Brief Original Article | Iran J Med Microbiol. 2023; 17(1): 112-116

10.30699/ijmm.17.1.112

Iranian Journal of Medical Microbiology | ISSN:2345-4342

Frequency of Influenza Infection in Symptomatic Patients Suspected of Having COVID-19

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ABSTRACT

Background and Aim: About one billion people have infected with the influenza A virus each year. The continued spread of SARS-CoV-2 especially in the winter season may increase the co-infection of SARS-CoV-2 with other respiratory viruses, which may worsen the severity of the disease and increase mortality. In respiratory infections, primary identification of the underlying source of infection is necessitated to find appropriate treatment and to improve individual patient management**.** Therefore, it is essential to accurately and immediately diagnose these two diseases. This study aimed to assess the frequency of influenza A, influenza B, and COVID-19 among individuals suspected of having a respiratory infection.

Materials and Methods: In this study, 861 patients presenting from 19 November 2021 to 18 January 2022 in Kavosh medical laboratory (Golestan, Gorgan, Iran) with suspected viral respiratory tract infection who underwent RT-PCR testing for SARS-CoV-2/influenza were included. Data analysis was performed using appropriate descriptive statistics.

Results and Conclusions: A total of 184 patients were confirmed with COVID-19/influenza. 90 patients with COVID-19 (48.9%) and 94 patients (51.1%) with influenza (92 with influenza A and 2 with influenza B) were collected in the present study. Influenza/COVID-19 ratio was 1/0.95. Two cases of co-infection with COVID-19/influenza were observed. During the influenza season, influenza/COVID-19 ratio in patients with suspected respiratory infection was 1/0.95. Patients with influenza were significantly younger than patients with COVID-19 and the proportion of males and females was not meaningfully different in the COVID-19 and influenza patients.

Keywords: COVID-19, influenza viruses, Seasonal influenza, Respiratory infection

Received: 2022/06/14; **Accepted**: 2022/10/10; **Published Online:** 2023/01/20

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Pourmomen M, Younesian O, Hosseinzadeh S, Hosseini Alarzi S S, Pourmomen M, Joshaghani H. Frequency of Influenza Infection in Symptomatic Patients Suspected of Having COVID-19. Iran J Med Microbiol. 2023; 17(1):112-16.

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1. Introduction

Seasonal influenza caused by the Orthomyxoviridae family of influenza viruses is an acute respiratory infection that is often characterized by fever, headache, cough, myalgia, fatigue, and the feeling of

malaise. The Orthomyxoviridae family classifies into three different types; influenza A, influenza B, and influenza C **(1)**.

Coronavirus disease 2019 (COVID-19) the first pandemic caused by the newest member of the family of coronaviruses (SARS-CoV-2) is an acute respiratory syndrome with nonspecific symptoms including fever and cough. It is often clinically similar to other respiratory infections such as seasonal influenza. COVID-19 and seasonal influenza have common characteristics ranging from mild symptoms to acute respiratory distress syndrome and death **(2)**. The continued spread of SARS-CoV-2 especially in the winter season may increase the co-infection of SARS-CoV-2 with other respiratory viruses, which may worsen the severity of the disease and increase mortality **(3)**. In respiratory infections, primary identification of the underlying source of infection is necessitated to find appropriate treatment and to improve individual patient management **(4)**. Therefore, now in the influenza season and with difficulty in clinically distinguishing between influenza and COVID-19, it is essential to accurately and immediately diagnose these two diseases. Nucleic acid detection in sputum samples or nasal/throat swabs and serological tests can be used to diagnose both COVID-19 and influenza **(5)**. Here we assessed the frequency of influenza A, influenza B, and COVID-19 in people with symptoms of a respiratory infection.

2. Materials and Methods

In this study, 861 patients presenting from 19 November 2021 to 18 January 2022 in Kavosh medical laboratory (Golestan, Gorgan, Iran) with suspected viral respiratory tract infection who underwent RT-PCR testing for SARS-CoV-2/influenza were included. Exclusion criteria were **(1)** patients comorbid with other infections such as individuals who were infected with avian influenza; **(2)** Patients who have received antiviral drugs for SARS-CoV-2 or influenza. Age and gender were recorded. According to the age distribution in this study, five age categories were assessed: ≤10 years, 11–30 years, 31–50 years, 51–70 years, and 70–90 years **(6)**.

After extracting the RNA from the nasal swab, all the samples were assayed in duplicates by BIOER Real-Time Thermocycler System using the Pishtaz Teb Diagnostic SARS-FLU PLUS OneStep RT-PCR Kit. FAM channel, ROX, VIC/HEX, and CY5 channel were selected for detection of coronavirus, influenza A virus, influenza B virus, and internal control, respectively. The mixture of primer and probe in this kit is capable of identifying the ORF1ab region of the coronavirus, the M1 region of the influenza A virus gene, and the NS1 region of the influenza B virus gene. The clinical Sensitivity and specificity of this kit were 100% and 100%, respectively.

Groups of patients were built according to RT-PCR-based virus detection: a COVID-19 group with RT-PCR positive for SARS-CoV-2 and an influenza group with RT-PCR positive for influenza A or B. Data analysis was performed using appropriate descriptive statistics in SPSS16. Data were expressed as mean ± standard deviation (SD), Median with (IQR), or numbers and percentages. A T-test was used to compare the two groups. A P-value < 0.05 was considered significant.

3. Results and Discussion

A total of 184 patients were confirmed with COVID-19/influenza. 90 patients with COVID-19 (48.9%), and 94 patients (51.1%) with influenza (92 with influenza A and 2 with influenza B) were collected in the present study. Influenza/COVID-19 ratio was 1/0.95. Two cases of co-infection with COVID-19/influenza were observed. The COVID-19 group included 44 (48.9%) males and 46 (51.1%) females, with ages ranging from 1 to 86 years (44 ± 16 years). The influenza group included 50 (53.2%) men and 44 (46.8%) women, with ages ranging from 1 to 76 years (32 ± 17 years). The proportion of males and females was not significantly different in the COVID-19 and influenza groups. Patients with influenza were significantly younger than patients with COVID-19 and the proportions of patients in the age categories ≤10 and 11–30 were meaningfully greater for influenza while most patients in the COVID-19 group were in the age categories of 31–50 years. The female/male ratio in the age category ≤10 years was 1/2 in influenza patients. There was a statistically significant difference in age between the COVID-19 and influenza groups (p <0·0001). The summary baseline characteristics of the participants are presented in Table 1.

In this study, our results showed that of the 861 patients with suspected viral respiratory tract infection during the influenza season, 94 patients had seasonal influenza and 90 had COVID-19, and the influenza/COVID-19 ratio was 1/0.95. In 94 influenza patients, 92 patients with influenza A and only 2 patients with influenza B were diagnosed. Influenza viruses A and B result in seasonal influenza epidemics and thousands of deaths each year worldwide. Influenza virus A can cause pandemics because of transmission from humans, pigs, horses, and migrating birds, while Influenza virus B is not involved in pandemics due to human-to-human transmission and the absence of another host **(1)**. Various studies have reported that the influenza A virus is more prevalent than other types of influenza virus **(7, 8)**, and the influenza B virus is responsible for about a

quarter of the yearly influenza burden (9). Influenza B viruses result in fewer and smaller epidemics, which can be due to the circulation of the Influenza B virus only in humans, lack of animal reservoir, and slower evolution of hemagglutinin (10).

Table 1. Baseline characteristics of the patients included in the present study

	COVID-19 n(90)	Influenza n(94)	P-value
Sex, no. (%)			
Female	46 (51.1)	44 (46.8)	>0.05
Male	44 (48.9)	50 (53.2)	
Age (years)			
Mean (SD)	44 ± 16	32 ± 17	
Median (IQR)	41(34 to 53)	30(23 to 38)	<0·0001*
Range	1 to 86	1 to 76	
Age category, years, no. (%)			
≤10	1(1.1)	12(13.5)	
11–30	12(13.3)	34(38.2)	
31–50	53(58.9)	29(32.6)	<0·0001*
51–70	17(18.9)	12(13.5)	
70–90	7(7.8)	2(2.2)	

IQR interquartile range, n; number, *SD;* standard deviation. *Significant group difference at $p < 0.05$. Data were expressed as median with IQR, mean ± SD, or numbers and percentages.

The continued spread of SARS-CoV-2 especially in the winter season may increase the co-infection of SARS-CoV-2 with other respiratory viruses, which may worsen the severity of the disease and increase mortality (3). The results of a meta-analysis of 30 studies in patients with SARS-CoV-2 infection showed that 7% of hospitalized patients had bacterial co-infections with SARS-CoV-2, and only 3% had viral coinfections with respiratory syncytial virus and influenza A virus (11). About one billion people have infected with the influenza A virus each year, so the virus can cause a co-infection with the SARS-CoV-2 during the influenza season. Previous studies have reported a few cases of co-infection with SARS-CoV-2, and influenza A virus (12). In our study, two cases of co-infection with these viruses were observed among 184 patients with positive RT-PCR testing for SARS-CoV-2/influenza.

Our results showed that the proportion of males and females was not meaningfully different in the COVID-19 and influenza patients. A study conducted on patients with COVID-19 and seasonal influenza at the University Medical Center Hamburg-Eppendorf reported that COVID-19 patients were younger than influenza patients and most of COVID-19 and influenza patients were men (13). Also in a study in China, COVID-19 patients were younger than influenza patients, but there was no significant difference in the ratio of males and females in the two diseases (14). Other studies found that there was no significant difference in age or sex between influenza and the COVID-19 group (15). Our study showed that patients with influenza were significantly younger than patients with COVID-19 and the proportions of patients in the age categories ≤10 and 11–30 were meaningfully greater for influenza. Our observation that seasonal influenza patients are younger than patients with SARS-CoV-2 infection is inconsistent with previous studies. This difference in study results may be due to the sample size.

Many studies have been performed on Sex differences in COVID-19 epidemiology. Although these studies did not show a sex difference in COVID-19 infection, the severity and mortality of COVID-19 were higher in male patients (16). These differences can be due to higher levels of angiotensin-converting enzyme (ACE) 2 and the cellular serine protease TMPRSS2 in males, as well as hormonal influences on the immune responses to viruses (17). However, a study of COVID-19 sex-disaggregated data from 133 countries found that women had less access to health care due to social norms and financial or non-financial barriers, which could affect female's testing

for COVID-19, and in countries where there is more discrimination against women, the difference in the incidence and mortality of COVID-19 is greater among male and female **(18)**.

In our study, the female/male ratio at the age category ≤10 years was 1/2 in influenza patients. In influenza infection, influenza A virus exposure is often higher in males, however, in females, fatality from exposure to the pathogenic influenza A virus is higher. Because boys are more active than girls, they are more exposed to environmental pathogens through touching contaminated surfaces or close contact with infected persons. The immunity of young children is relatively lower than that of young adults and boys had a weaker immune response to influenza infections than girls **(19)**.

4. Conclusion

In summary, this study assesses the frequency of influenza A, influenza B, and COVID-19 in patients suspected of viral respiratory tract infection during the influenza season. Influenza/COVID-19 ratio was 1/0.95. Patients with influenza were significantly younger than patients with COVID-19 and the proportion of males and females was not meaningfully different in the COVID-19 and influenza patients.

Acknowledgment

The authors would like to thank the Kavosh medical laboratory for its financial support.

Funding

No funds, grants, or other support were received.

Conflict of Interest

The authors declare no competing interests.

Availability of Data and Materials

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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