Original Article

Epidemiological characteristics of community-acquired *Mycoplasma* pneumoniae in hospitalized children around COVID-19 from Jiangsu Province, China: a multicenter retrospective study

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Background: It has been reported that the emergence of coronavirus disease 2019 (COVID-19) has changed the epidemiological characteristics of many pathogens, but the epidemiological characteristics of *Mycoplasma* (MP) infection in hospitalized children with community-acquired pneumonia (CAP) are not clear. The aim of this study was to answer this question.

Methods: Children with CAP in three tertiary hospitals (hospitals A, B and C) from 2018 to 2023 were selected. Data on gender, age, number and date of MP infection were obtained from the medical record. The intensity of the epidemic was measured as a percentage of the number of CAP.

Results: In hospitals A and B, before the pandemic (in 2018 and 2019), the number of hospitalized children with MP pneumonia and the proportion of total pneumonia had shown a significant upward trend, but the control measures led to a slight decline. In hospital C, the number and percentage of hospitalized children with MP pneumonia were low before and during the COVID-19 period. After the epidemic control was lifted, the number and percentage of children with MP pneumonia in the three hospitals increased sharply, and the proportion of children aged more than 7 years old increased significantly in 2022 and 2023.

Conclusions: From 2018 to 2019, there was already an epidemic trend of MP in the study hospital. From 2020 to 2022, after the outbreak of COVID-19, the incidence of MP pneumonia stabilized, but after the epidemic control was lifted, it broke out. This may be due to the severe restrictive measures taken early during the COVID-19 pandemic that effectively controlled the spread of MP, pausing its pandemic.

Keywords: *Mycoplasma* pneumonia (MP pneumonia); children; coronavirus disease 2019 (COVID-19); community-acquired pneumonia (CAP); pneumonia

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Introduction

Mycoplasma (MP) is an important pathogen causing respiratory tract infections in children and adults, and its infection rate has surpassed that of *Streptococcus* pneumoniae and has become one of the important pathogens of community-acquired pneumonia (CAP) in children and adults (1), which accounts for 10–40% of CAP in children (2-4). It is especially common in school-age children. Studies have found that the source of infection of *Mycoplasma* pneumoniae (MPP) is usually infected patients or carriers, and can be transmitted into the air through secretions from the nose, pharynx, throat and other parts, and epidemic transmission occurs through droplets and aerosols (5). It has a regional epidemic every 3–7 years, and each epidemic can last for 1–2 years, or even longer (6).

Hayes *et al.* found that the inhibition effect of non-pharmacological interventions (NPI) on the transmission of most pathogens continued until the measure was lifted, and only non-vaccine-preventable respiratory infections rebounded after the NPI was lifted, which supports the importance of NPI and vaccination, but does not support the "immune debt" hypothesis (7). It has been suggested that "immunity debt" is the main reason for the recurrence of respiratory tract infections in China in 2023 (8). However, Sweden has not implemented strict epidemic prevention measures since the outbreak of coronavirus disease 2019 (COVID-19), and has also suffered multiple rounds of influenza from the end of 2021 to June 2023. The epidemic of MPP had occurred in Beijing [2011–2013] and United Kingdom [2015–2016] (9,10). There was also a pandemic in 2019. After the outbreak of COVID-19 at the end of 2019, the positivity of MPP decreased significantly, and there was no significant difference in the relationship between the positivity and season, age, and sex before and during the COVID-19 (11). But it is unclear whether the epidemiological characteristics of MPP have changed since the occurrence of COVID-19. To answer this question, this study was conducted to analyze the prevalence of MPP on hospitalized CAP from 2018 to 2023 in three tertiary hospitals, and explored the epidemiological characteristics of MPP in children during and around COVID-19, aiming to provide more basis for the epidemic prevention and control of MPP. We present this article in accordance with the STROBE reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-24-281/rc).

Highlight box

Key findings

- In 2018–2019, there was an epidemic trend of *Mycoplasma* pneumonia in our study, and after the coronavirus disease 2019 (COVID-19) outbreak from 2020 to 2022, the incidence of *Mycoplasma* pneumonia stabilized, but it broke out after the epidemic control was lifted.

What is known and what is new?

- The emergence of the COVID-19 had an impact on the epidemiological characteristics of *Mycoplasma* pneumonia.
- The outbreak and control measures of the COVID-19 epidemic have slowed down the epidemic of *Mycoplasma* pneumonia, and have also led to some changes in epidemic characteristics.

What is the implication and what should change now?

- Authorities and medical institutions should learn from this experience and pay attention to the impact of control measures on the prevalence of non-target infectious diseases. The epidemiological characteristics of *Mycoplasma* pneumonia observed in this study can be used as a reference for future epidemic prediction.

Methods

Subjects

Children hospitalized for CAP between 2018 and 2023 in Changshu Hospital Affiliated to Nanjing University of Chinese Medicine (hospital A), The First People's Hospital of Lianyungang (hospital B) and Xuzhou Children's Hospital (hospital C) were included in this study. The three hospitals are all tertiary hospitals. Changshu Hospital Affiliated to Nanjing University of Chinese Medicine is located in the southeast of Jiangsu Province,

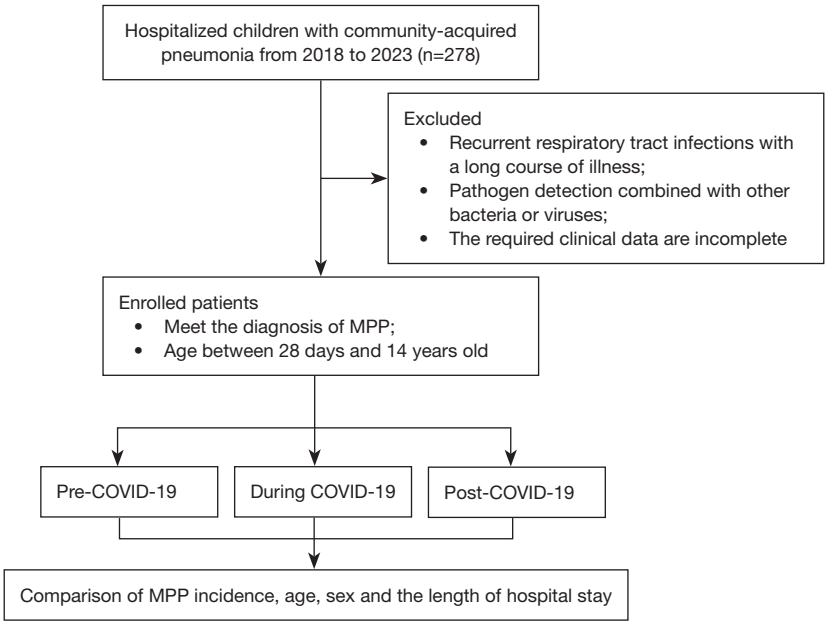

Figure 1 The flow chart of this study. MPP, *Mycoplasma* pneumoniae; COVID-19, coronavirus disease 2019.

The First People's Hospital of Lianyungang is located in the northeast of Jiangsu Province, and Xuzhou Children's Hospital is located in the northwest of Jiangsu Province. The geographical location of the three hospitals can well cover different areas of Jiangsu Province. The flow chart of this study is shown in *Figure 1*. The age, gender, onset time, clinical manifestations, diagnosis information of the children were derived from the electronic medical record. All children were divided into four age groups: <1 year, 1–<3 years, 3–<7 years, and ≥7 years group. This study does not involve the interventions on the patients. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional ethics board of Changshu Hospital Affiliated to Nanjing University of Chinese Medicine (No. 2017788), The First People's Hospital of Lianyungang (No. 2023CS034) and Xuzhou Children's Hospital (No. 2023-06-17-k17) and informed consent was taken from all the patients' parents/legal guardians.

Diagnostic criteria for CAP and MPP

The diagnosis of CAP is based on the guidelines for CAP in children (I and II) (12,13). Consistent with clinical and radiographic findings of MP infection, combined with any or both of the following, the diagnosis of MPP was made according to the following: (I) Single serum MP antibody titer ≥1:160 (particle agglutination method). During the course of the disease, the titer of MP antibody in double serum increased by 4-fold or more. (II) MP-DNA or RNA positive (14).

Statistical analysis

Counting data were described using frequency and percentage, and Chi-squared or Fisher exact probability methods were used to compare counting data. The incidence trend of MPP was described by comparing the number of hospitalized children with MPP to the total number of pneumonia patients. Excel and Graphpad software were used to make bar plots and graphs. A P value less than 0.05 was considered statistically significant (two-sided).

Results

Epidemiological characteristics of MPP before, during and post COVID-19

There were 777 patients from 2018 to 2023 enrolled in this study. The flow chart is showed in *Figure 1*. From 2018 to 2019, the number of patients with MP pneumonia in hospitals A and B increased significantly, decreased in

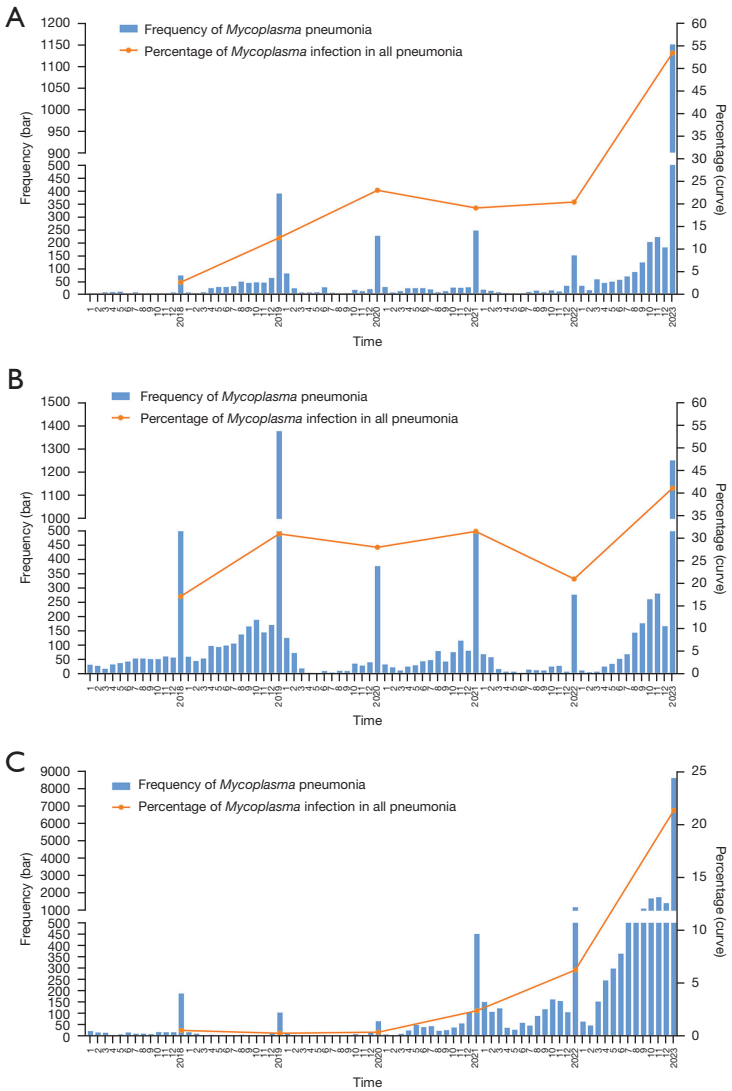

Figure 2 The number and proportion of *Mycoplasma* infection among hospitalized pneumonia patients by year. (A) Hospital A, (B) hospital B, (C) hospital C.

2020 and then flattened to 2022, and increased sharply after March 2023. The proportion of MP pneumonia in the total number of patients with CAP has also undergone a process of increasing-flat-sharply rising (*Figure 2A*,*2B*). The number of MP and the proportion of MP pneumonia in the total number of pneumonia patients in hospital C were at a relatively low level from 2018 to 2020 (*Figure 2C*), and increased sharply post 2021, especially post March, 2023 (P<0.001).

Proportion of MPP in hospitalized pneumonia stratified by sex

There was no statistically significant difference in the gender composition ratio of patients with MP pneumonia in hospitals B and C. The proportion of girls in hospital A in 2021 is lower than that in other years (P=0.009, *Table 1*). After stratification by sex, the proportion of boys and girls with MP pneumonia in the total number of pneumonia

Table 1 The number and composition ratio of *Mycoplasma* pneumonia by age and sex in each year

Hospital	Index	2018, n (%)	2019, n (%)	2020, n (%)	2021, n (%)	2022, n (%)	2023, n (%)	P
A	Age							<0.001
	<1	0 (0.00)	8 (2.05)	4 (1.76)	4 (1.62)	2 (1.32)	13 (1.13)	
	1–<3	11 (14.86)	71 (18.21)	73 (32.16)	58 (23.48)	29 (19.21)	167 (14.52)	
	3–<7	44 (59.46)	218 (55.90)	109 (48.02)	154 (62.35)	78 (51.66)	439 (38.17)	
	≥7	19 (25.68)	93 (23.85)	41 (18.06)	31 (12.55)	42 (27.81)	531 (46.17)	
	Gender							0.009
	Male	33 (44.59)	166 (42.56)	125 (55.07)	102 (41.30)	73 (48.34)	572 (49.74)	
	Female	41 (55.41)	224 (57.44)	102 (44.93)	145 (58.70)	78 (51.66)	578 (50.26)	
B	Age							<0.001
	<1	16 (3.00)	76 (5.52)	30 (7.94)	39 (6.25)	14 (5.04)	59 (4.72)	
	1–<3	131 (24.53)	324 (23.53)	105 (27.78)	148 (23.72)	53 (19.06)	153 (12.23)	
	3–<7	262 (49.06)	718 (52.14)	167 (44.18)	302 (48.40)	116 (41.73)	517 (41.33)	
	≥7	125 (23.41)	259 (18.81)	76 (20.11)	135 (21.63)	95 (34.17)	522 (41.73)	
	Gender							0.54
	Male	277 (51.87)	745 (54.10)	207 (54.76)	325 (52.08)	135 (48.56)	672 (53.72)	
	Female	257 (48.13)	632 (45.90)	171 (45.24)	299 (47.92)	143 (51.44)	579 (46.28)	
C	Age							<0.001
	<1	24 (12.70)	9 (8.49)	7 (10.45)	39 (8.65)	79 (6.58)	382 (4.43)	
	1–<3	50 (26.46)	27 (25.47)	15 (22.39)	113 (25.06)	249 (20.75)	1,155 (13.41)	
	3–<7	98 (51.85)	54 (50.94)	33 (49.25)	208 (46.12)	591 (49.25)	4,212 (48.89)	
	≥7	17 (8.99)	16 (15.09)	12 (17.91)	91 (20.18)	281 (23.42)	2,867 (33.28)	
	Gender							0.83
	Male	101 (53.44)	61 (57.55)	38 (56.72)	242 (53.66)	672 (56.00)	4,670 (54.20)	
	Female	88 (46.56)	45 (42.45)	29 (43.28)	209 (46.34)	528 (44.00)	3,946 (45.80)	

patients is consistent with that of the non-stratified patients, and the proportion of girls is always higher than that of boys in hospitals A and B (*Figure 3*, P<0.001).

Proportion of MPP in hospitalized pneumonia stratified by age

The age of patients with MP pneumonia is generally on the rise, and the median age of patients in hospital C has increased from 3 to 5 years old in 2023. The median age in hospitals A and B increase from 4 to 6 years old in 2023 (*Figure 4*, P<0.001). The change in the age of onset can also be reflected in the age composition ratio (P<0.001, *Table 1*), especially in the proportion of children aged more than 7 years old. However, the length of hospital stay in patients with MP pneumonia shows a decrease (*Figure 5*).

Discussion

MP infection is endemic worldwide and can present with a variety of clinical manifestations, including upper respiratory tract infection, pneumonia, and various extrapulmonary manifestations (e.g., encephalitis, Stevens-Johnson syndrome) (15). However, MPP is also the most common cause of hospitalization for MP infection in children. The outbreak of MPP began in Beijing in

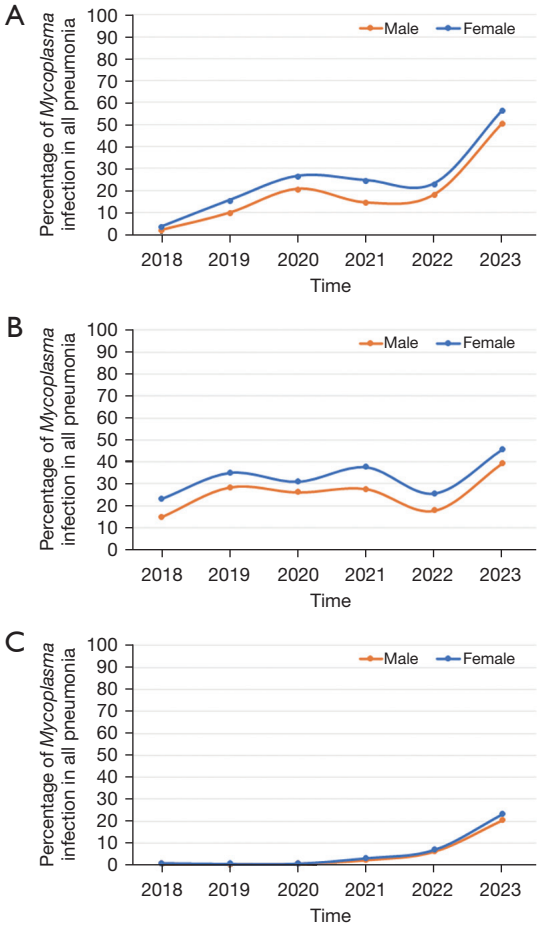

Figure 3 The proportion of *Mycoplasma* infection in hospitalized pneumonia patients grouped by sex in each year. (A) Hospital A, (B) hospital B, (C) hospital C.

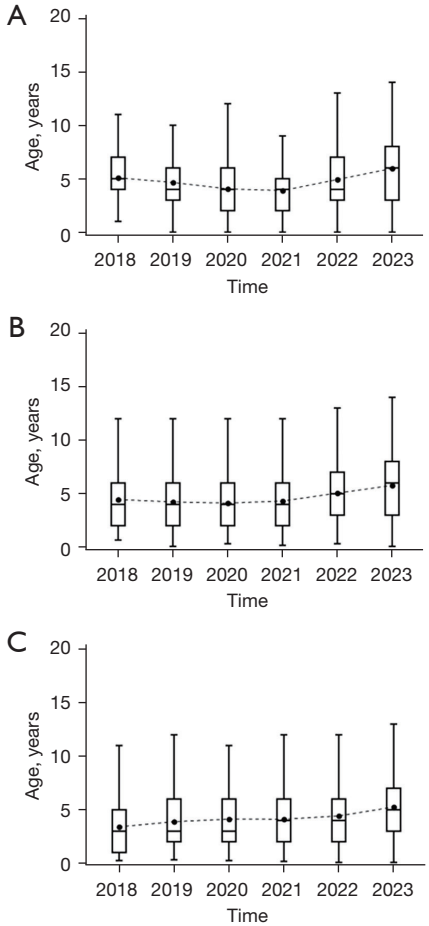

Figure 4 Curves of the proportion of *Mycoplasma* infection in hospitalized pneumonia patients stratified by age. (A) Hospital A, (B) hospital B, (C) hospital C.

the summer of 2019, and based on past experience, the epidemic of MPP may last from the Summer and Autumn of 2019 to the winter of 2020 or the spring of 2021 (11). Data from our analysis of hospitals in hospitals A and B showed that in 2018 and 2019, before the pandemic, the number of hospitalized children with MP pneumonia and the proportion of children suffering from the total number of pneumonia cases showed a significant upward trend, indicating that the two regions have entered an epidemic or there would be endemic. However, during the pandemic (from December 2019 to December 2022), there was no further growth, and even a slight moderation, which was slowed or interrupted, and it is clear that the impact of the intervention was brought about. NPIs, including mask-wearing, hand hygiene, surface disinfection, social distancing, and increased ventilation, have been effective in interrupting the spread of the virus, reducing the spread of the COVID-19 and reducing children's exposure to other pathogens, reducing the overall prevalence of respiratory illness among children (16). The epidemiological characteristics of hospital C were different from those of the other two hospitals, which may be related to the beginning of MP epidemic in 2021. Another important reason is the lack of diagnosis of MP pathogens before the pandemic, and the hospital only introduced pathogenic testing in 2020.

In the three months after all pandemic control measures were lifted (lifted in December 2022), the number of MP pneumonia cases and the proportion of acquired pneumonia began to rise sharply. It is not yet clear whether the continuation of this upward trend is exacerbated by the "immunity debt" brought about by the control measures. Many researchers have supported that this is due to immune

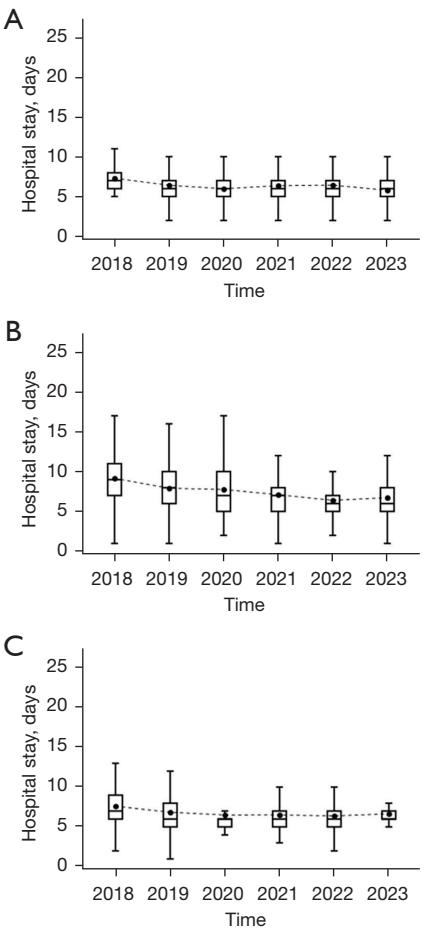

Figure 5 The length of hospital stay for *Mycoplasma* pneumonia in different years. (A) Hospital A, (B) hospital B, (C) hospital C.

paralysis, and that the control measures during COVID-19 have reduced the chance of exposure to pathogens, and routine immunization has been delayed or interrupted, resulting in insufficient population immunity stimulation, and thus resulting in a decline in herd immunity and the formation of an immune debt (17), while some researchers believe that this "immune debt" theory is controversial (18). It was noted that the sharp increase in the number of cases in such a short period of time had put tremendous pressure on medical resources, with patients overcrowding medical institutions, medical staff overworked, and medical resources seriously insufficient. Therefore, authorities and medical institutions should learn from this experience and pay attention to the impact of control measures on the prevalence of non-target infectious diseases. The epidemiological characteristics of MP pneumonia observed in this study can be used as a reference for future epidemic prediction.

In addition to the seasonal climate of the region, the epidemiological characteristics of MP may also vary according to age, sex, and genotype (19). MPP infection is closely related to age in children of different ages due to differences in immune status. A previous study has shown that the incidence of MPP infection increases significantly with age (20). In a study of children under 18 years of age with CAP requiring hospitalization at three hospitals in Memphis, Nashville, and Salt Lake City, MP infection was more common in children at the age of 5 years or older than in younger children (19% *vs.* 3%) (21). Our study found that from 2018 to 2023, the age of onset of MPP increased, especially at the age of more than 7 years. MP infection is not lifelong immunity and can be recurred. The age of children with MPP is increasing, which may be due to the fact that COVID-19 isolation measures have reduced antibodies in children who have been infected in the past, and older children have been reinfected as a result. MP is an ectoparasitic bacterium that rarely invades the blood and tissues, and the immune inflammatory response has an important relationship with the clinical manifestations of MPP (22). Children over 7 years old have relatively mature immune function, and after MP infection, they can activate adaptive immunity and induce antibody production, forming immune complexes against host tissues, which further exacerbates the autoimmune response and leads to damage to the lungs and extrapulmonary tissues (23), so children over 7 years old are more likely to suffer from lobar pneumonia and severe pneumonia, and the probability of hospitalization is higher. The overall shortening of hospital stay may be due to the increase in the proportion of patients with mild symptoms compared with children with severe disease, and the shortage of medical resources.

The correlation between sex and MP infection has been controversial, and a number of studies have shown that the detection rate of MP in girls is higher than that in boys, possibly because of differences in hormone levels between girls and boys, which makes girls susceptible to MP (11,24).

There are some limitations in this study. First, there is an inevitable selection bias in the design of the retrospective study, and the potential influence of unmeasured variables and unknown confounding factors cannot be ruled out in this study. Second, there is a lack of clinical data, such as the severity of the patient's condition, prognosis, oxygen therapy, etc., which may lead to our inadequate assessment of MP pneumonia.

Conclusions

In summary, our study found that MPP showed an increasing-flat-sharply increasing epidemic trend before, during, and post the COVID-19. Management departments and medical institutions should pay attention to the potential impact of control measures on the epidemic of non-target infectious diseases, make epidemic predictions, and prepare for response in advance.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tp.amegroups.com/article/view/10.21037/tp-24-281/rc

Data Sharing Statement: Available at https://tp.amegroups.com/article/view/10.21037/tp-24-281/dss

Peer Review File: Available at https://tp.amegroups.com/article/view/10.21037/tp-24-281/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-24-281/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional ethics board of Changshu Hospital Affiliated to Nanjing University of Chinese Medicine (No. 2017788), The First People's Hospital of Lianyungang (No. 2023CS034) and Xuzhou Children's Hospital (No. 2023-06-17-k17) and informed consent was taken from all the patients' parents/legal guardians.

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