Preplanned Studies

Trends in Respiratory Infectious Pathogens in Children Under the Age of 14 — Xiamen City, Fujian Province, China, 2017–2023

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Summary

What is already known about this topic?

Respiratory infections pose a significant burden on public health. Despite recent outbreaks occurring in various locations, there is limited information available on the prevalence trends of multiple common respiratory pathogens in China beyond 2022.

What is added by this report?

A retrospective analysis was conducted on respiratory pathogen infections in a Xiamen hospital over a seven-year period. The analysis revealed fluctuating trends, with the number of infections for certain viruses initially decreasing after 2019, only to rebound to previous or higher levels. Recently, there has been an observed collective increase in positive cases for certain pathogens.

What are the implications for public health practice?

The study improves understanding of respiratory pathogens, primarily in Xiamen, with potential implications for the improvement of strategies for the prevention and management of respiratory infectious diseases.

Respiratory tract infections (ICD-10/J00-J99) are infectious diseases caused by various microorganisms, including bacteria, viruses, mycoplasmas, fungi, and parasites. These infections are typically seasonal and have been extensively studied. The implementation of dynamic control measures in China from 2020 to 2023 may have helped reduce the spread of other respiratory pathogens. Certain regions have experienced a delayed outbreak of respiratory viruses due to these interventions (*1*–*5*). However, most existing studies have mainly focused on the period from 2020 to early 2022. Timely surveillance is crucial for understanding community health threats, especially when observed trends deviate from seasonal norms. This study aims to assess changes in the epidemiological trends of common respiratory pathogens among children in recent years. We conducted a retrospective analysis of the prevalence of various common respiratory pathogens among patients with respiratory infections admitted to the Women and Children's Hospital, School of Medicine, Xiamen University, in Fujian Province from 2017 to 2023.

The study was conducted at the Women and Children's Hospital, School of Medicine, Xiamen University, which serves as a regional medical center for maternal and child healthcare in southwestern Fujian. The study retrospectively analyzed pediatric patients with respiratory tract infections who visited the hospital between January 1, 2017, and November 30, 2023. The inclusion criteria included children tested for pathogens (bacteria, virus, or mycoplasma) and excluded those above 14 years old or who didn't undergo pathogen testing. The study focused on detecting five viruses [Respiratory syncytial virus (RSV), adenovirus, influenza A (Flu A), influenza B (Flu B), parainfluenza], five bacteria (*H. influenzae*, *M. catarrhalis*, *S. pneumoniae*, *S. aureus*, *K. pneumoniae*) and *Mycoplasma pneumoniae*. The five viruses were detected by polymerase chain reaction (PCR) capillary electrophoresis fragment analysis (multiple detection kits for 13 types of respiratory pathogens, Ningbo Health Gene Technologies Co., Ltd, Ningbo, China), probe-based PCR (Respiratory virus nucleic acid six-fold test kit, Beijing Zhuo Cheng Hui Sheng Biotechnology Co., Ltd., Beijing, China) or immunofluorescence (D$^{®3}$ Ultra DFA Respiratory Virus Screening and ID Kit, Diagnostic Hybrids Inc., Athens, USA) with nasal swabs. *Mycoplasma pneumoniae* was detected by Probe-based PCR (*Mycoplasma pneumoniae* nucleic acid test kit, Daan Gene Co., Ltd, Guangzhou, China). Sputum was tested for typical bacteria using conventional culture

method. A total of 25,506 virus detection samples, 21,640 bacterial detection samples, and 23,579 pneumonia detection samples were collected. Trend analysis was conducted using GraphPad Prism and ArcGIS.

According to the current addresses of the patients included in the study, the majority (77.71%) were from Xiamen, while 18.38% were from other cities in Fujian Province, and 3.91% were from other provinces (Figure 1A). The annual distribution of these samples is shown in Figure 1C. The number of outpatient visits for respiratory infections exceeded one hundred thousand from 2017 to 2019, decreased in 2020 and 2021, and then increased again in 2022 and 2023 (Figure 1B). The prevalence of various viruses declined between 2019 and 2023. However, cases of some pathogen infections have returned to previous levels, and in some cases, have even exceeded previous levels. Of particular note is the unprecedented surge in cases of *Mycoplasma pneumoniae* in recent months.

As previously described, there have been changes in the epidemiology of respiratory infections in recent years. Our study observed a significant reduction in circulating respiratory pathogens, including major viruses, bacteria, and mycoplasma, in early 2020. Subsequently, several viruses demonstrated a "peak" pattern over the following three years, while bacteria did not exhibit such a pattern. Respiratory syncytial virus (RSV) emerged as the predominant virus in pediatric respiratory infections, with a surge in infections occurring after 2020, resulting in an infection peak higher than usual in July 2021 (Figure 2A). Adenovirus did not display a distinct seasonal pattern. Although a relatively large number of infected patients and increase in positive rates were seen in the summer of 2019, the number of infections has remained low in subsequent years. However, in recent months, there has been a steady increase in the number of adenovirus infections and positive rates, surpassing the previous years' levels (Figure 2C). Before 2020, influenza A and influenza B traditionally alternated in dominance. In 2020 and 2021, the number of influenza A and influenza B infections was low. However, in the 2022–2023 period, influenza B re-emerged, while influenza A experienced two peaks, with a higher number of infections than the pre-March 2020 timeframe. Notably, both the number of influenza A and B infections and positivity rates rose simultaneously last month (Figure 2E, 2G). Since the winter of 2020, there has been a significant increase in parainfluenza infections and positive rates (Figure 2I). Among the five bacteria of interest (*H. influenzae*, *M. catarrhalis*, *S. pneumoniae*, *S. aureus*, *K. pneumoniae*), there was no observable trend of post-decline

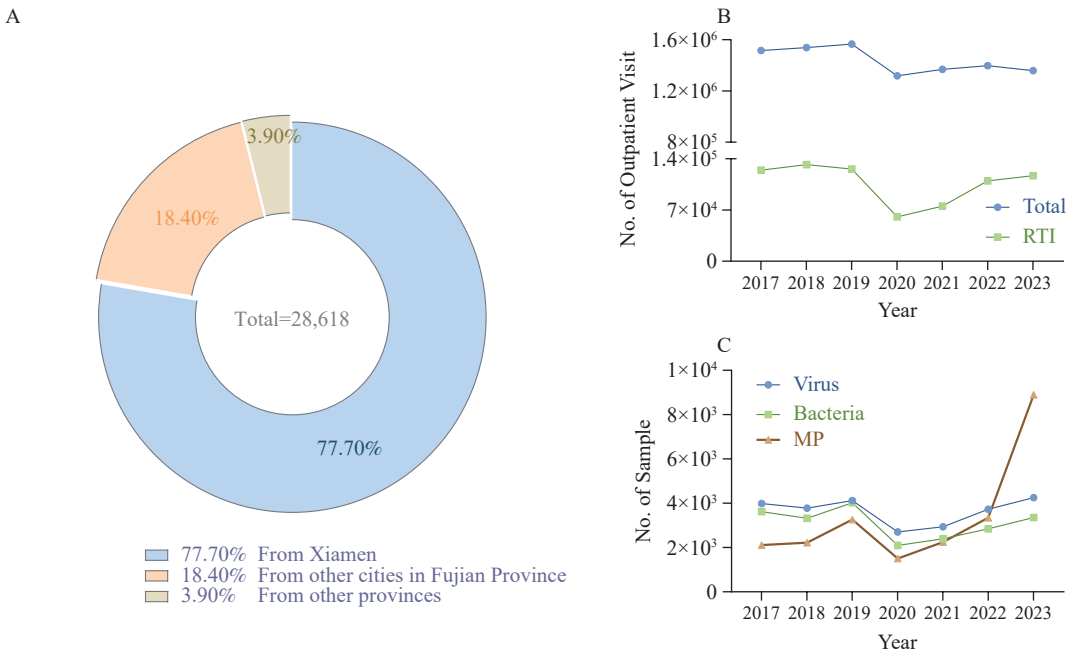

FIGURE 1. Information on the population and tested samples included in this study. (A) Distribution of patient sources included in this study; (B) total outpatient visits and visits for respiratory symptoms in the hospital over the past 7 years; (C) Number of samples tested for viruses, bacteria, and *Mycoplasma pneumoniae* in the last seven years.
Abbreviation: RTI=respiratory tract infection, MP=*Mycoplasma pneumoniae*.

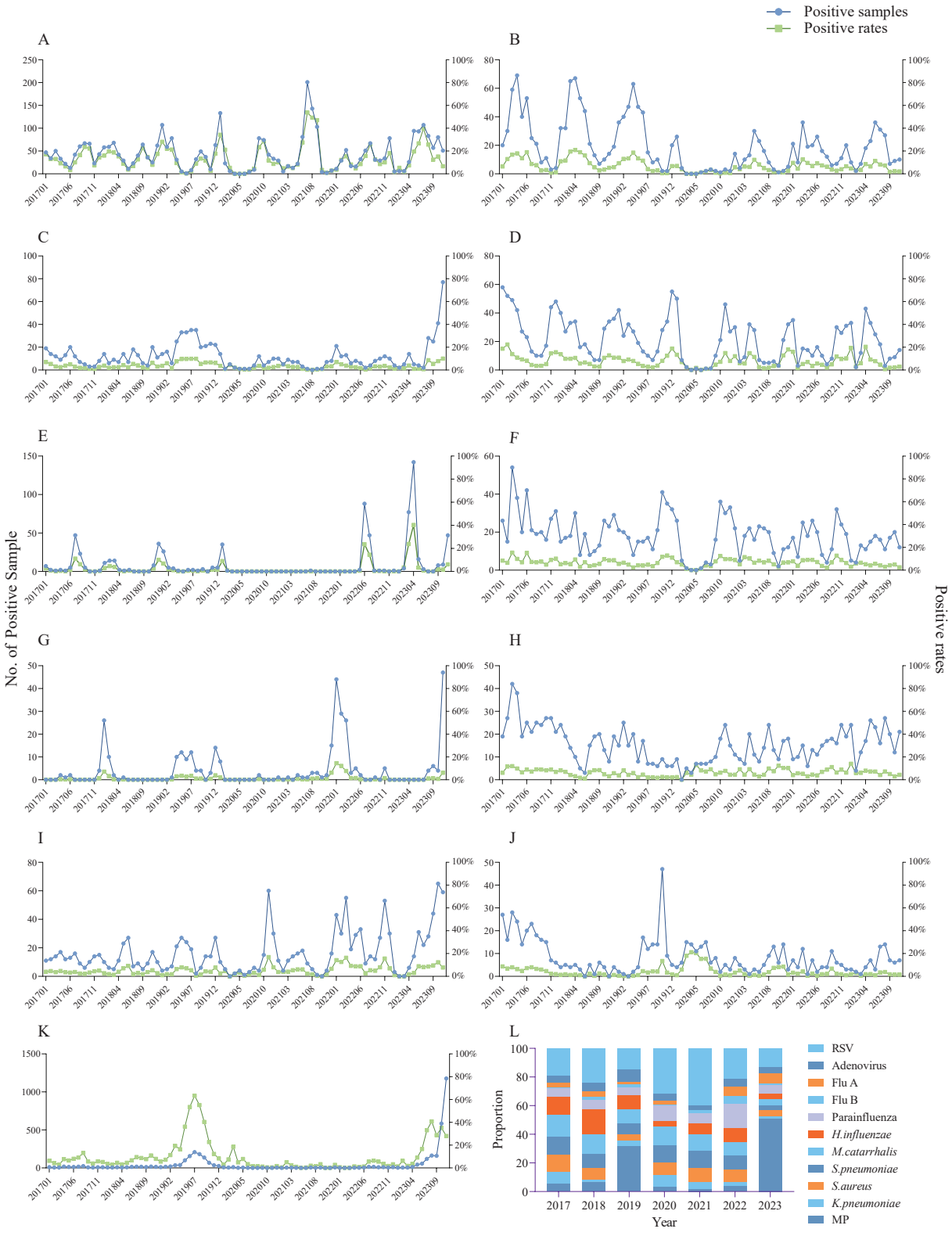

FIGURE 2. Changes in positive samples for different pathogens in the last seven years. (A) RSV; (B) *H. influenzae*; (C) Adenovirus; (D) *M. catarrhalis*; (E) influenza A; (F) *S. pneumoniae*; (G) Influenza B; (H) *S. aureus*; (I) Parainfluenza; (J) *K. pneumoniae*; (K) *Mycoplasma pneumoniae*; (L) Percentage of positive samples infected with different respiratory pathogens in different years (Number of positive samples for different pathogens divided by the sum of positive samples for all pathogens).
Abbreviation: RSV=respiratory syncytial virus.

"upsurge" (Figure 2B, 2D, 2F, 2H, 2J). The last significant outbreak of *Mycoplasma pneumoniae* occurred in 2019. After 2020, *Mycoplasma pneumoniae* infections remained at low levels until the second half of 2023. However, in the past two months, there has been a remarkable surge in *Mycoplasma pneumoniae* infections and positive rates, making it the primary pathogen in respiratory infections in 2023 (Figure 2K, 2L). It is important to note that cases where pathogenic microorganisms were not detected or could not be identified among patients were not included in Figure 2L.

DISCUSSION

The implementation of non-pharmaceutical interventions (NPIs) has played a significant role in reducing hospital utilization for respiratory tract infections (*4*,*6*–*7*). In this study, we conducted an analysis of major respiratory pathogens detected in our laboratory over a seven-year period. RSV, adenovirus, influenza A and B, parainfluenza, and *Mycoplasma pneumoniae* all exhibited "off-season" periods followed by surges, consistent with previous findings (*1*–*6*). Recent global surveillance data have indicated a resurgence of *Mycoplasma pneumoniae* infections in Europe and Asia (*8*). *Mycoplasma pneumoniae* infections occur year-round in various climates worldwide, with periodic epidemics every few years. Our study observed an outbreak of *Mycoplasma pneumoniae* in 2019, which took place from May to October, with the highest number of infections occurring in July. Additionally, Xiamen has experienced a recent re-emergence of *Mycoplasma pneumoniae*, with significantly more positive detections compared to 2019.

It is important to highlight that the findings of this study demonstrate an increase in the prevalence of *Mycoplasma pneumoniae* cases, as well as infections caused by various viruses in recent months. For instance, there was a surge in adenovirus infections starting from August 2023, surpassing previous levels. In addition, Influenza A reached peaks above previous levels in June 2022 and April 2023, respectively. Notably, there was a significant rise in positive cases of Influenza B in November and a substantial increase in parainfluenza viruses since the winter of 2020. These findings emphasize the need for monitoring and surveillance of these pathogens.

This study provides crucial epidemiological information on respiratory infections, including the seasonal and annual trends of various pathogens. First, this information can assist relevant authorities in enhancing their surveillance systems, increasing alertness, and disseminating early warning information to healthcare organizations and the public in a timely manner. By doing so, necessary measures can be implemented to control and prevent the spread of respiratory infections. Second, it can aid in optimizing the allocation and management of medical resources, ensuring timely diagnosis and accessible treatment. Lastly, identifying epidemiological trends in pathogens can guide clinicians in implementing targeted preventive measures, reducing the overuse of antibiotics, shortening the duration of medical care, and improving efficiency. The escalation in the number of infections has placed a significant burden on healthcare institutions, thus highlighting the urgent need for rapid pathogen diagnostics.

There are several limitations to this study. First, due to constraints in the laboratory testing projects, this study only analyzed the historical changes of 11 respiratory pathogens. Other common respiratory pathogens such as rhinovirus, human metapneumovirus, and bocavirus were not included. Additionally, some patients were not tested for all eleven pathogens, making it impossible to analyze co-infection scenarios. A positive test result does not necessarily indicate infection with the respective pathogen; it could be indicative of colonization. This study solely reported positive test results without distinguishing between colonization and infection. Second, this study did not differentiate between inpatients and outpatients or analyze patient symptoms. Therefore, it cannot determine if the observed increase in viral infections since 2020 has resulted in more severe disease outcomes. Lastly, the use of different pathogen detection methods in the laboratory over the course of this study's long time span limits the comparability of data. The viral epidemic trend observed can only be considered as a reference.

In conclusion, this study conducted a retrospective analysis to determine the prevalence of major respiratory pathogens over a seven-year period. The study focused on patients primarily from Xiamen, with some patients from other cities in Fujian Province and a few from other provinces. The findings provide important data on trends in respiratory pathogen prevalence. It was observed that there has been a concurrent increase in infections caused by different

viruses in recent months, highlighting the need for heightened attention.

Conflicts of interest: No conflicts of interest.

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