

Seasonal influenza activity in young children before the COVID-19 outbreak in Wuhan,
China

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Outbreak Alerts

Dear Editor,

During the first wave of COVID-19 in China, the attack rate of coronavirus disease 2019 (COVID-19) in children was much lower than in adults, and most child cases had mild symptoms (Dong et al 2020). However, the secondary attack rate of COVID-19 among close contacts was later found similar between children and other age groups (Bi et al). In Wuhan, Hubei province, China, there was only one paediatric case of COVID-19 officially reported before January 22, 2020. The reasons why children were exempted from COVID-19 infection in the early stage remain unclear. One hypothesis is the potential interference of seasonal influenza peaks with the newly-emerging COVID-19 outbreak among young children. Liu *et al* reported that 11% and 1.6% of 366 hospitalized children (≤ 16 years of age) were infected by influenza and SARS-CoV-2, respectively, in early January 2020 in Wuhan, China. Kong *et al* found that the incidence rates of influenza-illness-like (ILI) were substantially higher in the 2019-20 season than in the previous two years based on the surveillance data in two hospitals in Wuhan, China. The retrospective laboratory tests in the specimens from these ILI patients to January 2020 showed that an outbreak of seasonal influenza attacked the ≤ 30 age group in October-November 2019, followed by the COVID-19 cases in the > 30 -years age group that first emerged in December 2019 to January 2020. Surprisingly, no COVID-19 case was found in the ≤ 30 age group in their 120 samples (Table 1). Thus there is an apparent inconsistency between the studies by Kong *et al* and Liu *et al*, as one would expect some COVID-19 cases among the young age group of ILI patients by the mid-January in Wuhan, China.

We obtained the test results of 194,672 specimens from the Maternal and Child Health Hospital of Hubei Province in Wuhan. These specimens were collected from 1 January 2017 to 20 May 2020, for immunofluorescence tests of influenza type A and B. Around 75% of the specimens were taken from the outpatients and inpatients aged ≤ 6 years old. In consistent with the findings by Kong *et al*, we also found a peak of influenza A in early January, coinciding with the start of the COVID-19 outbreak. It is interesting to note that the winter peak of seasonal influenza in Wuhan appeared in early January 2020, nearly one month earlier than those in 2017-18 and 2018-19. The difference in the peak time could be associated with an international event in late October but the earlier lunar calendar cycle

could be another reason (e.g., Chongyang festival was on October 28 in 2017, October 17 in 2018 and October 7 in 2019).

We observe a sudden drop of influenza A cases in early January 2020, presumably due to social distancing and avoidance of hospital visits immediately after the official report of pneumonia clusters of COVID-19 and closure of the Huanan Seafood market on December 31, 2019.

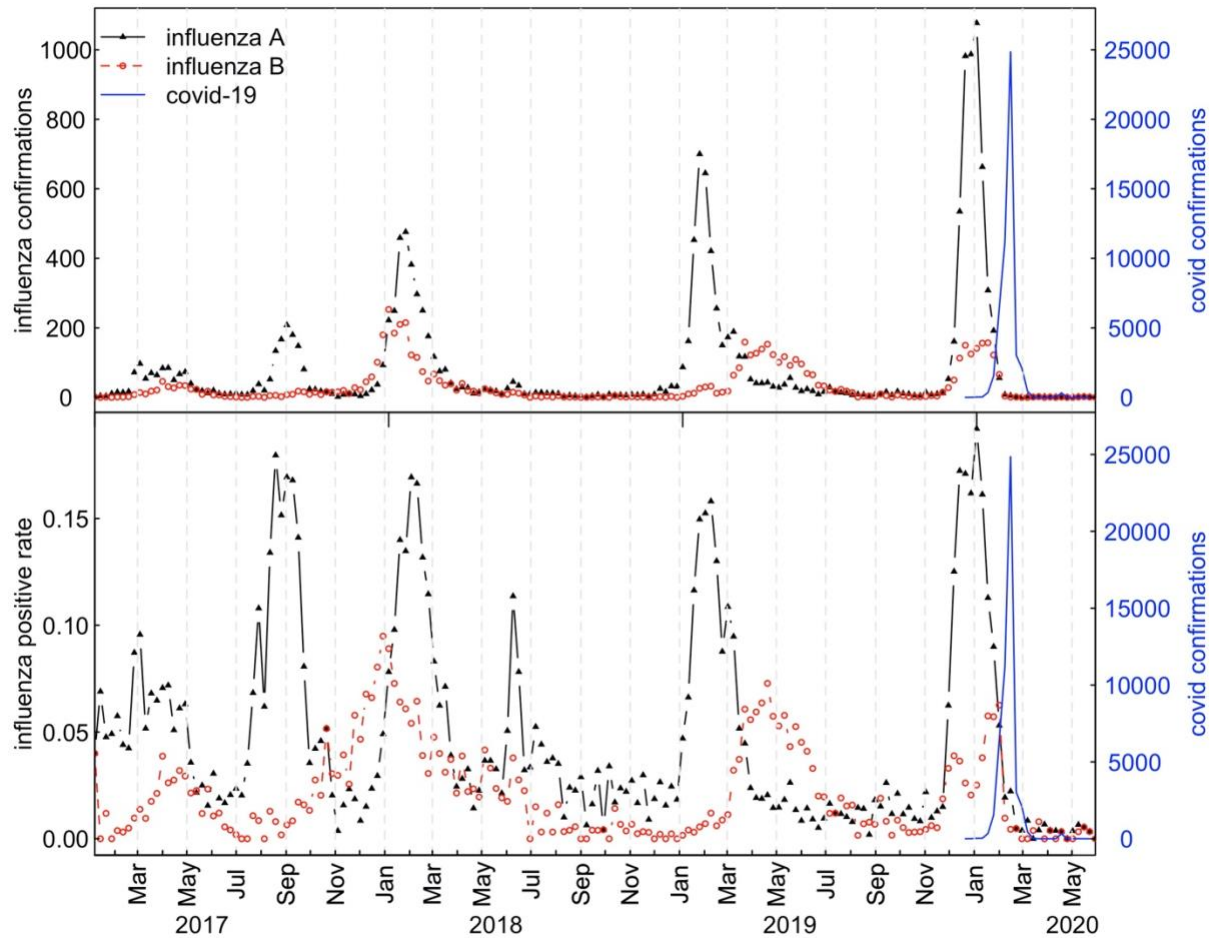


Figure 1. Influenza activity from January 2017 to May 2020 in Wuhan, China. The top panel shows weekly numbers of specimens positive for influenza A (black triangle) and influenza B (red square). The blue curve shows weekly numbers of reported COVID-19. The bottom panel shows weekly positive rate for influenza A and B.

Infection risk of COVID-19 was known to increase with age (Sun et al 2020). If we assume that the ratio of COVID-19 to influenza cases in the <30 age group was not less than that in the <16 age group and similar across different hospitals, we could derive a ratio of 0.136

(1.6% / 11.80%) based on reference (Liu et al 2020). Given the influenza positive rate of 60% from reference (Kong et al 2020), we would expect that around 8% of COVID-19 would have occurred in ILI patients under 30 years old. Hence, the chance of having zero COVID-19 cases in the <30 age group of ILI cases, as reported in reference (Kong et al 2020), was estimated to be very low ($0.002 = [(1-0.08)^{75}]$), given the total number of 75 specimens collected in their study for this age group.

Table 1 Influenza and COVID-19 positive tests from two studies

	Liu et al	Kong et al	Kong et al
Hospitals	One pediatric hospital and one general hospital	Pediatric inpatients and outpatients from three general hospitals	
Age	<16 years old	<30 years old	>30 years old
Sample size	366	75	45
Time	7-15 January, 2020	Jan. weeks 1-3	Jan. weeks 1-3
Sample	hospitalized children	ILI patients	ILI patients
influenza positive	11.80%	60%	15.6%
COVID-19 positive	1.60%	0%	20%

It is of note that Kong et al collected the data from pediatric inpatients and outpatients from three general hospitals in Wuhan, whereas Liu et al collected the data from one pediatric hospital and one general hospital. *We showed that the results from samples of such size from a few hospitals could not well match with each other in the initial stage of the pandemic.* Taken together, the exemption from COVID-19 infection in the <30 age group in the early phases of the COVID-19 outbreak might have been due to underreporting whereas the potential interference between influenza and COVID-19 cannot be ruled out. Studies with a large sample size from different regions are warranted to investigate the interaction between seasonal respiratory viruses and SARS-CoV-2, particularly in children.

Declaration

Ethical Approval and Consent to participate

The ethical approval has been obtained from the Maternal and Child Health Hospital of Hubei Province. Individual consents were exempted as the aggregated data were used in this study.

Availability of data and materials

All data used are from public domain.

Competing interests

DH was supported by an Alibaba (China) Co. Ltd. Collaborative Research project. Other authors declare no conflict of interest.

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Authors' contributions

All authors conceived and conducted the research and wrote the draft. All authors critically revised the manuscript, and all authors approved the submission.

Reference

Dong Y, Mo X, Hu Y, et al. Epidemiological Characteristics of 2143 Pediatric Patients With 2019 Coronavirus Disease in China. *Pediatrics* 2020.

Bi Q, Wu Y, Mei S, Ye C, Zou X, Zhang Z, Liu X, Wei L, Truelove SA, Zhang T, Gao W. Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study. *The Lancet Infectious Diseases*. 2020 Apr 27.

Liu, W., Zhang, Q., Chen, J., Xiang, R., Song, H., Shu, S., ... & Wu, P. (2020). Detection of Covid-19 in children in early January 2020 in Wuhan, China. *New England Journal of Medicine*, 382(14), 1370-1371.

Kong, W. H., Li, Y., Peng, M. W., Kong, D. G., Yang, X. B., Wang, L., & Liu, M. Q. (2020). SARS-CoV-2 detection in patients with influenza-like illness. *Nature Microbiology*, 1-4.

Sun, K., Chen, J., & Viboud, C. (2020). Early epidemiological analysis of the coronavirus disease 2019 outbreak based on crowdsourced data: a population-level observational study. *The Lancet Digital Health*.