandolia A. Pathogenesis of Mycoplasma pneumoniae: An update. Indian J Med Microbiol 2016;34:7-16.
8. Zou Y. Clinical significance of abnormal inflammatory indexes in Mycoplasma pneumoniae. Chinese Clinical Journal of Practical Pediatrics 2021;36:1209-14.
9. Guo X, Zhu P, Wang C, et al. Analysis of factors affecting 185 cases of severe Mycoplasma pneumoniae pneumonia in children. Fujian Medical Journal 2021;43:1-5.
10. Yang X, Lin R, Jin R, et al. Clinical significance of platelet parameters measurement in children with severe mycoplasma pneumonia. Chinese Electronic Journal of Diagnostics 2018;6:37-40.
11. Chen R, Zhou X, He G, et al. Clinical value of neutrophil/lymphocyte ratio in evaluating the severity of mycoplasmal pneumonia in children. China Maternal and Child Health 2022;37:641-4.
12. Chiu CY, Chen CJ, Wong KS, et al. Impact of bacterial and viral coinfection on mycoplasmal pneumonia in childhood community-acquired pneumonia. J Microbiol Immunol Infect 2015;48:51-6.
13. Jia J, Jia C. Predictive value of laboratory indicators for refractory Mycoplasma pneumoniae. Inner Mongolia Medical Journal 2021;53:1425-8.
14. Wang X, Zhong LJ, Chen ZM, et al. Necrotizing pneumonia caused by refractory Mycoplasma pneumonia pneumonia in children. World J Pediatr 2018;14:344-9.
15. Ku DM, Zhou JJ, Luo X, et al. Cytokines IL-6 and TNF-α assess the progression and prognosis of pediatric mycoplasma pneumonia. Chinese Journal of Lung Diseases (Electronic Edition) 2021;14:505-7.
16. Wang J, Mao J, Chen G, et al. Evaluation on blood coagulation and C-reactive protein level among children with mycoplasma pneumoniae pneumonia by different chest imaging findings. Medicine (Baltimore) 2021;100:e23926.
17. Zhang C, Zhang Q, Du JL, et al. Correlation Between the Clinical Severity, Bacterial Load, and Inflammatory Reaction in Children with Mycoplasma Pneumoniae Pneumonia. Curr Med Sci 2020;40:822-8.
18. Liu JL. Application of C-reactive protein lactate dehydrogenase level detection in the early recognition of severe Mycoplasma pneumoniae pneumonia. Chinese

Drugs and Clinics 2021;21:1858-60.
19. Li J, Yang J, Li Y, et al. Relationship between serum CRP PCT and ESR levels and severity of MPP in pediatric Mycoplasma pneumoniae. Western Medicine 2021;33:1374-8.
20. Jeong JE, Soh JE, Kwak JH, et al. Increased procalcitonin level is a risk factor for prolonged fever in children with Mycoplasma pneumonia. Korean J Pediatr 2018;61:258-63.
21. Wu H, Ding X, Zhao D, et al. Effect of montelukast combined with methylprednisolone for the treatment of mycoplasma pneumonia. J Int Med Res 2019;47:2555-61.
22. Uckan K, Sahin HG. Serum amyloid A, procalcitonin, highly sensitive C reactive protein and tumor necrosis factor alpha levels and acute inflammatory response in patients with hemolysis, elevated liver enzymes, low platelet count (HELLP) and eclampsia. J Obstet Gynaecol Res 2018;44:440-7.
23. Chen F, Chen P. Early diagnosis and medication indication of serum amyloid A in pediatric severe mycoplasma pneumonia. Hebei Medicine 2020;42:1351-4.
24. Zhang ML, Zhou H. Research progress of serum calcitoninogen and community-acquired pneumonia. Medical Review 2019;25:3175-9.
25. Specialized Committee on Hospital Infection Management and Control of the Chinese Medical Association Pediatrics. Expert consensus on the clinical application of serum procalcitoninogen test in pediatric infectious diseases. Chinese Journal of Pediatrics 2019;57:9-15.
26. Ke J, Xu J, Ran F, et al. Expert consensus on the use of SAA alone and in combination with CRP in pediatric infectious diseases. Laboratory Medicine 2021;36:685-90.
27. Wang C, Liu G, Wang S, et al. Clinical significance of pre-serum protein in children with severe Mycoplasma pneumoniae. Chinese Clinical Journal of Practical Pediatrics 2020;35:302-4.

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