DOI: 10.1002/jmv.26710

LETTER TO THE EDITOR

JOURNAL OF MEDICAL VIROLOGY WILEY

Comparison of COVID-19 and influenza in adult patients: Neurological symptoms input

To the Editor,

We have read with interest the article of Zhang et al.[1] entitled "Differentiation of COVID-19 from seasonal influenza: A multicenter comparative study" which compare the clinical features and outcomes of hospitalized coronavirus disease 2019 (COVID-19) patients ($n = 211$) with influenza patients ($n = 115$). Patients with influenza exhibited higher proportions of cough, expectoration, chest pain, dyspnea, and vomiting than patients with COVID-19 ($p < .05$). Compared to patients with COVID-19, hospitalized influenza patients were older and the incidence rates of comorbidities including cardiovascular diseases (hypertension and coronary heart disease) were significantly higher. In contrast, comorbidities such as bronchitis and immunocompromised conditions were significantly more common in COVID-19 compared to influenza patients. In this study, patients with influenza developed mild-to-moderate symptoms upon hospital admission, but none of the severe or fatal cases was recorded. By contrast, more than a fifth of patients in the COVID-19 cohort was later transferred to the intensive care unit (ICU).

We have recently published a retrospective and observational study in *Nord Franche-Comté* Hospital comparing clinical features and outcomes of mild-to-moderate forms of COVID-19 and seasonal influenza[2]. Between February 26th and March 14th, 2020, we enrolled 124 adult patients (≥18 years) with confirmed COVID-19 ($n = 70$) or confirmed influenza ($n = 54$) who consulted ($n = 59/124$) or were hospitalized ($n = 65/124$) in our hospital.

Comparing the article of Zhang et al.,[1] we noticed similar findings concerning the symptoms: patients with influenza presented more often fever ≥38 (92.6% vs. 75.7%; $p = .042$), dyspnea (59.3% vs. 34.3%; $p = .007$), expectoration (51.9% vs. 28.6%; $p = .006$), and vomiting (22.2% vs. 2.8%; $p = .001$) than patients with COVID-19; however, no significant difference was found about chest pain (25.7% vs. 18.5%; $p = .391$) and fatigue (92.9% vs. 87%; $p = .36$).

Patients with COVID-19 described more often neurological symptoms such as headache (44.3% vs. 13%, $p = .001$), anosmia (52.9% vs. 16.7%; $p < .001$), and dysgeusia (38.6% vs. 20.4%; $p < .001$), these data have not been analyzed in the review of Zhang et al.[1]

In our study, no significant differences were found in age, sex, and the different comorbidities between the two groups (Table 1). However, the Charlson comorbidity index was lower in patients with COVID-19 than patients with influenza A/B (2 [±2.5] versus 3 [±2.4]; $p = .003$).

Hospitalization and clinical aggravation appeared later in COVID-19 than in influenza, respectively: patients were hospitalized on Day 7 (±3) versus 5 (±2) ($p = .038$), patients had a respiratory rate ≥22/min on Day 9 (±0.8) versus 5 (±1.3) ($p < .001$), and patients were admitted in an ICU on Day 10 (±2.7) versus 7 (±2.4) ($p < .004$).

In contrast to the study of Zhang et al.,[1] there were no statistical differences about in-hospital mortality between patients with influenza or COVID-19 which was lower than 10% in both cases ($p = 1$). There was also no significant difference in the evolution of the two diseases (duration of hospitalization, oxygen therapy requirement, and invasive mechanical ventilation).

To conclude, we describe similar results as reported by Zhang et al.[1] about the comparison between COVID-19 and influenza, especially about clinical features. However, no significant differences were found between comorbidities and the outcome. Actually, most reports so far put the new loss of taste or smell to neurological symptoms instead of rhinolaryngological symptoms.[3] We have noticed that neurological symptoms are clearly more noticeable in COVID-19, especially anosmia, which is also described in another French study.[2,4] Unfortunately, in the review of Zhang et al.,[1] the authors did not emphasize the differences and similarities between the two viruses regarding neurological signs. This can help clinicians when dealing with cases of influenza-like illnesses during the period of co-circulation of influenza and severe acute respiratory syndrome coronavirus 2.

ACKNOWLEDGMENTS

The authors would like to thank all patients involved in the study and especially Dr. Hajer Zahra for her help.

AUTHOR CONTRIBUTIONS

Souheil Zayet, N'dri Juliette Kadiane-Oussou, and Timothée Klopfenstein collected the epidemiological and clinical data and processed statistical data. Souheil Zayet and Timothée Klopfenstein drafted the manuscript. Lynda Toko, Pierre-Yves Royer, and Vincent Gendrin revised the final manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

Due to the retrospective nature of the study, the Ethics Committee of Nord Franche-Comté Hospital determined that patient consent was not required. The authors make sure to keep patient data confidential and compliance with the Declaration of Helsinki.

TABLE 1 Characteristics, clinical symptoms, and outcomes with COVID-19 or seasonal influenza

		SARS-CoV-2 (*n* = 70)	Influenza (*n* = 54)	*p*
Demographics and baseline characteristics				
Age (y) (mean, extremes, *SD*)		56.7 (19–96) ±19.3	61.3 (25–98) ± 18.8	.176
Sex (number, %)				
Male	29 (41.4)	17 (31.5)	.192	
Healthcare worker (number, %)		22 (31.4)	3 (5.6)	**<.001**
Underlying diseases (number, %)				
Current smoking	10 (14.3)	11 (20.4)	.359	
Heart failure		4 (5.7)	2 (3.7)	0.696
Others cardiovascular diseases[a]		25 (35.7)	23 (42.6)	0.199
COPD or asthma		11 (15.7)	9 (16.7)	0.714
Immunosuppression[b]		3 (4.3)	3 (5.6)	0.206
Diabetes mellitus		10 (14.3)	15 (27.8)	0.074
Malignancy		3 (4.3)	7 (13)	0.101
Charlson comorbidity index (mean, extremes, *SD*)		1.7 (0–10) ± 2.5	3 (0–8) ± 2.4	**.003**
Symptoms statistically more frequents in the group COVID-19				
Headache (number, %, [95% CI])				
Frontal		18 (25.7, [15.8–37.1])	5 (9.3, [1.9–16.7])	**.021**
Retro-orbital or temporal		13 (18.6, [10–27])	2 (3.7, [0–9.3])	**.013**
Dysgeusia (number, %, [95% CI])		34 (48.6, [37.1–61.4])	11 (20.4, [11.1–31.5])	**.001**
Anosmia (number, %, [95% CI])		37 (52.9, [40.4–64.3])	9 (16.7, [7.4–27.8])	**<.001**
Diarrhea (number, %, [95% CI])		28 (40, [28.6–51.4])	11 (20.4, [11.1–31.5])	**.021**
Crackling sounds heard on pulmonary auscultation (number, %, [95% CI])		27 (38.6, [27.1–50])	11 (20.4, [9.3–31.5])	**.032**
Symptoms statistically more frequents in the group influenza				
Fever ≥38 (objective) (number, %, [95% CI])		53 (75.7, [65.8–85.7])	50 (92.6, [85.2–98.1])	**.042**
Sputum production/expectoration (number, %, [95% CI])		20 (28.6, [18.6–38.6])	28 (51.9, [38.9–64.8])	**.010**
Sneezing (number, %, [95% CI])		13 (18.6, [10–28.6])	25 (46.3, [33.3–59.3])	**.001**
Dyspnea/shortness of breath (number, %, [95% CI])		24 (34.3, [22.9–45.7])	32 (59.3, [46.3–72.2])	**.007**
Sore throat (number, %, [95% CI])		14 (20, [11.4–30])	24 (44.4, [29.6–57.4])	**.006**
Conjunctival hyperemia (number, %, [95% CI])		3 (4.3, [0–10])	16 (29.6, [18.5–42.6])	**<.001**
Tearing (number, %, [95% CI])		4 (5.7, [1.4–11.4])	13 (24.1, [13–37])	**.004**
Vomiting (number, %, [95% CI])		2 (2.8, [0–7.1])	12 (22.2, [13–33.3])	**.001**
Rhonchi sounds heard on pulmonary auscultation (number, %, [95% CI])		1 (1.4, [0–4.3])	9 (16.7, [5.6–27.8])	**.002**
Symptoms with no significant difference				
Fatigue (number, [%])		65 (92.9)	47 (87)	.362
Myalgia (number, [%])		41 (58.6)	38 (70.4)	.192
Chest pain (number, [%])		18 (25.7)	10 (18.5)	.391
Hemoptysis (number, [%])		6 (8.6)	3 (5.6)	.730
Rhinorrhea (number, [%])		34 (48.6)	30 (55.6)	.4
Nasal obstruction (number, [%])		13 (18.6)	19 (35.2)	.08

TABLE 1 (Continued)

	SARS-CoV-2 ($n = 70$)	Influenza ($n = 54$)	p
Nausea (number, (%))	22 (31.4)	11 (20.4)	.219
Abdominal pain (number, [%])	14 (20)	9 (16.7)	.816
Clinical outcomes			
Hospitalization (number, %)	33 (47.1)	32 (59.3)	.207
Duration of hospitalization (days) (mean, extremes, *SD*)	6.9 (1–21) ± 5.8	7.6 (1–22) ± 6.9	.667
Oxygen therapy (number, %)	23 (32.9)	20 (37)	.705
Patients admitted or transferred to ICU (number, %)	11 (15.7)	5 (9.3)	.499
Days from conventional hospitalization to ICU (mean, extremes, *SD*)	3.1 (1–13) ± 1.7	2.4 (1–6) ± 2.4	.458
IMV (number, %)	11 (15.7)	5 (9.3)	.499
Duration of hospitalization in ICU (mean, extremes, *SD*)	7.9 (2–21) ± 6.6	8.2 (2–12) ± 3.8	.924
Death	4 (5.7)	5 (9.3)	1

Note: Bold values indicate $p < .05$.

Abbreviations: 95% CI, 95% confidence interval; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; ICU, intensive care unit; IMV, invasive mechanical ventilation; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a]Defined by: Cardiac failure, cardiac arrhythmia, coronary heart disease, stroke, peripheral arterial obstructive disease, and thromboembolic disease.

[b]Defined by: Transplantation, cirrhosis, long-term steroids therapy, immunomodulators treatments, and human immunodeficiency virus.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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