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Characteristics and Outcome of Severe *Mycoplasma pneumoniae* Pneumonia Admitted to PICU in Shanghai: A Retrospective Cohort Study

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OBJECTIVES: We aimed to describe the characteristics and outcome in children with severe *Mycoplasma pneumoniae* pneumonia in a Chinese PICU.

DESIGN: A retrospective observational study from 2017 to 2019.

SETTING: A 36-bed university tertiary PICU at Shanghai Children's Hospital.

PATIENTS: Patients admitted to a tertiary PICU 29 days to 18 years old screened for laboratory-confirmed severe *M. pneumoniae* pneumonia.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: Descriptive analysis of baseline characteristics for patients included hospital mortality, organ dysfunctions, use of mechanical ventilation, continuous renal replacement therapy, and/or extracorporeal membrane oxygenation. A total of 817 children with severe pneumonia were admitted to PICU, and 203 of 817 cases (24.8%) with severe *M. pneumoniae* pneumonia were included in this study. The median age was 41 months (interquartile range, 20–67 mo), of which 77.3% (157/203) were younger than 6 years old. Among 163 patients with the test for macrolide resistance, 90.2% cases (147/163) were macrolide-resistant *M. pneumoniae*. Severe *M. pneumoniae* pneumonia-associated organ dysfunction included acute respiratory failure (203 cases, 100%), followed by cardiovascular disorder (79/203, 38.9%), gastrointestinal dysfunction (24/203, 11.8%). The main complications were pleural effusion (79/203, 38.9%), capillary leak syndrome (58/203, 28.6%), and plastic bronchitis (20/203, 9.9%). All patients needed respiratory support, including 64.5% patients (131/203) who received mechanical ventilation and 35.5% patients (72/203) who received high-flow nasal oxygen. Twenty-five patients (12.3%) treated with continuous renal replacement therapy and nine cases (4.4%) received extracorporeal membrane oxygenation. The case fatality rate was 3.9% (8/203). Furthermore, cardiovascular dysfunction, liver injury, or multiple organ dysfunction syndrome were associated with longer mechanical ventilation duration, delayed PICU discharge, and high hospital mortality. Coinfection was a risk factor of delayed PICU discharge.

CONCLUSIONS: Children with severe *M. pneumoniae* pneumonia mainly occur under the age of 6 years, showing a high proportion of extrapulmonary organ dysfunction and macrolide resistances. Extrapulmonary organ dysfunction and coinfection are associated with worse outcomes. The

DOI: 10.1097/CCE.0000000000000366

overall mortality is relatively low after treated with appreciate antibiotics, respiratory support, and extracorporeal life support.

KEY WORDS: child; mortality; severe *Mycoplasma pneumoniae* pneumonia; severe *Mycoplasma pneumoniae* pneumonia-associated organ dysfunction

Mycoplasma pneumoniae (MP) is considered one of the common etiologies of community-acquired pneumonia (CAP). The prevalence of MP infection is widely underestimated because of most patients are seldom symptomatic and may rarely seek medical attention. But the prevalence of severe MP pneumonia (SMPP) has been increased in recent years and represents a serious threat to both adult and children (1–3). The prevalence of MP pneumonia differs significantly by geographic area and age. Clinical manifestations vary from asymptomatic, suggesting a carrier state to severe complicated pneumonia (4, 5). Moynihan et al (6) identified only 30 (0.3%) confirmed MP cases by clinical and laboratory criteria in 11,526 PICU admissions from 2008 to 2013 in Queensland, Australia. In north China, it is showed that MP infections made up approximately 70% of all cases of CAP in children over 5 years old (7). However, there were little data available with large numbers of patients with SMPP in PICU in the past few years in China.

In order to highlight the epidemiology of SMPP in PICU, this retrospective study was conducted to describe the clinical characteristics, laboratory features, and appropriate therapies in patients with SMPP in a tertiary PICU in Shanghai, China (2017–2019).

MATERIALS AND METHODS

Study Population

From January 2017 to December 2019, patients 1 month to 18 years old admitted with severe pneumonia to PICU (36-beds in a tertiary hospital) of Shanghai Children's Hospital, Shanghai Jiao Tong University were collected in the study. SMPP were defined as children with both clinical presentation and positive laboratory results consistent with MP infection. The SMPP was diagnosed according to the following criteria: 1) dyspnea with transcutaneous oxygen saturation less than or equal to 92% in room air or Pao_2 less than 60 mm Hg, requiring advanced respiratory support (high-flow nasal oxygen [HFNO] or mechanical ventilation [MV]) and 2) identified acute extrapulmonary organ dysfunction according to the 2005 International Pediatric Sepsis Consensus Conference criteria (8). The exclusion included: 1) patient was hospital-acquired MP infection; 2) children transferred from other hospital within the last 7 days; and 3) children readmitted to the PICU without 7 days symptom-free period. The study was approved by the ethics committee of Hospital (Approval number: 2020R123-E01). Informed content was waived because of its retrospective design.

Identification of Macrolide Resistance

MP was defined by real-time polymerase chain reaction from an oropharyngeal swab or bronchoalveolar lavage collected by bronchoscopy after intubation, and/or MP serum immunoglobulin M greater than 1:160. Macrolide resistance-associated mutations were detected including at positions 2063 and 2064 in the 23S ribosomal RNA gene of MP according to literature available (9).

Antibiotic Treatment of Patients With SMPP

For patients with worse response to azithromycin or other macrolide antibiotics before admitted to PICU and patients infected with macrolide resistance MP, quinolone, or quinolone combined with minocycline were used in our PICU.

Clinical Data Collection

The Data were collected included the demographic characteristics, comorbidities, microbiological results, extrapulmonary organ dysfunction, the need of continuous renal replacement therapy (CRRT) or extracorporeal membrane oxygenation (ECMO), the duration of MV or HFNO, organ dysfunction, complications, length of PICU stay, and hospital mortality.

Statistical Analysis

Continuous variables were presented as median (interquartile range [IQR]), and all categorical variables were presented as numbers (percentage). The Mann-Whitney *U* test or Fisher exact test (two-tailed) was used for univariate testing of continuous and categorical variables, respectively. A two-sided *p* value of less than 0.05 was considered to indicate statistical significance. SPSS statistics Version 25 (SPSS, Chicago, IL) was used for all statistical analysis.

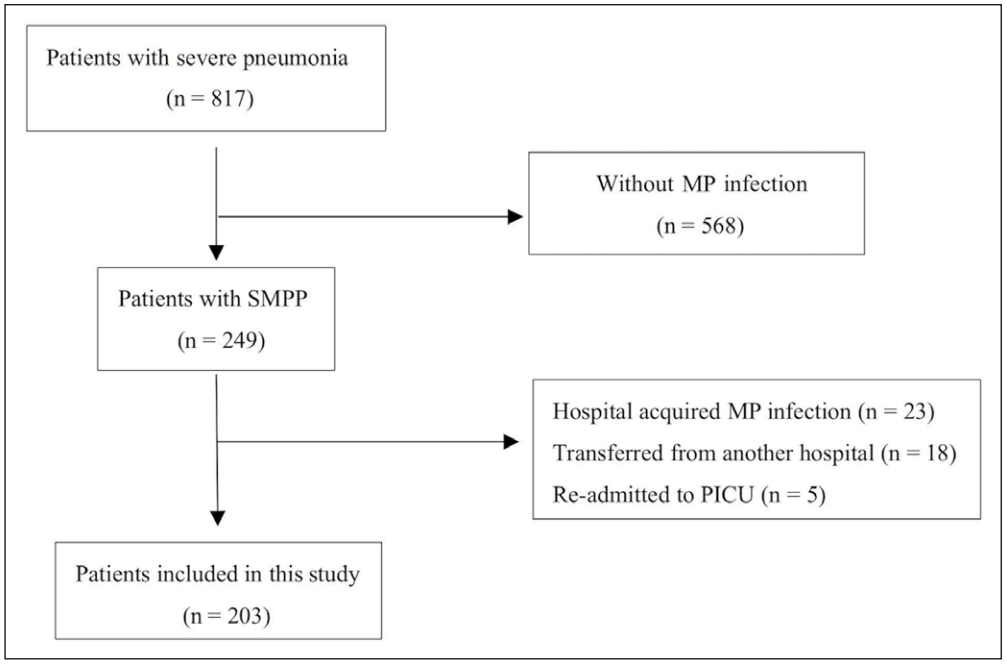

Figure 1. Patient enrollment and study profile. MP = *Mycoplasma pneumoniae*, SMPP = severe *Mycoplasma pneumoniae* pneumonia.

RESULTS

Characteristics of SMPP Patients

From January 2017 to December 2019, 817 patients diagnosed with severe pneumonia were admitted to PICU. Among of them, there were 568 cases without mycoplasma infection, and 30.5% cases (249/817) were diagnosed with SMPP. Twenty-three children were excluded due to hospital-acquired MP infection, 18 cases who transferred from another hospital were excluded, and five patients were excluded due to readmitted to PICU. Finally, 203 patients were included in this study (**Fig. 1**). Overall, 110 patients (54.2%) were male. The median age was 41 months (IQR, 20–67 mo), of which 77.3% (157/203) were younger than 6 years old. **Figure 2** shows the age distribution of SMPP admitted to PICU. The median duration from symptom onset to hospitalization and PICU admission were 7 days (IQR, 6–10 d) and 9 days (IQR, 7–10 d), respectively (**Table 1**). In addition, among 163 patients with test for macrolide resistance, there were 90.2% cases (147/163) infected with macrolide resistance MP.

SMPP-Associated Organ Dysfunctions and Complications

Of the 203 patients, all children (100%) were complicated with acute respiratory failure and medium to severe acute respiratory distress syndrome (ARDS) in 26 cases (12.8%). Cardiovascular dysfunction was the second most common organ dysfunction (79 [38.9%]), followed by gastrointestinal dysfunction (24 [11.8%]), liver injury (21 [10.3%]), acute kidney injury (11 [5.4%]), and neurologic involvement (10 [4.9%]). Pleural effusion was the most common complication (79 [38.9%]), followed by capillary leak syndrome (58 [28.6%]), plastic bronchitis (20 [9.9%]), and venous thromboembolism (7 [3.4%]) (Table 1).

Of the 203 children with SMPP, all patients needed respiratory support, including 64.5% patients (131/203) received MV and 35.5% (72/203) supported by HFNO. Nine patients (4.4%) with severe ARDS supported by ECMO and 25 cases (12.3%) received CRRT (Table 1). The other treatment included corticosteroids (methylprednisolone 0.5–2 mg/kg/d for 3–5 d in 184 patients [90.6%]) and IV immunoglobulin (400 mg/kg/d for 1–3 d in 144 children [70.9%]). The mean PICU stay

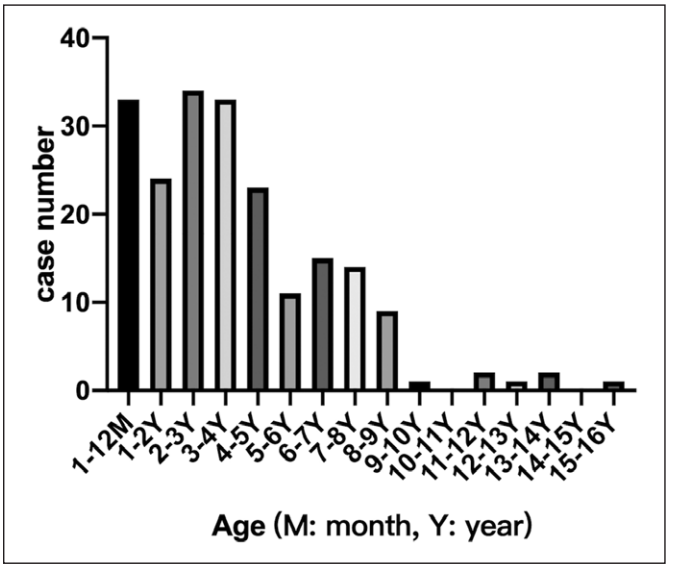

Figure 2. Age distribution of severe *Mycoplasma pneumoniae* pneumonia in PICU from 2017 to 2019.

TABLE 1.
Baseline Characteristics of Patients With Severe *Mycoplasma pneumoniae* Pneumonia Admitted to PICU

Characteristics	Total ($n = 203$)
Male, *n* (%)	110 (54.2)
Age, mo, median (Q1–Q3)	41 (20–67)
Underlying diseases, *n* (%)	
Leukemia and solid tumor	1
Congenital heart disease	16
Other	11
Percentage of macrolide resistance in subgroup with test for macrolide resistance ($n = 163$), *n* (%)	147/163 (90.2)
Body temperature on PICU admission, °C, median (Q1–Q3)	38.9 (38.3–39.5)
Associated organ dysfunction, *n* (%)	
Acute respiratory failure	203 (100)
Acute respiratory distress syndrome ($PaO_2/FIO_2 < 200$ mm Hg)	26 (12.8)
Cardiovascular dysfunction	79 (38.9)
Gastrointestinal disorder	24 (11.8)
Liver injury	21 (10.3)
Neurologic involvement	10 (4.9)
Acute kidney injury	11 (5.4)
Multiple organ dysfunction syndrome	34 (16.7)
Complications, *n* (%)	
Pleural effusion	79 (38.9)
Capillary leak syndrome	58 (28.6)
Venous thromboembolism	7 (3.4)
Plastic bronchitis	20 (9.9)
Coinfection, *n* (%)	
Bacterial coinfection	41 (20.2)
Viral coinfection	58 (28.6)
Bacterial and viral coinfection	28 (13.8)
Interval time between onset to hospital admission, d, median (Q1–Q3)	7 (6–10)
Interval time between onset to PICU admission, d, median (Q1–Q3)	9 (7–10)
Length of PICU stay, d, median (Q1–Q3)	7 (5–10)
Hospital mortality, *n* (%)	8 (3.9)
High-flow nasal oxygen support, *n* (%)	72 (35.5)
MV support	
n (%)	131 (64.5)
Duration, hr, median (Q1–Q3)	110 (79–177)
PaO_2/FIO_2 on initial MV, mm Hg, median (Q1–Q3)	180 (137–218)
Continuous renal replacement therapy support	
n (%)	25 (12.3)
Duration, hr, median (Q1–Q3)	31 (23–77)
Extracorporeal membrane oxygenation support	
n (%)	9 (4.4)
Duration, hr, median (Q1–Q3)	158 (106.5–171.5)
Methylprednisolone, *n* (%)	184 (90.6)
IV immunoglobulin, *n* (%)	144 (70.9)

MV = mechanical ventilation.

was 7 days (IQR, 5–10 d) and case fatality rate (CFR) was 3.9% (8/203) (Table 1).

Association of Organ Dysfunction With Outcomes in SMPP

Further analysis showed that cardiovascular dysfunction (10 d [7–15 d] vs 6 d [4–8 d]), liver injury (15 d [7–20.5 d] vs 7 d [5–9 d]), and multiple organ dysfunction syndrome (MODS) (13.5 d [8.5–19.5 d] vs 6 d [5–9 d])

were associated with delayed PICU discharge (all $p < 0.001$) and increased mortality (10.1% vs 0%, 23.9% vs 1.6%, 23.5% vs 0%, respectively; all $p < 0.001$). Higher proportion of patients required with MV in SMPP comorbidity with cardiovascular dysfunction or MODS (all $p < 0.001$). The rate of CRRT support was high in patients with cardiovascular dysfunction, liver injury, or MODS (all $p < 0.05$). Nine patients need ECMO support (**Table 2**).

Association of Coinfection With Outcomes in Patients With SMPP

Overall, the comorbidity with bacterial or viral infection in patients with SMPP were 41 (20.2%) or 58 (28.6%), respectively. Bacterial and viral coinfection was 28 (13.8%) (Table 1). Coinfected bacterial species included *Streptococcus pneumonia* in 23 patients, *Staphylococcus aureus* in nine cases, *Staphylococcus epidermidis* in seven cases, *Klebsiella pneumonia* in seven cases, *Acinetobacter baumannii* in five cases, *Pseudomonas aeruginosa* in three cases, *Haemophilus influenzae* in three cases, and *Enterobacteriaceae* in two cases. Coinfection in patients with SMPP resulted in longer length of PICU study (7 d [5–11 d] vs 6 d [5–9 d]; p = 0.037), but not higher hospital mortality (4.7% vs 2.6%; $p = 0.458$) (Table 2). Further subgroup analysis indicated that patients with SMPP with bacterial coinfection were prior to needing MV support compared with patients with virus coinfection or both coinfections (80.5% vs 56.9% vs 60.7%; $p = 0.044$; **Table 3**). However, there were no significant differences in length of hospital stay, hospital mortality, and ratio of CRRT or ECMO among patients with different coinfection (all $p > 0.05$; Table 3).

DISCUSSION

In this retrospective cohort study, 77.3% cases with SMPP were younger than 6 years old in PICU, and 90.2% of patients with SMPP were macrolide resistances in Shanghai. Over one-third of patients were with comorbidity of cardiovascular dysfunction and complicated with pleural effusion. About two-thirds of patients received MV. SMPP-associated cardiovascular dysfunction, liver injury, or MODS were associated with longer MV duration, delayed PICU discharge, and high hospital mortality. Patients with bacterial coinfection were prior to needing MV support compared with virus coinfection or both coinfections. To the best of our knowledge, this is the largest case-based study investigating characteristics of SMPP admitted to PICU in mainland China.

There is a little data available on the role of MP infection in critically ill children requiring PICU admission. In South Africa, Carrim et al (10) found age under 6 years to be an independent risk factor for severe disease (odds ratio, 7.1; 95% CI, 1.7–28.7). High levels of macrolide resistance have been noted in Japan (50–90%) (11) and China (90–100%) (12, 13). Routine macrolide resistance monitoring was not systematically in Europe and the United States, which may contribute to the under-detection of macrolide-resistant MP or reflect low levels of macrolide resistance reported (14, 15). Previous study indicated that the rate of antibiotic resistance was 53% in patients complicated by pneumonia with ICU admission in Taiwan, China (16). In our study, totally of 817 patients diagnosed with severe pneumonia were admitted to PICU and 249 of 817 (30.5%) were identified with SMPP from January 2017 to December 2019. Among 163 patients with test of macrolide-resistant, 90.2% of patients (147/163) were infected with macrolide resistance species. These results indicate that the rate of macrolide resistance is high in severe SMPP patients in PICU, which might give new insight to antibiotic selection for treatment of severe SMPP in PICU. In our experience, quinolone or quinolone combined with minocycline would be a better choice in patients with worse response to azithromycin or other macrolide antibiotics.

SMPP-associated organ dysfunction includes respiratory and extrapulmonary organ dysfunction. Extrapulmonary manifestations of MP infection can involve any organ. Gordon reports that 26% of children with extrapulmonary manifestations in MP infection (12). Extrapulmonary manifestations are not only directly related to the infection process but also due to vascular complications. Our results showed that the most comorbidity was cardiovascular dysfunction, followed by medium to severe ARDS, gastrointestinal dysfunction, liver injury, acute kidney injury, and neurologic involvement. The rate of cardiovascular involvement in our cohort was 38.9% (79/203), which was similar with the result reported in adult population (2). More importantly, SMPP-associated with cardiovascular dysfunction, liver injury, or MODS were associated with worse outcome in patients with SMPP.

TABLE 2.

Outcomes of Patients With Severe *Mycoplasma pneumoniae* Pneumonia-Associated Organ Dysfunction or Coinfection

	Cardiovascular Dysfunction			Liver Injury			Multiple Organ Dysfunction Syndrome			Coinfection		
	Yes (*n* = 79)	No (*n* = 124)	*p*	Yes (*n* = 21)	No (*n* = 182)	*p*	Yes (*n* = 34)	No (*n* = 169)	*p*	Yes (*n* = 127)	No (*n* = 76)	*p*
Length of PICU stay, d, median (Q1–Q3)	10 (7–15)	6 (4–8)	0.000	15 (7–20.5)	7 (5–9)	0.000	13.5 (8.5–19.5)	6 (5–9)	0.000	7 (5–11)	6 (5–9)	0.037
Hospital mortality, *n* (%)	8 (10.1)	0	0.000	5 (23.9)	3 (1.6)	0.000	8 (23.5)	0	0.000	6 (4.7)	2 (2.6)	0.458
Need of MV, *n* (%)	73 (92.4)	58 (46.8)	0.000	15 (71.4)	116 (63.7)	0.485	32 (94.1)	99 (58.6)	0.000	83 (65.4)	48 (63.2)	0.752
Duration of MV, hr, median (Q1–Q3)	146 (90.5–235)	88.5 (69.8–118.5)	0.000	240 (133–365)	107.5 (77.3–157.3)	0.000	177.5 (94.8–272.8)	103 (77–146)	0.001	118 (83–200)	101 (72.5–161.5)	0.092
Need of continuous renal replacement therapy, *n* (%)	22 (27.8)	3 (2.4)	0.000	6 (28.6)	19 (10.4)	0.017	9 (26.5)	16 (9.5)	0.006	19 (15.0)	6 (7.9)	0.138
Need of extracorporeal membrane oxygenation, *n* (%)	9 (11.4)	0	0.000	2 (9.5)	7 (3.8)	0.231	6 (17.6)	3 (1.8)	0.000	8 (6.3)	1 (1.3)	0.095

MV = mechanical ventilation.

TABLE 3.
Outcomes of Patients With Coinfection of Bacterial, Virus, or Both

	Bacterial Coinfection (*n* = 41)	Viral Coinfection (*n* = 58)	Bacterial and Viral Coinfection (*n* = 28)	*p*
Length of PICU stay, d, median (Q1–Q3)	7 (6–10.5)	6 (5–10.3)	8.5 (5.25–12.8)	0.200
Hospital mortality, *n* (%)	0	3 (5.2)	3 (10.7)	0.117
MV support, *n* (%)	33 (80.5)	33 (56.9)	17 (60.7)	0.044
Duration of MV, hr, median (Q1–Q3)	109 (71.5–157.5)	118 (87.5–228)	132 (83–205)	0.386
Continuous renal replacement therapy support, *n* (%)	7 (17.1)	8 (13.8)	4 (14.3)	0.898
Extracorporeal membrane oxygenation support, *n* (%)	4 (9.8)	3 (5.2)	1 (3.6)	0.520

MV = mechanical ventilation.

SMPP should be treated with antibiotics for MP or MP coinfected with other organisms. Timely adjustment and selection of antibiotics is an important clinical issue (12, 17, 18). Because of macrolide resistance MP and driven by antimicrobial pressure in our PICU, antibiotics included moxifloxacin (10 mg/kg/d) or ciprofloxacin (30 mg/kg/d) were treated for 7–21 days in suspected or confirmed macrolide resistance species infection. According to our observations, after 48 hours the use of quinolone drugs, clinical symptoms began to improve, such as fever began to decline, pulmonary exudation decreased, and ventilator parameters down-regulated. Limited studies suggest that glucocorticoid may be beneficial but still controversial (19, 20). We also used methylprednisolone (0.5–2 mg/kg/d for 3–5 d) for SMPP.

Some SMPP developed to severe hypoxic respiratory failure or severe ARDS and need ECMO rescue therapy (3). Nine patients were treated with ECMO support in our group, eight children survived and one died of combined infection with adenovirus and *Acinetobacter baumannii*. The survival rate of ECMO rescue SMPP complicated with severe ARDS is relatively higher than that of other pathogen-induced ARDS, but the timing ECMO still needs further investigation. In our study, in totally 203 children with SMPP, the CFR was 3.9% (8/203). Among the eight patients who died, five had adenovirus coinfection, one patient had bone marrow suppression after chemotherapy for acute lymphoblastic leukemia, one patient had a history of operation for congenital heart disease, and one patient had severe mycoplasma encephalitis. Totally, coinfection was not a risk factor for hospital mortality instead of delayed PICU discharge, as well as more prior to needing MV support. Finally, the patients with SMPP could be well rescued after appropriate antibiotics and organ support strategy with a CFR about 3.9%.

There were some limitations in our study. First, we presented a retrospective cohort study in PICU and did not focus on rare complications of MP. Second, the proportion of venous thromboembolism (3.4%) may have been underestimated because vascular ultrasound was not screened for all patients.

CONCLUSIONS

In conclusion, SMPP accounts for about one-third of severe CAP in PICU, and the majority of children SMPP are less than 6 years old. The rate of extrapulmonary organ dysfunctions is high, which is associated with worse outcomes. After treated with appreciate antibiotics, respiratory support, and extracorporeal life support, the overall rate of mortality of SMPP is relatively low in PICU.

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The study protocol was approved by the local ethics committee and conducted in accordance with the ethical standards laid down in the Declaration of Helsinki (Ethics Committee of Children's Hospital affiliated to Shanghai Jiao Tong University (Approval number: 2020R123-E01).

Requirement for consent was waived as the data were retrospective analysis.

All data generated or analyzed during this study are available from the corresponding author upon reasonable request.

Drs. Zhou and Shan contributed equally to this work.

Dr. Zhang conceived and designed the study. Drs. Zhou, Cui, Shi, Wang, and Miao collected and analyzed data. Drs. Zhou, Cui, Wang, and Zhang contributed analysis tools and discussion. Drs. Zhou, Wang, and Zhang wrote the article.

This study was supported by the Multicenter Clinical Research Program of Shanghai Jiao Tong University School of Medicine (DLY201618), funded by the Science and Technology Commission of Shanghai Municipality (20Y11901300, 18411951000).

The authors have disclosed that they do not have any potential conflicts of interest.

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REFERENCES

1. Inchley CS, Berg AS, Vahdani Benam A, et al: *Mycoplasma pneumoniae*: A cross-sectional population-based comparison of disease severity in preschool and school-age children. *Pediatr Infect Dis J* 2017; 36:930–936
2. Khoury T, Sviri S, Rmeileh AA, et al: Increased rates of intensive care unit admission in patients with *Mycoplasma pneumoniae*: A retrospective study. *Clin Microbiol Infect* 2016; 22:711–714
3. Ding L, Zhao Y, Li X, et al: Early diagnosis and appropriate respiratory support for *Mycoplasma pneumoniae* pneumonia associated acute respiratory distress syndrome in young and adult patients: A case series from two centers. *BMC Infect Dis* 2020; 20:367
4. Bajantri B, Venkatram S, Diaz-Fuentes G: *Mycoplasma pneumoniae*: A potentially severe infection. *J Clin Med Res* 2018; 10:535–544
5. Meyer Sauteur PM, Unger WW, Nadal D, et al: Infection with and carriage of *Mycoplasma pneumoniae* in children. *Front Microbiol* 2016; 7:329
6. Moynihan KM, Barlow A, Nourse C, et al: Severe *Mycoplasma pneumoniae* infection in children admitted to pediatric intensive care. *Pediatr Infect Dis J* 2018; 37:e336–e338
7. Gao LW, Yin J, Hu YH, et al: The epidemiology of paediatric *Mycoplasma pneumoniae* pneumonia in North China: 2006 to 2016. *Epidemiol Infect* 2019; 147:e192
8. Goldstein B, Giroir B, Randolph A; International Consensus Conference on Pediatric Sepsis: International pediatric sepsis consensus conference: Definitions for sepsis and organ dysfunction in pediatrics. *Pediatr Crit Care Med* 2005; 6:2–8
9. Lin C, Li S, Sun H, et al: Nested PCR-linked capillary electrophoresis and single-strand conformation polymorphisms for detection of macrolide-resistant *Mycoplasma pneumoniae* in Beijing, China. *J Clin Microbiol* 2010; 48:4567–4572
10. Carrim M, Wolter N, Benitez AJ, et al: Epidemiology and molecular identification and characterization of *Mycoplasma pneumoniae*, South Africa, 2012-2015. *Emerg Infect Dis* 2018; 24:506–513
11. Yamazaki T, Kenri T: Epidemiology of *Mycoplasma pneumoniae* infections in Japan and therapeutic strategies for macrolide-resistant *M. pneumoniae*. *Front Microbiol* 2016; 7:693
12. Liu Y, Ye X, Zhang H, et al: Antimicrobial suscepetibility of *Mycoplasma pneumoniae* isolates and molecular analysis of macrolide resistant from Shanghai, China. *Antimicrob Agents Chenother* 2009; 53:2160–2162
13. Wang Y, Ye Q, Yang D, et al: Study of two separate types of macrolide-resistant *Mycoplasma pneumoniae* outbreaks. *Antimicrob Agents Chemother* 2016; 60:4310–4314
14. Beeton ML, Zhang XS, Uldum SA, et al: *Mycoplasma pneumoniae* infections, 11 countries in Europe and Israel, 2011 to 2016. *Euro Surveill* 2020; 25:1900112
15. Kutty PK, Jain S, Taylor TH, et al: *Mycoplasma pneumoniae* among children hospitalized with community-acquired pneumonia. *Clin Infect Dis* 2019; 68:5–12
16. Lee KL, Lee CM, Yang TL, et al: Severe *Mycoplasma pneumoniae* pneumonia requiring intensive care in children, 2010-2019. *J Formos Med Assoc* 2021; 120:281–291
17. Waites KB, Ratliff A, Crabb DM, et al: Macrolide-resistant *Mycoplasma pneumoniae* in the United States as determined from a national surveillance program. *J Clin Microbiol* 2019; 57:e00968-19
18. Ha SG, Oh KJ, Ko KP, et al: Therapeutic efficacy and safety of prolonged macrolide, corticosteroid, doxycycline, and levofloxacin against macrolide-unresponsive *Mycoplasma pneumoniae* pneumonia in children. *J Korean Med Sci* 2018; 33:e268
19. Kim HS, Sol IS, Li D, et al: Efficacy of glucocorticoids for the treatment of macrolide refractory mycoplasma pneumonia in children: Meta-analysis of randomized controlled trials. *BMC Pulm Med* 2019; 19:251
20. Sun LL, Ye C, Zhou YL, et al: Meta-analysis of the clinical efficacy and safety of high- and low-dose methylprednisolone in the treatment of children with severe *Mycoplasma pneumoniae* pneumonia. *Pediatr Infect Dis J* 2020; 39:177–183