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ORIGINAL RESEARCH

Clinical Characteristics and Treatment Outcomes of Pediatric Drug-Resistant *Mycoplasma pneumoniae* Pneumonia in the Post-COVID-19 Era

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Video Abstract

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Background: *Mycoplasma pneumoniae* pneumonia (MPP) is a prevalent disease among children. Typically, macrolides are the first-line treatment for MPP in China. However, the number of cases resistant to macrolides has been rising, especially after the outbreak of the COVID-19 pandemic, which has further complicated the clinical management of macrolide-unresponsive *Mycoplasma pneumoniae* pneumonia (MUMPP) in children.

Objective: This study examined the clinical characteristics of MUMPP and the effects of various treatments on children with MUMPP during March 2023 to February 2024 in southern China.

Methods: We conducted a retrospective case–control study at a university-affiliated hospital in southern China. Patients were categorized based on their response to macrolide treatment into two groups: MUMPP and control group. The study included 549 pediatric patients. Of these, 297 were in the MUMPP group and 252 were in the control group. This categorization allowed us to compare clinical characteristics and laboratory indicators between the groups. The MUMPP group received one of the three treatments: combined antibiotics, additional steroids, or a switch to doxycycline. Subsequently, we analyzed differences in clinical outcomes, which included hospital stay, hospital cost, and recovery time.

Results: No significant differences were found in gender or pre-admission disease duration between the MUMPP and control group ($P>0.05$). However, subjects in MUMPP group was older, had longer fever durations, extended hospital stays, higher medical costs, and elevated levels of C-reactive protein, lactate dehydrogenase, IL-6, and γ-IFN. All of which showed statistically significant differences ($P<0.05$). Within the MUMPP group, patients switched to doxycycline had the shortest hospital stay and recovery time, significantly differing from those in other treatment groups ($P<0.05$).

Conclusion: Children in the MUMPP group exhibited higher inflammatory indicators than the control group. The early adaptation of treatment strategies, particularly the switch to doxycycline, is associated with improved clinical outcomes.

Keywords: *Mycoplasma pneumoniae* pneumonia, macrolide resistance, post-COVID-19, clinical characteristics, treatment

Introduction

Despite advancements in medical and microbiological research, pneumonia continues to be a leading cause of death among children.[1] *Mycoplasma pneumoniae* has become one of the important pathogens of community-acquired pneumonia in children, especially those over five years old worldwide, and it is increasingly affecting younger children.[2,3] In China, the infection of *M. pneumoniae* varies seasonally across different regions, being more common in the autumn and winter in the north, and in the summer and autumn in the south.[4,5] Notably, after the COVID-19 outbreak, there has been a peak in *M. pneumoniae* infections among children in China, especially in the latter half of 2023. According to data in Beijing, during the *M. pneumoniae* epidemic in 2023, the positive detection rate (by RT-PCR assay) of *M. pneumoniae* in outpatient patients can reach 25.4%.[6] The global prospective surveillance study on *M. pneumoniae* indicates the re-

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emergence of *M. pneumoniae* in Europe and Asia, more than three years after the introduction of COVID-19 pandemic restrictions. Data was collected from 45 sites across 24 countries within the four UN regions. The mean incidence of *M. pneumoniae* detected by PCR from April 1 to September 30, 2023, was 4.12%. Detections by IgM serology were 6.58% of 2403 samples, and detections by IgG serology were 12.35% of 2364 samples.[7] According to our observations, the number of *M. pneumoniae* infection cases has increased significantly, and the clinical manifestations are more severe. Severe cases of *M. pneumoniae* pneumonia (MPP) can be life-threatening, leaving some children with permanent respiratory impairments such as obliterative bronchiolitis.[8] Therefore, early and effective treatment of MPP is critical to prevent progression to severe or chronic conditions. Typically, macrolides such as azithromycin and erythromycin are the first-line treatments.[9] Historical data suggest that early and complete courses of macrolides are effective against MPP;[10] however, the incidence of macrolide-resistant strains which necessitates an adaptation of treatment strategies has increased globally in recent years.[11–13] Moreover, the COVID-19 outbreak has further complicated the clinical management of macrolide-resistant MPP in children in China,[14,15] presenting new diagnostic and therapeutic challenges.

Early identification of resistant strains is crucial for effective treatment, and the best treatment window is within 5 to 10 days after the onset of fever.[6] In clinical practice, identifying drug-resistant *M. pneumoniae* pneumonia early, and recognizing the clinical characteristics of these infections are important issues. When we find unresponsiveness to macrolide drugs early in the treatment process, we should be alert to the possibility of drug-resistant *M. pneumoniae*. A lack of expected response to macrolide treatment may indicate the presence of drug-resistant *M. pneumoniae*, leading to the classification of macrolide-unresponsive *M. pneumoniae* pneumonia (MUMPP). MUMPP is characterized by persistent fever and worsening clinical and radiographic findings despite 72 hours of standard macrolide therapy.[9] Early recognition of its clinical features is critical for managing this condition. In this article, we analyzed the clinical features of the MUMPP group compared to the control group, and evaluated the efficacy of different treatment strategies on clinical outcomes in the MUMPP group.

Materials and Methods

Study Subjects

The retrospective case–control study involved all individuals aged from 2 months to 16 years diagnosed with MPP from March 2023 to February 2024, at Shenzhen Maternity and Child Healthcare Hospital, affiliated with Southern Medical University, in southern China. Clinical data from individuals with clear treatment histories and recovery at discharge, and with comprehensive and available clinical data, were selected for the study. Each individual was identified through the hospital's electronic medical record system. Patients with underlying conditions (eg preterm bronchopulmonary dysplasia, primary immunodeficiency, congenital heart disease, severe hepatic or renal dysfunction), concurrent conditions such as Kawasaki disease and infectious mononucleosis, unclear treatment plans or grouping were excluded.

Inclusion Criteria

- Ages 2 months to 16 years.
- Diagnosis according to MPP criteria.
- Clear treatment history and recovery at discharge.
- Comprehensive clinical data available.

Exclusion Criteria

- Underlying conditions such as preterm bronchopulmonary dysplasia, primary immunodeficiency, congenital heart disease, severe hepatic or renal dysfunction.
- Concurrent conditions like Kawasaki disease, infectious mononucleosis.
- Ongoing treatment with long-term corticosteroids or immunosuppressants.
- Cases with insufficient clinical data.

Diagnostic Criteria and Related Indicators

M. pneumoniae Pneumonia (MPP) involved infection by *M. pneumoniae* leading to lung inflammation, potentially affecting bronchi, bronchioles, alveoli, and pulmonary interstitium.[9] The diagnostic criteria for MPP typically included: (1) clinical symptoms such as fever and cough; (2) radiographic evidence of pulmonary infiltrates on chest imaging; and (3) laboratory confirmation with a positive serum MP IgM test and a positive MP-RNA test from a pharyngeal swab.

Macrolide-unresponsive *M. pneumoniae* pulmonary (MUMPP) was defined when children with MPP exhibit persistent fever and no improvement or worsening in clinical signs and pulmonary imaging after 72 hours of standard macrolide treatment.[3] The condition can be related to drug resistance, abnormal immune responses, or co-infections.

The primary clinical outcomes were hospital stay, recovery time, and hospital costs. Recovery time was defined as the period required for the complete resolution of lung lesions or the complete disappearance of cough.

Collection of Clinical Data

The study employed a retrospective, case–control approach. We reviewed and collected data from the electronic health medical record system of Shenzhen Maternity and Child Healthcare Hospital, including general demographics, laboratory results at admission, treatment details, hospitalization outcomes, discharge follow-up information, and other relevant data. Patients were first categorized into an unresponsive (MUMPP) group and a responsive group (control group) based on their response to azithromycin or erythromycin after 72 hours. A total of 549 children diagnosed with MPP at the hospital were included in the study. Of these, 297 were in the MUMPP group (137 males, 160 females) and 252 were in the control group (123 males, 129 females). Then, patients in the MUMPP group were further divided into one of the three treatment subgroups based on subsequent clinical decisions: 1) combined use of antibiotics (third-generation cephalosporins: ceftriaxone 80 mg/kg/day once or ceftazidime 100 mg/kg/day twice); 2) addition of steroids (methylprednisolone 2 mg/kg/day); 3) switching to doxycycline (0.02 mg/kg/day).

Our study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cohort studies and was conducted in accordance with the Declaration of Helsinki. The study was approved by the Ethics Committee of Shenzhen Maternity and Child Healthcare Hospital and informed consent requirements were waived due to deidentification of the data.

Statistical Analysis

Data analysis was performed using SPSS version 25.0. The Mann–Whitney *U*-test was used to compare non-normally distributed quantitative data between the two groups, and the Kruskal–Wallis test was used among three groups. Categorical data were compared using the chi-square test. A P-value of less than 0.05 was considered statistically significant.

Results

General Data

There were no significant differences in gender or disease duration before admission between the groups ($P > 0.05$). Children in the MUMPP group were significantly older, had a longer fever duration and hospital stay, and higher hospital costs than the control group ($P < 0.05$) (Table 1).

Laboratory Indicators

Significant differences were observed in the levels of C-reactive protein, lactate dehydrogenase, IL-6, and γ-IFN between groups, with higher values in the MUMPP group ($P<0.05$) (Table 2).

Monthly Trend of Macrolide-Unresponsive MPP Proportion

From March 2023 to February 2024, the monthly trend of the MUMPP group was analyzed, and the proportion was calculated for each month. The MUMPP rate overall showed an upward trend from March to December and gradually declined after entering 2024. See Figure 1.

Table 1 Basic Clinical Characteristics

Clinical Characteristic	MUMPP Group (n=297)	Control Group (n=252)	P-value
Gender (Male: Female)	137:160	123:129	0.549
Age (y)	6.66 (4.5–7.0)	3.16 (1.6–5.84)	<0.001
Duration of Illness(d)	7(5–9)	6(4–9)	0.071
Duration of Fever (d)	6(4–7)	3(1–5)	<0.001
Hospital Stay (d)	5(4–7)	4(4–5)	<0.001
Hospital Costs (CNY)	4696 (3912–7073)	4519 (3861–5318)	0.003

Table 2 Comparison of Laboratory Indicators Between the Two Groups

Laboratory Indicators	MUMPP Group (n=297)	Control Group (n=252)	P-value
White Blood Cells (10^9/L)	7.58(5.80–9.50)	7.53(6.12–9.86)	0.221
Platelets (10^9/L)	275(221–343)	284(239–345)	0.179
C-reactive Protein (mg/L)	12.46(5.92–22.91)	7.01(1.47–17.83)	<0.001
Procalcitonin (ng/mL)	0.08(0.04–0.14)	0.07(0.04–0.11)	0.124
Lactate Dehydrogenase (U/L)	316(272–393)	296(256–351)	<0.001
IL-6 (pg/mL)	29.41(14.59–65.65)	23.26(12.59–47.62)	0.002
γ-IFN (pg/mL)	76.67(35.7–168.72)	35.32(18.37–56.18)	<0.001

Analysis of Clinical Outcomes for the MUMPP Group

Depending on the subsequent clinical decisions, the patients were divided into three treatment groups: Treatment Group 1 (combined use of antibiotics), Treatment Group 2 (added steroids), and Treatment Group 3 (switched to doxycycline). We compared hospital stay, recovery time, and hospital costs. In terms of clinical outcomes within the MUMPP group, significant differences between groups were found in hospital stay and recovery time. Those who switched to doxycycline (Treatment Group 3) had the shortest hospital stay and the fastest recovery time, respectively (P = 0.013, P = 0.007). There was no significant difference in hospital costs between groups (P = 0.453) (Table 3).

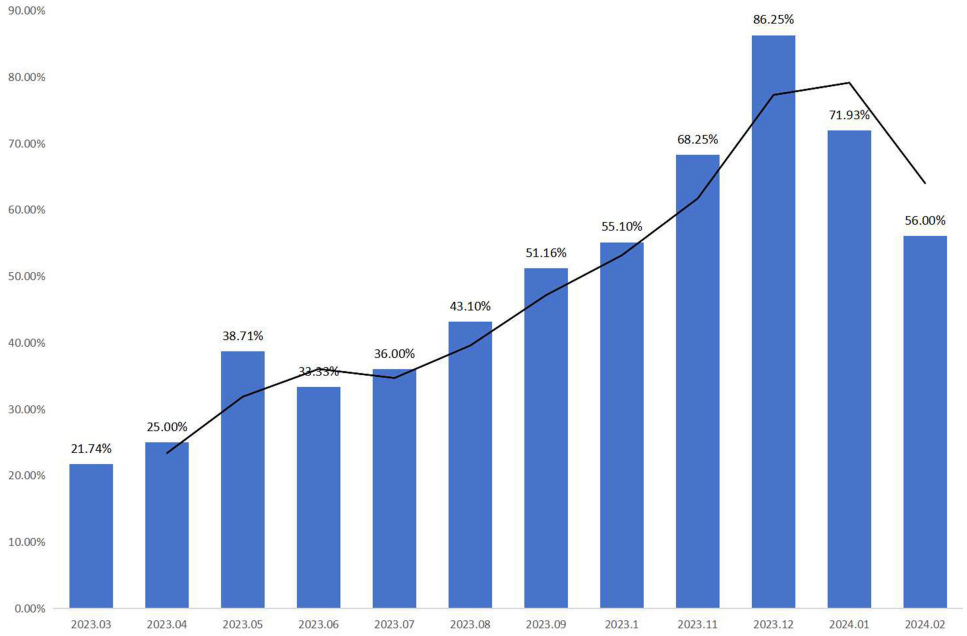

Figure 1 Monthly Change Trend of MUMPP Proportion in Children.

Table 3 Comparison of Clinical Outcomes After Changing Treatment Plans in the MUMPP Group

Clinical Outcomes	Treatment Group 1 (n=105)	Treatment Group 2 (n=112)	Treatment Group 3 (n=80)	P-value
Hospital Stay (d)	5(4–7)	5(4–6)	4.5(3–6)	0.013
Recovery Time (d)	12(10–15.5)	11.5(9~15)	11(9–12.75)	0.007
Hospital Costs (CNY)	4776(3908–6181)	4939(3966–6236)	4519(3776–6120)	0.453

Discussion

This study described the clinical characteristics of MUMPP in children and assessed the effectiveness of various treatment strategies during the one year following the COVID-19 outbreak in China. Our findings reveal that children in the MUMPP group, typically older with a mean age of 6.66 years, displayed prolonged fever duration and hospital stay, as well as elevated levels of inflammatory markers such as C-reactive protein (CRP), lactate dehydrogenase, IL-6, and γ-IFN. Research conducted by Di Weiwei et al[16] also indicates that in children with refractory *M. pneumoniae* infection, elevated levels of white blood cell count, CRP, procalcitonin, lactate dehydrogenase, and ferritin are associated with more severe radiological findings, longer hospital stays, and a higher incidence of hypoxemia. These indicators suggest a robust association with more severe clinical presentations and underscore the necessity for prompt and tailored treatment interventions to manage drug-resistant MPP effectively.

Notably, children who did not respond to conventional macrolide treatment benefited significantly from switching to doxycycline, which resulted in the shortest hospital stay and recovery time.[17] This outcome challenges the traditional reliance on macrolides and suggests that doxycycline could be a viable first-line therapy for macrolide-resistant cases. In contrast, treatments involving steroids or combined antibiotics were less effective, highlighting the need for strategic treatment adjustments based on the initial response to macrolide therapy. Doxycycline, a tetracycline antibiotic, offers broad-spectrum activity against various pathogens, including M. pneumoniae, and retains efficacy in the presence of macrolide resistance. Unlike macrolides, which bind to the 50S ribosomal subunit, doxycycline binds to the 30S subunit, inhibiting protein synthesis. This distinct mechanism of action allows doxycycline to overcome resistance associated with 23S rRNA mutations, such as A2063G, that confer resistance to macrolides. Consequently, doxycycline emerges as an effective alternative for treating MUMPP. Although tetracyclines offer a potential therapeutic alternative, the side effects, associated with tetracycline use in children under eight years of age, must be carefully considered.[18]

During the first year following the COVID-19 outbreak, the overall MUMPP rate showed an upward trend from March to December and gradually declined after entering 2024. The concept of "immune debt", introduced by Robert Cohen et al[19] resonates with our findings, suggesting that diminished natural immunity among children, due to reduced exposure to pathogens during the pandemic, has facilitated the resurgence of infections like MPP.[7,20] This scenario is compounded by the rise in macrolide-resistant strains,[21,22] emphasizing the urgent need for revising vaccination and the sensitive use of antibiotics.

The treatment with macrolides has become complicated due to the emergence of strains resistant to macrolides.[23] This resistance is associated with mutations in the peptidyltransferase region of the Mycoplasma 23S rRNA, particularly at positions 2063 and 2064, with 2063 being especially significant.[23,24] These mutations have been observed worldwide, and the prevalence of macrolide resistance varies significantly by region, with rates as high as 90% in Asia.[25] Genetic mutations in the 23S rRNA gene of *M. pneumoniae*, which are primarily responsible for macrolide resistance, have become increasingly prevalent.[26] These mutations, along with the upregulation of efflux pumps, pose a complex challenge for treating infectious diseases in the post-pandemic era.[27] Another possible reason for this increase might be associated with the overuse of antibiotics, especially macrolides. A recently published study showed that a decreased macrolide prescription rate was associated with a decreasing proportion of macrolide-resistant strains infections in Japan.[28]

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Concluding Remarks

In our research, children in the MUMPP group, those who did not respond to 72 hours of macrolide antibiotic treatment, exhibited higher inflammatory indicators at admission time. The early adaptation of treatment strategies, particularly the switch to doxycycline, is associated with improved clinical outcomes. Our study underscores the importance of vigilant monitoring for macrolide resistance in *M. pneumoniae* pneumonia and advocates for an early switch to alternative treatments, such as doxycycline, to enhance clinical outcomes.

As the global medical community continues to fight against the aftereffects of the COVID-19 pandemic, our findings contribute to a deeper understanding of how pandemic-related changes in human behavior and medical practice might continue to influence the epidemiology of respiratory infections. Furthermore, our research supports the need for integrated strategies that combine both pharmacological and public health interventions to manage the increasing challenge of antibiotic-resistant infections.

Future Directions

Further research is necessary to explore the long-term impacts of immune debt and its implications for global health security. Additionally, studies focusing on the development of new antimicrobial agents and vaccines against *M. pneumoniae* are crucial to prevent severe outcomes in pediatric populations.

The findings of this study have significant implications for pediatric healthcare providers and public health policy-makers, emphasizing the need for strategic planning and resource allocation to strengthen our health system against the evolving infectious diseases.

Limitations

This study has several limitations. First, as a retrospective observational cohort study, it is subject to inherent recall bias, particularly in the categorization of children based on body temperature, cough, and imaging findings post-medication. Second, we did not grade the severity of pneumonia in children with MPP, which may introduce confounding bias affecting our results. Third, the study did not monitor changes in laboratory indicators during and after treatment, leaving specific mechanisms of MUMPP unclear. Future research should aim to extend the monitoring period and conduct in-depth basic investigations to better understand these mechanisms and their clinical significance.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

References

1. Verani Jennifer R, Blau Dianna M, Gurley Emily S, et al. Child deaths caused by Klebsiella pneumoniae in sub-Saharan Africa and South Asia: a secondary analysis of child health and mortality prevention surveillance (CHAMPS) data. *Lancet Microbe*. 2024;5(2):e131–e141. doi:10.1016/S2666-5247(23)00290-2
2. Kumar S, Kumar S. *Mycoplasma pneumoniae*: among the smallest bacterial pathogens with great clinical significance in children. *Indian J Med Microbiol*. 2023;46:100480. doi:10.1016/j.ijmmb.2023.100480
3. Waites Ken B, Xiao L, Liu Y, et al. *Mycoplasma pneumoniae* from the respiratory tract and beyond. *Clin Microbiol Rev*. 2017;30(3):747–809. doi:10.1128/CMR.00114-16
4. Jiande C, Jing Z, Zhiwei L, et al. *Mycoplasma pneumoniae* among Chinese outpatient children with mild respiratory tract infections during the coronavirus disease 2019 pandemic. *Microbiol Spectr*. 2022;10(1):e0155021. doi:10.1128/spectrum.01550-21

5. Wang X, Li M, Luo M, et al. *Mycoplasma pneumoniae* triggers pneumonia epidemic in autumn and winter in Beijing: a multicentre, population-based epidemiological study between 2015 and 2020. *Emerg Microbes Infect*. 2022;11(1):1508–1517. doi:10.1080/22221751.2022.2078228
6. Chao Y, Guan-Hua X, Han-Qing Z, et al. Current status of *Mycoplasma pneumoniae* infection in China. *World J Pediatr*. 2024;20(1):1–4.
7. Meyer Sauteur Patrick M, Beeton Michael L, Pereyre S. *Mycoplasma pneumoniae*: delayed re-emergence after COVID-19 pandemic restrictions. *Lancet Microbe*. 2024;5(2):e100–e101. doi:10.1016/S2666-5247(23)00344-0
8. Liu J, He R, Zhang X, et al. Clinical features and ”early” corticosteroid treatment outcome of pediatric *Mycoplasma pneumoniae* pneumonia. *Front Cell Infect Microbiol*. 2023;13:1135228. doi:10.3389/fcimb.2023.1135228
9. China national health commission of the people’s republic of guidelines for the diagnosis and treatment of *Mycoplasma pneumoniae* pneumonia in children (2023 edition). Electronic Journal of Emerging Infectious Diseases. 2024.
10. Brown RJ, Macfarlane-Smith L, Phillips S, et al. Detection of macrolide resistant *Mycoplasma pneumoniae* in England, September 2014 to September 2015. *Euro Surveill*. 2015;20(48):30078. doi:10.2807/1560-7917.ES.2015.20.48.30078
11. Lanata MM, Wang H, Everhart K, et al. Macrolide-resistant *Mycoplasma pneumoniae* infections in children, Ohio, USA. *Emerg Infect Dis*. 2021;27(6):1588–1597. doi:10.3201/eid2706.203206
12. Oishi T, Ouchi KR. Trends in the epidemiology, diagnosis, and treatment of macrolide-resistant *Mycoplasma pneumoniae*. *J Clin Med*. 2022;11(7). doi:10.3390/jcm11071782
13. Joon Kee L, Taekjin L, Yae-Jean K, et al. Clinical manifestations, macrolide resistance, and treatment utilization trends of *Mycoplasma pneumoniae* pneumonia in children and adolescents in South Korea. *Microorganisms*. 2024;12(9):1806. doi:10.3390/microorganisms12091806
14. Ding G, Zhang X, Vinturache A, et al. Challenges in the treatment of pediatric *Mycoplasma pneumoniae* pneumonia. *Eur J Pediatr*. 2024;183(7):3001–3011. doi:10.1007/s00431-024-05519-1
15. Du H, L J, Li X, et al. Impact of the COVID-19 pandemic on epidemiological and clinical characteristics of *Mycoplasma pneumoniae* pneumonia in children: a multicenter study from Hubei, China. *Front Pediatr*. 2024;12:1388132. doi:10.3389/fped.2024.1388132
16. Wei D, Zhao Y, Zhang T, et al. The role of LDH and ferritin levels as biomarkers for corticosteroid dosage in children with refractory *Mycoplasma pneumoniae* pneumonia. *Respir Res*. 2024;25(1):266. doi:10.1186/s12931-024-02892-1
17. Xu Y, Yang C, Sun P, et al. Epidemic features and megagenomic analysis of childhood *Mycoplasma pneumoniae* post COVID-19 pandemic: a 6-year study in southern China. *Emerg Microbes Infect*. 2024;13(1):2353298. doi:10.1080/22221751.2024.2353298
18. Lee H, Yun KW, Lee HJ, et al. Antimicrobial therapy of macrolide-resistant *Mycoplasma pneumoniae* pneumonia in children. *Expert Rev Anti Infect Ther*. 2018;16(1):23–34. doi:10.1080/14787210.2018.1414599
19. Robert C, Marion A, Muhamed-Kheir T, et al. Pediatric infectious disease group (GPIP) position paper on the immune debt of the COVID-19 pandemic in childhood, how can we fill the immunity gap? *Infect Dis Now*. 2021;51(5):418–423. doi:10.1016/j.idnow.2021.05.004
20. Maeve B, Penelope J, Mihiri W, et al. Impact of COVID-19 on people with non-functioning spleens in Australia. *J Infect Public Health*. 2024;17(4):657–662. doi:10.1016/j.jiph.2024.02.007
21. Li X, Li T, Chen N, et al. Changes of *Mycoplasma pneumoniae* prevalence in children before and after COVID-19 pandemic in Henan China. *J Infect*. 2023;86(3):256–308.
22. Li-Na Z, Ling C, Meng L-H. Meng Ling-Hui.Pathogenic changes of community-acquired pneumonia in a children’s hospital in Beijing, China before and after COVID-19 onset: a retrospective study. *World J Pediatr*. 2022;18(11):746–752. doi:10.1007/s12519-022-00592-8
23. Kim K, Jung S, Kim M, et al. Global trends in the proportion of macrolide-resistant *Mycoplasma pneumoniae* Infections. *JAMA Network Open*. 2022;5(7):e2220949. doi:10.1001/jamanetworkopen.2022.20949
24. Jiang Y, Kang H, Dou H, et al. Comparative genomic sequencing to characterize *Mycoplasma pneumoniae* genome, typing, and drug resistance. *Microbiol Spectr*. 2024;12(8):e0361523. doi:10.1128/spectrum.03615-23
25. Yen MH, Yan DC, Wang CJ, et al. The clinical significance of and the factors associated with macrolide resistance and poor macrolide response in pediatric *Mycoplasma pneumoniae* infection: a retrospective study. *J Microbiol Immunol Infect*. 2023;56(3):634–640. doi:10.1016/j.jmii.2023.01.010
26. Dekyi XY, Xia W, Wang X, et al. Predominance of A2063G mutant strains in the *Mycoplasma pneumoniae* epidemic in children: a clinical and epidemiological study in 2023 in Wuhan China. *Int J Infect Dis*. 2024;145:107074. doi:10.1016/j.ijid.2024.107074
27. Han HY, Park KC, Yang EA, et al. Macrolide-resistant and macrolide-sensitive *Mycoplasma pneumoniae* pneumonia in children treated using early corticosteroids. *J Clin Med*. 2021;10(6):1309. doi:10.3390/jcm10061309
28. Nakamura Y, Oishi T, Kaneko K, et al. Recent acute reduction in macrolide-resistant *Mycoplasma pneumoniae* infections among Japanese children. *J Infect Chemother*. 2021;27(2):271–276. doi:10.1016/j.jiac.2020.10.007