RESEARCH



Epidemiological change of influenza virus in hospitalized children with acute respiratory tract infection during 2014–2022 in Hubei Province, China

Song Yi^{1†}, Wan-Xue Zhang^{2†}, Yi-Guo Zhou³, Xin-Rui Wang⁴, Juan Du⁵, Xing-Wen Hu^{6*} and Qing-Bin Lu^{2,3,4,5,7*}

Abstract

Purpose Influenza virus (IFV) causes acute respiratory tract infection (ARTI) and leads to high morbidity and mortality annually. This study explored the epidemiological change of IFV after the implementation of the universal two-child policy and evaluated the impact of coronavirus disease 2019 (COVID-19) pandemic on the detection of IFV.

Methods Hospitalized children under 18 years with ARTI were recruited from Hubei Maternal and Child Healthcare Hospital of Hubei Province from January 2014 to June 2022. The positive rates of IFV were compared among different periods by the implementation of the universal two-child policy and public health measures against COVID-19 pandemic.

Results Among 75,128 hospitalized children with ARTI, the positive rate of IFV was 1.98% (1486/75128, 95% CI 1.88–2.01). Children aged 6–17 years had the highest positive rate of IFV (166/5504, 3.02%, 95% CI 2.58–3.50). The positive rate of IFV dropped to the lowest in 2015, then increased constantly and peaked in 2019. After the universal two-child policy implementation, the positive rate of IFV among all the hospitalized children increased from 0.40% during 2014–2015 to 2.70% during 2017–2019 (RR 6.72, 95% CI 4.94–9.13, P<0.001), particularly children under one year shown a violent increasing trend from 0.20 to 2.01% (RR 10.26, 95% CI 5.47–19.23, P<0.001). During the initial outbreak of COVID-19, the positive rate of IFV decreased sharply compared to that before COVID-19 (0.35% vs. 3.37%, RR 0.10, 95% CI 0.04–0.28, P<0.001), and then rebounded to 0.91%, lower than the level before COVID-19 (RR 0.26, 95% CI 0.20–0.36, P<0.001).

Conclusion IFV epidemiological pattern has changed after the implementation of the universal two-child policy. More attention should be emphasized to comprehend the health benefits generated by COVID-19 restrictions on IFV transmission in future.

Keywords Influenza virus, Epidemiology, The universal two-child policy, COVID-19, Hospitalized children

[†]Song Yi and Wan-Xue Zhang contributed equally to this work.

*Correspondence: Xing-Wen Hu xingwenhu0107@126.com Qing-Bin Lu qingbinlu@bjmu.edu.cn Full list of author information is available at the end of the article



© The Author(s) 2023. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

Introduction

Influenza is an acute respiratory disease caused by influenza virus (IFV) infections that have led to heavy health burden [1, 2]. Circulating among the population by the infection of respiratory tract, IFV usually activates during colder periods, particularly in spring and winter in China [3, 4]. Patients with influenza mostly show self-limited upper respiratory tract infections (URTI) and some develop into lower respiratory tract infection (LRTI) with pneumonia or bronchitis [5]. Despite marvelous efforts have been made to eliminate the transmission of IFV, it is still epidemic worldwide and contributes to a billion cases and about half a million deaths annually [6]. The prevention of IFV is still one of the important global public health issues.

China had implemented the one-child policy since 1979 to alleviate population growth [7]. For the past few decades, a series of social issues such as population ageing, labor shortages were arisen, suggesting an adjustment of population policy [8]. Subsequently, starting on 1 January, 2016, the universal two-child policy was implemented by the government of China, allowing all Chinese married couples to have two children. In the era of the universal two-child policy, the number of live births increased, with a boosting newborn population in Wuhan city increasing from 100,784 in 2014 to 131,409 in 2017. This brought new challenges to the control of various infectious diseases. Changes in age structure caused by an increased number of newborns may affect the epidemiological characteristics of infectious diseases. Besides, young children infected with pathogens such as IFV can have serious symptoms resulting in hospital admissions or even death [9]. However, since the universal two-child policy was implemented, the changes of epidemiological features of IFV remain uninvestigated.

The coronavirus disease 2019 (COVID-19) is a new infectious disease that has rapidly spread worldwide through close human interactions or the contaminated secretions of the infected people, which has a similar transmission route to IFV [10]. Besides massive vaccination, nonpharmaceutical interventions (NPIs), including mask-wearing, physical distancing, hygiene promotion, and targeted restrictions on gathering and movement have been implemented and demonstrated effectiveness in limiting the spread of COVID-19 [11]. Studies have explored the impact of COVID-19 pandemic and related NPIs on the epidemiological pattern of respiratory infections [12, 13]. Early studies reported that during the first wave of the pandemic, a nearly immediate reduction of influenza was observed, but the impact of COVID-19 restrictions during the regular epidemic prevention and control period on IFV transmission still needs to be systematically studied [14].

This study aimed to illustrate the overall detection of IFV in Hubei Province and compare its epidemiological patterns before and after the universal two-child policy and COVID-19 pandemic. The findings might assist in the understanding of how the universal two-child policy affects the epidemiological patterns of infectious disease and may help policy makers comprehend the health benefits generated by NPIs.

Materials and methods

Study setting and participants

In this observational study, hospitalized children with ARTI were recruited in Hubei Maternal and Child Health Hospital, Hubei Province, China between 1 January 2014 and 30 June 2022. Hubei Maternal and Child Health Hospital undertakes the medical and health care for women and children at provincial level, dominating in the development of diagnosis and treatment management of children's respiratory diseases in Hubei Province. There are more than 3000 beds in total and nearly three million outpatients and 100,000 inpatients every year. The research was reviewed and approved by the human ethics committee of Hubei Maternal and Child Health Hospital (2022IEC052).

Hospitalized children under eighteen years with ARTI were recruited by using the case definition as follows: (1) aged under 18 years; (2) at least one of the following conditions: fever, abnormal white blood cell (WBC) differentials, leukocytosis or leukopenia; (3) at least one of the following symptoms/signs: cough, chills, sore throat, expectoration, nasal congestion, chest pain, tachypnea, and abnormal pulmonary breath sounds [15]. Pneumonia was diagnosed according to the guidelines carried by Chinese Thoracic Society [16]. The ARTI was categorized into URTI and LRTI. Hospitalized children with bronchitis and pneumonia were classified into LRTI.

Testing and IFV detection

Within the first 24 h of admission to hospital, fresh nasopharyngeal swabs were collected from all participants. The nasopharyngeal swabs were placed in 3 mL normal saline, and transported to the laboratory and stored at -80 °C.

The D³ Ultra DFA Respiratory Virus Screening & ID kit produced by DIAGNOSTIC HYBRIDS (1055 East State St., Suite 100, Athens, Ohio, USA) were used to detect IFV-A and IFV-B in the nasopharyngeal swab. After mixing on the vortex oscillator, the swab was removed. Through centrifugation at 708 g/min for 10 min, part of the supernatant was discarded, and about 100–150 μ L of supernatant was left to mixed to form a turbidized cell suspension. The suspension was mixed with a straw to form a cell suspension. About 15 μ L of the suspension was taken on the spot sample slide, and was first airdried, then immersed in cold acetone solution and fixed for 10 min. Approximately 25 μ L of the corresponding fluorescent antibody was added to each spot sample. Then the slides were placed in a wet box and incubated at 37 °C for 30 min. After removing the slides, the blocking solution was dropped and the slides were covered. A specimen was defined as positive if two or more positive cells were found in a 200-fold magnification field of view when viewed under an OLYMPUS BX53 fluorescence microscope.

Data resource

Demographic data including gender and age, clinical data including diagnosis and IFV detection results were collected from all hospitalized children. Children were categorized into age groups of <1 year, 1-2 years, 3-5 years and 6-17 years.

In order to analyze the effect of the universal twochild policy, the time intervals were categorized into 2014–2015 (before the universal two-child policy implementation) and 2017–2019 (one year after the universal two-child policy implementation). For the COVID-19 and related NPIs, we split the time into Stage I (the combined period during February–June of 2017–2019), Stage II (the combined period during February–June of 2020) and Stage III (the combined period during February– June of 2021 and 2022).

In this study, we defined the seasons of spring (from March to May), summer (from June to August), autumn (from September to November) and winter (from December to February next year).

Statistical analysis

Categorical variables were summarized as frequencies and proportions. The positive rate of IFV as well as the 95% confidence interval (95% CI) were estimated by Wilson method. To evaluate the association between demographic variables (gender and age groups) and diagnosis and the positive rate of IFV, a logistic regression model was performed to calculate the adjusted odds ratio (OR) and its 95% CI.

Temporal trends of influenza and weekly positive rates of IFV were illustrated using time series plot and heatmap based on the age groups and gender in the overall, URTI and LRTI children.

To demonstrate the impact of the universal two-child policy and the COVID-19 and related NPIs on the activity of IFV, the positive rate of IFV during different periods were calculated and compared by using rate ratio (RR) as well as its 95% CI. All statistical tests were two-sided, and a level of P < 0.05 was used to declare statistical significance.

Data description, graphing and analysis were conducted using R 4.2.1 (R Foundation, Vienna, Austria) and GraphPad Prism 9.3.0 (La Jolla, CA, USA).

Results

Characteristics of the hospitalized children and IFV detection

During 1 January 2014 to 30 June 2022, 75,128 hospitalized children under 18 years with ARTI in Hubei Maternal and Child Health Hospital were included in this study, with 44,961 (59.85%) male and 30,167 (40.15%) female (Table 1). There were 26,498 (35.27%) children under one year, 23,919 (31.84%) aged 1–2 years, 19,207 (25.57%) aged 3–5 years and 5504 (7.33%) aged 6–17 years. The diagnosis of those hospitalized children were grouped into URTI (23,922, 29.26%) and LRTI (60,049, 70.74%). Among all the children, 1486 (1.98%, 95% CI 1.88–2.01) was positive for IFV, including 954 (64.20%) for single IFV-A, 521 (35.06%) for single IFV-B and 11 (0.74%) with co-infection.

The positive rates of IFV in different gender were similar (1.96% in male and 2.00% in female). Among different age groups, children under one year were the most but their positive rate of IFV was the lowest (1.36%, 95% CI 1.22–1.50), while children aged 6 to 17 years had the highest positive rate of IFV (3.02%, 95% CI 2.58–3.50). There were more hospitalized children with LRTI and higher positive rate of IFV than the children with URTI (70.74% vs. 29.26%, OR 1.13, 95% CI 1.01–1.27).

Temporal distribution

There were some shifts in the timing of the peak of IFV infection (Fig. 1a). For all the children and the children with URTI or LRTI, the peak of IFV infections mostly occurred during winter, and some small peaks were also observed in autumn and spring. The positive rate of IFV remained at low levels from 2014 to 2016, except for a high peak in the beginning of 2016. Since the autumn and winter in 2017, there has been a large increase in the infection of IFV. The peak of IFV infection was observed in 2019, and then a sharp decrease of IFV detections occurred. There were no IFV infections from March to August in 2020, followed by a slight increase during winter, and the IFV activity remained minimal in 2021 and 2022. Similar trends of the positive rate of IFV were observed in children with URTI and LRTI (Fig. 1b and c). For different types of IFV, a shift of the dominant type happened in 2020, with IFV-B took the predominant prevalence instead of IFV-A after 2020 (Fig. 1d). However, the epidemiological pattern of the two types of viruses shared a similar trend.

Table 1 The positive rate of IFV in the hospitalized children during January 2014 to June 2022

Group	No. of children (%)	Positive (%)			Positive rate (95% CI), %	OR (95% CI)	Р
		Total	IFV-A	IFV-B			
Overall	75,128	1486 (100)	954 (64.20)	521 (35.06)	1.98 (1.88–2.01)		
Gender							
Male	44,961 (59.85)	882 (59.35)	580 (60.80)	295 (56.62)	1.96 (1.84–2.10)	1.01 (0.91–1.12)	0.830 ^a
Female	30,167 (40.15)	604 (40.65)	374 (39.20)	226 (43.38)	2.00 (1.85–2.17)	Reference	
Age, year							
< 1	26,498 (35.27)	358 (24.09)	271 (28.41)	83 (15.93)	1.36 (1.22–1.50)	Reference	
1-2	23,919 (31.84)	536 (36.07)	361 (37.84)	174 (33.40)	2.24 (2.06–2.44)	1.70 (1.48–1.95)	< 0.001 ^b
3–5	19,207 (25.57)	426 (28.67)	251 (26.31)	172 (33.01)	2.22 (2.01-2.44)	1.68 (1.46–1.94)	< 0.001 ^b
6–17	5504 (7.33)	166 (11.17)	71 (7.44)	92 (17.66)	3.02 (2.58–3.50)	2.32 (1.92–2.80)	< 0.001 ^b
Diagnosis							
URTI	21,983 (29.26)	420 (28.26)	248 (26.00)	170 (32.63)	1.91 (1.73–2.10)	Reference	
LRTI	53,145 (70.74)	1066 (71.74)	706 (74.00)	351 (67.37)	2.01 (1.89–2.13)	1.13 (1.01–1.27)	0.032 ^c

IFV Influenza virus, URTI, Upper respiratory tract infection, LRTI, Lower respiratory tract infection, CI, Confidence interval, OR, Odds ratio, P P value

^a Adjusted for gender and diagnosis

^b Adjusted for age and diagnosis

^c Adjusted for age and gender. There were 11 children mixed infection with IFV-A and IFV-B



Fig. 1 The positive rate of IFV by month in the hospitalized children during January 2014 to June 2022. **a** The positive rate of IFV among the overall children; **b** The positive rate of IFV among children with URTI; **c** The positive rate of IFV among children with URTI; **c** The positive rate of IFV among the overall children in different age groups; **f** The positive rate of IFV among the overall children of different gender

Weekly positive rate of IFV revealed that there were some differences in the prevalence and the timing of the influenza peak from year to year (Fig. 2). In

general, influenza mostly activated in the few weeks at the beginning and end of the years. Longer time periods of IFV detection were observed in 2018 and 2019, with



Fig. 2 The heatmap of weekly positive rate of IFV among different diagnosis, type, gender and age groups during January 2014 to June 2022. **a** Weekly positive rate of IFV among the overall children; **b** Weekly positive rate of IFV-A among the overall children; **c** Weekly positive rate of IFV-B among the overall children; **d** Weekly positive rate of IFV among the overall children under one year; **e** Weekly positive rate of IFV among the overall children aged 1–2 years; **f** Weekly positive rate of IFV among the overall children aged 3–5 years; **g** Weekly positive rate of IFV among the overall children; **i** Weekly positive rate of IFV among the overall children; **i** Weekly positive rate of IFV among the overall children; **j** Weekly positive rate of IFV among the overall female children; **j** Weekly positive rate of IFV among children with URTI; **k** Weekly positive rate of IFV among children with LRTI

a constant positivity of IFV until week 13 and week 22, respectively.

Similar temporal epidemiological patterns were found among different age groups and gender (Fig. 1e and c, Additional files 1: Fig. S1 and 2: Fig. S2). The positive rate of IFV shown no difference between male and female. The distribution of the prevalence of influenza was similar in different age groups. The positive rate was highest in the group of 6-17 years, followed by the groups of 1-2 years, 3-5 years and < 1 year.

Impact of the universal two-child policy on IFV detection

The positive rate of IFV in overall children was 0.40% during 2014 to 2015, while there was a huge increase to 2.70% during 2017–2019 after the policy implementation (RR 6.72, 95% CI 4.94–9.13, P<0.001) (Table 2). The same trend was observed in children with URTI (from 0.41% to 2.67%, RR 6.54, 95% CI 3.59–11.91, P<0.001) and LRTI (from 0.40% to 2.71%, RR 6.78, 95% CI 4.74–9.69, P<0.001).

Compared to the period before the policy implemented, the effect values of RR were higher in children under one year in the overall and LRTI group, from 0.20% to 2.01% (RR 10.26, 95% CI 5.47–19.24, P<0.001), 0.12% to 1.99% (RR 16.33, 95% CI 6.74–39.56, P<0.001), respectively. For the children with URTI, children aged 1–2 years shown the biggest change of IFV positive rate (RR 12.74, 95% CI 3.15–51.49, P<0.001).

Impact of the COVID-19 pandemic and NPIs on IFV detection

Hospitalized children were divided into three stages according to the outbreak of COVID-19. For all the children, the positive rate of IFV during Stage I (3.37%, 95% CI 3.11-3.65) was significantly higher compared to that during Stage II (0.35%, 95% CI 0.14-0.90, RR 0.10, 95% CI 0.04–0.28, P<0.001) and Stage III (0.91%, 95% CI 0.69–1.19, RR 0.26, 95% CI 0.20–0.36, P<0.001) (Fig. 3a and Additional file 3: Table S1). Among all the children, different gender and age groups were further analyzed. Except for children aged 3-5 years, children with URTI under one year, female children and children aged 1-2 years, 3-5 years and 6-17 years with LRTI, the positive rate of IFV in stage II was significantly lower than that in stage I (P < 0.05), respectively. During the regular epidemic prevention and control period in 2021 and 2022 after the outbreak of COVID-19, we observed a slight increase in the frequency of IFV

Table 2 The positive rate of IFV in Hubei Province stratified by the universal two-child policy implementation

Group	2014-2015			2017–2019		RR (95% CI)	P	
	No. of children	Positive	Positive rate (95% CI), %	No. of children	Positive	Positive rate (95% CI), %		
Overall	10,446	42	0.40 (0.30–0.54)	43,916	1186	2.70 (2.55–2.86)	6.72 (4.94–9.13)	< 0.001
Gender								
Male	6438	27	0.42 (0.29–0.61)	26,183	712	2.72 (2.53–2.92)	6.48 (4.42–9.51)	< 0.001
Female	4008	15	0.37 (0.23–0.62)	17,733	474	2.67 (2.45–2.92)	7.14 (4.28–11.93)	< 0.001
Age, year	-							
< 1	5105	10	0.20 (0.11–0.36)	14,977	301	2.01 (1.80–2.25)	10.26 (5.47–19.24)	< 0.001
1-2	2984	16	0.54 (0.33–0.87)	14,248	429	3.01 (2.74–3.30)	5.62 (3.41–9.23)	< 0.001
3–5	1850	13	0.70 (0.41–1.20)	11,224	321	2.86 (2.57–3.18)	4.07 (2.34–7.07)	< 0.001
6–17	507	3	0.59 (0.20–1.73)	3467	135	3.89 (3.30–4.59)	6.58 (2.10–20.58)	< 0.001
URTI	2691	11	0.41 (0.23–0.73)	11,340	303	2.67 (2.39–2.99)	6.54 (3.59–11.91)	< 0.001
Gender								
Male	1559	7	0.45 (0.22-0.92)	6682	175	2.62 (2.26-3.03)	5.83 (2.75–12.39)	< 0.001
Female	1132	4	0.35 (0.14–0.90)	4658	128	2.75 (2.32–3.26)	7.78 (2.88–20.99)	< 0.001
Age, yeai								
< 1	1001	5	0.50 (0.21–1.16)	2713	57	2.10 (1.63–2.71)	4.21 (1.69–10.46)	< 0.001
1-2	956	2	0.21 (0.06–0.76)	4164	111	2.67 (2.22-3.20)	12.74 (3.15–51.49)	< 0.001
3–5	536	2	0.37 (0.10–1.35)	3282	88	2.68 (2.18–3.29)	7.19 (1.77–29.10)	< 0.001
6–17	198	2	1.01 (0.28–3.61)	1181	47	3.98 (3.01–5.25)	3.94 (0.96–16.09)	< 0.001
LRTI	7755	31	0.40 (0.28–0.57)	32,576	883	2.71 (2.54–2.89)	6.78 (4.74–9.69)	< 0.001
Gender								
Male	4879	20	0.41 (0.27-0.63)	19,501	537	2.75 (2.53–2.99)	6.72 (4.30–10.49)	< 0.001
Female	2876	11	0.38 (0.21–0.68)	13,075	346	2.65 (2.38–2.94)	6.92 (3.80–12.59)	< 0.001
Age, yeai	r							
< 1	4104	5	0.12 (0.05-0.28)	12,264	244	1.99 (1.76–2.25)	16.33 (6.74–39.56)	< 0.001
1–2	2028	14	0.69 (0.41-1.16)	10,084	318	3.15 (2.83–3.51)	4.57 (2.68–7.78)	< 0.001
3-5	1314	11	0.84 (0.47-1.49)	7942	233	2.93 (2.58–3.33)	3.50 (1.92–6.40)	< 0.001
6–17	309	1	0.32 (0.06–1.81)	2286	88	3.85 (3.14–4.72)	11.90 (1.66–85.08)	< 0.001

IFV influenza virus, URTI upper respiratory tract infection, LRTI lower respiratory tract infection, CI confidence interval, RR rate ratio, P P value



Fig. 3 Dynamics of the positive rate of IFV before and after COVID-19 in Hubei Province from 2014 to 2021. **a** The positive rate of IFV among the overall children during three stages; **b** The positive rate of IFV among children with URTI during three stages; **c** The positive rate of IFV among children with URTI during three stages. The blue line presents the positive rate of IFV during Stage I, the combined period during February–June of 2017–2019. The red line presents the positive rate of IFV during Stage II, the combined period during February–June of 2020. The yellow line presents the positive rate of IFV during State III, the combined period during February–June of 2021 and 2022. "*" was represented *P*<0.05. COVID-19, coronavirus disease 2019

detection, but the positive rate was still significantly lower than that in the same period during 2017–2019.

Discussion

Our results showed the changing pattern of IFV in hospitalized children with ARTI during 2014–2022 varied year by year. The overall positive rate of IFV increased after the implementation of the universal two-child policy. The incidence pattern of IFV had significant reductions during the time of COVID-19 outbreak and related NPIs implemented, but those measures did not continuously sustain IFV infections at low levels. The rebound of IFV infections was observed during the regular epidemic prevention and control period in 2021 and 2022.

Consistent with prior studies, the positive rate of IFV in children varied by gender and age, which may be

related to the different vaccination rate, immune system ability and behavior patterns [17]. This study showed the positive rate of IFV in patients with LRTI was higher than that in patients with URTI, reminding that IFV is an important pathogen associated with LRTI [18]. Strengthening surveillance for IFV is critical for preventing illness and reducing hospitalization [19].

The influenza seasonality observed in our study was similar to other regions such as Chongqing city, which located at the same latitude as Hubei Province [20]. The main peak occurred during winter, since influenza activity frequently followed low seasonal temperatures [21]. Besides, children's summer vacations reduce the frequency of them gathering and interacting, preventing the IFV from being transmitted among children. The impact of other climate conditions such as humidity, precipitation and sunshine on the IFV activity were also found in some studies, which may explain the difference of the specific epidemic patterns every year [22, 23]. During the influenza seasons, the IFV-A co-circulated with the IFV-B and there were some co-infections occurred. Same phenomenon has been described in other studies conducted in the same area [24, 25]. It should be noted that after the outbreak of COVID-19, IFV-B is predominant in hospitalized children instead of IFV-A. This transition may be related to that children infected with IFV-A have a higher frequency of symptoms, leading to more medical attention and early identification of children at higher risk during the COVID-19 pandemic, which may reduce the proportion of hospitalization [26]. Besides, the COVID-19 may have an impact on the types of IFV, which needs to be further investigated.

Implemented on 1 January 2016, the universal two child policy has been associated with a rise in births in China [27]. In 2017–2019, the prevalence of IFV in hospitalized children increased, and children under one year had demonstrated a rapid boost in the positive rate of IFV. Newborns increased the population density in family, causing more exposure and transmission within households especially in the infants who lacks of protective antibodies [28]. What's more, evidence provided by previous studies suggested that there were more multiparous mothers and mother aged 35 years and over on the scale, increasing the risk of birth outcomes such as preterm birth and birth defects [27, 29–31]. With unmature immune system, the burden of newborn infectious disease has always been considered as the highest across the entire human life span [32]. We evaluated the impact of this policy on the epidemiology of influenza with a large sample size. Our findings suggest that with the implementation of the universal two-child policy, influenza prevention and control targeted to the children especially newborns should be strengthened and developed in facing the assault of increasing susceptible population.

In the early stage of COVID-19, the spread of influenza reduced, implying that rigorous implementation of NPIs was likely to benefit the control of influenza [33, 34]. Studies conducted in other regions and countries have shown similar results in the epidemiology of influenza and other respiratory viral diseases [13, 35, 36]. In Western Australia, the COVID-19 related NPIs also reduced the circulation of respiratory syncytial virus, altering its seasonality [37]. At the beginning of COVID-19 outbreak, Wuhan city was closed and traffic restricted under the strong control of the government. Almost all people were quarantined at home, minimizing the transmission of the infection to others [14]. A series of measures were taken to limit the possibility of IFV transmission.

After success in early elimination local transmission of severe acute respiratory syndrome coronavirus-2 (SAR-CoV-2), the resumption of work and life was advanced, followed by a resurgence of influenza infections [38]. The rebound of influenza was likely attributed to the accumulation in population susceptibility coupled with relaxed NPIs. The decline in child vaccination coverage during COVID-19 outbreak increased the risk of infection [39]. Besides, the threshold for respiratory virus testing in the context of the regular epidemic prevention and control for COVID-19 was lowered, facilitating more patients get tested and virus get detected [12].

However, the epidemic level of influenza has not returned to the level before COVID-19. This phenomenon reveals that COVID-19 outbreak and related NPIs has altered influenza epidemiology and seasonality. Daily protective measures such as mask wearing have interrupted a significant portion of the transmission of IFV [40]. However, large number of people wear mask for long periods of time may increase population susceptibility to pathogens, which may lead to a huge bounce of infectious disease. Influenza vaccine has demonstrated effectiveness in the prevention of influenza and reducing severe disease [41]. Promoting the influenza vaccination to increase vaccination coverage in the population is still vital to prevent the epidemic of influenza.

There were several limitations in this research. Firstly, this study was a retrospective analysis based on historical data, so there are some unmeasured biases and the causal inferences cannot be concluded. Secondly, only outpatient under 18 years in a single center were included in our study, lacking more data from the population to illustrate the whole situation. Due to the impact of COVID-19 outbreak, the hospitalization and the isolation of the viruses may be delayed and suspended, possibly leading to biased results.

Conclusion

IFV has been activating continuously in Hubei Province. The universal two-child policy increased the possibility of IFV transmission especially in newborns. Influenza activity among children declined sharply at the beginning of COVID-19 outbreak and rebounded during the regular epidemic prevention and control period in 2021 and 2022. NPIs has altered influenza epidemiology. More attention should be emphasized to comprehend the health benefits generated by COVID-19 restrictions on IFV transmission in future.

Supplementary Information

The online version contains supplementary material available at https://doi. org/10.1186/s12985-023-02092-1.

Additional file 1: Figure S1. The positive rate of IFV among children with URTI and LRTI in different gender and age groups during January 2014 to June 2022. The positive rate of IFV—A and IFV—B among children with URTI; The positive rate of IFV among children with URTI in different age groups; The positive rate of IFV—A and IFV—B among children with URTI in different gender; The positive rate of IFV—A and IFV—B among children with LRTI; The positive rate of IFV among children with LRTI in different age groups; The positive rate of IFV among children with LRTI in different gender; The positive rate of IFV among children with LRTI in different age groups; The positive rate of IFV among children with LRTI in different gender.

Additional file 2: Figure S2. The heatmap of weekly positive rate of IFV among children with URTI and LRTI in different diagnosis, gender and age groups during January 2014 to June 2022. Weekly positive rate of IFV–A and IFV–B among children with URTI;Weekly positive rate of IFV among children with URTI in different gender;Weekly positive rate of IFV among children with URTI in different age groups;Weekly positive rate of IFV–A and IFV–B among children with LRTI;Weekly positive rate of IFV among children with LRTI in different gender;Weekly positive rate of IFV among children with LRTI; Weekly positive rate of IFV among children with LRTI in different gender;Weekly positive rate of IFV among children with LRTI in different age groups.

Additional file 3: Table S1. The positive rate of IFV in Hubei Province from 2017-2022, stratified by COVID-19 outbreak.

Acknowledgements

Not applicable.

Author contributions

Conceptualization, SY and W-XZ; methodology, SY; formal analysis, W-XZ; writing—original draft preparation, SY, W-XZ, Y-GZ and X-RW; writing—review and editing, JD, X-WH; visualization, W-XZ; supervision, Q-BL; funding acquisition, Q-BL. All authors have read and agreed to the published version of the manuscript.

Funding

This work was supported by Joint Research Fund for Beijing Natural Science Foundation and Haidian Original Innovation (L222029 and L202007) and Fundamental Research Funds for the Central Universities and Peking University Health Science Center (BMU2021YJ041), Peking University Medicine Fund of Fostering Young Scholars' Scientific and Technological Innovation (BMU2021PY005).

Availability of data and materials

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

Declarations

Ethics approval and consent to participate

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of Hubei Maternal and Child Health Hospital (protocol code 2022IEC052).

Informed consent

Informed consent was obtained from all subjects involved in the study.

Competing interests

The authors declare there are no competing interests.

Author details

¹Department of Medical Genetic Center, Maternal and Child Health Hospital of Hubei Province, Wuhan 430070, People's Republic of China. ²Department of Epidemiology and Biostatistics, School of Public Health, Peking University, Beijing 100191, People's Republic of China. ³Department of Health Policy and Management, School of Public Health, Peking University, Beijing 100191, People's Republic of China. ⁴Department of Laboratorial Science and Technology and Vaccine Research Center, School of Public Health, Peking University, 38th Xueyuan Road, Haidian District, Beijing 100191, People's Republic of China. ⁵Global Center for Infectious Disease and Policy Research and Global Health and Infectious Diseases Group, Peking University, Beijing 100191, People's Republic of China. ⁶Department of Clinical Laboratory, Maternal and Child Health Hospital of Hubei Province, 745th Wuluo Road, Hongshan District, Wuhan 430070, People's Republic of China. ⁷Key Laboratory of Epidemiology of Major Diseases (Peking University), Ministry of Education, Beijing, China.

Received: 13 January 2023 Accepted: 4 June 2023 Published online: 13 June 2023

References

- 1. Uyeki TM, Hui DS, Zambon M, et al. Influenza. Lancet. 2022;400(10353):693–706.
- Iuliano AD, Roguski KM, Chang HH, et al. Estimates of global seasonal influenza-associated respiratory mortality: a modelling study. Lancet. 2018;391(10127):1285–300.
- Shu Y, Fang L, de Vlas SJ, et al. Dual seasonal patterns for influenza, China. Emerg Infect Dis. 2010;16(4):725–6.
- Yu H, Alonso WJ, Feng L, et al. Characterization of regional influenza seasonality patterns in China and implications for vaccination strategies: Spatio-Temporal modeling of surveillance data. PLoS Med. 2013;10(11):e1001552.
- Kwong JC, Schwartz KL, Campitelli MA, et al. Acute myocardial infarction after laboratory-confirmed influenza infection. N Engl J Med. 2018;378(4):345–53.
- Javanian M, Barary M, Ghebrehewet S, et al. A brief review of influenza virus infection. J Med Virol. 2021;93(8):4638–46.
- Hesketh T, Lu L, Xing ZW. The effect of China's one-child family policy after 25 years. N Engl J Med. 2005;353(11):1171–6.
- Hesketh T, Zhou X, Wang Y. The End of the one-child policy. JAMA. 2015;314(24):2619.
- 9. Paules C, Subbarao K. Influenza. Lancet. 2017;390(10095):697–708.
- Al-Harrasi A, Bhatia S. Epidemiology respiratory infections: types, transmission, and risks associated with co-infections, 2022. p. 7–17.
- Ryu S, Ali ST, Noh E, et al. Transmission dynamics and control of two epidemic waves of SARS-CoV-2 in South Korea. BMC Infect Dis. 2021;21(1):1–9.
- 12. Saravanos GL, Hu N, Homaira N, et al. RSV epidemiology in Australia before and during COVID-19. Pediatrics. 2022;149:2.
- Uppala R, Sitthikarnkha P, Niamsanit S, et al. Effect of the COVID-19 pandemic on lower respiratory tract infection determinants in Thai hospitalized children: national data analysis 2015–2020. Trop Med Infect Dis. 2022;7(8):151.
- 14. Wu D, Lu J, Liu Y, et al. Positive effects of COVID-19 control measures on influenza prevention. Int J Infect Dis. 2020;95:345–6.

- Li Z, Zhang H, Ren L, et al. Etiological and epidemiological features of acute respiratory infections in China. Nat Commun. 2021;12(1):5026.
- Cao B, Huang Y, She DY, et al. Diagnosis and treatment of communityacquired pneumonia in adults: 2016 clinical practice guidelines by the Chinese Thoracic Society, Chinese Medical Association. Clin Respir J. 2018;12(4):1320–60.
- Jiang Y, Tong Y, Fang B, et al. Applying the moving epidemic method to establish the influenza epidemic thresholds and intensity levels for agespecific groups in Hubei Province, China. Int J Environ Res Public Health. 2022;19(3):1677.
- Wang X, Li Y, O'Brien KL, et al. Global burden of respiratory infections associated with seasonal influenza in children under 5 years in 2018: a systematic review and modelling study. Lancet Glob Health. 2020;8(4):e497–510.
- 19. Radin JM, Katz MA, Tempia S, et al. Influenza surveillance in 15 countries in Africa, 2006–2010. J Infect Dis. 2012;206(Suppl 1):S14–21.
- Meng X, Zhao H, Ou R, et al. Epidemiological and clinical characteristics of influenza outbreaks among children in Chongqing, China. Front Public Health. 2022;10.
- Azziz Baumgartner E, Dao CN, Nasreen S, et al. Seasonality, timing, and climate drivers of influenza activity worldwide. J Infect Dis. 2012;206(6):838–46.
- 22. Park JE, Son WS, Ryu Y, et al. Effects of temperature, humidity, and diurnal temperature range on influenza incidence in a temperate region. Influenza Other Respir Viruses. 2019;14(1):11–8.
- Ali ST, Cowling BJ, Wong JY, et al. Influenza seasonality and its environmental driving factors in mainland China and Hong Kong. Sci Total Environ. 2022;818:151724.
- Chen L, Guo J, Guo W, et al. Molecular epidemiology and vaccine compatibility analysis of seasonal influenza viruses in Wuhan, 2016–2019. Virologica Sinica. 2020;35(5):556–65.
- He Z, Tao H. Epidemiology and ARIMA model of positive-rate of influenza viruses among children in Wuhan, China: A nine-year retrospective study. Int J Infect Dis. 2018;74:61–70.
- Mosnier A, Caini S, Daviaud I, et al. Clinical characteristics are similar across type A and B influenza virus infections. PLoS ONE. 2015;10(9):e136186.
- Li H, Xue M, Hellerstein S, et al. Association of China's universal two child policy with changes in births and birth related health factors: national, descriptive comparative study. BMJ. 2019;2019:14680.
- 28. Kumar V. Influenza in children. Indian J Pediat. 2017;84(2):139-43.
- Zhang X, Chen L, Wang X, et al. Changes in maternal age and prevalence of congenital anomalies during the enactment of China's universal twochild policy (2013–2017) in Zhejiang Province, China: an observational study. PLoS Med. 2020;17(2):e1003047.
- Deng K, Liang J, Mu Y, et al. Preterm births in China between 2012 and 2018: an observational study of more than 9 million women. Lancet Glob Health. 2021;9(9):e1226–41.
- 31. Viboud C, Boëlle PY, Cauchemez S, et al. Risk factors of influenza transmission in households. Br J Gen Pract. 2004;54(506):684–9.
- Brook B, Harbeson D, Ben-Othman R, et al. Newborn susceptibility to infection vs. disease depends on complex in vivo interactions of host and pathogen. Semin Immunopathol. 2017;39(6):615–25.
- Zheng L, Qi J, Wu J, et al. Changes in influenza activity and circulating subtypes during the COVID-19 outbreak in China. Front Med. 2022;9:627.
- Liu Y, Morgenstern C, Kelly J, et al. The impact of non-pharmaceutical interventions on SARS-CoV-2 transmission across 130 countries and territories. BMC Med. 2021;19(1):1–12.
- Sullivan SG, Carlson S, Cheng AC, et al. Where has all the influenza gone? The impact of COVID-19 on the circulation of influenza and other respiratory viruses, Australia, March to September 2020. Eurosurveillance. 2020;25(47):2001847.
- Kuo S, Shih S, Chien L, et al. Collateral benefit of COVID-19 control measures on influenza activity, Taiwan. Emerg Infect Dis. 2020;26(8):1928–30.
- Foley DA, Phuong LK, Peplinski J, et al. Examining the interseasonal resurgence of respiratory syncytial virus in Western Australia. Arch Dis Child. 2022;107(3):e1–2.
- Huang W, Cheng Y, Tan M, et al. Epidemiological and virological surveillance of influenza viruses in China during 2020–2021. Infect Dis Pov. 2022;11(1):74.

- Bramer CA, Kimmins LM, Swanson R, et al. Decline in child vaccination coverage during the COVID-19 pandemic — Michigan care improvement registry, May 2016–May 2020. MMWR Morb Mortal Wkly Rep. 2020;69(20):630–1.
- Chaabna K, Doraiswamy S, Mamtani R, et al. Facemask use in community settings to prevent respiratory infection transmission: a rapid review and meta-analysis. Int J Infect Dis. 2021;104:198–206.
- 41. Bosaeed M, Kumar D. Seasonal influenza vaccine in immunocompromised persons. Hum Vaccin Immunother. 2018;14(6):1311–22.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

