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Impact of non-pharmaceutical interventions during the COVID-19 pandemic on common childhood respiratory viruses – An epidemiological study based on hospital data

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A B S T R A C T
Considering common childhood respiratory viruses and SARS-CoV-2 share similar transmission routes, non-pharmaceutical interventions (NPIs) to prevent SARS-CoV-2 may affect the epidemiology of respiratory viruses. Therefore, our study aimed to observe the epidemiologic characteristics of common childhood respiratory viruses in 2020 (after the pandemic) compared with 2019 (before the pandemic) in Hangzhou, China. The data were compared between 2019 and 2020 based on age and month, respectively. One or more viruses were detected in 3135/21452 (14.61%) specimens in 2019, which was significantly lower in 1110/8202 (13.53%) specimens in 2020. Respiratory syncytial virus (RSV) was the most commonly detected virus in 2019 and 2020. The positive rate of adenovirus (ADV), parainfluenza virus (PIV)1, PIV2, and PIV3 in 2020 was significantly decreased in 2019. In 2020, RSV replaced ADV as the most predominant virus in children aged 1–6 years, and the positive rate of influenza virus A (FluA), influenza virus B (FluB), PIV1, and PIV2 was not correlated to age. FluA, FluB, and PIV2 were not almost detected from February 2020. The positive rates of ADV and PIV1 were uncorrelated to the month in 2020. By strict NPIs, besides controlling the COVID-19 pandemic, incredible progress has been made to reduce the prevalence of common childhood respiratory viruses.

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Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a contagious disease worldwide [1,2]. COVID-19 is mainly transmitted through respiratory droplets and contact, and the population is generally susceptible [3–5]. A series of non-pharmaceutical interventions (NPIs) were taken to block the transmission of SARS-CoV-2 to contain the outbreak of COVID-19, such as wearing masks, washing hands frequently, keeping a social distance, and paying attention to indoor ventilation. In addition, the Chinese government has delayed the start of the spring semester in primary and secondary schools and stopped all offline training courses [6]. Therefore, children in China could only stay at home and study online courses during the pandemic until the school reopened [7]. An important fact must be realized that before the COVID-19 pandemic, there had never been such strict measures and large-scale lockdown.

Lower respiratory tract infections, such as pneumonia and bronchiolitis, remain a global public health problem and one of the leading causes of morbidity and mortality in children younger than five years [8]. In China, approximately 16.5% of deaths in children younger than five years were caused by pneumonia in 2008 [9]. Because common childhood respiratory viruses, such as influenza and respiratory syncytial virus (RSV), and SARS-CoV-2 share similar routes and means of transmission, these NPIs prevent the spread of SARS-CoV-2 are also likely to affect the epidemiology of common childhood respiratory viruses to some extent [10]. Therefore, our study aimed to observe the epidemiologic characteristics of common childhood respiratory viruses in 2020 (after the pandemic) compared with 2019 (before the pandemic) in Hangzhou, China.

1. Methods

1.1. Study design

The present study enrolled all children with respiratory tract infection who came to the Children's Hospital of Zhejiang University School of Medicine for treatment during 2019 and 2020. The patients' demographics, clinical features, and laboratory results were recorded. The diagnosis of respiratory tract infection was based on the symptoms and signs of respiratory tract infection, such as cough, fever, and respiratory distress. The positive rate of respiratory viruses was calculated as the number of children with a positive result divided by the number of children tested.

The present study was approved by the Ethics Committee of the Children's Hospital of Zhejiang University School of Medicine. The participants and their guardians were fully informed about the study and provided written informed consent.

The present study was conducted in accordance with the Declaration of Helsinki and the Good Clinical Practice guidelines.

The results were analyzed using the SPSS software (version 22.0). The chi-square test was used to compare the positive rates of respiratory viruses between 2019 and 2020. The level of significance was set at p<0.05.

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University between January 2019 and December 2020 to explore the variations in the prevalence of common childhood respiratory viruses of children in Hangzhou, China, during the COVID-19 pandemic. Based on the criteria of the U.S. Centers for Disease Control and Prevention, the enrolled children met the following criteria: (1) children aged younger than 18 years; (2) confirmed fever (a body temperature above 37.5 °C); (3) one or more respiratory symptoms within 14 days of onset (cough, sore throat, sputum, shortness of breath, lung auscultation abnormality (rale or wheeze), tachypnea, and chest pain) [11]. The exclusion criteria for this study were (1) children with repeated visits within a week; (2) children with hospital infection; (3) children with congenital pulmonary airway malformation and an impaired immune system; (4) children infected with COVID-19. All the enrolled children were divided into five age groups: under 28 days of age (0–28 d), 1–12 months of age (>1–12 mo), 1–3 years of age (>1–3 y), 3–6 years of age (>3–6 y) and more than six years of age (>6 y). From January 2020, the important events about the COVID-19 pandemic in Hangzhou, China, are in Fig. 1.

1.2. Data and specimen collection

Demographic characteristics from enrolled children were obtained from their electronic medical records. Respiratory specimens (nasopharyngeal aspirates/bronchoalveolar lavage fluid) were obtained from all the enrolled children as soon as they were

Fig. 1. The important events about the COVID-19 pandemic in Hangzhou, China.
admitted by trained staff following standard operating procedures. The specimens were immediately transferred to the clinical laboratory for respiratory virus detection.

1.3. Specimen detection

A multiplex direct immunofluorescence assay kit (Diagnostic Hybrids, Athens Ohio, USA) was used to detect respiratory viruses, including adenovirus (ADV), influenza virus A (FluA), influenza virus B (FluB), parainfluenza virus (PIV) 1–3, and RSV. The specimens were diluted in PBS and centrifuged for 10 min at 1500 rpm at room temperature. The supernatant was discarded. The pellet containing cells and cells debris was resuspended in 1 mL PBS. Twenty-five microliters of the resuspension were pipetted into a single 6 mm diameter well and dried for 30 min at 37 °C. The dried samples were fixed in acetone and incubated with the test monoclonal antibodies for 30 min at 37 °C. Finally, one drop of mounting fluid reagent was added to the middle of each well. A coverslip was placed over the slide, and reading was performed using a fluorescence microscope.

1.4. Statistical analysis

Categorical variables were presented as count with percentage. Proportions for categorical variables were compared using the chi-square test or Fisher’s exact test. A value of P < 0.05 was considered statistically significant. Statistical analyses were conducted in SPSS version 26.0 software (IBM, New York, USA).

2. Results

2.1. Patient characteristic

Twenty-nine thousand six hundred fifty-four specimens from consecutive children were detected between Jan 2019 and December 2020, including 21452 specimens in 2019 and 8202 specimens in 2020. The age of enrolled children ranged from 0 day to 17 years old. Most patients were 1–12 months old (32.68% in 2019, 34.44% in 2020). No significant differences in gender were observed between the years 2019 and 2020 (Table 1).

2.2. Overall detection of respiratory viruses

One or more viruses were detected in 3135/21452 (14.61%) specimens in 2019, which was significantly lower in 1110/8202 (13.53%) specimens in 2020 (Table 1). As shown in Fig. 2, RSV was the most commonly detected virus in 2019 and 2020, accounting for 43.19% of positive specimens in 2019 and 64.29% of positive specimens in 2020. Meanwhile, the positive rate of RSV in 2020 was significantly higher than that in 2019 (9.35% vs. 6.31%, P < 0.05). However, the positive rate of ADV, PIV1, PIV2, and PIV3 in 2020 were significantly decreased compared with 2019 (P < 0.05). No significant differences were found in the positive rate of FluA and FluB between 2019 and 2020 (P > 0.05) (Table 1).

In the present study, a total of 49 specimens detected two viruses, among which there were 35 specimens in 2019 and 14 specimens in 2020 (0.16% vs. 0.17%, P > 0.05) (Fig. 2). In 2019, ADV and PIV3 were the most frequently detected viruses in 20/35 (57.14%) mixed infection specimens, and the detection of ADV plus PIV3 was the most common type of mixed infection, making up 25.71% of mixed infection specimens. However, in 2020, RSV was the most frequently detected virus in 13/14 (92.86%) mixed infection specimens, and the detection of RSV plus PIV3 was the most common type of mixed infection, making up 64.29% of mixed infection specimens. No specimens detected more than two viruses both in 2019 and 2020.

2.3. Age distribution

All the patients were divided into five age groups. The detection of each virus-positive specimen based on 2019 and 2010 was described in Fig. 3 and Fig. 4. In 2019 and 2020, the total positive rate reached the peak in children aged 1–12 months, with the peaks of 27.29% and 27.43%, respectively, and after that declined with the rising age of the enrolled children (Fig. 4a). Compared to 2019, the total positive rate in children aged 1–12 months in 2020 was almost identical (27.29% vs. 27.43%, P > 0.05), whereas the total positive rate in other age groups was dramatically decreased in 2020 (P < 0.05) (Table 2). In 2020, the positive rate of ADV, PIV3, RSV followed a similar pattern as their counterparts in 2019, but the positive rate of RSV was higher than that in 2019 (Fig. 4b, g. 4h). However, the positive rate of FluA and PIV1 in 2020 was not correlated to the age of the enrolled children (P > 0.05) (Table 3).

The predominant viruses among different age groups vary. In 2019, although all seven viruses were detected in each age group, the most dominant viruses in each age group were RSV, PIV3, and ADV, contributing to 82.66–93.13% of all infections in each age group. In children aged <1-year, RSV was predominant; in children aged >1 year, ADV was predominant (Fig. 5a). In 2020, not all seven viruses were detected in each age group; RSV accounted for the highest proportion of all infections in children aged <6 years, with a range from 47.79% to 87.29%, followed by PIV3 (8.47–36.03%); PIV3 was the most dominant virus in children aged >6 years, accounting for 42.86%, followed by RSV (35.71%) (Fig. 5b).
2.4. Season distribution

The detection of each virus-positive specimen based on the month in 2019 and 2020 was shown in Fig. 6 and Fig. 7. Overall, common childhood respiratory viruses in 2019 and 2020 were detected more often in January and December than in other months, with total positive rates of 25.04% and 26.28% in 2019, 31.33%, and 28.01% in 2020, respectively (Fig. 7a). Compared with 2019, the total positive rates in October and December in 2020 were not a significant difference (7.07% vs. 6.75% in October, 26.28% vs. 28.01% in December, P > 0.05); the total positive rates in January and November in 2020 increased significantly (25.04% vs. 31.33% in January, 8.44% vs. 19.70% in November, P < 0.05); the total positive rates in other months in 2020 decreased significantly (P < 0.05) (Table 4). More specifically, in 2019, ADV, PIV1, PIV3, and RSV were detected throughout the whole year of 2019 (Fig. 7b–h). The positive rate of each virus was found to be associated with the month (P < 0.05) (Table 5). However, in 2020, FluA, FluB, and PIV2 were not almost detected from the beginning of February (Fig. 7c, d, f). The positive rates of ADV and PIV1 were found to be uncorrelated to month (P > 0.05) (Table 5).

3. Discussion

In response to the COVID-19 pandemic, Zhejiang province initiated the 1-level emergency response on Jan 23, 2020. A range of NPIs was implemented to suppress or mitigate the spread of the virus. The present study demonstrated that apart from the control of the COVID-19 pandemic, incredible progress has also been made to reduce the prevalence of common childhood respiratory viruses. In the present study, the number of children with respiratory symptoms in our hospital in 2020 decreased by 61.77%, and the overall number of virus-positive specimens decreased by 64.59% compared to 2019. More specifically, a substantial decline in the
Fig. 3. The number of each virus-positive specimens based on age in 2019 and 2020.
Fig. 4. The percentage of each virus-positive specimens based on age in 2019 and 2020.
The prevalence of ADV and PIV 1–3 was found in 2020, and even children with FluA and FluB infection disappeared in our hospital from the beginning of February 2020, compared to the previous year. Similar results have been described by reports from Italy [12], Finland [13], Brazil [14], New Zealand [15], France [16], Turkey [17], England [18], and the US [19]. Given this situation, a hypothesis has been proposed that the effectiveness of these NPIs in reducing viral transmission may depend on the characteristics of each virus, such as viral structure. NPIs, especially hand hygiene, have a strong negative effect on enveloped viruses, reducing transmission of the enveloped virus, such as FluA, FluB, and PIV1-3 [20]. However, in the present study, unexpectedly, despite being an enveloped virus, the prevalence of RSV also exited a substantial augmentation in 2020. So, the potential mechanisms by which NPIs disrupt respiratory virus transmission should be further investigated.

In the present study, children aged 1–12 months were the most vulnerable to respiratory viruses, mainly RSV and PIV3, both before and after the pandemic, and their prevalence of respiratory infection after the pandemic was almost consistent with that before the pandemic. On the other hand, in other age groups, the prevalence of respiratory infection significantly decreased after the pandemic. During virus infections, the host activates the immune system to fight the pathogenic microorganism [21]. In children aged 1–12 months, due to the lack of complete immune memory and reduced innate and adaptive immunity, the immaturity of the immune system may be responsible for their vulnerability to respiratory viruses, and NPIs have little impact [22]. However, for neonates who obtained massive passive antibodies from mothers and older children whose immune systems are more thoroughly developed, the implementation of NPIs may play a vital role in protecting them.

### Table 2

| Age          | 2019   | 2020   | \( \chi^2 \) value | \( p \) value |
|--------------|--------|--------|---------------------|---------------|
| 0–28 d       | 393/2335 (16.83) | 118/943 (12.51) | 9.516             | 0.002         |
| >1–12 mo     | 1913/7010 (27.29) | 775/2825 (27.43) | 0.021             | 0.885         |
| >1–3 y       | 480/5053 (9.50) | 136/1985 (6.85) | 12.512            | <0.001        |
| >3–6 y       | 286/4283 (6.08) | 81/1603 (5.05) | 5.265             | 0.022         |
| >6 y         | 58/2771 (3.54) | 14/846 (1.65) | 7.649             | 0.006         |

Data was expressed as the positive number/the total number (%).

### Table 3

Detection of each virus based on age in the year of 2020 (COVID-19 pandemic) compared with the year of 2019 (before COVID-19 pandemic).

| Virus | Year 0-28 d | >1-12 mo | >1-3 y | >3-6 y | >6 y | \( \chi^2 \) value | \( p \) value |
|-------|-------------|----------|--------|--------|------|---------------------|---------------|
| ADV   | 2019 13     | 154      | 184    | 159    | 41   | 100.395             | <0.001        |
|       | 2020 0      | 5        | 10     | 6      | 0    | 10.932              | 0.027         |
| FluA  | 2019 5      | 61       | 19     | 12     | 4    | 37.736              | <0.001        |
|       | 2020 0      | 5        | 14     | 5      | 9    | 8.842               | 0.065         |
| FluB  | 2019 2      | 13       | 12     | 12     | 8    | 3.688               | 0.450         |
|       | 2020 0      | 11       | 3      | 2      | 2    | 7.643               | 0.106         |
| PIV1  | 2019 11     | 64       | 18     | 14     | 3    | 36.305              | <0.001        |
|       | 2020 5      | 11       | 3      | 4      | 1    | 5.077               | 0.279         |
| PIV2  | 2019 9      | 13       | 10     | 6      | 2    | 7.443               | 0.114         |
|       | 2020 0      | 2        | 1      | 0      | 0    | 2.249               | 0.690         |
| PIV3  | 2019 86     | 655      | 141    | 40     | 26   | 639.877             | <0.001        |
|       | 2020 10     | 167      | 49     | 18     | 6    | 129.010             | <0.001        |
| RSV   | 2019 267    | 953      | 96     | 43     | 14   | 1244.253            | <0.001        |
|       | 2020 103    | 565      | 65     | 42     | 5    | 619.740             | <0.001        |
| Total | 2019 393    | 1913     | 480    | 286    | 98   | 1492.186            | <0.001        |
|       | 2020 118    | 775      | 136    | 81     | 14   | 735.551             | <0.001        |

Data was expressed as the positive number/the total number (%).

**Fig. 5.** Respiratory viruses were reported in different age groups in 2019 (a) and 2020 (b).
Fig. 6. The number of each virus-positive specimen based on months in 2019 and 2020. The two gray blocks represented the reopening of primary and secondary schools in Hangzhou from April to June in 2020 and the fall semester from September to December in 2020.
Fig. 7. The percentage of each virus-positive specimen based on the month in 2019 and 2020. The two gray blocks represented the reopening of primary and secondary schools in Hangzhou from April to June in 2020 and the fall semester from September to December in 2020.
against respiratory viral infections. In addition, we also reported that during the pandemic, RSV was the most predominant respiratory virus in children. RSV is among childhood’s most critical pathogenic infections and makes up 13–22% of mortality from acute lower respiratory infections in young children [23]. Generally, most children will experience at least one RSV infection by two years [24]. Given the decrease in the number of children with respiratory symptoms in our hospital during the pandemic, although the positive number of RSV was lower than that before the pandemic, the prevalence of RSV still showed a significant increase, which was also exacerbated by a marked decrease in the detection of other respiratory viruses.

Since the strictest NPIs were implemented in Hangzhou on Jan 23, 2020, the morbidities of respiratory infection have remained extremely low level even during the first resumption of school. This is largely attributed to the most comprehensive and rigorous prevention and control measures with a high sense of responsibility for students’ health during the first resumption of school. However, when the fall semester began in September 2020, there was a sharp increase in the detection of respiratory viruses, especially PIV3 and RSV. The prevalence of respiratory viruses even exceeded or was comparable to the same period in 2019. In fact, under the fall semester began in September 2020, there was a sharp increase in the detection of respiratory viruses, especially PIV3 and RSV.

Table 5 Detection of each virus based on month in the year of 2020 (COVID-19 pandemic) compared with the year of 2019 (before COVID-19 pandemic).

Table 4 The overall positive rate of virus based on month in the year of 2020 (COVID-19 pandemic) compared with the year of 2019 (before COVID-19 pandemic).

| Month      | 2019       | 2020       | χ² value | p value |
|------------|------------|------------|----------|---------|
| January    | 604/2412   | 463/1478   | 18.184   | <.001   |
| February   | 291/1980   | 5/384      | 52.684   | <.001   |
| March      | 269/1970   | 3/380      | 48.527   | <.001   |
| April      | 266/1994   | 4/349      | 43.316   | <.001   |
| May        | 313/2026   | 4/467      | 72.816   | <.001   |
| June       | 210/1526   | 2/537      | 77.230   | <.001   |
| July       | 199/1685   | 1/527      | 61.129   | <.001   |
| August     | 191/1587   | 7/523      | 52.932   | <.001   |
| September  | 137/1520   | 16/588     | 24.937   | <.001   |
| October    | 107/1513   | 4/467      | 72.816   | <.001   |
| November   | 127/1504   | 18/944     | 65.934   | <.001   |
| December   | 456/1735   | 386/1378   | 1.164    | 0.281   |

Data was expressed as the positive number/total number (%).
4. Conclusions

By the strict NPIs, apart from the control of the COVID-19 pandemic, incredible progress has also been made to reduce the prevalence of common childhood respiratory viruses.

Declaration of competing interest

The authors declare that they have no conflicts of interest.

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