Explore the Predictive Value of Peripheral Blood Cell Parameters in Refractory *Mycoplasma pneumoniae* Pneumonia in Children Over 6 Years Old

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**Background:** To determine the predictive value of peripheral blood cell parameters for refractory *Mycoplasma pneumoniae* pneumonia (RMPP) in children over 6 years old.

**Methods:** A retrospective study was conducted in children with RMPP admitted to the respiratory department of Tianjin Children’s Hospital from September 2017 to September 2019, and non-refractory *Mycoplasma pneumoniae* pneumonia (NRMPP) was selected by the propensity score method and matched according to the ratio of 1:1.5. We analyzed the differences in clinical characteristics, peripheral blood cell parameters, imaging findings, and treatments between the two groups, and further determined the predictive value of peripheral blood cell parameters on RMPP.

**Results:** There were 76 patients in the RMPP group and 114 patients in the NRMPP group. We found that the RMPP group had a longer clinical course and a higher incidence of intrapulmonary and extrapulmonary complications (p < 0.01). Moreover, the proportion of children in the RMPP group who received immunotherapy (such as glucocorticoid, gamma immunoglobulin) and fiberoptic bronchoscopy intervention was higher than that in the NRMPP group (p < 0.01). Meanwhile, the level of neutrophil, neutrophil/lymphocyte ratio (NLR), platelet count/lymphocyte ratio (PLR), mean platelet volume/lymphocyte ratio (MPVLR), C-reactive protein (CRP), lactic dehydrogenase (LDH), and interleukin (IL)-6 in the RMPP group was significantly higher (p < 0.01) than those in the NRMPP group. The incidence of pulmonary consolidation, atelectasis, and pleural effusion was also higher in the RMPP group (p < 0.05). ROC curve and binary logistic regression analysis showed that NLR > 3.92 (OR = 3.243; 95% CI = 1.485–7.081; p = 0.003), MPVLR > 5.29 (OR = 2.700; 95% CI = 1.258–5.795; p = 0.011), and pleural effusion (OR = 3.023; 95% CI = 1.424–6.420; p = 0.004) were significant factors in predicting RMPP. Our study showed that NLR had higher accuracy in predicting RMPP than CRP.

**Conclusions:** The parameters of peripheral blood cells might be a predictor of RMPP. NLR > 3.92, MPVLR > 5.29, and pleural effusion might have important predictive value for RMPP in children over 6 years old.

**Keywords:** refractory *Mycoplasma pneumoniae* pneumonia, neutrophil/lymphocyte, mean platelet volume/lymphocyte, predictive value, children


INTRODUCTION

*Mycoplasma pneumoniae* (MP) is a common pathogen of pediatric community-acquired pneumonia (CAP) (1). *Mycoplasma pneumoniae* pneumonia (MPP) is usually considered as a mild/self-limiting disease, which has a good response to macrolides, but sometimes it may develop into a refractory case. Refractory *Mycoplasma pneumoniae* pneumonia (RMPP) is mainly referred to as MPP characterized by persistent fever and progressive exacerbations of clinical symptoms, signs, and related imaging manifestations after standard treatment with macrolide drugs for more than 1 week (2). RMPP is more likely to cause severe pulmonary and extrapulmonary complications, including atelectasis, necrotizing pneumonia, encephalitis, arthritis, pericarditis, hemolytic anemia, and disseminated intravascular coagulation, and even endangers life (3–8).

Peripheral blood cell parameters, such as neutrophil/lymphocyte ratio (NLR), platelet count/lymphocyte ratio (PLR), and mean platelet volume/lymphocyte ratio (MPV/LR) are markers of systemic inflammation, and their changes are related to inflammatory stress response (9). In recent years, peripheral blood cell parameters have attracted more and more attention. A study showed that NLR contributes to risk stratification and prognosis in patients with acute coronary syndromes (10). Lattanzi et al. found that NLR was associated with 30-day mortality and morbidity after intracerebral hemorrhage, which could improve outcome prediction of acute intracerebral hemorrhage (11). They also played an important role in the prognosis of acute ischemic stroke patients undergoing revascularization treatment (12, 13), and had a certain predictive value in the occurrence, efficacy, and prognosis of tumors (14–16). The above evidence shows the significance and broad potential of serum biomarkers that are easy to obtain and inexpensive in daily clinical practice. Therefore, we aim to explore the predictive value of peripheral blood cell parameters in children with RMPP. Besides, due to the specificity of blood images of preschool children, this study mainly explored the predictive value of peripheral blood cell parameters for children over 6 years old.

METHODS

Study Population

A retrospective case–control study was conducted to select RMPP children admitted to the Respiratory Department of Tianjin Children’s Hospital from September 2017 to September 2019, and non-refractory *Mycoplasma pneumoniae* pneumonia (NRMPP) was selected by the propensity score method and matched according to a ratio of 1:1.5.

Diagnostic Criteria

All patients had signs and symptoms indicative of pneumonia (such as fever and cough) on admission, and pneumatic infiltrations in the chest radiograph. MP acute infection was based on the titer of MP-IgM antibody in single serum persisting at 1:160, and whether MP-DNA and/or MP-RNA was positive in nasopharyngeal secretions, or the titration of MP-antibody had a significant conversion in a double serum interval of 2 weeks (17). RMPP is mainly referred to as MPP characterized by progressive exacerbations of clinical symptoms, persistent fever, and aggravated lung imaging after standard treatment with macrolide drugs for 7 days or longer (2).

Inclusion Criteria

(1) Children who meet the diagnostic criteria; and (2) are more than 6 years old but <15 years old.

Exclusion Criteria

(1) Individuals with basic diseases such as asthma, chronic cardiopulmonary disease, rheumatism, and immune deficiency; (2) those with other respiratory pathogen infections and tuberculosis confirmed using the following tests: blood cultures, nasopharyngeal aspirate cultures, nasopharyngeal aspirate for virus reverse transcriptase real-time multiplex PCR, and serology of common respiratory pathogens; (3) those who had used glucocorticoids and antibiotics before the blood routine test; and (4) those whose clinical data were incomplete.

Data Collection

Hospitalization demographics, clinical information, peripheral blood cell parameters, lactic dehydrogenase (LDH), interleukin (IL)-6, radiological findings, and treatments of all patients were collected in the study.

After admission, all patients had their body temperature (axillary temperature) monitored daily and their respiratory symptoms were evaluated, such as cough, wheezing, dyspnea, and chest pain. According to the eighth edition of Zhu Futang’s Practical Pediatrics, a body temperature (axillary temperature) of above 37.5°C is defined as fever. Dyspnea refers to the exertion of breathing movement, which may result in mouth opening breathing, nasal flapping, inspiratory depression of chest wall, etc. We also evaluated extrapulmonary complications. Liver function damage is defined as an increase in alanine aminotransferase (ALT) of more than double the usual level. The diagnosis of thromboembolism is based on the related clinical symptoms of MPP children and imaging examination (such as ultrasound, CT, MRI, MRA, MRV, CTA, etc.) promoting thrombosis. Toxic encephalopathy refers to the symptoms of the nervous system, normal cerebrospinal fluid, negative etiological examination, and abnormal electroencephalogram; treatment of primary disease symptoms results in a gradual recovery. Skin and mucous membrane damage refers to systemic or local erythema multiforme, maculopapular and urticaria, and even Steven–Johnson syndrome.
We used the blood routine results of the first blood collection of the patients and calculated the related inflammatory indexes: NLR, PLR, and MPVLR. In addition, blood culture, sputum culture, sputum virus RT-PCR, blood biochemistry, LDH, IL-6, and blood pathogen examinations were completed within 24 h after admission.

Chest radiography was performed before admission or during hospitalization. Patients had a CT scan if he or she had one of the following situations: (1) the clinical manifestations were inconsistent with the chest radiograph; (2) airway and lung malformations were suspected; (3) there were serious complications associated with pneumonia; (4) patients failed to respond to treatment and other diseases needed to be excluded such as interstitial lung disease, pulmonary tuberculosis, and so on (18, 19).

In terms of treatment, the indications of glucocorticoids used in this study were as follows: (1) patients with obvious wheezes and increasing respiratory secretions; (2) severe pneumonia with obvious poisoning symptoms; (3) a lot of pleural effusion exudation for a short time; and (4) persistent high fever of pneumonia with strong inflammatory reaction (20). When combined with central nervous system disease, immune hemolytic anemia, immune thrombocytopenic purpura, and other autoimmune diseases, gamma immunoglobulin could be considered (20). Patients with atelectasis or inflammatory consolidation of one or more lung segments and no obvious improvement in chest imaging after routine intravenous anti-infection therapy could be considered for fiberoptic bronchoscopy therapy (20).

**Ethics**

This study was approved by the medical ethics committee of Tianjin Children’s Hospital, and informed consent was signed by the guardians of children before the collection of clinical case data.

**Data Analysis**

SPSS 22.0 was used for statistical analysis. The normal distribution data were represented by mean ± SD (x ± s). The skewed distribution data were expressed as median (P25, P75), whose comparisons were made by the Mann–Whitney U-test. Chi-squared tests or Fisher’s exact test were used to compare categorical data. Receiver operating characteristic (ROC) curves were calculated to determine the sensitivity and specificity of candidate peripheral blood cell parameters related to RMPP. Then, logistic regression analysis was carried out to further determine the independent variables related to RMPP. The difference was considered statistically significant at \( p < 0.05 \).

**RESULTS**

**Clinical Characteristics of Patients**

A total of 190 patients were enrolled in this study, including 76 in the RMPP group and 114 in the NRMPP group. The average age was 7.93 ± 1.91 years old, and the ratio of boys to girls was about 1.26. There was no difference in age and gender distribution between these two groups. All patients had cough and fever. Besides, intrapulmonary and extrapulmonary complications were more common in the RMPP group, especially toxic encephalopathy, mucous plugging, and dyspnea (all \( p < 0.05 \)) (Table 1).

**Clinical Course and Treatment of Patients**

Regarding the clinical course, the median duration of fever in the RMPP and NRMPP groups was 11.5 (10.0–14.0) and 9.0 (7.0–11.0) days, respectively \(( p < 0.01 \)) (Table 1).

**Laboratory Parameters and Imaging Features of Patients**

The average level of neutrophil count (N), MPV, NLR, PLR, and MPVLR in the RMPP group was 6.17 × 10⁹/L, 10.23 fl, 4.65, 219.37, and 8.50, respectively, which were higher than those in the NRMPP group (all \( p < 0.05 \)). Lymphocyte count (L) was lower in RMPP, while no difference was found in total peripheral leukocyte count and platelet count. Besides, we compared the levels of C-reactive protein (CRP), LDH, and IL-6 between
and pleural effusion was higher in the RMPP group (all p < 0.05). The incidence of pulmonary consolidation, atelectasis, and pleural effusion in the RMPP group was 93.42 and 19.30%, respectively. Besides, the radiological abnormalities in the RMPP group were more serious. The incidence of pulmonary consolidation, atelectasis, and pleural effusion was higher in the RMPP group (all p < 0.05) (Table 3).

### Predictive Value of Peripheral Blood Cell Parameters in Patients With RMPP

To explore the predictive value of peripheral blood cell parameters in RMPP, a ROC curve (Figure 1) was calculated and the critical value with maximum sensitivity and specificity was determined. ROC curve analysis showed that NLR, PLR, and MPVLR were helpful to predict the incidence of RMPP. When the cutoff values of NLR, PLR, and MPVLR were 3.92, 159.56, and 5.29, the sensitivity and specificity were 0.539 and 0.842, 0.697 and 0.561, and 0.789 and 0.544, respectively. The areas under the curve of NLR, PLR, and MPVLR were 0.718, 0.658, and 0.685 (Table 4). In addition, we also conducted ROC analysis for CRP. The cutoff value, sensitivity, specificity, and the areas under the curve of CRP were 33.55 mg/L, 0.474, 0.825, and 0.667, respectively (Figure 2).

### Multiple Logistic Regression Analysis for the Related Factors Predicting the Risk of RMPP

To further evaluate the predictors associated with RMPP, multiple logistic regression was performed. The results showed that NLR > 3.92 (OR: 3.243, p = 0.003), MPVLR > 5.29 (OR: 2.700, p = 0.011), and pleural effusion (OR: 3.023, p = 0.004) were significant predictors of the incidence of RMPP (Table 5).

### DISCUSSION

Although MP infection is a benign disease in most cases, the prevalence of RMPP has rapidly increased in recent years (21). It is significant for pediatricians to recognize RMPP earlier and treat it promptly. A blood routine examination is easy and low-priced. To the best of our knowledge, our study is the first to focus on the predictive role of peripheral blood cell parameters in children with RMPP.

So far, the pathogenesis of RMPP has not been fully understood. It is generally known that RMPP may be related to an excessive inflammatory reaction, MP resistance, abnormal secretion of airway mucus, mixed infection, and community-acquired respiratory distress syndrome toxins (22, 23). The host cell immune response can affect the clinical characteristics of MP infection. The proportion of pulmonary consolidation, atelectasis, and pleural effusion in the RMPP group was significantly higher than that in the NRMPP group, which was similar to the results of Zhang et al. (24). Children with RMPP were more likely to have extrapulmonary complications, such as dyspnea, toxic encephalopathy, and mucous plugging, which were mainly related to the immune response after MP infection. In addition, the days of fever and hospitalization...
TABLE 4 | Predictive value of peripheral blood cell parameters in patients with RMPP.

| Independent factors | Cut-off value | Sensitivity | Specificity | AUC | P-value | 95% CI Lower | 95% CI Upper |
|---------------------|--------------|-------------|-------------|-----|---------|--------------|--------------|
| NLR                 | 3.92         | 0.539       | 0.842       | 0.718 | 0.000   | 0.642        | 0.795        |
| PLR                 | 159.56       | 0.697       | 0.561       | 0.658 | 0.000   | 0.579        | 0.738        |
| MPVLR               | 5.29         | 0.789       | 0.544       | 0.685 | 0.000   | 0.607        | 0.762        |

FIGURE 2 | The ROC curve of predictive value of CRP in patients with RMPP.

TABLE 5 | Multiple logistic regression analysis for the related factors predicting the RMPP.

| Variable        | OR     | 95% CI          | P-value |
|-----------------|--------|-----------------|---------|
| NLR             | 3.243  | 1.485–7.081     | 0.003   |
| MPVLR           | 2.700  | 1.258–5.795     | 0.011   |
| Pleural effusion| 3.023  | 1.424–6.420     | 0.004   |

Neutrophils and lymphocytes are essential cellular components of human host defense. Neutrophils are the first cell line of defense against infection in the non-specific immune system. They induce and activate an inflammatory response, while lymphocytes play a role in adaptive immunity (25). In our study, the average levels of neutrophils and lymphocytes in the RMPP group were $6.17 \times 10^9/L$ and $1.53 \times 10^9/L$, respectively. This was similar to other studies where the children with RMPP showed a higher proportion of neutrophils and a lower percentage of lymphocytes (26, 27). NLR refers to the ratio of neutrophils to lymphocytes in peripheral blood. Our study showed that the children with RMPP had a higher NLR value. Nowadays, many studies have shown the prediction of CRP in RMPP (28–30). In ROC curve analysis, the area under the curve of CRP was 0.667, which was lower than that of NLR (0.718). Therefore, NLR had a higher accuracy rate than CRP in predicting the incidence of RMPP. It has been reported that NLR could better predict the clinical outcomes of patients with systemic inflammation (31). Besides, NLR is a more easily quantified biomarker than other inflammatory factors, such as tumor necrosis factor and interleukin (32). This may indicate the role of excessive inflammatory response in RMPP. MP infection can stimulate the activation of T lymphocytes, promote the high expression of inflammatory factors and cytokines, and further aggravate the body’s inflammatory response (33). However, an excessive inflammatory reaction may activate apoptosis of lymphocytes, resulting in the decrease of lymphoid count (25).

Platelets are considered to be inflammatory reactants in the acute phase, which can release inflammatory mediators, such as chemokines and cytokines, thus aggravating the inflammatory response (34). MPV is a marker of platelet function and activation (35), which may be more sensitive than platelets. We found that PLR and MPVLR in the RMPP group were significantly higher than those in the NRMPP group, which may further suggest that there is an excessive inflammatory reaction in RMPP.

To better predict the predictive value of peripheral blood cell parameters, we conducted ROC curves and logic regression analysis. The results showed that NLR > 3.92 (OR = 3.243; 95% CI = 1.485–7.081; $p = 0.003$), MPVLR > 5.29 (OR = 2.700; 95% CI = 1.258–5.795; $p = 0.011$), and pleural effusion (OR = 3.023; 95% CI = 1.424–6.420; $p = 0.004$) had a positive value in predicting the risk of disease. Besides, the areas under the curve of NLR and MPVLR were 0.718 and 0.685, respectively.

Many studies have explored some important predictive indicators of RMPP, including C-reactive protein, lactate dehydrogenase, and interleukin-6 (24, 36, 37). There has been no study until now showing that peripheral blood cell
parameters could be significant factors in predicting the risk of RMPP, and that they have the advantages of low cost and simple operation.

**Limitations and Strengths**

The advantage of our study was exploring the predictive effect of peripheral blood cell parameters on RMPP for the first time, which was easy to obtain. Besides, we excluded the influence of age on peripheral blood cells. However, our study was a retrospective study, and the subjects may have selective bias. In future work, we should further carry out long-term multi-center and larger sample prospective studies to further prove the predictive value of peripheral blood cell parameters on RMPP.

**CONCLUSION**

Our study showed that excessive inflammatory response might play an important role in RMPP and the parameters of peripheral blood cells might be a predictor of RMPP. NLR > 3.92, MPVLR > 5.29, and pleural effusion might have important predictive value for RMPP in children over 6 years old.

**REFERENCES**

1. Liu WK, Liu Q, Chen DH, Liang HX, Chen XK, Chen MX, et al. Epidemiology of acute respiratory infections in children in Guangzhou: a three-year study. *PloS ONE*. (2014) 9:e96674. doi: 10.1371/journal.pone.0096674

2. Zhou Y, Wang J, Chen W, Shen N, Tao Y, Zhao R, et al. Impact of viral coinfection and macroside-resistant mycoplasma infection in children with refractory *Mycoplasma pneumoniae* pneumonia. *BMC Infect Dis*. (2020) 20:633. doi: 10.1186/s12879-020-05356-1

3. Kannan TR, Hardy RD, Coalson JJ, Cavuoti DC, Siegel JD, Eagle M, et al. Fatal outcomes in family transmission of *Mycoplasma pneumoniae*. *Clin Infect Dis*. (2012) 54:225-31. doi: 10.1093/cid/cir769

4. Demitsu T, Kawase M, Nagashima K, Takazawa M, Yamada T, Kakurai M, et al. *Mycoplasma pneumoniae*-associated mucositis with severe blistering stomatitis and pneumonia successfully treated with azithromycin and infusion therapy. *J Dermatol*. (2019) 46:e38-39. doi: 10.1111/1346-8138.14510

5. Tsai YG, Ou TY, Wang CC, Tsai MC, Yuh YS, Hwang B. Intraosseous gamma-globulin therapy in myocarditis complicated with complete heart block: report of one case. *Acta Paediatr Taiwan*. (2001) 42:311-3. doi: 10.7097/AFT.200110.0311

6. Kurugol Z, Ozen SS, Koturç G. Severe hemolytic anemia associated with mild pneumonia caused by *Mycoplasma pneumoniae*. *Case Rep Med*. (2012) 2012:694850. doi: 10.1155/2012/694850

7. Gu L, Chen X, Li H, Qu J, Miao M, Zhou F, et al. Severe hemolytic anemia associated with severe pneumonia caused by *Mycoplasma pneumoniae*. *Chin Med J*. (2014) 127:3839. doi: 10.3760/cma.j.issn.0366-6999.20141015

8. Park SJ, Pai KS, Kim AR, Lee JH, Shin JI, Lee SY. Fulminant and fatal multiple organ failure in a 12-year-old boy with *Mycoplasma pneumoniae* infection. *Allergy Asthma Immunol Res*. (2012) 4:55-7. doi: 10.4168/aiar.2012.4.1.55

9. Damar Çakirca T, Torun A, Çakirca G, Portakal RD. Role of NLR, PLR, ELR and CLR in differentiating COVID-19 patients with and without pneumonia. *Int J Clin Pract*. (2021) 75:e14781. doi: 10.1111/ijcp.14781

10. Tamhane UU, Aneja S, Montgomery D, Rogers EK, Eagle KA, Gurm HS. Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. *Am J Cardiol*. (2008) 102:653-7. doi: 10.1016/j.amjcard.2008.05.006

11. Lattanzi S, Cagnetti C, Rinaldi C, Angelocola S, Provinciali L, Silvestrini M. Neutrophil-to-lymphocyte ratio improves outcome prediction of acute intracerebral hemorrhage. *J Neurol Sci*. (2018) 387-398. doi: 10.1016/j.jns.2018.01.038

12. Lattanzi S, Norata D, Divani AA, Di Napoli M, Broggi S, Rocchi C, et al. Systemic inflammatory response index and futile recanalization in patients with ischemic stroke undergoing endovascular treatment. *Brain Sci*. (2021) 11:1614. doi: 10.3390/brainsci11091164

13. Swiñor ME, Piekúł-Słomka N, Slomka A, Sokal P, Zekanowska E, Lattanzi S. Neutrophil-to-lymphocyte ratio and symptomatic hemorrhagic transformation in ischemic stroke patients undergoing revascularization. *Brain Sci*. (2020) 10:771. doi: 10.3390/brainsci1010771

14. Mungan I, Dicle Ç, Bektas S, Sari S, Yamanyar S, Cavuş M, et al. Does the preoperative platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio predict morbidity after gastrectomy for gastric cancer. *Mil Med Res*. (2020) 7:9. doi: 10.1186/s40779-020-00234-y

15. Pu D, Xu Q, Zhou LY, Zhou YW, Liu JY, Ma XL. Inflammation-nutritional markers of peripheral blood could predict survival in advanced non-small-cell lung cancer patients treated with PD-1 inhibitors. *Thorac Cancer*. (2021). doi: 10.1111/1759-7714.14152

16. García-Alfonso P, Muñoz A, Jiménez-Castro J, Jiménez-Fonseca P, Pernicay C, Longo-Muñoz F, et al. Early clinical experience with trifluridine/tipiracil for refractory metastatic colorectal cancer: the ROS study. *Cancers*. (2021) 13:4514. doi: 10.3390/cancers13184514

17. Expert consensus on laboratory diagnostics and clinical practice of *Mycoplasma pneumoniae* infection in children in China (2019). *J Pediatr*. (2020) 58:366–73. doi: 10.3767/jcmj.cn121140-20200304-00176

18. Subspecialty Group of Respiratory Diseases, The Society of Pediatrics, Chinese Medical Association The Editorial Board, Chinese Journal of Pediatrics. [Guidelines for management of community acquired pneumonia in children](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7765999/). (2020) 58:366–73. doi: 10.3767/jcmj.cn121140-20200304-00176

19. Subspecialty Group of Respiratory Diseases, The Society of Pediatrics, Association AM, Editorial Board, Chinese Journal of Pediatrics. [Guidelines for management of community acquired pneumonia in children](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7765999/). (2020) 58:366–73. doi: 10.3767/jcmj.cn121140-20200304-00176

**DATA AVAILABILITY STATEMENT**

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

**ETHICS STATEMENT**

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

**AUTHOR CONTRIBUTIONS**

YL and YX: conception and design. YL: extraction of data and drafting the article. JN and YX: revising the article for intellectual content. YL, JN, and YX: final approval of the completed article. All authors read and approved the final manuscript.

**FUNDING**

This work was supported by Tianjin Science and Technology Committee (20JCXJC00170).
for management of community acquired pneumonia in children (the revised edition of 2013) (I)]. Zhonghua Er Ke Za Zhi. (2013) 51:745-52
31. Wang L, Lu S, Feng Z, Li L, Niu B, Shuai J, et al. The early examination of neutrophil-lymphocyte ratio, monocyte-to-lymphocyte ratio, platelet-to-lymphocyte ratio and red blood cell distribution width in distinguishing between reactive lymphadenopathy and lymphoma in children. Bratisl Lek Listy. (2020) 121:287-92. doi: 10.4149/BLL_2020_045
32. Lu A, Wang C, Zhang X, Wang L, Qian L. Lactate dehydrogenase as a potential markers to predict refractory Mycoplasma pneumoniae pneumonia in Chinese children: a case control study. Respir Res. (2021) 22:89. doi: 10.1186/s12931-020-01577-9
33. Gong H, Sun B, Chen Y, Chen H, Li H. The risk factors of children acquiring refractory Mycoplasma pneumoniae pneumonia: a meta-analysis. Medicine. (2021) 100:e24894. doi: 10.1097/MD.0000000000024894
34. Chen P, Huang Z, Chen L, Zhuang S, Lin H, Xie J, et al. The relationships between lncRNA NNT-AS1, CRP, PCT and their interactions and the refractory Mycoplasma pneumoniae pneumonia in children. Sci Rep. (2021) 11:2059. doi: 10.1038/s41598-021-81853-w
35. Yilmaz H, Yalcin KS, Namuslu M, Celik HT, Sozen M, Inan O, et al. Neutrophil-Lymphocyte Ratio (NLR) could be better predictor than C-reactive protein (CRP) for liver fibrosis in non-alcoholic steatohepatitis (NASH). Ann Clin Lab Sci. (2015) 45:278-86.
36. Lou M, Luo P, Tang R, Peng Y, Yu S, Huang W, et al. Relationship between neutrophil-lymphocyte ratio and insulin resistance in newly diagnosed type 2 diabetes mellitus patients. BMC Endocr Disorders. (2015) 15:9. doi: 10.1186/s12902-015-0002-9
37. Kazama I, Nakajima T. Acute bronchitis caused by bordetella pertussis possibly co-infected with Mycoplasma Pneumoniae. Am J Case Rep. (2019) 20:60-4. doi: 10.12659/AJCR.913430
38. Balta S, Demirkol S, Kucuk U. The platelet lymphocyte ratio may be useful inflammatory indicator in clinical practice. Hemodial Int. (2013) 17:668-9. doi: 10.1111/hdi.12058
39. Sahin A, Sahin M, Yuksel H, Turkcu FM, Cinar Y, Cingi AK, et al. The mean platelet volume in patients with retinal vein occlusion. Ophthalmol. (2013) 2013:236371. doi: 10.1155/2013/236371
40. Liu JR, Peng Y, Yang HM, Li HM, Zhao SY, Jiang ZF. [Clinical characteristics and predictive factors of refractory Mycoplasma pneumoniae pneumonia]. Zhonghua Er Ke Za Zhi. (2012) 50:915-8. doi: 10.1007/s11783-011-0280-z
41. Inamura N, Miyashita N, Hasegawa S, Kato A, Fukuda Y, Sai toh A, et al. Management of refractory Mycoplasma pneumoniae pneumonia: utility of measuring serum lactate dehydrogenase level. J Infect Chemother. (2014) 20:270-3. doi: 10.1016/j.jiac.2014.01.001

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