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The Impact of COVID-19 Pandemic on the Etiological Spectrum of Respiratory Infections in Children

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Abstract

Objective: Following the outbreak of the novel coronavirus pandemic, a series of preventive and control measures were adopted by the public, which have had a certain impact on the occurrence of respiratory infectious diseases and changes in their etiology. This article aims to explore the changes in respiratory pathogens among children with respiratory infections during the COVID-19 pandemic and after the comprehensive lifting of restrictions, providing a basis for the clinical diagnosis and treatment of pediatric respiratory infections in the post-pandemic era. **Methods:** We retrospectively reviewed and analyzed the targeted sequencing results of multiple respiratory pathogens in children with respiratory infections treated at the Children's Hospital affiliated with Shandong University from January 2022 to December 2023. **Results:** A total of 16,571 targeted sequencing results of pathogens from children with respiratory infections were included in the analysis (2,810 cases in 2022 and 13,761 cases in 2023). The overall positive detection rates of pathogens in 2022 and 2023 were 95.19% and 96.56%, respectively. The positive detection rates for single pathogens were 16.01% vs. 19.29%, while the rates for two or more pathogens were 79.18% vs. 77.27%. The top three viral pathogens with the highest positive detection rates in both 2022 and 2023 were rhinovirus, parainfluenza virus, and respiratory syncytial virus. In 2023, the top three bacterial pathogens were *Streptococcus pneumoniae, Haemophilus influenzae,* and *Staphylococcus aureus,* whereas in 2022, they were *Streptococcus pneumoniae, Haemophilus influenzae,* and *Bordetella pertussis*. The positive detection rates of *Haemophilus influenzae, Staphylococcus aureus, Mycoplasma pneumoniae,* respiratory syncytial virus, adenovirus, influenza A virus, and rhinovirus in 2023 were significantly higher than those in 2022 (all $P < 0.05$). However, the positive detection rates of *Streptococcus pneumoniae*, *Bordetella pertussis*, and parainfluenza virus were significantly lower in 2023 than in 2022 (all $P < 0.001$). Differences in the positive detection rates of respiratory pathogens were observed across different age groups. **Conclusion:** Significant changes in the prevalence of certain pathogens occurred during the COVID-19 pandemic and after the lifting of restrictions. It is essential to strengthen long-term monitoring of common respiratory infectious diseases to guide early clinical intervention.

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Objective: Following the outbreak of the novel coronavirus pandemic, a series of preventive and control measures were adopted by the public, which have had a certain impact on the occurrence of respiratory

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infectious diseases and changes in their etiology. This article aims to explore the changes in respiratory pathogens among children with respiratory infections during the COVID-19 pandemic and after the comprehensive lifting of restrictions, providing a basis for the clinical diagnosis and treatment of pediatric respiratory infections in the post-pandemic era.**Methods:** We retrospectively reviewed and analyzed the targeted sequencing results of multiple respiratory pathogens in children with respiratory infections treated at the Children's Hospital affiliated with Shandong University from January 2022 to December 2023.**Results:** A total of 16,571 targeted sequencing results of pathogens from children with respiratory infections were included in the analysis (2,810 cases in 2022 and 13,761 cases in 2023). The overall positive detection rates of pathogens in 2022 and 2023 were 95.19% and 96.56%, respectively. The positive detection rates for single pathogens were 16.01% vs. 19.29%, while the rates for two or more pathogens were 79.18% vs. 77.27%. The top three viral pathogens with the highest positive detection rates in both 2022 and 2023 were rhinovirus, parainfluenza virus, and respiratory syncytial virus. In 2023, the top three bacterial pathogens were *Streptococcus pneumoniae, Haemophilus influenzae,* and *Staphylococcus aureus,* whereas in 2022, they were *Streptococcus pneumoniae, Haemophilus influenzae,* and *Bordetella pertussis* . The positive detection rates of *Haemophilus influenzae, Staphylococcus aureus, Mycoplasma pneumoniae,* respiratory syncytial virus, adenovirus, influenza A virus, and rhinovirus in 2023 were significantly higher than those in 2022 (all $P < 0.05$). However, the positive detection rates of *Streptococcus pneumoniae* , *Bordetella pertussis* , and parainfluenza virus were significantly lower in 2023 than in 2022 (all $P < 0.001$). Differences in the positive detection rates of respiratory pathogens were observed across different age groups.**Conclusion:** Significant changes in the prevalence of certain pathogens occurred during the COVID-19 pandemic and after the lifting of restrictions. It is essential to strengthen long-term monitoring of common respiratory infectious diseases to guide early clinical intervention.

Keywords: Children; Respiratory Infections; Pathogens; COVID-19

Background

In December 2019, Coronavirus Disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), broke out in Wuhan, Hubei Province, China [1]. COVID-19 is primarily transmitted throuh contact and droplets, and all populations are susceptible [2–4]. To interrupt the spread of the novel coronavirus, a series of public health protection measures have been implemented worldwide since January 2020, including maintaining social distance, wearing masks, hand hygiene, travel restrictions, etc. These non-pharmaceutical interventions (NPIs) have effectively curbed the spread of the novel coronavirus and also reduced the transmission of other pathogens [5]. Additionally, SARS-CoV-2 triggers an excessive immune response, leading to a "cytokine storm" and subsequent immune dysregulation. This results in a decrease in the number and function of T lymphocyte subsets, making the body more susceptible to viral infections and causing changes in the epidemic spectrum of multiple pathogens[6]. As is well known, the prevention and control measures in China during the COVID-19 pandemic were strict and lasted for a long time. Therefore, it is more symbolic to study the changes in etiology before and after the epidemic in China. This study retrospectively analyzed the changes in the respiratory pathogen spectrum of children treated at our hospital in 2022 and 2023, aiming to find the epidemiological characteristics of etiology in the post-pandemic period and provide guidance for clinical practice.

Methods

Study Population We conducted a retrospective study on children aged 0-17 years diagnosed with respiratory infections at the Children's Hospital Affiliated to Shandong University (Jinan Children's Hospital) from January 1, 2022, to December 23, 2023. Specimens were collected from throat swabs, sputum, or bronchoalveolar lavage fluid and targeted sequencing for multiple pathogens. This retrospective study has been approved by the Ethics Committee of the Children's Hospital Affiliated to Shandong University(Approval Number: SDFE-IRB/P-2024097).All participants in this study provided informed consent prior to inclusion in the study.

Targeted Sequencing (NGS) Detection of Multiple Respiratory Pathogens

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Multiplex PCR combined with NGS technology was used, targeting the highly conserved regions of 103 respiratory pathogens to design specific primers. PCR amplification was performed in a single tube to enrich target pathogens. In the second round of PCR, sequencing adapters distinguishing sample sources were connected. High-throughput sequencing was carried out using a gene sequencer (model: KM MiniSeqDx-CN) to obtain sequencing data. Bioinformatics software was used to filter the sequencing data and align it with reference genomes to interpret the detection results of pathogens. The quality of samples was monitored by simultaneously detecting human DNA in the samples. All operations were completed by Guangzhou KingMed Diagnostics Co., Ltd.

3. Statistical Methods

Statistical analysis was performed using the SPSS v25.0 software package. Categorical variables were expressed as frequencies and percentages. The comparison of proportions of categorical variables was conducted using the chi-square test or Fisher's exact test. A p-value of less than 0.05 was considered statistically significant.

Results:

Basic Information of Enrolled CasesA total of 16,571 children with respiratory infections were included in the analysis, comprising 2,810 cases in 2022 and 13,761 cases in 2023. The age of the children ranged from 1 hour after birth to 17 years (median age was 3 years). The enrolled children were divided into three age groups: infants and toddlers (age $<$ 3 years), preschool children (3-5 years), and school-age children (6-17 years). In 2023, the overall positive detection rate of pathogens in children was 96.56%, with 19.29% of the children testing positive for one pathogen and 77.27% testing positive for two or more pathogens. In 2022, the overall positive detection rate of pathogens was 95.19%, with 16.01% of the children testing positive for one pathogen and 79.18% testing positive for two or more pathogens. The positive detection rate of pathogens in school-age children(6-17 years) in 2023 was significantly higher than that in 2022, while the positive detection rates in infants and toddlers (<3 years) and preschool children (3–5 years) were significantly lower than in 2022. The positive detection rate for a single pathogens in children in 2023 was significantly higher than that in 2022, whereas the positive detection rate for two or more pathogens in 2023 was significantly lower than in 2022. All these differences were statistically significant (all $P < 0.05$) (Table 1).

Table 1:The basic information of the patient

		2022 N=2810（%）	2023 N=13761（%）	X^2	P-value
Gender	boys	1676（59.64%）	8078（58.7%）	0.855	0.366
	girls	1134（40.36%）	5683（41.3%）		
<3 years old		1355（48.22%）	6336（46.04%）	4.45	0.036
3-5 years old		854（30.39%）	3594（25.12%）	21.71	<0.001
6-17 years old		597（9.5%）	3734（27.13%）	41.92	<0.001
Single pathogen		450（16.01%）	2655（19.29%）	16.48	<0.001
⩾2 pathogens		2225（79.18%）	10633（77.27%）	4.91	0.028

Positive Detection Rates of Pathogens in Different Years Regarding bacteria, the top three pathogens in 2023 were*Streptococcus pneumoniae, Haemophilus influenzae* , and*Staphylococcus aureus* . In 2022, the top three bacterial pathogens were *Streptococcus pneumoniae, Haemophilus influenzae* , and *Bordetella pertussis* . Among these, the positive detection rates of *Haemophilus influenzae* and*Staphylococcus aureus* in 2023 were significantly higher than those in 2022 (P <0.001), while the positive detection rates of *Streptococcus pneumoniae* and *Bordetella pertussis* were significantly lower than those in 2022 (both$P$ <0.001). In 2023, the positive detection rate of *Mycoplasma pneumoniae* was significantly higher than that in 2022 (P <0.001). Regarding viruses, the top three pathogens with the highest positive detection rates in both 2023 and 2022 were rhinovirus, parainfluenza virus, and respiratory syncytial virus. In 2023, the positive detection rates

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of respiratory syncytial virus, adenovirus, influenza A virus, and rhinovirus were significantly higher than in 2022 (all$P$ <0.05).However, the positive detection rate of parainfluenza virus in 2023 was significantly lower than that in 2022 (all P <0.001). The results are shown in Table 2.

Table 2: Positive Detection Rates of Pathogens in Different Years

Pathogens	2022 N=2810（%）	2023 N=13761（%）	X^2	P-value
Bacteria				
Streptococcus pneumoniae	701（24.95%）	3025（21.98%）	11.764	<0.001
Haemophilus influenzae	429（15.27%）	3149（22.88%）	79.061	<0.001
Staphylococcus aureus	283（10.07%）	1966（14.29%）	35.353	<0.001
Bordetella pertussis	409（14.56%）	417（3.03%）	654.415	<0.001
Atypical pathogens				
Mycoplasma pneumoniae	221（7.86%）	2022（14.67%）	92.981	<0.001
Virus				
Respiratory Syncytial Virus	215（7.65%）	2146（15.59%）	120.516	<0.001
Bocavirus	133（4.73%）	689（5%）	0.371	0.143
Metapneumovirus	155（5.5%）	834（6.06%）	1.233	0.015
Adenovirus	174（6.19%）	1014（7.37%）	4.853	0.029
Influenza A virus	204（7.26%）	1150（8.36%）	3.744	
Rhinovirus	570（20.28%）	3050（22.24%）	5.198	0.012
Parainfluenza virus	426（15.15%）	1742（12.66%）	12.838	<0.001

3. Positive Detection Rates of Pathogens in Different Months

The positive detection rates of common respiratory pathogens in different months of 2023 and 2022 also varied.

Regarding bacteria, Streptococcus pneumoniae was detected throughout the year in 2023. Haemophilus influenzae had a higher positive detection rate after July 2023, and both Streptococcus pneumoniae and Haemophilus influenzae reached their peaks in November 2022 (Figure 1A, Figure 1B). Bordetella pertussis had a low positive detection rate in 2023, while in 2022, it had two detection peaks in March and September (Figure 1C). The positive detection rate of Mycoplasma pneumoniae reached its peak in November 2023, and it remained at a low level in 2022 (Figure 1D).

For viruses, compared to 2023, in 2022, respiratory syncytial virus, adenovirus, rhinovirus, bocavirus, and metapneumovirus all reached their positive detection rate peaks in November 2022. The positive detection rate of influenza A virus significantly increased from August 2022 and reached its peak in October (Figure 1E-J). In 2023, respiratory syncytial virus had positive detection rate peaks in May and December (Figure 1E). Influenza A virus had positive detection rate peaks in March and November 2023 (Figure 1J). Rhinovirus had positive detection rate peaks in May and November 2023 (Figure 1G).

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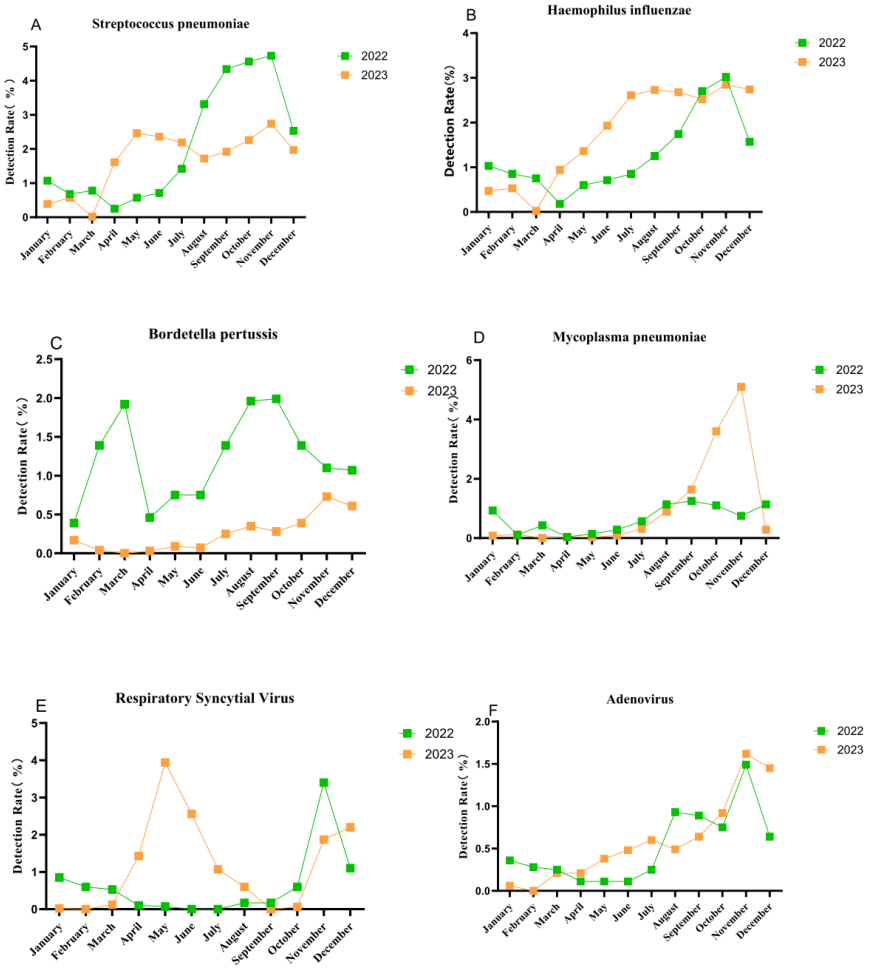

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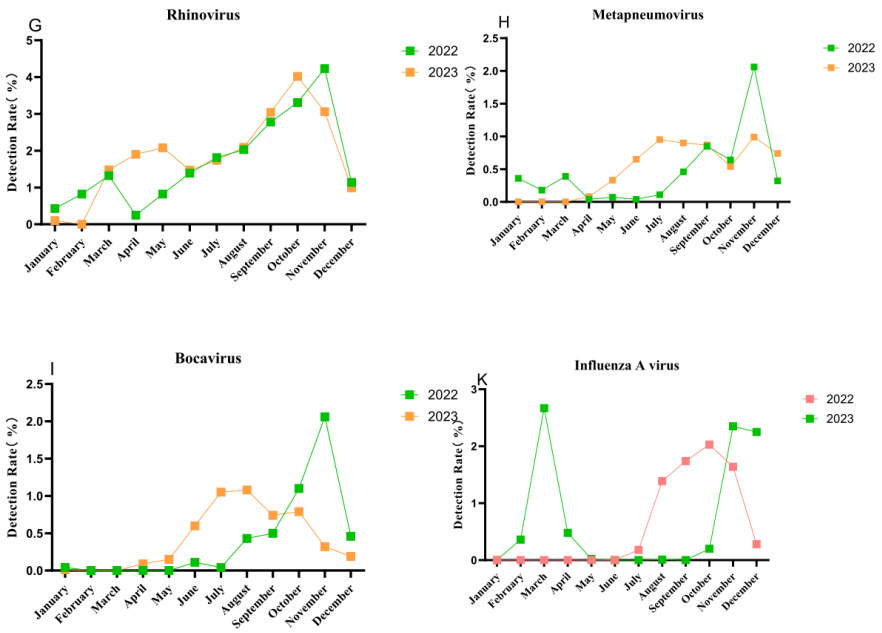

Figure 1:Positive Detection Rates of Pathogens in Different Months

4.Positive Detection Rates of Respiratory Pathogens in Different Age Groups

An analysis was conducted on the top 10 respiratory pathogens with the highest detection rates in 2023 and 2022, revealing differences in pathogen detection rates among children of different ages(Figure 2).

For the acterial pathogens, the positive detection rate of Streptococcus pneumoniae in children aged 3-5 years in 2023 was significantly lower than that in 2022 (P <0.001); the positive detection rate of Haemophilus influenzae in all age groups in 2023 was significantly higher than that in 2022 (all$P$ <0.001); however, the detection rate of Bordetella pertussis in children of all age groups was significantly lower than that in 2022 (all P <0.001).

In 2023, the positive detection rate of Mycoplasma pneumoniae in children under 3 years old and those aged 6-17 years was significantly higher than that in 2022 (both P <0.001).

For viral pathogens, the positive detection rate of respiratory syncytial virus (RSV) in all age groups in 2023 was significantly higher than that in 2022 (all P<0.001). The positive detection rates of human metapneumovirus (hMPV) and bocavirus in children under 3 years old in 2023 were significantly lower than those in 2022 (both$P$ <0.05). The positive detection rate of adenovirus in children aged 6-17 years in 2023 was significantly higher than that in 2022 (P <0.001). The positive detection rates of influenza A virus in children under 3 years old and those aged 6-17 years in 2023 were significantly higher than those in 2022 (both$P$ <0.001), while the positive detection rate of influenza A virus in children aged 3-5 years in 2023 was significantly lower than that in 2022 (P <0.001). The positive detection rate of rhinovirus in children under 3 years old in 2023 was significantly lower than that in 2022 (P <0.05), while the positive detection rate of rhinovirus in children aged 3-5 years in 2023 was significantly higher than that in 2022 (P <0.001).

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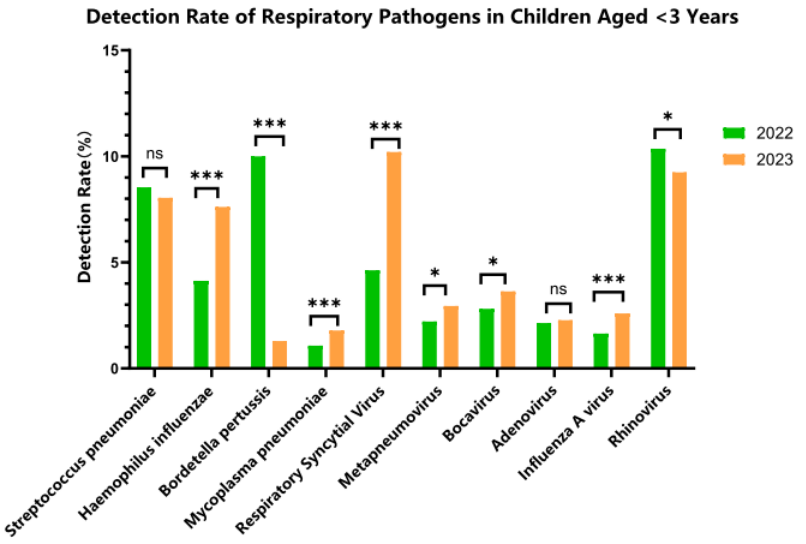

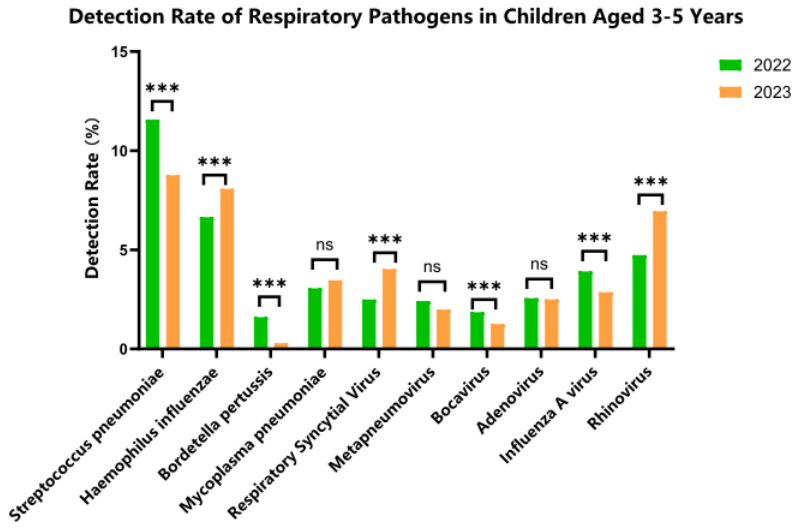

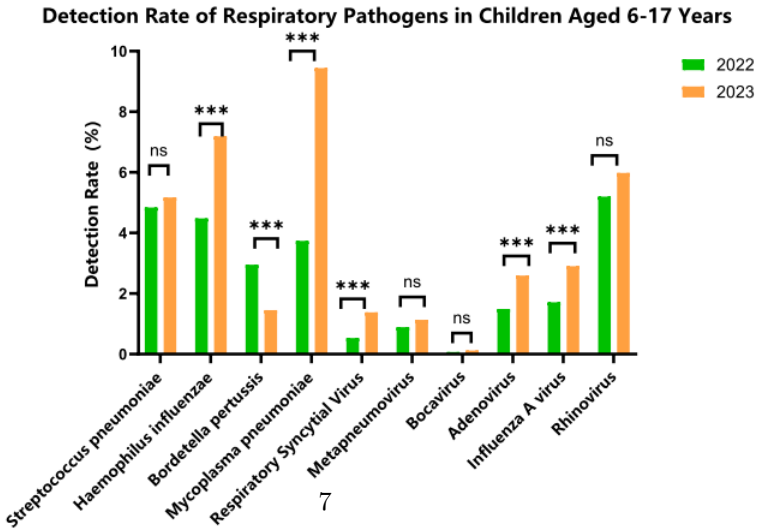

Figure 2:Positive Detection Rates of Respiratory Pathogens in Different Age Groups

Discussion

Through this retrospective study, we analyzed the epidemiological characteristics and the evolution of the pathogen spectrum of respiratory tract infections in children in Shandong, China, during and after the COVID-19 pandemic. We confirmed that the COVID-19 pandemic had a certain impact on the changes in the pathogen spectrum of respiratory tract infections in children, especially for pathogens such as Mycoplasma pneumoniae, Bordetella pertussis, and some viruses, which showed more significant changes.

Since the outbreak of the COVID-19 pandemic in 2019, multiple countries both domestically and internationally have implemented NPIs (Non-Pharmaceutical Interventions) during the COVID-19 pandemic. These measures effectively curbed the spread of COVID-19 in 2020 and 2021, while also affecting the epidemiological patterns of other respiratory pathogens. In 2022, as the domestic epidemic situation eased, people in low-risk areas had largely returned to normal work and life. With the lifting of NPIs, the incidence rates of various respiratory pathogens changed. Regarding viral pathogens, the "viral interference" mechanism between the novel coronavirus and other viruses can influence the epidemiological trends of some viruses. The current understanding of the mechanisms of viral interference includes the direct blocking of one virus from entering receptors by another virus and competition among viruses for host cells, as well as the induction of innate or adaptive immune responses by viruses to prevent infections from related or different viruses[7]. For bacterial pathogens, strict NPIs were implemented during the COVID-19 pandemic, but this also affected the vaccination rates of children. The delay or interruption of routine immunizations led to insufficient immune stimulation in the population, failing to build an effective immune protective barrier, resulting in what is known as an "immune gap" or "immune debt"[8]. In the current domestic multi-child family model, infections of Mycoplasma pneumoniae or Bordetella pertussis in children under 3 years old are mostly caused by cross-infections from older children in the family. During the COVID-19 pandemic, older children studied at home, which also reduced the risk of cross-infections for children under 3 years old. Moreover, the emergence of drug-resistant strains is an important reason for the surge in Mycoplasma pneumoniae and Bordetella pertussis in 2023.

It is well known that respiratory virus infections are the most common respiratory pathogens [9]. Studies have confirmed that in acute respiratory infections of children under 5 years old, the detection rate of viruses is the highest, among which influenza virus, respiratory syncytial virus (RSV), and rhinovirus are the top three viral pathogens with the highest positive detection rates[10]. The results of this study also confirm the important status of these viruses in pediatric respiratory infections, but they have also been affected by the epidemic. As one of the most common viral pathogens in children, RSV is the most important viral pathogen for acute lower respiratory infections in children under 5 years old worldwide[10]. The results of this study show that the positive detection rate of RSV in all age groups in 2023 was significantly higher than that in 2022. However, there are differences in the incidence of RSV infections in different age groups. In 2023, the highest positive detection rate of RSV infection was found in children under 3 years old, followed by those aged 3-5 years, and the lowest in those aged 6-17 years. A recent birth cohort study also confirmed the differences in the incidence of RSV in different age groups, and that children under 3 years old are the most susceptible to RSV infections[11]. Due to the resumption of normal work and life in low-risk areas in the winter of 2022 and the lifting of NPIs in some areas, this may be the reason for the significant increase in the detection rate of RSV at the end of 2022 and in 2023. Domestic scholars' research also believes that the surge in RSV infections is related to this[12]. In this study, it was found that in 2023, the detection rates of rhinovirus and RSV showed a trend of one rising and the other falling. A study on pathogen detection in infants also confirmed a negative correlation between the co-detection of RSV and rhinovirus, that is, immune defense can suppress RSV infections, but may simultaneously increase the risk of rhinovirus infections[13], which also supports the viral interference hypothesis. However, in this study, rhinovirus infections maintained their usual circulation levels. One reason is that medical masks can block the transmission of coronaviruses and influenza viruses, but cannot block rhinoviruses transmitted through droplets and aerosols[14]. In addition, rhinovirus is a non-enveloped virus, so it may be inherently

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more difficult to inactivate with soap and water or alcohol-based hand sanitizers[15,16]. Moreover, the poor handwashing quality of children also makes it difficult to prevent the spread of rhinovirus. After the lifting of NPIs, the global detection rate of influenza viruses has significantly increased, with influenza A virus infections being predominant. WHO influenza surveillance data show that from October 2022 to February 2023, there was a significant peak in global influenza cases. Europe experienced a peak in November 2022, the United States in December 2022, and northern China in February 2023[17]. The detection trend of influenza viruses in this study is consistent with the global influenza trend. At the end of 2022, China fully lifted NPIs, during which there was a surge in COVID-19 infection cases. However, in this study, the detection rate of influenza viruses in December 2022 was at a low level, which may be due to the "viral interference" mechanism between COVID-19 and influenza viruses mentioned earlier. Compared with other countries, the peak of influenza virus infections in China occurred later, which may be related to the strict and long-term implementation of NPIs in our country. The increase in the incidence of influenza viruses in China after the lifting of NPIs was also delayed, which may also be affected by the "viral interference" mechanism between the two[18]. The COVID-19 pandemic has changed people's medical-seeking behaviors and increased their attention to non-pharmaceutical interventions. People have reduced the risk of infection through measures such as maintaining social distance, hand hygiene, and cough etiquette, leading to changes in the pathogen spectrum[19]. Therefore, continuous pathogen monitoring and a series of prevention and treatment measures for positive pathogens can affect the epidemiological characteristics of pathogens. Early intervention and treatment may reduce the incidence and prognosis of pediatric respiratory infections.

Research by domestic scholars on the etiology and epidemiological characteristics of acute respiratory infections indicates that, in terms of bacterial positive detection rates, Streptococcus pneumoniae is the most common bacterium, followed by Haemophilus influenzae and Klebsiella pneumoniae. In terms of age distribution, the top three bacterial pathogens in preschool children are Streptococcus pneumoniae, Haemophilus influenzae, and Staphylococcus aureus. In school-age children, Mycoplasma pneumoniae ranks first, followed by Streptococcus pneumoniae and Haemophilus influenzae[9]. This study found that the most common bacteria in 2022 and 2023 were Streptococcus pneumoniae and Haemophilus influenzae. The World Health Organization's 2008 "Global Action Plan for the Prevention and Control of Pneumonia" listed the immunization coverage rates for Haemophilus influenzae and Streptococcus pneumoniae, as well as immunizations for pertussis and measles, as primary prevention strategies. Given that our country does not routinely use vaccines covering these two bacteria, Haemophilus influenzae and Streptococcus pneumoniae, the infection rates of pneumococcal and Haemophilus influenzae infections in children are relatively high[20]. In this study, the positive detection rates of Haemophilus influenzae in all age groups in 2023 were significantly higher than those in 2022. Moreover, the positive detection rates of Streptococcus pneumoniae and Haemophilus influenzae both peaked at the end of 2022. The possible reasons are that during the NPIs period, the microbial exposure of people in different age groups was reduced, the proportion of susceptible children increased, and the group immunity decreased due to the delay or interruption of immunizations, forming an "immune debt" during the COVID-19 pandemic[21]. In the post-epidemic period, as people's epidemic prevention measures were relaxed and NPIs were gradually lifted, a peak in bacterial detection rates occurred when the COVID-19 pandemic was about to be fully lifted in 2022.

According to data from the World Health Organization, from 2019 to 2021, the coverage rate of the DTP (diphtheria, pertussis, and tetanus) vaccine for children decreased by 5%, with the global DTP vaccine coverage rate dropping to 81%. NPIs (Non-Pharmaceutical Interventions) reduced the spread of Bordetella pertussis among children, leading to a decrease of about 90% in the number of infection cases[22]. In this study, the positive detection rates of Bordetella pertussis in all age groups in 2023 were significantly lower than those in 2022, which may be related to the fact that children under 3 years old did not receive the pertussis vaccine on time during the COVID-19 period, and the antibody levels against pertussis in children over 5 years old gradually decreased. Studies have shown that after the cancellation of NPIs in our country, the number of reported pertussis cases increased from 1,512 in June 2023 to a significant surge at the beginning of 2024, reaching 97,669 cases by May 2024[23]. This study has not yet statistically analyzed the detection rates of Bordetella pertussis in this region for 2024. Factors such as increased awareness among

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healthcare professionals, strengthened surveillance measures, decreased vaccination rates in specific areas, insufficient vaccine efficacy, and the emergence of macrolide-resistant Bordetella pertussis are associated with the resurgence of pertussis[24]. The pertussis vaccination strategy in China mainly targets infants and young children, and the national immunization program does not include vaccination for infants under 3 months and children over 6 years old. Studies have shown that pertussis infections in infants under 3 months are more likely to develop into severe infections with higher mortality rates[25]. Given the high-density contact environment in schools, the risk of transmission of Bordetella pertussis among school-age children is higher. Research in Germany and the United Kingdom has shown that administering a booster dose at the age of 4-6 can reduce the incidence of pertussis in the entire population and prevent household transmission[26,27].

Mycoplasma pneumoniae (MP) is one of the most common pathogens of respiratory infections in children and adolescents, accounting for 40% of community-acquired pneumonia in children over 5 years old[28]. The research results of this study in 2023 showed that the most common pathogen in school-age children was Mycoplasma pneumoniae. From September to December 2023, the detection rate of Mycoplasma pneumoniae remained high. It has been reported that in the autumn and winter of 2023, there was a significant increase in the prevalence of Mycoplasma pneumoniae in northern China, the Netherlands, and the United States[29–31]. The sharp increase in Mycoplasma pneumoniae infections from October to November 2023 attracted close attention from the World Health Organization[32]. The epidemic of Mycoplasma pneumoniae pneumonia is cyclical, with regional outbreaks occurring every 3 to 7 years, and each outbreak can last for 1 to 1.5 years[33] In this study, the positive detection rates of Mycoplasma pneumoniae in children under 3 years old and those aged 6-17 years in 2023 were significantly higher than those in 2022. This may be related to the inherent cyclical pattern of Mycoplasma pneumoniae and the potential "immune debt" [8], as well as the structure of multi-child families. In addition, the emergence of macrolide-resistant Mycoplasma pneumoniae (MRMP) in 2023 was also one of the reasons for this result[34,29].

This article compares the epidemiological characteristics of common pathogens in respiratory infections among children in China during the COVID-19 pandemic and after the full reopening. However, this study also has some limitations. First, this study was conducted in a single center, which may lead to bias in the selection of patients. Second, during the pandemic, many public health interventions were implemented, some of which (such as wearing masks) still existed in some populations later on. Therefore, the sample size should be further expanded, and pathogens should be assessed for at least two years before and after COVID-19 to check which of these measures may be the most effective in preventing the spread of respiratory pathogens.

Conclusions:

The strict public health intervention measures for COVID-19 in our country have effectively curbed the spread of the novel coronavirus. Non-pharmaceutical interventions during the COVID-19 pandemic have had different impacts on the prevalence of various respiratory pathogens. We observed a decrease in the incidence of respiratory syncytial virus, influenza virus, and Mycoplasma pneumoniae in children during the COVID-19 epidemic, with differences in the positive detection rates of respiratory pathogens among different age groups. However, its effect on some bacteria and rhinoviruses and other pathogens is much more limited. With the large-scale administration of COVID-19 vaccines and the relaxation of control measures, the positive detection rates of multiple pathogens have returned to previous levels. Therefore, in order to ensure preparedness and rapid response to public health challenges, it is necessary to conduct more epidemiological surveillance of respiratory pathogens, especially large-scale multicenter studies, to provide a theoretical basis for the effective prevention and control of pediatric respiratory infections.

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Declaration of competing interests

The authors have no conflicts of interest, financial or otherwise, to declare.

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5. Final approval of manuscript: All authors**References:**[1] Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019[J]. New England Journal of Medicine, 2020, 382(8): 727-733.[2] Soy M, Keser G, Atagündüz P. Pathogenesis and treatment of cytokine storm in COVID-19[J]. Turkish Journal of Biology, 2021, 45(4): 372-389.[3] Ye Q, Wang B, Mao J, et al. Epidemiological analysis of COVID-19 and practical experience from China[J]. Journal of Medical Virology, 2020, 92(7): 755-769.[4] Yang R, Xu H, Zhang Z, et al. The Epidemiology of Pathogens in Community-Acquired Pneumonia Among Children in Southwest China Before, During and After COVID-19 Non-pharmaceutical Interventions: A Cross-Sectional Study[J]. Influenza and Other Respiratory Viruses, 2024, 18(8): e13361.[5] Li Q, Guan X, Wu P, et al. Early transmission dynamics in wuhan, china, of novel coronavirus–infected pneumonia[J]. New England Journal of Medicine, 2020, 382(13): 1199-1207.[6] Redlberger-Fritz M, Kundi M, Aberle S W, et al. Significant impact of nationwide SARS-CoV-2 lockdown measures on the circulation of other respiratory virus infections in Austria[J]. Journal of Clinical Virology, 2021, 137: 104795.[7] Agrawal B. Heterologous immunity: role in natural and vaccine-induced resistance to infections[J]. Frontiers in Immunology, 2019, 10: 2631.[8] Cohen R, Pettoello-Mantovani M, Somekh E, et al. European pediatric societies call for an implementation of regular vaccination programs to contrast the immunity debt associated to coronavirus disease-2019 pandemic in children[J]. Journal of Pediatrics, 2022, 242: 260-261.e3.[9] Li Z J, Zhang H Y, Ren L L, et al. Etiological and epidemiological features of acute respiratory infections in China[J]. Nature Communications, 2021, 12(1): 5026.[10] Causes of severe pneumonia requiring hospital admission in children without HIV infection from Africa and Asia: the PERCH multi-country case-control study[J]. Lancet (London, England), 2019, 394(10200): 757-779.[11] Teoh Z, Conrey S, McNeal M, et al. Burden of respiratory viruses in children less than 2 years old in a community-based longitudinal US birth cohort[J]. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America, 2023, 77(6): 901-909.[12] Ye Q, Liu H. Impact of non-pharmaceutical interventions during the COVID-19 pandemic on common childhood respiratory viruses – an epidemiological study based on hospital data[J]. Microbes and Infection, 2022, 24(1): 104911.[13] Achten N B, Wu P, Bont L, et al. Interference between respiratory syncytial virus and human rhinovirus infection in infancy[J]. Journal of Infectious Diseases, 2017, 215(7): 1102-1106.[14] Leung N H, Chu D K, Shiu E Y, et al. Respiratory virus shedding in exhaled breath and efficacy of face masks[J]. Nature Medicine, 2020, 26(5): 676-680.[15] Savolainen-Kopra C, Korpela T, Simonen-Tikka M L, et al. Single treatment with ethanol hand rub is ineffective against human rhinovirus—hand washing with soap and water removes the virus efficiently[J]. Journal of Medical Virology, 2012, 84(3): 543-547.[16] Britton P N, Hu N, Saravanos G, et al. COVID-19 public health measures and respiratory syncytial virus[J]. The Lancet. Child & Adolescent Health, 2020, 4(11): e42-e43.[17] Ziegler T, Moen A, Zhang W, et al. Global influenza surveillance and response system: 70 years of responding to the expected and preparing for the unexpected[J]. Lancet, 2022, 400(10357): 981-982.[18] Oishi K, Horiuchi S, Minkoff J M, et al. The host response to influenza a virus interferes with SARS-CoV-2 replication during coinfection[J]. Journal of Virology, 96(15): e00765-22.[19] De St. Maurice A, Martin-Blais R, Halasa N. Preparing for the 2020—2021 influenza season[J]. Pediatric Transplantation, 2021, 25(5): e14025.[20] Walker C L F, Rudan I, Liu L, et al. Global burden of childhood pneumonia and diarrhoea[J]. Lancet (London, England), 2013, 381(9875): 1405-1416.[21] Han Peng, Zheng Yuejie, Yang Yonghong, et al. The Immunization Debt and Its Impact in Children During the COVID-19 Pandemic [J]. Chinese Journal of Practical Pediatrics, 2022, 38(1).[22] Cohen R, Bechet S, Gelbert N, et al. New approach to the surveillance of pediatric infectious diseases from ambulatory pediatricians in the digital era[J]. Pediatric Infectious Disease Journal, 2021, 40(7): 674-680.[23] Yahong H, Mengyang G, Meng Q, et al. Rising pertussis cases and deaths in China: current trends and clinical solutions[J]. Emerging Microbes &

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