

An open call for influenza vaccination pending the new wave of COVID-19

Dear Editor,

We have read the study of Yue et al¹ with great interest. They reported influenza coinfection among 307 coronavirus disease 2019 (COVID-19) patients as 57.3%. The study included a period of 12 January to 21 February 2020 in Wuhan, China. On the other hand, we have recently detected the influenza coinfection among COVID-19 patients as 0.54% in Turkey.² This huge difference between the rates of coinfection can be explained by the seasonality of the influenza virus. Our study included a period of 10 March to 10 May.

There have been other reports describing rates of the coinfection. Another study from Wuhan, including the period of 28 January 2020 to 29 February 2020, reported the rate of influenza coinfection among critically ill COVID-19 patients as 49.5%.³ Zhu et al⁴ reported 31.5% viral coinfections among COVID-19 patients, 2.7% being influenza viruses, in their study from 22 January to 2 February 2020. Similar to our low rate of coinfection, two studies from the United

States reported low rates of 0.08% in 16 March to 20 April 2020,⁵ and 0.9% in 3 March to 25 March.⁶

In China, Turkey, and United States, influenza cases began to increase significantly by the first week of December 2019.⁷⁻⁹ It peaked at the first week of January 2020 in China, then decreased to low levels by mid-February 2020. In Turkey, it peaked at third week of January 2020 and sharply declined by the end of February 2020. In the United States, it showed a plateau from December to the first week of March and then declined (Figure 1). Therefore, the studies from the influenza season reported very high rates of coinfection. When the COVID-19 came to Europe and America, the influenza season was almost over and thus the coinfection rates are low¹⁻⁶ (Figure 1).

A very recent research published in the Journal analyzed epidemiological evidence for an association between higher influenza vaccine uptake in the elderly and lower COVID-19 deaths in Italy.¹⁰ They found a moderate to strong correlation ($r = -0.5874$; $n = 21$; $P = .0051$), suggesting that the higher the influenza vaccination rate,

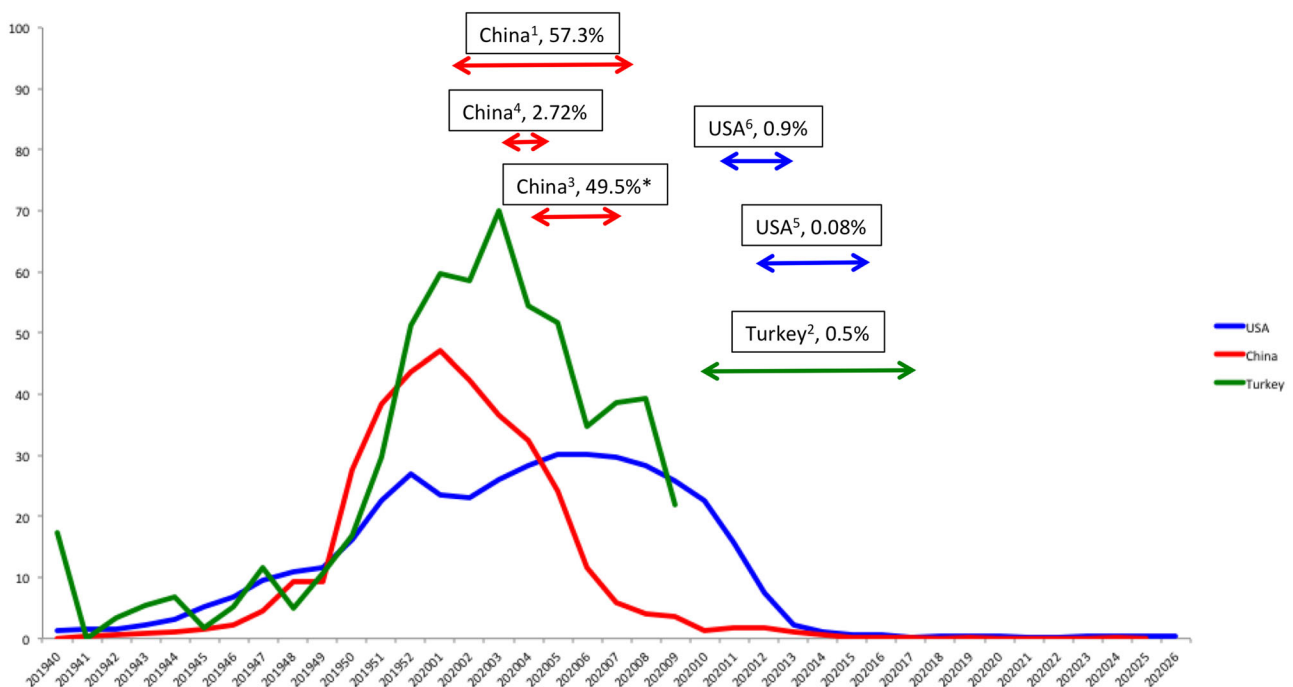


FIGURE 1 The percentage of influenza among patients admitted with influenza-like illness and prevalence of influenza coinfection among COVID-19 Patients. The percentage of influenza among patients admitted with influenza-like illness (y-axis) in weeks of 2019 and 2020 (x-axis) in China (red line), Turkey (green line) and United States (blue lines) and prevalence of influenza coinfection among COVID-19 patients in these countries (arrows and boxes)

the lower the death from COVID-19. There might be several explanations of this association: vaccination against influenza can foster the immunity against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) considering the similarity of the quality of immunity toward both viruses. Besides this cross-reactivity effect, the anti-influenza immune responses can induce bystander immunity, which can be expected to nonspecifically augment immunity against other viral infections including as SARS-CoV-2.¹¹

The higher uptake of influenza vaccination may represent a higher economic group with better general health and thus it may not be a direct function of vaccination. A third explanation is the prevention of influenza coinfection. The data of the mortality of influenza-COVID-19 coinfection compared to monoinfection of either virus is lacking. However, the information about this coinfection is accumulating and there have been case reports in the literature including patients who died (n = 3) and those living ventilator-dependent or still under mechanical ventilation.^{2,12} Most probably the increased severity is due to the combined effects of both viruses on the lungs, which can lead to pneumonia and acute respiratory distress syndrome.

In elderly, both influenza and COVID-19 have higher rates of mortality.^{13,14} Therefore, the impact of prevention of influenza in this fragile group is higher. Metaanalyses report the effectiveness of influenza vaccines in decreasing influenza and also reducing pneumonia- and influenza-related hospitalizations.^{15,16}

Current influenza-COVID-19 coinfection reports suggest that coinfection rates are as high as 57% when influenza is circulating. Besides, influenza vaccine induces immunity against SARS-CoV-2. Therefore, pending the new waves of COVID-19, it is reasonable to recommend influenza vaccination especially for elderly, but most probably, to general population. Countries should have access to enough numbers of influenza vaccines for the coming autumn and the World Health Organization should have a role in emphasizing the critical role of influenza vaccine.

KEYWORDS

coronavirus, disease control, influenza virus, vaccines, vaccine strains, virus classification

Resat Ozaras MD¹ , Prof
 Rasim Cirpin MD², Fellow
 Habibe Duman MD³, Fellow
 Arif Duran MD⁴, Fellow
 Ozgur Arslan MD², Fellow
 Hakan Leblebicioglu MD⁵, Prof

¹Infectious Diseases Department, Medilife Health Group, Istanbul, Turkey

²Radiology Department, Medilife Health Group, Istanbul, Turkey

³Internal Medicine Department, Medilife Health Group, Istanbul, Turkey

⁴Emergency Medicine Department, Medilife Health Group, Istanbul, Turkey

⁵Infectious Diseases Department, Liv Hospital, Samsun, Turkey

Correspondence

Resat Ozaras, MD, Prof, Infectious Diseases Department,
 Medilife Hospital, TR-34524 Beylikdüzü, Istanbul, Turkey.

Email: rozaras@yahoo.com

ORCID

Resat Ozaras  <http://orcid.org/0000-0002-8130-676X>

REFERENCES

1. Yue H, Zhang M, Xing L, et al. The epidemiology and clinical characteristics of co-infection of SARS-CoV-2 and influenza viruses in patients during COVID-19 outbreak. *J Med Virol*. 2020. <https://doi.org/10.1002/jmv.26163>
2. Ozaras R, Cirpin R, Duran A, et al. Influenza and COVID-19 coinfection: report of 6 cases and review of the literature. *J Med Virol*. 2020. <https://doi.org/10.1002/jmv.26125>
3. Ma S, Lai X, Chen Z, Tu S, Qin K. Clinical characteristics of critically ill patients co-infected with SARS-CoV-2 and the influenza virus in Wuhan, China. *Int J Infect Dis*. 2020;96:683-687. <https://doi.org/10.1016/j.ijid.2020.05.068>
4. Zhu X, Ge Y, Wu T, et al. Co-infection with respiratory pathogens among COVID-2019 cases. *Virus Res*. 2020;285:198005. <https://doi.org/10.1016/j.virusres.2020.198005>
5. Nowak MD, Sordillo EM, Gitman MR, Paniz Mondolfi AE. Co-infection in SARS-CoV-2 infected patients: where are influenza virus and rhinovirus/enterovirus? *J Med Virol*. 2020. <https://doi.org/10.1002/jmv.25953>
6. Kim D, Quinn J, Pinsky B, Shah NH, Brown I. Rates of co-infection between SARS-CoV-2 and other respiratory pathogens. *JAMA*. 2020;323(20):2085-2086. <https://doi.org/10.1001/jama.2020.6266>
7. https://www.cdc.gov/flu/weekly/weeklyarchives2019-2020/data/whoAllregt_cl26.html (last accessed July 5, 2020).
8. <https://grip.gov.tr/haftalik-influenza-raporu> (last accessed July 5, 2020).
9. http://www.chinaivdc.cn/cnic/en/Surveillance/WeeklyReport/index_1.htm (last accessed July 5, 2020).
10. Marín-Hernández D, Schwartz RE, Nixon DF. Epidemiological evidence for association between higher influenza vaccine uptake in the elderly and lower COVID-19 deaths in Italy. *J Med Virol*. 2020. <https://doi.org/10.1002/jmv.26120>
11. Salem ML, El-Hennawy D. The possible beneficial adjuvant effect of influenza vaccine to minimize the severity of COVID-19. *Med Hypotheses*. 2020;140:109752. <https://doi.org/10.1016/j.mehy.2020.109752>
12. Konala VM, Adapa S, Naramala S, et al. A case series of patients coinfecting with influenza and COVID-19. *J Investig Med High Impact Case Rep*. 2020;8:2324709620934674. <https://doi.org/10.1177/2324709620934674>
13. Pop-Vicas A, Gravenstein S. Influenza in the elderly: a mini-review. *Gerontology*. 2011;57(5):397-404. <https://doi.org/10.1159/000319033>
14. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395(10229):1054-1062. [https://doi.org/10.1016/S0140-6736\(20\)30566-3](https://doi.org/10.1016/S0140-6736(20)30566-3)
15. Demicheli V, Jefferson T, Di Pietrantonj C, et al. Vaccines for preventing influenza in the elderly. *Cochrane Database Syst Rev*. 2018;2(2):CD004876. <https://doi.org/10.1002/14651858.CD004876>
16. Heo JY, Song JY, Noh JY, et al. Effects of influenza immunization on pneumonia in the elderly. *Hum Vaccin Immunother*. 2018;14(3):744-749. <https://doi.org/10.1080/21645515.2017.1405200>