Effect of COVID-19 on Childhood *Mycoplasma Pneumoniae* Infection in Chengdu, China

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Abstract

Background. Following the outbreak of the COVID-19 pandemic, a change in the incidence and transmission of respiratory pathogens was observed. Here, we retrospectively analyzed the impact of COVID-19 on the epidemiologic characteristics of *Mycoplasma pneumoniae* infection among children in Chengdu, one of the largest cities of western China.

Method. *M. pneumoniae* infection was diagnosed in 33,345 pediatric patients with respiratory symptoms at the Chengdu Women's & Children's Central Hospital between January 2017 and September 2020, based on a titer of ³1:160 measured by the passive agglutination assay. Differences in infection rates were examined by sex, age, and temporal distribution.

Results. Two epidemic outbreaks occurred between October–December 2017 and April–December 2019, and two infection peaks were detected in the second and fourth quarters of 2017, 2018, and 2019. Due to the public health response to COVID-19, the number of positive *M. pneumoniae* cases significantly decreased in the second quarter of 2020. The rate of *M. pneumoniae* infection among children aged 3–6 years was higher than that in other age groups.

Conclusion. Preschool children are more susceptible to *M. pneumoniae* infection and close contact appears to be the predominant factor favoring pathogen transmission. The public health response to COVID-19 can effectively control the transmission of *M. pneumoniae*.

Introduction

Mycoplasma pneumoniae (*M. pneumoniae*) is one of the most common pathogens of respiratory infections in children and adolescents, accounting for up to 40% of community-acquired pneumonia (CAP) in children over 5 years of age [1], and this percentage rises during epidemics. In most cases, *M. pneumoniae* infections are self-limiting, but they can cause refractory pneumonia and extrapulmonary injuries, leading to severe complications and even death. The growing severity of this disease [2–4] and the occurrence of *M. pneumoniae* epidemics [5] have been associated with macrolide resistance [6–11], which is much higher in Asia than in Europe and North America due to the unregulated use of antibiotics.

Since the first COVID-19 outbreaks in Wuhan, China, in December 2019, the Chinese government responded rapidly and effectively to controlling the pandemic with restrictive measures that significantly affected the transmission of other respiratory pathogens, including *M. pneumoniae*. In this study, we conducted a retrospective epidemiologic analysis of data from January 2017 to September 2020 in order to evaluate the impact of the public health response to COVID-19 on the epidemiological characteristics and transmission of *M. pneumoniae* among children in western China.

2. Method And Materials

2.1 Study subjects

Data were retrospectively analyzed for children between 1 month and 18 years of age who came to Chengdu Women's & Children's Central Hospital from January 2017 to September 2020 due to respiratory symptoms. The patients' demographic features, clinical information, and laboratory data were retrospectively collected from the hospital records. The pediatric patients were divided into four groups depending on their age in years: 0–2, 3–6, 7–12, and 13–18.

2.2 Detection of M. pneumoniae

IgM antibodies against *M. pneumoniae* in serum were detected using a passive agglutination kid (Fujirebio, Japan) based on the manufacturer's instructions. A single titer of ≥1:160 was considered an indicator of *M. pneumoniae* infection.

2.2 Statistical analysis

All data were analyzed using the SPSS software package (version 20.0, IBM, USA). Categorical data were reported as ratios or n (%).

3. Results

3.1 Demographic characteristics of pediatric patients withM. pneumoniaeinfection

A total of 33,345 pediatric patients were enrolled in the study, including 16,253 males and 17,092 females. The male/female ratios were 0.92:1 for 2017, 0.94:1 for 2018, 0.96:1 for 2019, and 1.03 for 2020 (Fig. 1). In each year, the rate of *M. pneumoniae* infection was higher for the age group of 3–6 years than for other age groups, especially in 2019 (Fig. 2).

3.2 Temporal distribution of pediatric patients withM. pneumoniaeinfection

Our data provide the first evidence that two *M. pneumoniae* epidemic outbreaks occurred in western China between 2017 and 2020; the first between October 2017 and December 2017, and the second between April 2019 and January 2020. Analysis of the monthly distribution in the indicated period revealed that the number of *M. pneumoniae* positive cases was the highest in January 2020 and decreased sharply after February 2020 (Fig. 3). In addition, two epidemic peaks were identified in the second and fourth quarters of 2017, 2018 and 2019 (Fig. 4). Interestingly, these peaks decreased significantly after the COVID-19 pandemic outbreak, especially during the second quarter of 2020 (Fig. 4).

3.3 Inpatient/outpatient ratio of pediatric patients withM. Pneumoniaeinfection

The annual hospitalization rates between 2017 and 2020 were 28.5%, 30.7%, 47.3%, and 48.9%. The highest absolute total number of pediatric patients with *M. pneumoniae* infection, including both outpatients and inpatients, was observed in 2019. The number of inpatients was much higher in 2019–2020 than in 2017–2018. In contrast, the total number of positive cases was significantly reduced in 2020, but the inpatient/outpatient ratio remained almost the same as in 2019 (Fig. 5).

4. Discussion

Although epidemiological studies on *M. pneumoniae* infection have indicated that epidemics usually occur every 3–7 years [12–14], infection incidence in Europe and Asia significantly increased in 2011–2012, 2015, and 2017 [2, 9, 14, 15]. Our study retrospectively analyzed the impact of the public health response to COVID-19 on the occurrence of *M. pneumoniae* infection among children in western China, based on analysis of data from 2017 to 2020. In particular, we found that a small-scale epidemic outbreak of 3 months occurred in 2017, while a large-scale outbreak of 10 months occurred in 2019, confirming the uniform global epidemic pattern of *M. pneumoniae* infection. It has also been reported that a long epidemic affecting a large area can lead to a secondary peak in the same epidemic [16]. The average number of *M. pneumoniae* infections per month was approximately two times higher during each epidemic than between the epidemics.

Although substantial numbers of children were diagnosed with *M. pneumoniae* infection throughout the study period, the epidemic peaked in the fourth quarter of each year between 2017 and 2019, which was consistent with the results obtained previously in South Korea [2, 13], USA [3], Israel, and 11 countries of Europe [16]. However, the tendencies in these studies differ from the data reported in epidemiological studies in Italy [17], South Africa [18], and other regions of China [8, 19, 20]. The peaks of *M. pneumoniae* infection between 2017 and 2019 in our study coincided with the school semesters, and the number of infections fell significantly after schools were closed to limit the COVID-19 pandemic. These results indicate that closed settings with closer contacts promoted the *M. pneumoniae* transmission, consistent with studies reporting that *M. pneumoniae* infections are transmitted mainly through droplets spread during close contact [21], and that closed or semi-closed communities, such as military bases, hospitals, religious communities, schools, and institutions are areas associated with the highest rates of transmission, which can more easily lead to epidemics [22–24].

It has also been reported that climate conditions, such as humidity and temperature, can significantly affect the survival and spread of airborne *M. pneumoniae* [19, 25–27]. However, these studies have come to conflicting conclusions, suggesting that climatic factors are not the primary determinants of *M. pneumoniae* transmission patterns.

Furthermore, no clear differences were observed in sex distribution of pediatric cases of *M. pneumoniae* infection, but the number of positive cases varied significantly depending on age. Some studies have shown that *M. pneumoniae* infections are more common in children over 5 years of age [13, 22], although they also occur in infants [14, 17, 28, 29]. However, other studies have variably suggested higher rates of infection among preschool children or among school-age children [2, 8, 19, 20]. In the present study, the highest number of infections was detected among children 3–6 years old, which included children sent to a childcare center in Chengdu, where inter-child contact was closer than in primary and secondary schools [23], thus favoring the transmission of *M. pneumoniae*.

In the present study, the rate of hospitalization due to *M. pneumoniae* infection was within the rates reported in recent studies (18–67%) [13, 30, 31]. The significant increase in 2019 suggests that infections were more severe during an *M. pneumoniae* epidemic. Nevertheless, the incidence of infections decreased significantly in 2020 due to the restrictive measures and strong isolation policy applied from February 2020 by the Chinese government after the COVID-19 outbreak. In fact, the number of *M. pneumoniae* infections in the second quarter of 2020 was 63.3%, 60.3%, and 77.5% smaller, respectively, than the numbers in the second quarter of 2017, 2018, and 2019. This suggests that a comprehensive public health response can effectively control *M. pneumoniae* transmission.

Our study had some limitations, including the fact that *M. pneumoniae* infection was diagnosed based only on a single passive agglutination method [16] and a single acute-phase serum test for the presence of anti-*M. pneumoniae* IgM. In children with pneumonia, testing paired samples of acute- and convalescent-phase sera for *M. pneumoniae* antibody may be more sensitive than testing a single sample [32], and a titer of 1:640 may be a more suitable diagnostic criterion [13]. However, paired serum samples are difficult to obtain from inpatients and outpatients with self-limiting *M. pneumoniae* infection, and the optimal antibody level is difficult to define, because it can depend on the patient's immune state [33]. Therefore, our retrospective study relied mainly on clinical manifestations of respiratory infection combined with a single antibody titer of ≥1:160, as recommended in a Chinese study [34].

In conclusion, we demonstrate that two epidemic outbreaks of *M. pneumoniae* infection occurred during 2017–2020 in western China. Preschool children were more susceptible to infection, and the predominant factor influencing *M. pneumoniae* transmission appeared to be close contact, especially in childcare centers. The significant differences in the temporal distribution and the decrease in the number of positive cases in the first three quarters of 2020 indicated that the public health response to the COVID-19 pandemic may have effectively controlled the transmission of *M. pneumoniae* infection.

Abbreviations

M. pneumoniae: *Mycoplasma pneumoniae*; COVID-19: Coronavirus disease 2019; CAP: community-acquired pneumonia.

Declarations

Acknowledgements

Not applicable.

Authors' contributions

Conceptualization and methodology: Hanmin Liu. Data analysis, writing, original draft preparation: Ying Zhang and Yijie Huang. Data analysis: Jun Luo. Writing-review and editing: Tao Ai. Approval of final manuscript: all authors.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The study protocol was approved by the Chengdu Women's and Children's Central Hospital institutional review board. The included data were retrospective data from medical records and did not include any identifying information. Consent to participate is not applicable for this study.

Consent for publication

No identifiable patient data or identified individual responses are used in this publication.

Competing interests

All authors declare that they have no competing interests.

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Figures

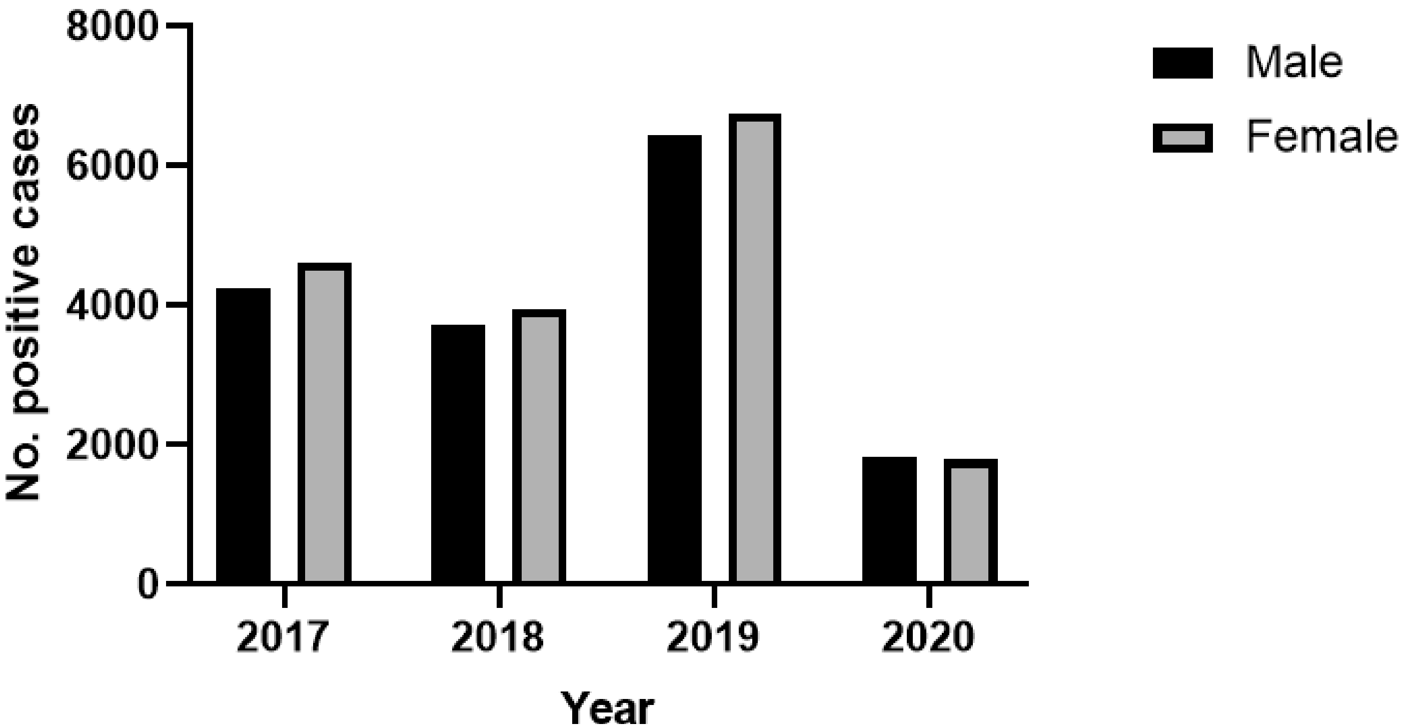

Figure 1

Sex distribution of pediatric patients with Mycoplasma pneumoniae infection between January 2017 and September 2020.

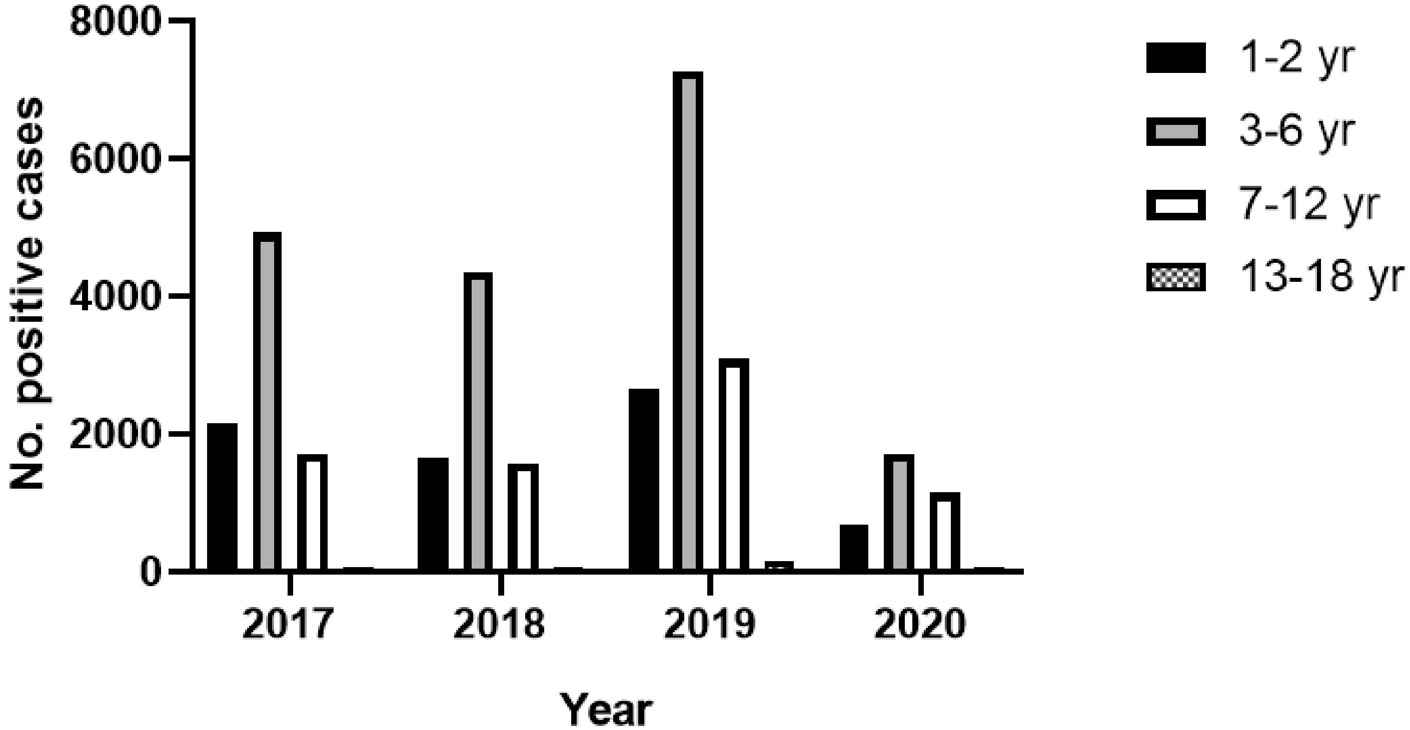

Figure 2

Age distribution of pediatric patients with Mycoplasma pneumoniae infection between January 2017 and September 2020.

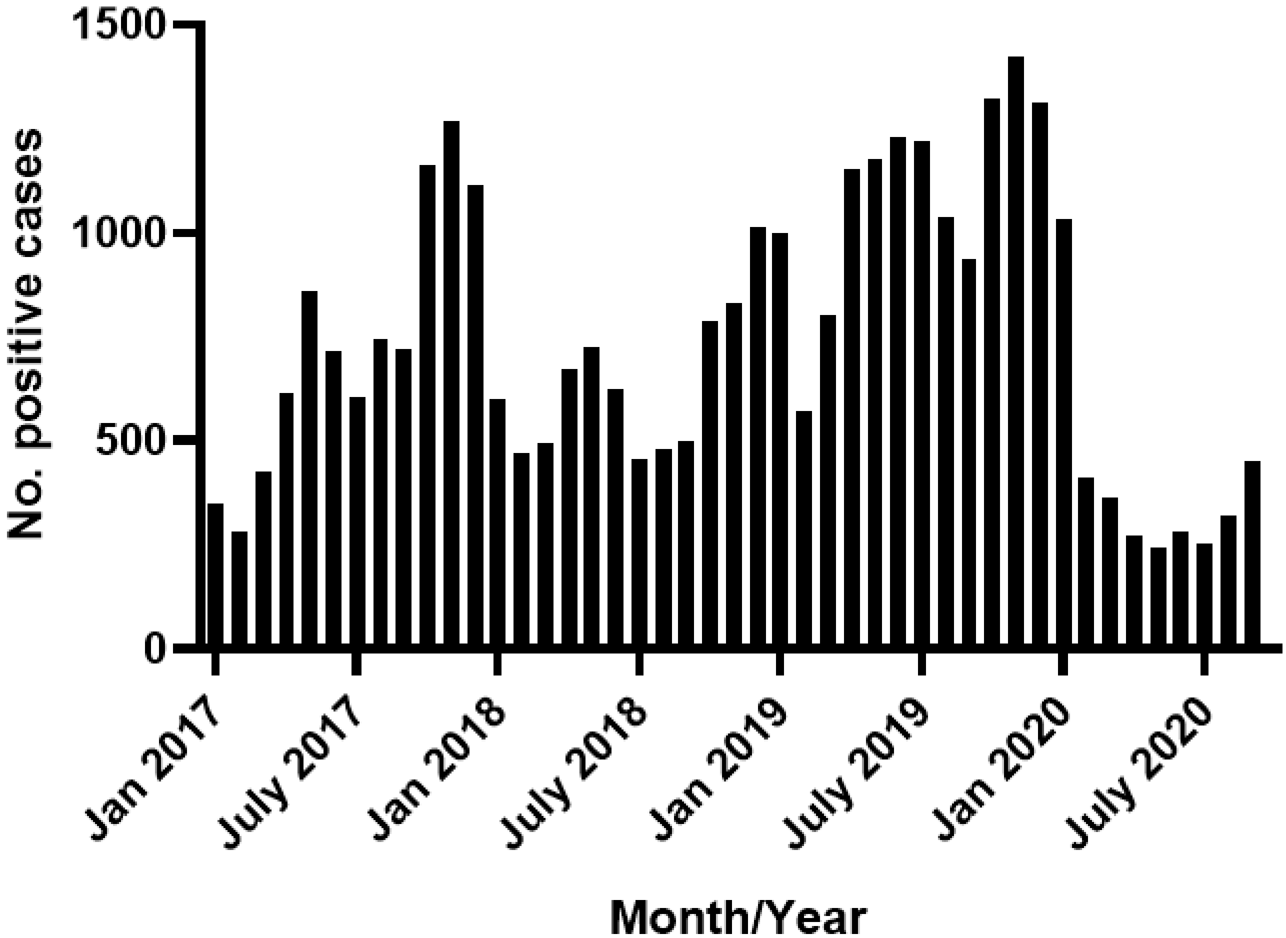

Figure 3

Monthly of pediatric patients with Mycoplasma pneumoniae infection between January 2017 and September 2020.

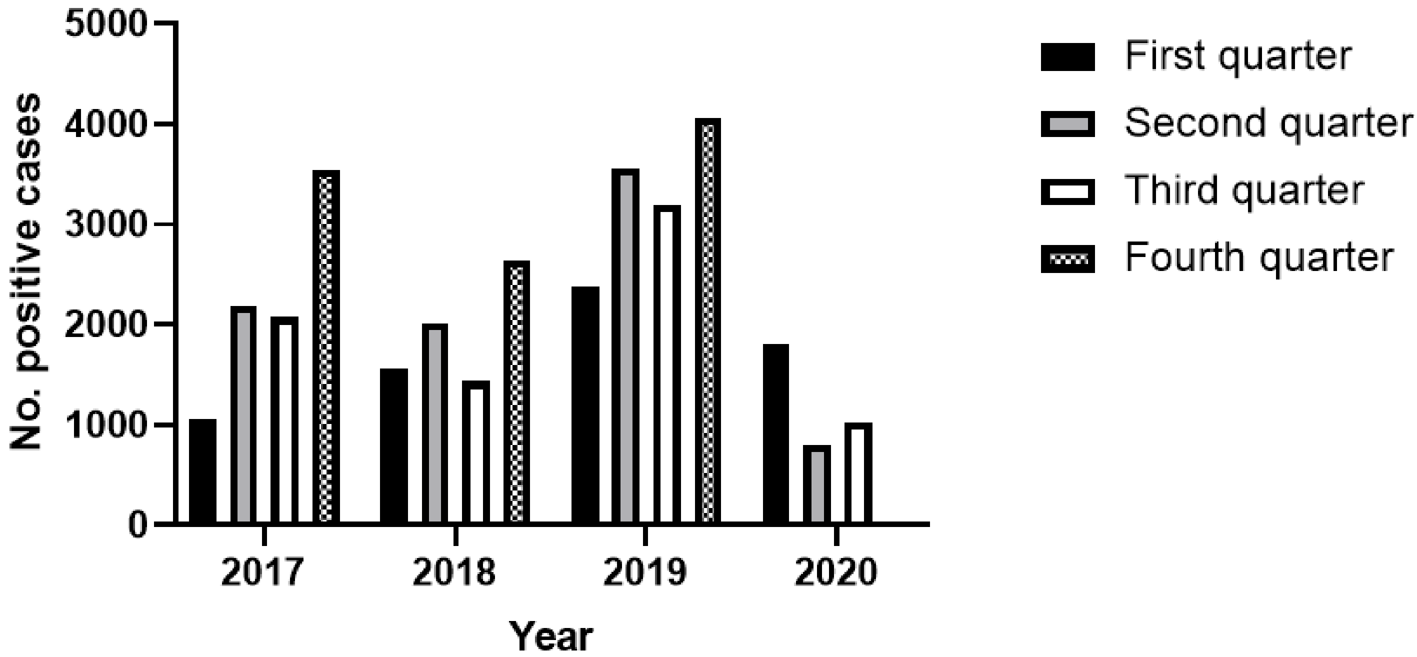

Figure 4

Quarterly distribution of pediatric patients with Mycoplasma pneumoniae infection between January 2017 and September 2020.

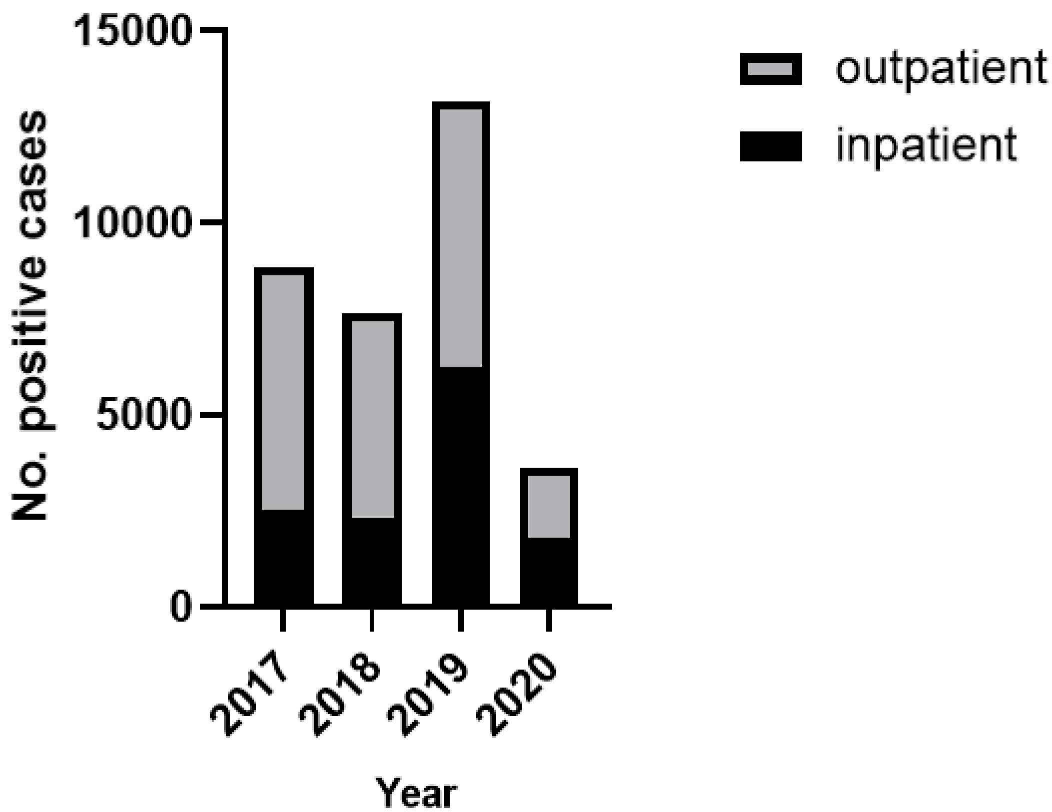

Figure 5

Populations of inpatients and outpatients among pediatric cases of Mycoplasma pneumoniae infection between January 2017 and September 2020.