

Influenza and COVID-19 co-infection; a cross-sectional study from northern Iran

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Editorial

Every year, Influenza epidemics occur during the cold season of the year. So far, four Influenza epidemics have been reported: the H1N1 (1918), the H2N2 (1957), the H3N2 (1967), and the H1N1 (2009).¹ During 1918 influenza pandemic was the greatest pandemic of the 20th century with a high death through the world.² There are four types of Influenza viruses: Influenza type A, B, C, and D.³ Influenza type A and B are the most common types which spread in humans routinely and are responsible for seasonal flu epidemics in cold season each year.³ Influenza mortality is determined by the patient's age and the underlying diseases.³

Fever, cough, and rhinitis are the most common flu symptoms.^{4,5} Other respiratory viruses, such as coronaviruses, have caused respiratory infections over the previous 20 years, in addition to the Influenza viruses.³ Coronavirus disease (COVID-19) is an infectious disease caused by the virus strain of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).⁶ Since its appearance, it has caused many devastating effects on health care system and societies.⁷ The transmission and clinical symptoms of Influenza and Covid have some similarities.^{8,9} The most common symptoms of COVID-19 are fever, dry cough, dyspnea, headache, myalgia, and fatigue, similar to Influenza.¹⁰⁻¹² Both of these viruses can be transmitted through respiratory droplets.^{10,11} As a result, social distancing strategies against COVID-19 can also be beneficial in reducing the spread of the Influenza viruses.¹³ Infection with a co-occurring pathogen is referred to as co-infection.¹³ Recent studies reported co-infection with viruses, bacteria, and fungus in hospitalized patients with COVID-19, among them Influenza type A is one of the main viral pathogens associated with COVID-19 as a co-infection.¹⁴

We aimed to study the epidemiology of Influenza and COVID-19 Co-infection in a cross-sectional study. We included 92 participants who suspected to COVID-19 and their swab samples referred to Central HIV Laboratory, Sari in northern of Iran, during autumn, 2021 (which delta variant was dominant in country). The Detection of influenza viruses type A&B and the new coronavirus by multiplex real time kit in form of qualitative diagnosis of covid 19 factor, influenza viruses type A&B are done by the method of probe-based reverse-transcription or Real Time PCR (RT-qPCR).

This reaction is in the form of Multiplex TaqMan assay that can differentiate the product of three named multiplied viruses and one internal control gene with using four different Fluorescence colors. in this test specific signal for SARS-Cov2 virus is read in orange and green channels, influenza A&B in yellow channel and internal endogen control is read in red channel. It is noticeable that in order to detection of SARS-Cov2 virus, oligonucleotide sequences are designed for N and RdRp genes for this virus and M2 gene for influenza A and NP gene for influenza B. Due to ability of most Real time cyclers to read 4 colors, specific probes for both types of influenza are labeled with one color (HEX/JOE/VIC).

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Descriptive results of demographic variables are shown in Table 1. There were 85 (92.3%) individuals with COVID-19 and 20 (21.7%) individuals with COVID-19 and Influenza in the study. Accordingly, the variables of age and hospitalization were significantly associated with patients with COVID-19 and Influenza. Besides, most of patients who positive for both COVID-19 and Influenza (55%) were under 17 years of old ($P < 0.001$). According to our study, there can be a substantial percentage of patients with the co-infection of Influenza and COVID-19 living with Covid throughout the cold season of the year.

Children with flu usually experience severe symptoms. By contrast, COVID-19 is frequently asymptomatic or with minimal symptoms in children.^{15,16} But new variant of covid 19, omicron has different and more clinical symptoms in children and adolescents.¹⁷ Hence, our understanding of the overall burden of Covid disease in children is incomplete.^{18,19} The elderly, people with underlying disease, and people with immunodeficiency are more prone to get the more severe form of both the flu and Covid.²⁰ As a result, these groups of people are of great concern.

Co-infection of respiratory viruses is a source of worry. According to studies, respiratory viruses have been demonstrated to cause severe disease in immunocompromised patients. For instance, co-infection with respiratory syncytial virus and human meta pneumo virus lead to more severe infection in children less than 3 years.²¹ Those with two

viral respiratory diseases had higher hospital admissions and oxygen demand than patients with a viral respiratory infection.²² Another retrospective study on COVID-19 patients, which was held in China demonstrated that microbial co-infection can increase the risk of disease severity in COVID-19 patients.²³ In the systematic review and meta-analyses, four studies with a total number of 3253 patients

were studied which were on the mortality rate of Covid patients with concurrent Influenza infection. These studies reported an increased risk of mortality. Furthermore, patients with Influenza type A had a worse prognosis than those with Influenza type B in the subgroup analysis.²⁴

Table 1 Demographic and characteristics of the patients with COVID-19 and COVID-19 + influenza

Variables	% of total (N)	COVID-19	P-value	COVID-19 + Influenza	P-value
% of total (N)	100(92)	100(85)		100(20)	
Sex					
male %(n)	53.3(49)	53(45)	0.516	65(13)	0.152
female %(n)	46.7(43)	47(40)		35(7)	
Age					
Adolescent %(n)	25(23)	23.5(20)	0.004	55(11)	<0.001
Young %(n)	25(23)	25.9(22)		20(4)	
Middle-aged %(n)	27.2(25)	29.4(25)		10(2)	
Old %(n)	22.8(21)	21.2(18)		15(3)	
Hospitalization					
Hospitalized %(n)	80.4(74)	82.4(70)	0.054	95(19)	0.012
Outpatient %(n)	19.6(18)	17.6(15)		5(1)	

Note:Age: <17 Adolescent, 17-48 young, 49-69 middle-aged, >69 old. p values resulted from Chi-square tests.

Conclusion

The co-infection of COVID-19 and Influenza viruses is predictable, especially during cold season of the year and in younger age. Considering the fact that Influenza viruses and COVID-19 share many similarities in terms of how they spread and clinical manifestations, we should investigate management strategies in the early diagnosis and treatment of these viral infections.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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