

Prevalence of influenza co-infection in a real-world cohort of COVID-19 patients in the U.S.

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Prevalence of SARS-CoV-2 and influenza virus co-infection was low



We used **electronic health records (EHR)** to evaluate SARS-CoV-2 and influenza virus **co-infection** in U.S. patients



Co-infection was **rare**, even in **hospitalized patients**, though broader influenza circulation was low this season



Hospitalized patients with co-infection had a **higher likelihood of respiratory failure** and other complications

INTRODUCTION

- Since January 2020, over 40 million people have been infected with SARS-CoV-2 in the U.S. alone.¹ While COVID-19, the disease caused by SARS-CoV-2 infection, carries serious morbidity and mortality², the potential for co-infection with other respiratory infections, such as influenza virus, remains unclear
- In this study, we aimed to:
 - (1) estimate co-infection prevalence of SARS-CoV-2 and influenza virus
 - (2) compare demographics and clinical outcomes of co-infected patients to those of SARS-CoV-2 singly-infected patients using U.S. electronic health records (EHR)

METHODS

- Patients with diagnosed COVID-19 between February 2020 and January 2021 were identified from the Optum de-identified COVID-19 EHR database
 - COVID-19 diagnosis defined as positive diagnostic test (e.g. molecular or antigen test) or ICD diagnostic code of U07.1 or U07.2, or a B97.29 diagnostic code with no negative diagnostic test within 14 days
 - In this study, the terms 'SARS-CoV-2-infected' or 'COVID-19 patients' refer to patients with either suspected or confirmed SARS-CoV-2 infection
- A subset of COVID-19 hospitalized patients was also identified, comprising patients hospitalized up to 7 days before and 21 days after COVID-19 diagnosis date who spent at least 1 night in hospital (emergency room or inpatient visits)
- The incidence of influenza virus co-infection (defined as influenza diagnosis, lab confirmed or ICD code, within 10 days of COVID-19 diagnosis) was determined for all COVID-19 patients and for the subset of hospitalized COVID-19 patients
 - A sensitivity analysis using only positive diagnostic tests to define influenza cases was also conducted, to understand confirmed influenza cases and provide a potential lower bound to the co-infection proportion

RESULTS

- Among all COVID-19 patients identified from the database (n=549,532), 1,794 patients (0.3%) were co-infected with influenza virus (Table 1)
- Of 80,192 hospitalized patients with COVID-19 identified, 242 patients (0.3%) were co-infected with influenza virus
- In the sensitivity analysis, 0.1% of all COVID-19 patients and 0.2% of hospitalized COVID-19 patients had co-infection with influenza virus
- Baseline characteristics were generally comparable between co-infected and singly-infected patients; no meaningful differences were observed (Table 2)
- In hospitalized patients, those with influenza virus co-infection had significantly higher rates of respiratory failure and pneumonia than those with COVID-19 only (Table 3)

Table 1. Prevalence of influenza virus co-infection among SARS-CoV-2-infected patients, overall and hospitalized

	Cohort	Total SARS-CoV-2-infected patients, n	Patients with influenza co-infection, n (%)
Original analysis	Overall	549,532	1,794 (0.3%)
	Hospitalized	80,192	242 (0.3%)
Sensitivity analysis*	Overall	549,532	809 (0.1%)
	Hospitalized	80,192	124 (0.2%)

*Sensitivity analysis using only positive diagnostic tests to define influenza cases

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Table 2. Patient characteristics of overall SARS-CoV-2-infected patients and patients co-infected with influenza virus

	Overall		Hospitalized	
	SARS-CoV-2-infected patients (n=549,532)	Influenza co-infection patients (n=1,794)	SARS-CoV-2-infected patients (n=80,192)	Influenza co-infection patients (n=242)
Mean age (SD)	45.02 (20.01)	43.95 (19.50)	56.80 (18.97)	57.01 (18.32)
Age, n (%)				
<18	44,849 (8.2)	147 (8.2)	1,723 (2.1)	2 (0.8)
18–29	92,642 (16.9)	338 (18.8)	6,214 (7.7)	18 (7.4)
30–39	82,834 (15.1)	269 (15.0)	7,385 (9.2)	28 (11.6)
40–49	82,021 (14.9)	296 (16.5)	8,868 (11.1)	31 (12.8)
50–64	136,839 (24.9)	421 (23.5)	21,279 (26.5)	62 (25.6)
65–74	58,888 (10.7)	188 (10.5)	15,323 (19.1)	45 (18.6)
75–84	33,390 (6.1)	89 (5.0)	11,934 (14.9)	38 (15.7)
>85	6,509 (1.2)	16 (0.9)	2,685 (3.3)	6 (2.5)
Missing	11,560 (2.1)	30 (1.7)	4,781 (6.0)	12 (5.0)
Sex, n (%)				
Female	304,869 (55.5)	908 (50.6)	40,079 (50.0)	123 (50.8)
Missing	576 (0.1)	4 (0.2)	48 (0.1)	1 (0.4)
Region, n (%)				
Midwest	260,030 (47.3)	888 (49.5)	31,068 (38.7)	82 (33.9)
Northeast	132,281 (24.1)	195 (10.9)	20,752 (25.9)	45 (18.6)
South	100,783 (18.3)	549 (30.6)	19,842 (24.7)	84 (34.7)
West	37,217 (6.8)	99 (5.5)	5,930 (7.4)	25 (10.3)
Missing	19,221 (3.5)	63 (3.5)	2,600 (3.2)	6 (2.5)
BMI category*, n (%)				
Normal	60,179 (11.0)	172 (9.6)	9,944 (12.4)	19 (7.9)
Obese	117,277 (21.3)	420 (23.4)	25,311 (31.6)	69 (28.5)
Overweight	74,611 (13.6)	236 (13.2)	14,240 (17.8)	37 (15.3)
Underweight	8,151 (1.5)	18 (1.0)	1,219 (1.5)	1 (0.4)
Missing	289,314 (52.6)	948 (52.8)	29,478 (36.8)	116 (47.9)
Other characteristics, n (%)				
Asthma	45,766 (8.3)	159 (8.9)	8,574 (10.7)	24 (9.9)
Chronic lung disease	81,078 (14.8)	264 (14.7)	20,231 (25.2)	56 (23.1)
Heart disease	61,032 (11.1)	189 (10.5)	21,326 (26.6)	78 (32.2)
Blood disorders	81,280 (14.8)	217 (12.1)	26,534 (33.1)	76 (31.4)
Endocrine disorders	120,516 (21.9)	376 (21.0)	32,217 (40.2)	102 (42.1)
Kidney disorders	35,491 (6.5)	99 (5.5)	14,229 (17.7)	43 (17.8)
Liver disorders	16,936 (3.1)	49 (2.7)	4,390 (5.5)	14 (5.8)
Metabolic disorders	180,161 (32.8)	572 (31.9)	47,893 (59.7)	152 (62.8)
Extreme obesity	25,966 (4.7)	92 (5.1)	6,906 (8.6)	24 (9.9)
Pregnancy	13,052 (2.4)	38 (2.1)	3,470 (4.3)	7 (2.9)
Mean CCI (SD)	0.89 (1.81)	0.80 (1.64)	1.92 (2.47)	1.88 (2.29)

*Normal: 18.5 to <25; obese: >30; overweight: 25 to <30; underweight: <18.5. CCI, Charlson comorbidity index

Table 3. Comparison of clinical outcomes among hospitalized SARS-CoV-2-infected patients, overall and subset to patients co-infected with influenza virus

n (%)	SARS-CoV-2-infected patients (n=80,192)	Influenza co-infection patients (n=242)	p-value
Mortality	10,913 (13.6)	32 (13.2)	0.936
Any ventilation	12,103 (15.1)	45 (18.6)	0.153
Invasive ventilation	7,840 (9.8)	31 (12.8)	0.140
Intensive care unit	18,486 (23.1)	66 (27.3)	0.139
Respiratory failure	37,370 (46.6)	136 (56.2)	0.003
Pneumonia	47,246 (58.9)	169 (69.8)	0.001
Bacterial pneumonia	5,582 (7.0)	23 (9.5)	0.154
Sepsis	16,046 (20.0)	55 (22.7)	0.330

LIMITATIONS

- Low incidence of circulating influenza during the study period³
- Study was limited to patients who sought care, leading to potential missing data bias
- No comparator cohort; data on non-COVID-19 patients were unavailable, so it was not possible to assess whether the risk of influenza was higher in COVID-19 patients versus non-COVID-19 patients

CONCLUSIONS

- Co-infection with influenza virus among SARS-CoV-2-infected patients was rare, although this may have been affected by the low incidence of influenza during the study period
- Among hospitalized patients, co-infected patients had a significantly higher likelihood of respiratory failure and pneumonia than singly-infected patients, but there was no significant difference in mortality
- Future studies when influenza circulation is high are needed to better understand co-infection