doi.org/10.36721/PJPS.2026.39.2.REG.13247.1

The impact of non–pharmaceutical interventions on the epidemiological characteristics and macrolide resistance of *Mycoplasma pneumoniae* infection in children during COVID–19 in single centre

Hong Liu[1], Fadi Liu[2]*, Lijuan Xiong[1], Shuai Liu[3], Fen Yang[3] and Qiang Chen[4]*

[1]Department of Emergency, Jiangxi Provincial Children's Hospital, Nanchang, Jiangxi, People's Republic of China
[2]Laboratory Medicine, Jiangxi Provincial Children's Hospital, Nanchang, Jiangxi, People's Republic of China
[3]Medical School of Nanchang University, Nanchang, Jiangxi, People's Republic of China
[4]Pneumology Department, Jiangxi Provincial Children's Hospital, Nanchang, Jiangxi, People's Republic of China

Abstract: **Background**: Non-pharmaceutical interventions (NPIs) implemented during the COVID-19 period may have influenced epidemiological characteristics of *Mycoplasma pneumoniae* (MP) infection and macrolide resistance in Children. Objective: To investigate the impact of NPIs on the epidemiological characteristics and macrolide resistance of MP infection in children from Jiangxi. **Methods**: Clinical data from patients tested for MP-DNA between 2019 and. 2023 were analyzed and categorized into pre-NPIs (2019), during-NPIs (2020-2022), and post-NPIs (2023) periods. **Results**: Among 19,862 specimens, 2,913 (14.67%) were MP-DNA positive, with·71.13% carrying macrolide-resistant mutations. The MP. Infection rate dropped significantly during NPIs (3 .76%) compared to pre-NPI (22.19%) and post-NPI· (29.78%) periods (χ^{2}·=. 2327.01, p <·0.01). The macrolide-resistant mutation rate was lowest during NPIs (59.26%) versus pre-NPI· (70.21%) and post-NPI (73 89%) (χ^{2} = 35.19, p < 0.01). Resistance rates did not differ by gender but were highest in children aged 3-<6 years (74.20%). The age distribution of resistant cases shifted, with the highest proportion in 3-<6·years pre-NPIs (33.25%) and in >6·years post-NPIs (55.07%). **Conclusion**: NPls temporarily reduced, MP incidence and overall macrolide resistance, especially in older children, but created an immune debt, leading to a significant post-NPI surge. Targeted public health strategies in schools and childcare settings may help control MP spread and resistance.

Keywords: Children; Epidemiology; *Mycoplasma pneumonia*; Macrolide resistance; Non–pharmaceutical interventions

Submitted on 16-08-2024 – Revised on 17-02-2025 – Accepted on 30-07-2025

INTRODUCTION

Mycoplasma pneumoniae (MP), classified under Mollicutes and the Mycoplasma genus, is the smallest microorganism known to grow on solid media without relying on living cells. MP is one of the most common pathogens causing respiratory infections in children, primarily transmitted through respiratory droplets and direct contact. It can cause both upper and lower respiratory tract infections, as well as severe extrapulmonary complications (Waites and Talkington, 2004). Currently, there is no vaccine available for MP and regional epidemics occur every 3 to 7 years. Children are susceptible to MP infection due to the relatively narrow airway lumen and incomplete development of the respiratory and immune systems. MP is the most important pathogen causing community acquired pneumonia (CAP) in children over the age of 5. At the peak of the epidemic, *Mycoplasma pneumoniae* pneumonia (MPP) accounts for up to 50% of CAP in children. MP is also the third most frequent pathogen causing lower respiratory tract infections following *Streptococcus pneumoniae* and viral pathogens (GBD, 2024). Macrolide antibiotics are the first–line treatment for MP infections in children (Ning *et al*., 2017). Since 2000, infections with macrolide–resistant *Mycoplasma pneumoniae* (MRMP) have rapidly increased in some parts of the world (Kim *et al*., 2022). Detection of MP macrolide resistance mutations is a rapid clinical method to identify MRMP. In some regions of China, the detection rate of MP resistance mutations exceeds 90% (Jiang *et al.,* 2023).

After the outbreak of COVID-19 at the end of 2019, widely implemented non-pharmaceutical interventions (NPIs) limited the spread of the virus in communities and also impacted other infectious diseases in children (Principi *et al*., 2023). The issue of immune debt, resulting from insufficient immune stimulation in children and reduced herd immunity under NPIs, may lead to negative consequences once NPIs are reduced or lifted (Cohen *et al.,* 2021). The impact of immune debt under NPIs on the epidemiological characteristics and drug resistance of MP in this region is currently unclear. This study aims to analyze the changes in the epidemiological characteristics and drug resistance of MP in children across three stages (before the implementation of NPIs, during the full implementation of NPIs and after the reduction of NPIs), thus providing a basis for the prevention and control of MP in children.

MATERIALS AND METHODS

Study subjects

A total of 19,862 patients with acute respiratory tract

**Corresponding author:* e-mail: panda12366@163.com, liufadi@ncmc.edu.cn

infection who visited Jiangxi Provincial Children's Hospital and underwent MP DNA testing from January 1, 2019, to December 31, 2023 were collected as screening subjects. Inclusion criteria: (1) Patients with positive MP DNA results from throat swabs, sputum, or bronchoalveolar lavage samples; (2) Patients who also underwent MP resistance mutation site detection; (3) Only one MP positive result was counted for the same patient during a single hospitalization. Exclusion criteria: Incomplete clinical data. A total of 2,913 MP DNA-positive patients were selected as study subjects, with 574, 24, 137, 244 and 1,934 cases in the five years, respectively. Patients' inclusion flowchart is shown in fig. 1. According to the occurrence time of COVID-19 pandemic, the patients were divided into three groups: pre–NPIs (2019), during–NPIs (2020-2022) and post–NPIs (2023).

Research methods

Clinical information collection

Patient age, gender, visit time, primary diagnosis, specimen type and collection time were gathered using the hospital information system.

MP nucleic acid and resistance mutation detection

MP nucleic acid and resistance mutation detection kits (Jiangsu Mole Bioscience Co., Ltd.) were used. PCR combined with TaqMan fluorescent probe technology was applied to qualitatively detect the MP nucleic acid target P1 gene and the two resistance mutation sites of 23S rRNA (A2063G and A2064G) in the specimens. The limit of detection (LOD) is 500 copies/mL. The detection sensitivity and specificity of this kit were more than 90%. Result determination: VIC fluorescence signal Ct value < 35.01 indicated MP positive; FAM fluorescence signal Ct value < 35.33 indicated A2063G or A2064G resistance mutation, while ≥ 35.33 indicated no A2063G or A2064G resistance mutation.

Statistical analysis

Data was statistically analyzed using SPSS 25.0 software. Categorical data was expressed as rate or percentage (%). Comparisons between groups were performed using the chi–squared test or Fisher's exact test. Mantel–Haenszel chi–squared test was used to determine if there was a linear relationship. $P < 0.05$ was considered as statistically significant.

RESULTS

Detection of MP–DNA from 2019 to 2023

Among the 19,862 respiratory specimens collected between 2019 and 2023, 2,913 were positive for MP–DNA, with an overall positivity rate of 14.67%. The MP–DNA positive rate was 3.76% in during–NPIs group, which was significantly lower than that in pre-NPIs (22.19%) and post–NPIs (29.78%) groups ($\chi^2 = 2327.01$, $P < 0.01$). And the MP-DNA positive rate in post–NPIs group was significantly higher than that in pre-NPIs group ($\chi^2 = 53.30$, $P < 0.01$). As for the gender stratification, the MP–DNA positive rate in females (17.08%) was higher than that in males (13.22%), showing a significant difference (χ^2=55.54, $P < 0.01$). Stratified by age, the positive rates from highest to lowest were ≥6 years (27.58%), 3–<6 years (16.66%), 1–<3 years (8.40%) and <1 year (3.12%). The result of Mantel–Haenszel chi-squared test indicated a linear relationship between age and MP–DNA positive rate ($\chi^2 = 1225.73$, $P < 0.01$). The result of Pearson correlation showed R=0.25, $P < 0.01$, indicating a positive correlation between age and MP–DNA positivity rate. Grouped by quarters, MP-DNA positive rates were 21.02%, 17.71%, 12.66%, and 3.61% in the third quarter, fourth quarter, second quarter and first quarter, respectively, with significant differences ($\chi^2 = 618.90$, $P < 0.01$). The MP–DNA positivity rates in different periods are shown in table 1.

Detection of macrolide-resistant mutations in MP in different periods

Comparison among different periods

Among the 2,913 MP–DNA positive specimens from 2019 to 2023, 2,072 were found to have macrolide–resistant mutations, with a positivity rate of 71.13%. There were significant differences in the detection rates of macrolide-resistant mutations in different NPIs periods ($\chi^2 = 35.19$, $P < 0.01$), as shown in table 2. The positive rate in during–NPIs group was 59.26% (240/405), which was significantly lower than that in pre–NPIs group (χ^2 =12.63, $P < 0.01$) and post–NPIs group (χ^2 =35.06, $P < 0.01$). There was no significant difference between the post–NPIs and pre–NPIs groups (χ^2 =3.04, $P = 0.08$).

Comparison by gender and age group

The positive rate for macrolide–resistant mutations was 70.40% (1156/1642) in male children and 72.07% (916/1271) in female children, with no significant differences (χ^2=0.97, $P = 0.33$). The overall positive rate for macrolide–resistant mutations was highest in the 3–<6 years group (74.20%), followed by the ≥6 years group (70.52%), the 1–<3 years group (69.69%) and the <1 year group (60.00%). There were significant differences among age groups ($\chi^2 = 11.55$, $P < 0.01$), as shown in table 2. The changes in the detection rates of macrolide-resistant mutations stratified by age across different NPI periods are shown in table 3. The highest detection rate was ≥6 years before NPIs, followed by 1–<3 years during NPIs and 3–<6 years pre–NPIs. Significant differences were found in the detection rates of macrolide-resistant mutations between the ≥6 years group ($\chi^2 = 16.61$, $P < 0.01$) and the 3–<6 years group ($\chi^2 = 13.84$, $P < 0.01$).

Comparison by quarter

The detection rates of MP macrolide resistance mutations in different quarters are shown in table 2. There was no statistical difference in the detection rates of macrolide-resistant mutations among the four quarters ($\chi^2 = 3.97$, $P = 0.27$).

Table 1: MP–DNA positive rates in different periods

Item	Total	MP–DNA Positive rate (%; cases)	Chi–Square value (χ^2)	*P* value
NPIs group				
pre–NPI	2587	22.19% (574)	2327.01	<0.01
during–NPI	10780	3.76% (405)		
post–NPI	6495	29.78% (1934)		
Gender				
Male	12422	13.22% (1642)	55.54	<0.01
Female	7440	17.08% (1271)		
Age				
<1 year	3526	3.12% (100)	1225.73	<0.01
1–<3 years	5777	8.40% (485)		
3–<6 years	5443	16.66% (907)		
≥6 years	5116	27.58% (1411)		
Quarter				
1 (Jan–Mar)	3994	3.61% (144)	618.9	<0.01
2 (Apr–Jun)	4203	12.66% (532)		
3 (Jul–Sep)	5181	21.02% (1089)		
4 (Oct–Dec)	6484	17.71% (1148)		

Table 2: Detection rates of macrolide–resistant mutations in MP in different periods

Item	Total	Macrolid–resistant mutation detection rate (%; cases)	Chi–Square value (χ^2)	*P* value
NPIs group				
Pre–NPIs	574	70.21% (403)	35.19	<0.01
During–NPIs	405	59.26% (240)		
Post–NPIs	1934	73.89%（1429）		
Gender				
Male	1642	70.40% (1156)	0.97	0.33
Female	1271	72.07% (916)		
Age				
<1 year	110	60.00% (66)	11.55	<0.01
1–<3 years	485	69.69% (338)		
3–<6 years	907	74.20% (673)		
≥6 years	1411	70.52% (995)		
Quarter				
1 (Jan–Mar)	144	65.28% (94)	3.97	0.27
2 (Apr–Jun)	532	70.86% (377)		
3 (Jul–Sep)	1089	70.43% (767)		
4 (Oct–Dec)	1148	72.65% (834)		

Table 3: Comparison of macrolid–resistant mutation detection rates in groups stratified by age (%; cases)

Period	<1 year	1–<3 years	3–<6 years	≥6 years	Chi–Square Value (χ^2)	*P* Value
Pre–NPIs	64.86% (24/37)	67.17% (133/198)	72.43% (134/185)	72.73% (112/154)	2.28	0.52
During–NPIs	47.83% (11/23)	62.92% (56/89)	61.60% (77/125)	57.14% (96/168)	2.34	0.51
Post–NPIs	62.00% (31/50)	75.25% (149/198)	77.39% (462/597)	72.27% (787/1089)	9.12	0.02
Chi–Square (χ^2)	1.87	5.43	13.84	16.42		
P Value	0.39	0.07	<0.01	<0.01		

Table 4: Age Distribution of MP–DNA and macrolid–resistant mutation positive cases in different periods (cases and composition ratio)

Item	Age	Pre–NPIs	During–NPIs	Post–NPIs
MP–DNA positive				
	<1 year	37 (6.45%)	23 (5.68%)	50 (2.59%)
	1–<3 years	198 (34.49%)	89 (21.98%)	198 (10.24%)
	3–<6 years	185 (32.23%)	125 (30.86%)	597 (30.87%)
	≥6 years	154 (26.83%)	168 (41.48%)	1089 (56.31%)
Macrolid–Resistant Positive	Mutation			
	<1 year	24 (5.96%)	11 (4.59%)	31 (2.17%)
	1–<3 years	133 (33.00%)	56 (23.33%)	149 (10.43%)
	3–<6 years	134 (33.25%)	77 (32.08%)	462 (32.33%)
	≥6 years	112 (27.79%)	96 (40.00%)	787 (55.07%)

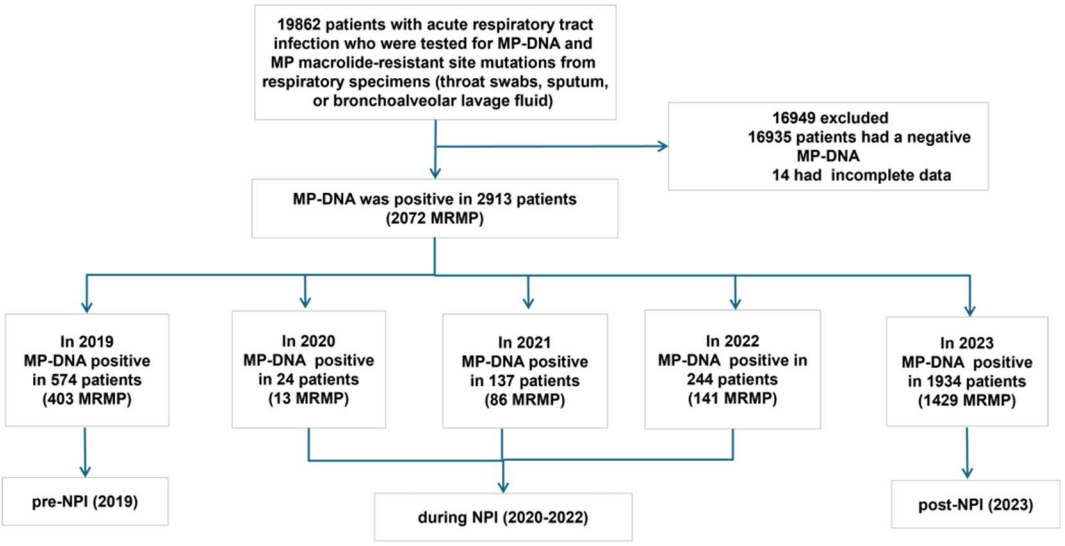

Fig. 1: Patients' inclusion flowchart.
A total of 19,862 patients with acute respiratory tract infection who visited Jiangxi Children's Hospital and underwent MP DNA testing from January 1, 2019, to December 31, 2023, were collected as screening subjects. 16935 patients with negative MP–DNA and 14 patients with incomplete data were excluded. Finally, a total of 2,913 MP DNA–positive patients were selected as study subjects, with 574, 24, 137, 244 and 1,934 cases in the five years, respectively.

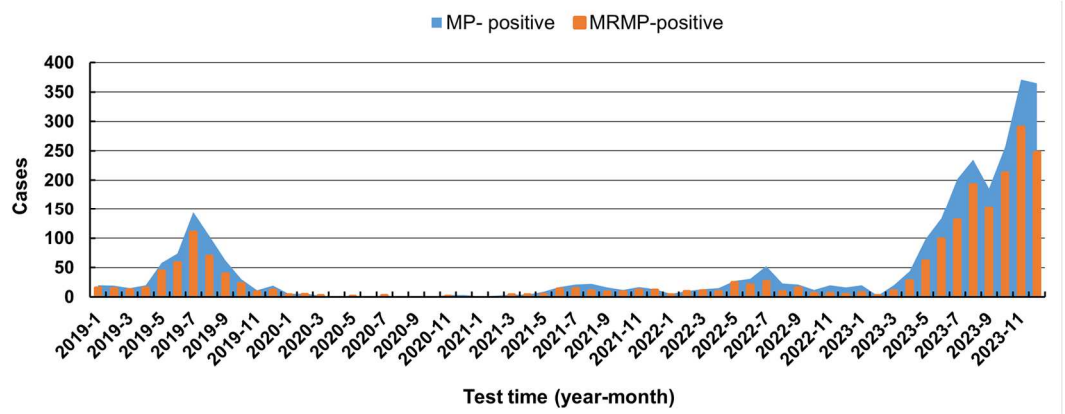

Fig. 2: The temporal distribution characteristics of MP–DNA positive and MRMP positive cases.
The peak months of resistant mutation positivity coincided with that of MP–DNA positivity, which was in July, 2019, and August 2023, as well as November 2023, no clear peaks were shown from 2020 to 2022.

Distribution characteristics of MRMP cases from 2019 to 2023

Temporal distribution characteristics

The monthly distribution of MRMP cases from 2019 to 2023 is shown in fig. 2. The peak months of resistant mutation positivity coincided with that of MP–DNA positivity, which was in July, 2019 and August 2023, as well as November 2023, no clear peaks were shown from 2020 to 2022.

Gender distribution characteristics

From 2019 to 2023, among the 2,913 MP–DNA positive cases, 1,642 were male and 1,271 were female, with a male–to–female ratio at 1.29:1 (1642/1271). The ratio of male to female in pre–NPIs group was 1.59:1, which was higher than that in during–NPIs (1.40:1) and post–NPIs groups (1.20:1) (χ^2=9.08, $P < 0.05$). There was total 2072 MP–resistant mutation positive cases, with a male–to–female ratio at 1.26:1 (1156/916). There was no significant difference among different NPIs groups.

Age distribution characteristics

As shown in table 4, there were significant differences in composition ratio of each age group in MP–DNA positive cases among different NPIs groups (χ^2=271.98, $P < 0.01$). The 1–<3 years group had the highest proportion at 34.49% in pre–NPIs group. In post–NPIs and during–NPIs groups, the proportion of MP–DNA positive cases in the ≥6 years group was significantly higher than that in other age groups. As for resistant mutation positive cases, the composition ratios of different age groups were significantly different among NPIs groups (χ^2=173.75, $P < 0.01$). The 3– < 6 years group accounted for the highest proportion (33.25%) in pre–NPIs group and the ≥6 years group accounted for the highest proportion in post–NPIs and during–NPIs groups.

DISCUSSION

During the COVID-19 pandemic, most countries implemented extensive NPIs such as wearing masks, maintaining hand hygiene, social distancing, travel restrictions and remote work and learning, which reduced the incidence of respiratory infectious diseases in children. MP detection rates showed NPI–related declines in multiple countries and regions (Meyer Sauteur *et al*, 2022a; Meyer Sauteur *et al*, 2022b). Our data indicate that during the NPIs period, the number of children diagnosed with MP infection significantly decreased. In our region, the MP–DNA detection rate in children dropped by 95.81% in the first year of NPIs (2020). The detection rate remained low in the second (2021) and third (2022) years of NPIs. However, in 2023, after the reduction of NPIs, the MP–DNA detection rate rapidly increased, with a total detection number being 3.36 times that before NPIs (2019). And the total number of detected cases from 2020 to 2023 was 2,339, which is 4.07 times that in 2019. The increase in the positivity rate of MP may be related to the widespread application of molecular diagnostic technologies such as PCR or mNGS. And it also indicates that the number of MP infections in children surged and compensated for the decrease during the NPIs period within one year after reducing NPIs. During the NPIs period, the seasonality of MP infections was not apparent, gender composition differences decreased, and the predominant age group increased each year. After NPIs, the MP epidemic peak extended, with the proportion of the ≥6 years group exceeding 50%.

The immune debt caused by NPIs in our region resulted in a surge of MP cases within one year after reducing NPIs, consistent with the reports from Shanghai and Europe (Zhang *et al*., 2024; Meyer Sauteur and Beeton, 2024). A study in Denmark showed a 3–fold increase in hospitalization of MP infection in 2023–2024 compared with pre–COVID–19 years (Edouard *et al*., 2024). This is consistent with the results of our study, which is attributed to immune debt caused by reduced infection rate during the COVID–19 pandemic. It was also confirmed by a contemporaneous study from Marseille, France (Dungu *et al*., 2024). In addition, due to the high infection rate of MP in children and the large number of transmissions, MP infection in adults is also increasing (Dungu *et al*., 2024). Whether all these changes can quickly establish herd immunity and their impact on MP resistance requires further research.

Macrolide antibiotics are the first–line treatment for MP infections in children. They inhibit bacterial peptide synthesis and prevent ribosome assembly, leading to reduced bacterial protein synthesis capability and inhibiting the growth of MP. The binding sites for macrolide antibiotics on ribosomes are located at positions 2063 and 2064 of the 23S rRNA. Mutations at these sites can reduce the binding ability of antibiotics to bacterial ribosomes, resulting in resistance, with the A2063G mutation being the most common (Xu *et al*., 2024a). Recent meta–analyses have shown that the global proportion of MRMP infections increased from 18.2% in 2000 to 76.5% in 2019, mainly concentrated in the Western Pacific region, particularly in China (Ning *et al*., 2017). Our study data indicate that the positive detection rate of MP resistance mutations in children in our region from 2019 to 2023 was 71.13% (2072/2913), which is lower than that reported by Beijing Children's Hospital from 2016 to 2019 (90.04%,1386/1524) (Wang *et al*., 2022) and Zhejiang from 2019 to 2020 (91.90%, 410/446) (Xu *et al*., 2024b), but close to the rate reported by Ningbo Women and Children's Hospital from 2019 to 2021 (73.41%, 947/1290) (Liu, 2023).

These results indicate regional differences in China, with high overall detection rates of MP resistance mutations in children, significantly higher than those in Europe and the

Americas (Ning *et al*., 2017). The specific factors contributing to the continuous increase in MRMP remain unclear.

In our study, we observed a decrease in the overall detection rate of MP resistance mutations in children in our region, dropping from 70.21% (403/574) before NPIs to 59.26% (240/405) during NPIs. Specifically, from 2020 to 2022, the quarterly detection rates of MP resistance mutations fluctuated between 16.67% and 100%. The reasons for this fluctuation during the NPIs period are multifaceted. Firstly, the way and habit of seeking medical treatment for patients has changed; secondly, during NPIs, the number of patients seeking medical attention for MP infections and other respiratory infectious diseases significantly decreased, leading to a substantial reduction in macrolide antibiotic prescriptions.

This reduced the selective pressure for MP resistance mutations. Additionally, decreased activities of humans during NPIs limited the spread of resistant MP strains in the community. Nevertheless, it remains unclear how the trend of MP resistance mutation detection rates in treated children during NPIs corresponds to the actual resistance levels of MP in the community. Concurrent studies in other regions of China did not find a decrease in MP resistance detection rates among hospitalized patients. For instance, in Foshan, the rates were 88.57% (31/35) in 2019 and 86.11 % (31/36) in 2020 (Xie *et al*., 2023); in Baoding, the rate was 92.69% (482/520) in 2021 (Kim *et al*., 2022). This disparity suggests that the impact of NPIs on MP resistance varies by region. In areas with higher MP resistance levels, no decrease in MP resistance mutation detection rates was observed during NPIs. In comparison, a multicenter study conducted in China among children with mild respiratory infections attending outpatient clinics (January 2020 – June 2021) reported a MP resistance mutation detection rate of 7.7% (6/78) (Chen *et al*., 2022), which is significantly lower than that in hospitalized children during the same period. This indicates that the impact of NPIs on MP resistance mutations in children is complex and requires broader population studies.

After the reduction of NPIs in 2023, the detection rate of MP resistance mutations in our region reached pre-NPIs levels in the third quarter, which was lower than the contemporaneous rate of 80% (348/434) in Shanghai (Zhang *et al*., 2024). In this study, the impact of NPIs on the detection rate of MP resistance mutations was more pronounced in the ≥6 years and 3–<6 years age groups. This indicates that the increase in the detection rate of MP resistance mutations in post–NPIs group is closely related to the increase in MP infection incidence, particularly among preschool and school-aged children who participate in group activities. This suggests that schools and childcare institutions are critical locations for MP transmission. Implementing public health strategies targeting these settings will help reduce MP infection rates and also decrease MP resistance.

CONCLUSION

In summary, the NPIs implemented during the COVID–19 pandemic reduced MP infections but also resulted in an immune debt phenomenon in children, leading to excess cases after the relaxation of NPIs. NPIs can reduce the overall detection rate of MP resistance mutations in children in this region, with a more pronounced effect on the ≥6 years and 3–<6 years age groups. Public health strategies targeting schools and childcare institutions will help reduce MP infection rates and subsequently decrease MP resistance. However, this study has certain limitations. It is a single–center study with limited subject coverage, not encompassing all respiratory infection patients. Longer observation is needed for post–NPIs to monitor the immune debt phenomenon for MP. There are only two drug–resistant sites (A2063G and A2064G) that were detected, which is relatively limited. Future research needs to evaluate the mechanisms of NPIs' impact on MRMP in children from multiple perspectives.

Acknowledgement
We thank LetPub for its linguistic assistance during the preparation of this manuscript.

Author's contribution
Hong Liu: Analyzed the data and wrote the draft of the manuscript.
Fadi Liu: Participated in collecting, assessing and interpreting the data.
Lijuan Xiong: Participated in assessing the data and editing the manuscript.
Shuai Liu and Fen Yang: Participated in collecting the data.
Qiang Chen: Reviewing the manuscript.
All authors read and approved the final manuscript.

Funding
This work is supported by Jiangxi province key research and development plan project (20202BBGL73062), Jiangxi Provincial Clinical Medical Research Center for Pediatric Infectious Diseases (20223BCG74013).

Data availability statement
All data generated or analyzed during this study are included in this published article [and its supplementary information files].

Ethical approval
This study was approved by the ethics committee of Jiangxi Provincial Children's Hospital and exempted from informed consent (approval number JXSETYY-YXKY-20230097-A1).

Conflict of interest
The author(s) report no conflicts of interest in this work.

REFERENCES

Cohen R, Ashman M, Taha M K, Varon E, Angoulvant F, Levy C, Rybak A, Ouldali N, Guiso N and Grimprel E (2021). 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*. **51**(5): 418-423.

Chen J, Zhang J, Lu Z, Chen Y, Huang S, Li H, Lin S, Yu J, Zeng X, Ji C, Zheng Y, Dai F, Dong W, Xu H, Chen W, Jin X, Cui Z, Qiao J, Qin W, Chen H, Jiang W, Zhang X, Song J, Shao J, Su W, Wang C, Liu F, Zhao Y, Zou Y, Guo R, Zhang L, Wu J, Yuan S, Tang M, Wu Y, Lin J, Dong W, Chen X, Sun X and Yin Y (2022). *Mycoplasma pneumoniae* among Chinese outpatient children with mild respiratory tract infections during the Coronavirus Disease 2019 Pandemic. *Microbiol Spectr.,* **10**(1): e0155021.

Dungu KHS, Holm M, Hartling U, Jensen LH, Nielsen AB, Schmidt LS, Toustrup LB, Hansen LH, Dahl KW, Matthesen KT, Nordholm AC, Uldum S, Emborg HD, Rytter MJH and Nygaard U (2024). *Mycoplasma pneumoniae* incidence, phenotype and severity in children and adolescents in Denmark before, during, and after the COVID-19 pandemic: A nationwide multicentre population-based cohort study. *Lancet Reg Health Eur.* **47**: 101103.

Edouard S, Boughammoura H, Colson P, La Scola B, Fournier PE and Fenollar F (2024). Large-scale outbreak of *Mycoplasma pneumoniae* infection, Marseille, France, 2023-2024. *Emerg Infect Dis*. **30**(7): 1481-1484.

GBD 2021 Lower Respiratory Infections and Antimicrobial Resistance Collaborators (2024). Global, regional and national incidence and mortality burden of non-COVID-19 lower respiratory infections and aetiologies, 1990-2021: A systematic analysis from the Global Burden of Disease Study 2021. *Lancet Infect Dis*. **24**(9): 974-1002.

Jiang TT, Sun L, Wang TY, Qi H, Tang H, Wang YC, Han Q, Shi XQ, Bi J, Jiao WW and Shen AD (2023). The clinical significance of macrolide resistance in pediatric *Mycoplasma pneumoniae* infection during COVID-19 pandemic. *Front Cell Infect Microbiol*., **13**: 1181402.

Kim K, Jung S, Kim M, Park S, Yang HJ and Lee E (2022). Global trends in the proportion of macrolide-resistant *Mycoplasma pneumoniae* infections: A systematic review and meta-analysis. *JAMA Netw Open.* **5**(7): e2220949.

Liu X (2023). Analysis of *Mycoplasma pneumoniae* infection and drug resistance in hospitalized children in Ningbo, Zhejiang Province from 2019 to 2021. *Chin. J. Prev. Med.,* **35**(2): 154-158.

Meyer Sauteur PM, Beeton ML, Uldum SA, Bossuyt N, Vermeulen M, Loens K, Pereyre S, Bebear C, Kese D, Day J, Afshar B, Chalker VJ, Greub G, Nir-Paz R, Dumke R and Team ESMS (2022a). *Mycoplasma pneumoniae* detections before and during the COVID-19 pandemic: Results of a global survey, 2017 to 2021. *Euro Surveill.* **27**(19): 2100746.

Meyer Sauteur PM, Chalker VJ, Berger C, Nir-Paz R, Beeton ML, Esgmac and the EMsg (2022b). *Mycoplasma pneumoniae* beyond the COVID-19 pandemic: where is it*? Lancet Microbe*. **3**(12): e897.

Meyer Sauteur PM, Beeton ML, European Society of Clinical M, Infectious Diseases Study Group for M, Chlamydia I and the EMpSsg (2024). *Mycoplasma pneumoniae:* Delayed re-emergence after COVID-19 pandemic restrictions. *Lancet Microbe*. **5**(2): e100-e101.

Ning G, Wang X, Wu D, Yin Z, Li Y, Wang H and Yang W (2017). The etiology of community-acquired pneumonia among children under 5 years of age in mainland China, 2001-2015: A systematic review. *Hum Vaccin Immunother*., **13**(11): 2742-2750.

Principi N, Autore G, Ramundo G and Esposito S (2023). Epidemiology of Respiratory Infections during the COVID-19 Pandemic. Viruses. **15**(5): 1160.

Waites KB and Talkington DF (2004). *Mycoplasma pneumoniae* and its role as a human pathogen. *Clin Microbiol Rev*. **17**(4): 697-728, table of contents.

Wang, YC, Wu XR, Liu F, Yin QQ, Li JQ, Wang YH, Quan ST, Tian X, Xu BP and Shen ED (2022). Epidemiological characteristics and drug resistance of *Mycoplasma pneumoniae* infection in hospitalized children in Beijing from 2016 to 2019. *Chin Pediatr. Emerg. Med.*, **7**(14): 1082-1085.

Xie JJ, Zhang JF, Su JD, Li BH, Xiao TL, Wang B and Yang LH (2023). Genotyping of *Mycoplasma pneumoniae* in children with *Mycoplasma pneumoniae* pneumonia and analysis of macrolide resistance gene mutations. *Chin Pediatr. Emerg. Med.*, **30**(09): 660-664.

Xu M, Li Y, Shi Y, Liu H, Tong X, Ma L, Gao J, Du Q, Du H, Liu D, Lu X and Yan Y (2024a). Molecular epidemiology of *Mycoplasma pneumoniae pneumonia* in children, Wuhan, 2020-2022. *BMC Microbiol*., **24**(1): 23.

Xu D, Zhang A L, Zheng JS, Ye MW, Li F, Qian GC, Shi HB, Jin XH, Huang LP, Mei JG, Mei GH, Xu Z, Fu H, Lin JJ, Ye HZ, Zheng Y, Hua LL, Yang M, Tong JM, Chen LL, Zhang YY, Yang DH, Zhou YL, Li HW, Lan YL, Xu YL, Feng JY, Chen X, Gong M, Chen ZM and Wang YS (2024b). A multicenter prospective study on early identification of refractory *Mycoplasma pneumoniae* pneumonia in children. Zhonghua Er Ke Za Zhi., **62**(4): 317-322.

Zhang X B, He W, Gui Y H, Lu Q, Yin Y, Zhang J H, Dong X Y, Wang Y W, Ye Y Z, Xu H, Wang J Y, Shen B, Gu D P, Wang L B and Wang Y (2024). Current *Mycoplasma pneumoniae* epidemic among children in Shanghai: Unusual pneumonia caused by usual pathogen. *World J. Pediatr*. **20**(1): 5-10.