Published online 2022 September 20.

Editorial

## Influenza and COVID-19 Co-infection

Masoud Mardani 💿<sup>1</sup> and Mohammad Javad Nasiri 💿<sup>1,\*</sup>

<sup>1</sup>Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>\*</sup> Corresponding author: Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: mj.nasiri@hotmail.com

Received 2022 September 13; Accepted 2022 September 13.

Keywords: COVID-19, SARS-CoV-2, Influenza

Since the beginning of the COVID-19 pandemic, there have been concerns about the possibility of an influenza outbreak in the middle of the COVID-19 pandemic, and coinfection with SARS-CoV-2 and Influenza viruses in a single host was not far from expected (1). Patients with simultaneous positive tests for both COVID-19 and influenza were reported recently in the ongoing surge of Omicronassociated COVID-19 cases, which was alarming to health systems (2). A recent study conducted by Pawlowski et al. Analyzed epidemiological data to evaluate trends in COVID-19 and influenza co-infection across the entire United States about trends in SARS-CoV-2 and influenza strain prevalence showed that confirmed co-infections are rare due to lower laboratory testing rates. However, coinfection with SARS-CoV-2 and influenza is not more frequent than expected (3).

Although the COVID-19 and Influenza co-infection rate is low, the importance of such co-infection may complicate the diagnosis, treatment, and prognosis of COVID-19, especially in high-risk individuals like the elderly and children (who have considerably higher rates of co-infection) (4) cannot be ignored (2).

Diagnosing such co-infections could be challenging due to the clinical manifestations and paraclinical similarities between the two infections (5, 6). Also, the dynamic of infection of each pathogen adds to the challenge of COVID-19 diagnosis, especially when the patient may test negative for COVID-19 but positive for other viruses and then turns SARS-COV-2 positive. This leads to COVID-19 under diagnosis, causing a delay in medical treatment (7). The mean incubation and viral shedding periods of influenza viruses are shorter than SARS-CoV-2 virus (8, 9). It is likely that in some patients who have co-infection, the influenza virus is no longer detectable when the SARS-CoV-2 infection is diagnosed, and the time window of co-detectability may be too short of identifying the co-infection (10). The treatment can also be challenging since coinfection can lead to complications and increased virulence and severity of the disease (11). In a systematic review conducted by Shah et al., co-infected patients were treated with antiviral agents, antibacterial drugs, or a combination of both. The antiviral drug of choice for most of the patients was oseltamivir. Moreover, they showed that for effective treatment, it is imperative to conduct proper tests quickly to differentiate between the two viruses or establish co-infection (12).

Likewise, from a public health standpoint, SARS-CoV-2 and influenza virus co-infection combined with variable clinical prognosis poses a greater challenge. A systematic review by Krumbein et al. revealed that a higher case-fatality rate was associated with COVID-19 and other viruses' co-infection (13). This is consistent with other studies showing a positive relation between co-infection and increased mortality risk and severity of the disease in these patients (11, 14). However, there are studies like the systematic review conducted by Guan et al. revealing that COVID-19 and Influenza co-infection did not affect overall mortality or critical outcomes involving shock, being admitted to ICU, or requiring ventilatory support in co-infected patients in comparison to COVID-19 mono-infection and the associations detected from different regions and samples were controversial (15). These contradictory results show the need for further well-designed controlled studies with adjustment of confounding factors like influenza strains, the order of infection, and other concomitant infections and comorbidities.

With the influenza season upon us, exploring the relationship between influenza vaccination and COVID-19 susceptibility is also important. Studies showed that one of the simplest ways to prevent co-infection is to get vaccinated against influenza, especially in the at-risk population (16). Also, studies report more benefits to influenza

Copyright © 2022, Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (http://creativecommons.org/licenses/by-nc/4.0/) which permits copy and redistribute the material just in noncommercial usages, provided the original work is properly cited.

vaccination, such as the significantly lower odds of testing positive for COVID-19 in patients who got an influenza vaccine compared to those who did not receive the vaccine. In addition, in patients who tested positive for COVID-19, those vaccinated against influenza had considerably better clinical outcomes (17, 18).

## Footnotes

Authors' Contribution: All authors contributed equally. Conflict of Interests: None

## References

- Rubin R. What Happens When COVID-19 Collides With Flu Season? JAMA. 2020;324(10):923-5. [PubMed ID: 32818229]. https://doi.org/10.1001/jama.2020.15260.
- Dadashi M, Khaleghnejad S, Abedi Elkhichi P, Goudarzi M, Goudarzi H, Taghavi A, et al. COVID-19 and Influenza Co-infection: A Systematic Review and Meta-Analysis. *Front Med (Lausanne)*. 2021;8:681469.
  [PubMed ID: 34249971]. [PubMed Central ID: PMC8267808]. https://doi.org/10.3389/fmed.2021.681469.
- Pawlowski C, Silvert E, O'Horo JC, Lenehan PJ, Challener D, Gnass E, et al. SARS-CoV-2 and influenza coinfection throughout the COVID-19 pandemic: an assessment of coinfection rates, cohort characteristics, and clinical outcomes. *PNAS Nexus*. 2022;1(3):pgac071. [PubMed ID: 35860600]. [PubMed Central ID: PMC9291226]. https://doi.org/10.1093/pnasnexus/pgac071.
- Kanji JN, Zelyas N, Pabbaraju K, Granger D, Wong A, Murphy SA, et al. Respiratory virus coinfections with severe acute respiratory coronavirus virus 2 (SARS-CoV-2) continue to be rare one year into the coronavirus disease 2019 (COVID-19) pandemic in Alberta, Canada (June 2020-May 2021). *Infect Control Hosp Epidemiol*. 2021:1–4. [PubMed ID: 34866560]. [PubMed Central ID: PMC8692847]. https://doi.org/10.1017/ice.2021.495.
- Osman M, Klopfenstein T, Belfeki N, Gendrin V, Zayet S. A Comparative Systematic Review of COVID-19 and Influenza. *Viruses*. 2021;13(3):452. [PubMed ID: 33802155]. [PubMed Central ID: PMC8001286]. https://doi.org/10.3390/v13030452.
- Kondo Y, Miyazaki S, Yamashita R, Ikeda T. Coinfection with SARS-CoV-2 and influenza A virus. *BMJ Case Rep.* 2020;13(7). e236812. [PubMed ID: 32611659]. [PubMed Central ID: PMC7358105]. https://doi.org/10.1136/bcr-2020-236812.
- Wu X, Cai Y, Huang X, Yu X, Zhao L, Wang F, et al. Co-infection with SARS-CoV-2 and Influenza A Virus in Patient with Pneumonia, China. *Emerg Infect Dis.* 2020;**26**(6):1324–6. [PubMed ID: 32160148]. [PubMed Central ID: PMC7258479]. https://doi.org/10.3201/eid2606.200299.

- Lau LL, Cowling BJ, Fang VJ, Chan KH, Lau EH, Lipsitch M, et al. Viral shedding and clinical illness in naturally acquired influenza virus infections. J Infect Dis. 2010;201(10):1509–16. [PubMed ID: 20377412]. [PubMed Central ID: PMC3060408]. https://doi.org/10.1086/652241.
- Cevik M, Tate M, Lloyd O, Maraolo AE, Schafers J, Ho A. SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and metaanalysis.*Lancet Microbe*. 2021;2(1):e13–22. https://doi.org/10.1016/s2666-5247(20)30172-5.
- Dao TL, Hoang VT, Colson P, Million M, Gautret P. Co-infection of SARS-CoV-2 and influenza viruses: A systematic review and meta-analysis. J Clin Virol Plus. 2021;1(3):100036. [PubMed ID: 35262019]. [PubMed Central ID: PMC8349735]. https://doi.org/10.1016/j.jcvp.2021.100036.
- Alosaimi B, Naeem A, Hamed ME, Alkadi HS, Alanazi T, Al Rehily SS, et al. Influenza co-infection associated with severity and mortality in COVID-19 patients. *Virol J.* 2021;**18**(1):127. [PubMed ID: 34127006]. [PubMed Central ID: PMC8200793]. https://doi.org/10.1186/s12985-021-01594-0.
- Shah MUFA, Sohail A, Jaffry AA, Khurshid M, Nashwan A, Ullah I. Influenza a and COVID-19 Coinfection: A Systematic Review of Cases. Rochester, NY: SSRN; 2022, [cited 2022]. Available from: https://papers. ssrn.com/sol3/papers.cfm?abstract\_id=4077063.
- Krumbein H, Kummel LS, Fragkou PC, Tholken C, Hunerbein BI, Reiter R, et al. Respiratory viral co-infections in patients with COVID-19 and associated outcomes: A systematic review and meta-analysis. *Rev Med Virol.* 2022. e2365. [PubMed ID: 35686619]. [PubMed Central ID: PMC9347814]. https://doi.org/10.1002/rmv.2365.
- Musuuza JS, Watson L, Parmasad V, Putman-Buehler N, Christensen L, Safdar N. Prevalence and outcomes of co-infection and superinfection with SARS-CoV-2 and other pathogens: A systematic review and meta-analysis. *PLoS One.* 2021;**16**(5). e0251170. [PubMed ID: 33956882]. [PubMed Central ID: PMC8101968]. https://doi.org/10.1371/journal.pone.0251170.
- Guan Z, Chen C, Li Y, Yan D, Zhang X, Jiang D, et al. Impact of Coinfection With SARS-CoV-2 and Influenza on Disease Severity: A Systematic Review and Meta-Analysis. *Front Public Health*. 2021;9:773130.
  [PubMed ID: 34957025]. [PubMed Central ID: PMC8703010]. https://doi.org/10.3389/fpubh.2021.773130.
- Ghaznavi H, Shirvaliloo M, Sargazi S, Mohammadghasemipour Z, Shams Z, Hesari Z, et al. SARS-CoV-2 and influenza viruses: Strategies to cope with coinfection and bioinformatics perspective. *Cell Biol Int.* 2022;46(7):1009–20. [PubMed ID: 35322909]. [PubMed Central ID: PMC9083817]. https://doi.org/10.1002/cbin.11800.
- Conlon A, Ashur C, Washer L, Eagle KA, Hofmann Bowman MA. Impact of the influenza vaccine on COVID-19 infection rates and severity. *Am J Infect Control*. 2021;49(6):694–700. [PubMed ID: 33631305]. [PubMed Central ID: PMC7899024]. https://doi.org/10.1016/ji.ajic.2021.02.012.
- Alizadeh N, Tabatabaei FS, Borran M, Dianatkhah M, Azimi A, Forghani SN, et al. Evaluation of the Possible Effect of the Influenza Vaccine on the Severity, Mortality, and Length of Hospitalization among Unvaccinated COVID-19 Patients; An Observational, Cross-Sectional Study. J Pharm Care. 2022;10(1):11–6. https://doi.org/10.18502/jpc.v10i1.9123.