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Letter to the Editor

Different patterns of Influenza A and B detected during early stages of COVID-19 in a university hospital in São Paulo, Brazil



Dear editor,

As recently reported in this journal, measures implemented to contain COVID-19 infection also seems to be effective in reducing influenza activity in Singapore [1]. The same effect was also reported to reduce the spread of viral respiratory diseases, particularly influenza viruses, in countries such as Taiwan, Japan [2,3], Australia, and New Zealand (<https://info.flutracking.net>).

São Paulo is the largest city in Brazil and aggregates the majority of COVID-19 cases registered in the country so far. Since the first detection of SARS-CoV-2 in Brazil, on February 25, the country accounts (on May 9) 148,670 confirmed cases and 10,100 deaths of which 41,830 and 3416 were registered in São Paulo, respectively.

According to the weekly epidemiological records for influenza viruses in the city of São Paulo, comprising the corresponding period of our study (11th to 16th epidemiological weeks), in the last four years, influenza A and B viruses were circulating and sometimes at the peak of the season (Fig. 1).

It is important to mention that the influenza vaccination campaign began on March 23, initially targeting priority groups such as the elderly (≥ 60 years) and health professionals, continuing until April 15 for those groups.

At the same time, on March 13, the first contingency act of the Health Department was adopted to prevent the contagion of COVID-19, suspending public events with an audience of over 500 people, in addition to recommending the suspension of classes in schools and universities. On March 22, the first quarantine act was implemented, allowing only essential activities related to health, food, supply, and security.

To investigate the impact of quarantine in the local community, we assessed the presence of SARS coronavirus 2 (SARS-CoV-2), influenza A virus (IV-A), B (IV-B), and human metapneumovirus (hMPV) in 244 hospitalized patients with acute respiratory illness. Human respiratory syncytial virus (RSV) was tested only in children. The study was approved by the National Research Ethics Commission (CONEP no. 29,407,720.4.0000.5505).

All patients were suspected of COVID-19 infection according to the World Health Organization case definition criteria. They were admitted at Hospital São Paulo, a university reference hospital with special wards for medical care of COVID-19 cases, from March 12 to April 16, presenting symptoms of severe acute respiratory syndrome (SARS), including fever, dry cough, dyspnea or respiratory distress. Some patients also experienced diarrhea.

Patients included 36 children (≤ 12 years) and 209 adults, with ages ranging from one month to 96 years (mean \pm SD = 48.49 ± 24.93 , median = 55.00).

Nasal and oropharyngeal swabs were collected and stored in 2 mL of sterile Ringer's lactate solution prior to RNA extraction with QIAamp Viral RNA Mini Kit (QIAGEN, Hilden, Germany), following the manufacturer's instructions.

Virus screening was carried out with AgPath-ID One-Step RT-PCR Reagents on 20 μ L of total reaction volume. SARS-CoV-2 detection was performed with oligonucleotides described by the Centers for Disease Control and Prevention (CDC) [5]. The detection of IV-A, IV-B, hMPV, and RSV was performed with oligonucleotides described elsewhere [6–8].

Overall, 115 patients were positive for SARS-CoV-2, four for IV-B, nine children for RSV, and none for IV-A and hMPV (Table 1). A 36-year-old patient was co-infected with SARS-CoV-2 and IV-B, who had a favorable outcome and was discharged after six days.

We observed the absence of IV-A and only 1.64% of IV-B and 0.41% of hMPV, which demonstrates a reduction of expected cases of infection by influenza virus in relation to the registered cases in the city during the same period, in the last 4 years (Fig. 1). Interestingly, during the pandemic influenza A (H1N1) pdm09 in 2009, hMPV was the second most prevalent virus in adults in a study carried out by our research group [9]. For RSV, 25% of investigated children were positive. However, the RSV infection rate in hospitalized children is usually higher than 50% at this time of year [10]. The results suggest that the containment measures adopted in the city for COVID-19 restraint contributed to reducing the spread of influenza viruses and RSV among children.

Table 1
Virus detection rates (%) by age groups.

Age group (in years)	no. patients	Virus detection no. (%)				
		SARS-CoV-2	IV-A	IV-B	hMPV	RSV
0–5	26	1 (3.58)	0	1 (3.85)	0	9 (36.61)
6–12	10	1 (10)	0	2 (20)	0	0
13–19	8	1 (12.5)	0	0	0	ND
20–39	30	12 (40)	0	1 (3.33)*	1 (3.33)	ND
40–59	71	40 (56.34)	0	0	0	ND
≥ 60	99	60 (60.61)	0	0	0	ND
total	244	115 (47.13)	0	4 (1.64)	1 (0.41)	9 (25)†

SARS-CoV-2, SARS coronavirus 2. IV-A, Influenza A virus. IV-B, Influenza B virus. hMPV, human metapneumovirus. ND, not done.

* SARS-CoV-2/IV-B codetection.

† Only children.

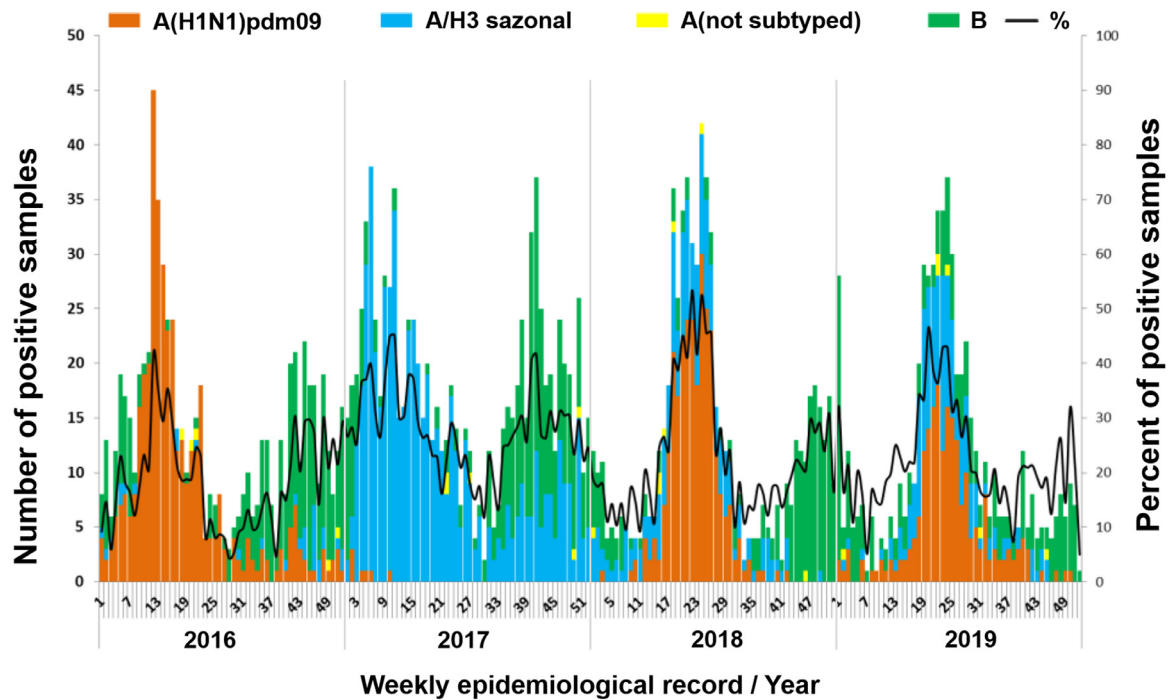


Fig. 1. Weekly epidemiological records of influenza viruses in Sao Paulo city from 2016 to 2019 [4].

One limitation of the present study was not to retrieve the vaccination status of the elderly, although the vaccination and study time frame overlapped and it is expected that the production of antibodies will take at least 15 days after vaccination.

Declaration of Competing Interest

None.

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References

1. Chow A, Hein AA, Kyaw WM. Unintended consequence: Influenza plunges with public health response to COVID-19 in Singapore. *J Infect* 2020 pp. doi:10.1016/j.jinf.2020.04.035.
2. Kuo SC, Shih SM, Chien LH, Hsiung CA. Collateral benefit of covid-19 control measures on Influenza activity, Taiwan. *Emerg Infect Dis* 2020;26(8) pp. doi:10.3201/eid2608.201192.
3. Sakamoto H, Ishikane M, Ueda P. Seasonal Influenza activity During the SARS-CoV-2 outbreak in Japan. *JAMA* 2020 pp. doi:10.1001/jama.2020.6173.
4. C.V.E. Influenza - 2019 aeasonality. (2019) http://www.saude.sp.gov.br/recursos/cve-centro-de-vigilancia-epidemiologica/areas-de-vigilancia/doencas-de-transmissao-respiratoria/influenza/doc/infoflu_se52_2019.pdf (Accessed April 4 2020.)
5. CDC. CDC 2019-novel coronavirus (2019-nCoV) real-time RT-PCR diagnostic panel. (2020) <https://www.fda.gov/media/134922/download> (Accessed April 2)
6. Fry AM, Chittaganpitch M, Baggett HC, Peret TC, Dare RK, Sawatwong P, et al. The burden of hospitalized lower respiratory tract infection due to respiratory syncytial virus in rural Thailand. *PLoS ONE* 2010;5(11):e15098. doi:10.1371/journal.pone.0015098.
7. Kuypers J, Wright N, Corey L, Morrow R. Detection and quantification of human metapneumovirus in pediatric specimens by real-time RT-PCR. *J Clin Virol* 2005;33(4):299–305. doi:10.1016/j.jcv.2004.11.023.
8. Selvaraju SB, Selvarangan R. Evaluation of three influenza A and B real-time reverse transcription-PCR assays and a new 2009 H1N1 assay for detection of influenza viruses. *J Clin Microbiol* 2010;48(11):3870–5. doi:10.1128/JCM.02464-09.
9. Watanabe AS, Carraro E, Moreira L, Camargo C, Sinohara J, Puerari D, et al. Respiratory virus infections among hospitalized patients with suspected influenza A H1N1 2009 virus during the first pandemic wave in Brazil. *Braz J Infect Dis* 2011;15(3):220–4. doi:10.1016/s1413-8670(11)70179-9.
10. Nascimento MS, Souza AV, Ferreira AV, Rodrigues JC, Abramovici S, Silva Filho LV. High rate of viral identification and coinfections in infants with acute bronchiolitis. *Clinics (Sao Paulo)* 2010;65(11):1133–7. doi:10.1590/s1807-59322010001100014.

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