Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Co-infection of SARS-CoV-2 and Influenza virus in Early Stage of the COVID-19 Epidemic in Wuhan, China

Dear Editor,

In this Journal, Tang *et al.* have report the symptoms of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection appear very similar to influenza (1). We would like to share our findings for co-infection of SARS-CoV-2 and influenza virus. In December, 2019, a novel coronavirus (SARS-CoV-2) caused Coronavirus disease 2019 (COVID-19) in Wuhan City, Hubei province, China (2,3). The epidemic of SARS-CoV-2 has rapidly spread worldwide and affected more than 4 million patients with more than 300 000 deaths in more than 230 countries (4). Both SARS-CoV-2 and influenza virus can cause highly similar respiratory symptoms, including high fever, cough, headache and even pneumonia (2,5,6). In early stage of COVID-19 epidemic in Wuhan, SARS-CoV-2 activities overlapped with influenza winter peak season and may have result in undetected co-infection. Here we performed a retrospective analysis of 1001 influenza patients, and confirmed the co-infection of SARS-CoV-2 and influenza virus in early stage of COVID-19 in Wuhan, China.

Samples for this study were collected during the routine influenza surveillance in Union Hospital in Wuhan. Union Hospital is a major comprehensive hospital and located within 5 kilometers to Huanan Seafood Market. The study protocol was reviewed and approved by the ethics committee of Union Hospital of Tongji Medical College, Huazhong University of Science and Technology (2019S940). Verbal informed consent was obtained from parents or caretakers of underage patients. Throat swab samples were collected from an outpatient or inpatient have an influenza-like illness (ILI) symptoms, such as a sudden onset of a fever $>38\,^{\circ}C$ as well as a cough or sore throat. Samples were tested for influenza A & B viruses with real-time reverse transcription polymerase chain reaction (rRT-PCR) assays. We then screened all the influenza positive samples using rRT-PCR for SARS-CoV-2 RNA, with primers and probes targeting the N and ORF1ab genes of SARS-CoV-2. Those samples have SARS-CoV-2 and influenza virus co-infection were further determined the presence of SARS-CoV-2 genome with next generation sequencing (NGS), and the influenza subtype with specific rRT-PCR (details of screening in the Supplementary Methods).

A total of 1001 influenza positive patients were analyzed. Amongst, 45 (4.5%) patients were sampled from January to November 2019, the time before the early COIVD-19 cases reported (Fig. 1). From December 2019 to January 2020 (as of January 19), in the early stage of COIVD-19 in Wuhan, 956 patients (95.6%) were enrolled (Fig. 1, Supplementary Table 1). As for the 1001 patients have influenza positive, the mean age of the patients was 30.6 years (range, one day to 89), and 463 (46.3%) were male (Supplementary Table 1). Among the 1001 influenza positive samples, 602 (60.1%) were influenza A viruses, 397 (39.7%) were influenza B viruses, and 2 (0.2%) were influenza A & B positive samples, respectively (Fig. 1, Supplementary Table 1).

Among enrolled 1001 patients, four patients (0.4%) in January 2020 were detected co-infection of SARS-CoV-2 and influenza virus (Fig. 1). There was no SARS-CoV-2 virus in influenza patients in December 2019 and earlier (Fig. 1). We then collected the clinical and laboratory features of the four patients have co-infection. Patient 1 and 2, 3 and 4 were co-infected with H3N2 virus, B/Victoria lineage virus, respectively (Supplementary Table 2). Patient 1, 3, and 4 were outpatients and aged 33, 30 and 15 years, respectively, and patient 2 was inpatient and aged 62 years. Patient 1, 3, and 4 experienced mild symptoms and showed high fever and cough. Besides, patient 3 showed unilateral pneumonia (Supplementary Table 2). Patient 1, 3, and 4 were treated with Oseltamivir and/or antibiotics and recovered within 5 days. Patient 2 experienced with malignant tumor and had worse outcomes from COVID-19, such as long-term fever (24 days), bilateral pneumonia, and oxygen support requirement. After 24 days treatment, patient 2 didn't show clinical improvement and was transferred to designated hospital for COVID-19. Of note, patient 2 have cycle threshold (Ct) values below 30 for both SARS-CoV-2 and influenza virus at sampling time, indicating high viral load in respiratory tract (Supplementary Table 2).

Our results revealed co-infection of SARS-CoV-2 and influenza viruses but with low rate in Wuhan, China. However, the risk of co-infection of SARS-CoV-2 with influenza viruses in winter influenza activity peak season is concerning. In January, when the testing capacity is insufficient, co-infection of SARS-CoV-2 with influenza viruses in winter influenza activity peak season may contribute the expansion of SARS-CoV-2 in the local population. Besides patients in this study, patients with both SARS-CoV-2 and influenza virus infection showed similar clinical characteristics as those patients with SARS-CoV-2 infection only (7,8). However, more studies are needed to assess the effect of the SARS-CoV-2 and influenza co-infection in clinical outcomes. This study has limitation that only a single center was enrolled. Nevertheless, our results highlight the importance of screening SARS-CoV-2 viruses among influenza patients.

Declaration of Competing Interest

None.

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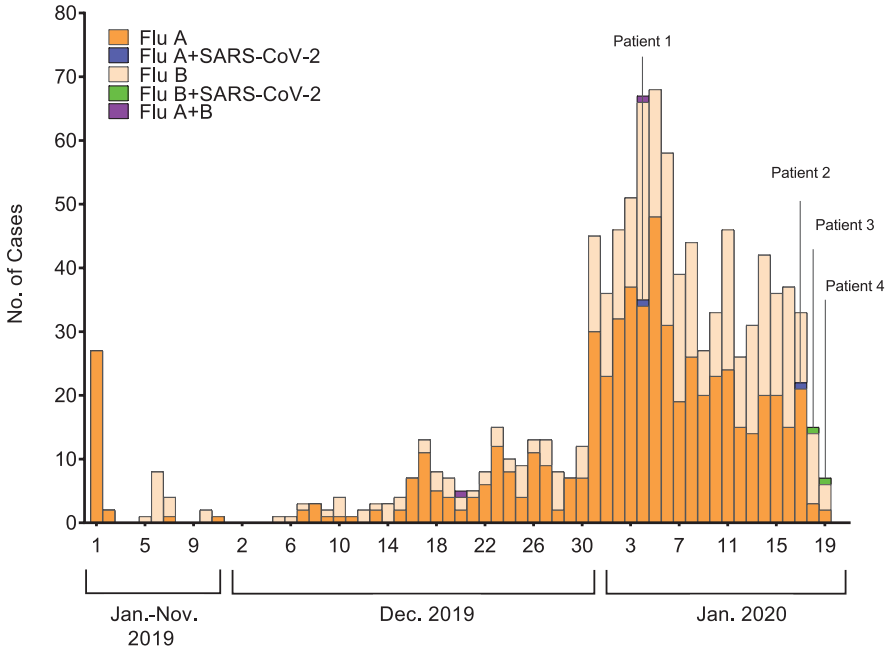

Fig. 1. SARS-CoV-2 in influenza positive cases in Wuhan, China. Number of influenza and SARS-CoV-2 cases were sampled between 4 January 2019 and 19 January 2020. The vertical columns scaled on the left y axis report the monthly or daily influenza and SARS-CoV-2 case numbers and the color blocks in the columns represent the single infection or co-infection.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jinf.2020.05.041.

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