

ORIGINAL ARTICLE

Evaluation of the Clinical Parameters of Patients with Influenza and Covid-19 using Blood Test Data

MUHAMMAD JAVED AKHTAR¹, ALEENA JAVED²

¹MBBS, MCPS Pulmonology, MCPS Community Medicine, MCPS Forensic Medicine Nishtar Medical College and Hospital, Multan

²MBBS Research Assistant, USA

Correspondence to: Muhammad Javed Akhtar, Email: dr.raojavedakhtar@yahoo.com

ABSTRACT

Objective: The characteristics of the novel corona virus ailment 2019 (COVID-19) vs influenza were not described, such as blood test data. As a result, we compared the diagnostic features of COVID-19 and flu, along with blood test data.

Materials and Methods: A cross-sectional study was conducted at Nishtar Hospital, Multan. We enrolled individuals diagnosed with COVID-19 between January 1, 2020, and December 31, 2020, and had they undergo blood tests. In comparing, we enlisted an equal percentage of participants who'd been identified with flu that had blood tests.

Results: During the course of the study, 228 people were identified of COVID-19 (men:women ratio, 123 [54.0 percent]:105 [46.0 percent]; age, 54.68 18.98 years). We also enlisted the help of 228 flu clients (male:female, 129 [56.6 percent]:99 [43.4 percent]; age, 69.6 21.25 years). Clients with COVID-19 had a vastly greater age range of 15 to 70 years (vs. 71 years), respiratory problems, as well as ennu than someone with flu. Nevertheless, discomfort, a body temperature greater than 38.1oC, as well as a white blood cell count greater than 9000/L were far more prevalent in flu patient populations.

Conclusions: Our findings are helpful in distinguishing COVID-19 from flu, so they'll be remarkably helpful for future practice as we understand to interoperate with COVID-19.

Keywords: Medical aspects, COVID-19, influenza, Critical respiratory syndrome coronavirus-2, blood test, malaise, respiratory problems, leukocytosis, vomiting.

INTRODUCTION

A sequence of pneumonias with unidentified etiology and diagnostic discussions which imitate bacterial meningitis had been announced in December 2019 (1–3). The virus outbreak of a novel corona virus disease (COVID-19) poses a danger to humanity. Numerous specific instance works have been reported on the commonalities among COVID-19 as well as influenza (4–7), and yet illness display persists to differ among persons. Signs distinct out of those seen in previous virus infection also were noted. There have been indications of individuals diagnosed with considerable decrease of flavor and aroma, for instance (8,9). The diverse variety of disclosed characteristics is thought to reflect effects on non-respiratory processes, as well as they suggest that indications may well be noticed in people with the disease who do not have obvious breathing problems (10).

Prior to 2019, flu seems to have been a prevalent disease that caused fever, particularly during different seasons outbreaks. Even so, distinguishing seasonal flu from COVID-19 is hard because much emphasis is given on identifying the other situation. Several analyses actually linked the burdens of COVID-19 as well as flu (11–14). In a past analysis, clients to COVID-19 had markedly so much alopecia (53 percent vs. 17 percent, P 0.001), dysgeusia (49 percent vs. 20 percent, P 0.001), diarrhoea (40 percent vs. 20 percent, P 0.021), frontal migraine (26 percent vs. 9 percent, P 0.021), and reciprocal tinkling noises (24 percent vs. 9 percent, P 0.034). Sputum creation, on the other hand (52 percent vs. 29 percent, P 14 0.010), dyspnea (59% vs. 34%, 0.007), sore throat (44% vs. 20%, P0.006), conjunctival hyperemia (30% vs. 4%, P<0.001), tearing (24% vs. 6%, P 0.004), vomiting (22% vs. 3%, P 0.001), and rhonchi sounds (17% vs. 1%, P 0.002) occurred more frequently in patients with influenza than in those with COVID-19 (15). To date, no research findings have always used blood test information to track COVID-19 as well as flu. In a past analysis, clients to COVID-19 who had an increased red blood cell allocation width (RDW) at the hospitalization but also an enhanced RDW throughout hospitalization used to have an expanded danger of mortality.¹⁵ In a study conducted, the fibrinogen-to-albumin fraction and WBC count had been found to be significant predictors for serious infection (16). Thus, COVID-19 can be identified solely on medical illnesses

and also blood test results, as well as a contrast of COVID-19 as well as flu utilizing blood test results is thought to be clinically significant. Physical assessments were also executed in symptoms suggestive flu to evaluate important properties like seasonal flu follicular; even so, since about the COVID-19 eruption, tangible evaluations have been frequently omitted. As a result, the purpose of this cross-sectional research was to assess the qualities of COVID-19 vs flu utilizing blood training dataset to assist in their differentiation.

MATERIALS AND METHODS

We enrolled COVID-19 clients who seemed to have blood tests among January 1 and December 31, 2020. For comparing, between 11 January 2020 and 31 December 2020, we enlisted an equivalent proportion of visitors afflicted to flu who also had blood tests. Children under the age of 14 who had COVID-19 or flu were not eligible. COVID-19 had been identified using a polymerase chain reaction for the identification of SARS-CoV-2 nucleic acids, whereas flu had been identified to use a quick flu diagnosing equipment. In addition, every prognosis was the result of the collaboration of further over health experts. A cross-sectional study was conducted at Nishtar Hospital, Multan. The diagnostic data gleaned through systematic review included social data, health complications, symptomatology, vitals, as well as lab results.

STATISTICAL ANALYSIS: Bivariate comparisons of each variable between COVID-19 and influenza were performed using an independent-samples t-test for data analysis or the chi-square test for ordinal attributes. P 0.05 had been used to determine whether or not the variations had been statistically meaningful. Multivariate logistic regression analysis was performed on major factors in the bivariate analysis. The area underneath the receiver operating characteristic curve was used to evaluate the accuracy of multivariate logistic regression models (AUC). The ethics committee of Nishtar Hospital, Multan, approved this retrospective study, which was carried out in compliance to pertinent rules and standards. The necessity for verbal or written consent form was waived by the ethics commission due to the retrospective survey methodology. The STROBE requirements were met in the preparation of this survey's report.

RESULTS

228 people were diagnosed with COVID-19 during the period studied (male:female ratio, 123 [54.0 percent]:105 [46.0 percent]; age, 54.68 18.98). Prior to SARS-CoV-2 infestation, neither of the clients had a background of COVID-19 vaccination. In the meantime, 228 flu subjects were enrolled (129 [56.6 percent]

male:99 [43.4 percent] female; age, 69.6 21.25). Type A disease was diagnosed in all flu clients. As shown in Table 1, 456 health care workers were included in study (male:female, 252 [55.3 percent]:204 [44.7 percent]; age, 62.12 21.47 years). Table 1 also provides an overview of COVID-19 patients' vs flu clients, as well as the outcomes of a bivariate analysis (Table 1).

Table 1: Patient variables and univariate analysis results

Variable	COVID-19	Influenza	Test performed	P value
Demographic factors				
Age	54.68 18.98	69.6 21.25	t-test	<0.001*
Female sex, n (%)	105 (46.0%)	99 (43.4%)	χ ²	0.64
Underlying condition				
Diabetes mellitus, n (%)	26 (11.4%)	29 (12.7%)	χ ²	0.77
Asthma	29 (12.7%)	12 (5.2%)	χ ²	<0.01*
Heart disease	61 (26.7%)	91 (39.9%)	χ ²	<0.01*
Symptoms				
Headache	27 (11.8%)	31 (13.6%)	χ ²	0.67
Cough	98 (43.0%)	79 (34.6%)	χ ²	0.08
Sore throat	35 (15.4%)	29 (12.7%)	χ ²	0.50
Breathing difficulty	48 (21.6%)	26 (11.4%)	χ ²	<0.01*
Chills	8 (3.5%)	32 (14.0%)	χ ²	<0.001*
Joint pain	16 (7.0%)	20 (8.8%)	χ ²	0.60
Diarrhea	3 (1.3%)	21 (9.2%)	χ ²	<0.001*
Malaise	14 (6.1%)	10 (4.3%)	χ ²	<0.001*
Vital signs				
Body Temperature	36.93 ± 0.76	38.22 ± 1.00	t-test	<0.001*
Systolic BP	128.21 ± 19.82	141.01 ± 26.31	t-test	<0.001*
Diastolic BP	79.36 ± 14.34	79.59 ± 15.65	t-test	0.88
Heart Rate	85.00 ± 15.82	96.94 ± 18.14	t-test	<0.001*
Respiratory Rate	17.25 ± 3.24	18.96 ± 4.37	t-test	<0.001*
Saturation	95.85 ± 3.59	94.90 ± 4.00	t-test	<0.01*
Lab Data				
White Blood Cells	5249.12 ± 2269.90	7249.56 ± 3304.15	t-test	<0.001*
Neutrophils	3464.79 ± 2278.0	5419.01 ± 2908.82	t-test	<0.001*
Lymphocytes	1247.82 ± 535.57	931.23 ± 736.39	t-test	<0.001*
Hemoglobin	13.96 ± 1.93	13.62 ± 1.48	t-test	0.04
Red Blood Cells distribution width	12.84 ± 1.47	17.52 ± 5.49	t-test	<0.001*
Platelet	21.51 ± 9.07	13.42 ± 1.95	t-test	<0.001*
Blood Urea Nitrogen	15.88 ± 13.79	17.84 ± 12.92	t-test	0.12
Creatinine	0.95 ± 0.79	1.09 ± 1.29	t-test	0.16
Total Protein	7.08 ± 0.69	7.08 ± 0.67	t-test	0.92
Albumin	3.97 ± 0.60	3.86 ± 0.57	t-test	0.07
Total Bilirubin	0.57 ± 0.52	0.64 ± 0.34	t-test	0.09
Lactate Dehydrogenase	246.76 ± 101.40	258.76 ± 105.67	t-test	0.23
Aspartate aminotransferase	32.26 ± 22.57	38.36 ± 38.15	t-test	0.04
Alanine aminotransferase	32.76 ± 38.48	27.32 ± 25.85	t-test	0.08
Sodium	138.39 ± 3.51	136.38 ± 4.01	t-test	<0.001*
Potassium	4.07 ± 0.46	4.05 ± 0.61	t-test	0.79
Chloride	103.36 3.85	101.24 ± 3.99	t-test	<0.001*
Creatine phosphokinase	121.44 198.79	500.25 ± 1968.86	t-test	<0.01*
Glucose	113.76 36.53	128.13 ± 38.90	t-test	<0.001*
C-reactive protein	3.19 4.66	4.56 ± 6.23	t-test	<0.01*

Table 2: Multivariate logistic regression model

Variable	Multivariate OR	Multivariate 95% CI	Multivariate P
Age	7.11	3.97–12.70	<0.001*
Chills	0.63	0.18–2.16	0.47
Breathing difficulty	3.33	1.51–7.36	<0.01*
Nausea	0.92	0.02–0.43	<0.01*
Malaise	2.21	1.09–4.48	0.03*
Body temperature <35.9°C	1.02	0.28–3.61	0.98
36.0–38.0°C	–	Reference	–
>38.1°C	0.04	0.02–0.09	<0.001*
White blood cell count >9000/L	0.07	0.02–0.24	<0.001*
Lymphocyte count >1800/L	1.87	0.66–5.34	0.24
Creatine phosphokinase >300 U/L	0.75	0.28–2.02	0.56

Basis of the findings of the bivariate analysis, we performed

multivariate logistic regression analysis (Table 2). We included elements that were thought to be clinically useful. If the variation was substantial, we exempted variables with either a big variation so over average limits. According to the Based on the results of the bivariate analysis, we performed multivariate logit model (Table 2). We included elements that were thought to be clinically useful. Unless the distinction was substantial, we exempted variables with such a big variation over the normal range. Body temperature was classified as hypothermia (35.9oC) or hyperthermia (>38.1oC) based on the cutoff value, with a body temperature range of 36 to 38oC used as the reference range. Furthermore, the cutoff white blood cell (WBC) count was greater than 9000/L, which was greater than the normal upper bound.

Since the ratios of neutrophils and lymphocytes have been strongly linked, the portion of lymphocytes has been used as an indicative in the statistical tests. The important considerations in the multivariate have been age (vs. 71 years; odds ratio [OR] 7.11; 95 % credible frequency [CI] 3.97–12.70; P 0.001), chest tightness (OR 3.33; 95 percent CI 0.18–2.16; P 0.01), nausea (OR 0.92; 95

percent CI 0.02–0.43; P 0.01), malaise (OR 2.21; 95 percent CI 1.09–4.48; P 0.03), body temperature $> 38.1^{\circ}\text{C}$ (P 0.001). We used the AUC to examine the effectiveness of this multivariate logistic regression that was 0.91 (95 percent CI 0.88–0.94). As a result, the model of the study was powerful enough.

To the best of the researcher, it's the first research to use lab test cases out of a university hospital to make comparisons clients of COVID-19 as well as many with flu. Clients with COVID-19 had a vastly greater age range of 15 to 70 years (vs. 71 years), respiratory problems, and malaise while, those with influenza. Even so, nausea, body temperature $> 38.1^{\circ}\text{C}$, and WBC count $> 9000/\text{IL}$ have been highly prevalent in flu clients than in COVID-19 clients. According to a few research, the age at which COVID-19 manifests itself is children below the age at which flu manifests itself. 14,21 The findings of these studies back up the findings of the research. Many COVID-19 patients in Japan are hospitalized to regulate the virus's expansion, sometimes whether they are youthful and show no symptoms. Cases with COVID-19 are typically handled in a health centre, where samples taken can be examined; even so, young patients with flu do not hospitalized and stay in the house, making blood testing difficult.

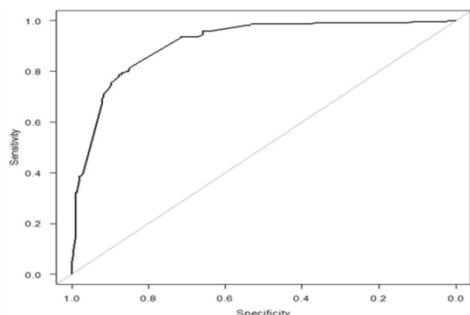


Figure 1: The area under the receiver operating characteristic curve of the multivariate logistic regression model was 0.91

DISCUSSION

SARS-CoV-2 primarily infiltrates breathing epithelium by strict adherence to angiotensin-converting enzyme 2; as a result, diseased individuals may suffer mild-to-severe inflammation and respiratory failure (22). Some other analysis revealed that COVID-19 creates respiratory distress fail due to flu primacy (14). These findings back up our findings, which show that COVID-19 causes more dyspnea than flu. Malaise has also been noted in a large number of COVID-19 sick people (14). In an earlier study, 63 percent of COVID-19 clients complained of malaise (23). All such conclusions back up the research results of our analysis that also found that the pervasiveness of malaise was greater in COVID-19 clients than in flu clients. Malaise could be caused by an expanded infectivity and antibody activation to infestation (24). Furthermore, malaise is associated with insufficient power supply metabolic needs (25).

A WBC rely greater than 9000/IL had been more commonly associated to flu in our research even than COVID-19, a having found backed by the findings of some other research (26). Concerning the discrepancy White blood cell count, one meta-analysis found lymphopenia in 62.5 percent of COVID-19 clients (95 percent CI 45–72; P 0.001), that were greater than the percentage of 49 percent in influenza type A clients (95 percent CI 35–56.4; P 0.001) (27). A further analysis revealed reduced lymphocyte numbers in COVID-19 sick people (28).

Although our study showed no significant lymphopenia, the Number of white blood cells could be important in differentiating COVID-19 from flu. CRP stages were also found to be ineffective in distinguishing COVID-19 from flu in our research. Correspondingly, a previous study suggested that the CRP level would not be an efficient determiner between COVID-19 and non-COVID-19 (29). CRP levels, on the other hand, have been way

greater in the serious COVID-19 community than in the non-COVID-19 group, confirming prior reports regarding clinical utility of the CRP level as an indicator of severe disease and progressive inflammation (30,31). Because none of the patients with COVID-19 had severe disease, no significant difference in CRP levels was observed in our study.

In relation to the results of a prior meta-analysis (32), a recent meta-analysis found that procalcitonin levels did not vary seen between serious and non-severe factions. Because procalcitonin stages have only been measured within few instances in this study, we did not include them as an extraction item. Even so, we presume that procalcitonin stages will be beneficial in the long run for distinguishing COVID-19 from flu. Clients with flu had a higher body temperature than COVID-19 clients. There have been numerous reports of COVID-19 instances without disease (33,34). These research results, we presume, are in accordance with the fact. This could have happened, even so, since people who receive antipsychotics could not be ruled out. Moreover, numerous clients of COVID-19 want more of the characteristics of the patients with flu. There have been numerous reports of COVID-19 instances without infection. (33,34). These research results, we assume, are in line with results. This could have happened, even so, even though people who receive antipsychotics could not be ruled out. Moreover, many COVID-19 clients had to be hospitalized for clinical care, and they had been subjected to tests conducted even while they were symptom free. Nausea is more commonly linked to flu than COVID-19. In one research, about 3.9 percent of COVID-19 (33) patients experienced nausea. The prevalence of nausea is also unidentified, but flu can induce gastrointestinal issues. The framework underpinning nausea is unknown and needs to be studied quite far. Whenever a virus gets digestive mucosal spurring blood cells, inflammation reactions have been reported, and gastrointestinal signs like nausea are thought to occur. The substantially lower rate of nausea in COVID-19 patient groups may be due to the drug's greater effect on the lower airways rather than the gastrointestinal tract. Esophageal spasms were actually more prevalent in COVID-19 clients than in flu clients, suggesting that our hypothesis is correct.

Flu and COVID-19 co-infection should then be addressed. As per the World Health Organization's disease surveillance study, the occurrence of flu after it COVID-19 eruption declined significantly both worldwide and in Japan. It seems as many folks were practicing prevention efforts for COVID-19 (wearing a mask as well as hand washing), that either lowered the amount of patient populations with flu. Since flu is communicated via droplets or aerosols and touch in the same way that COVID-19 is, it is assumed that COVID-19 preventative measures also safeguard against flu. Moreover, it is presumed that the decrease in cross-country travel helped contribute to a decline in the amount of flu clients. Co - infected cases also weren't found by researchers, but co - infection may become more popular over time. Animal research disclosed that with something worsens pneumonia (35). This subject will need to be discussed further in the years ahead.

There were some drawbacks to this study. First, health care workers with COVID-19 may have been hospitalized more commonly than is needed by Japanese law. Many COVID-19 cases, including children and the show no symptoms, are hospitalized for solitude to help control the spread of this extremely contagious disease. In addition, a multi-year flu filtration method is chosen. Seasonal flu symptoms can vary year to year, which may have impacted the study's findings. However, because no clients with influenza B had blood tests, the flu form had no influence on the outcomes.

Furthermore, obtaining a flu vaccine background from a retrospective analysis was tricky. As a result, we seem unable to investigate the effects of influenza vaccination in this research. A chart analysis also made it hard to compare the symptomology. Future research should look into these problems. Furthermore, since the information for three conditions (taste disruption,

dysosmia, and conjunctival hyperemia) had been incorrect, they were not included in chart feedback of clients with flu. Furthermore, only patients from a particular hospital were included in this survey. Eventually, this was a follow-up study. As a result, a multicenter study with a larger number of patients is needed to validate our findings.

CONCLUSIONS

Our findings can help distinguish COVID-19 from flu. Clients of COVID-19 had a vastly greater age range of 15 to 70 years (vs. 71 years), respiratory problems, as well as malaise while those with seasonal flu. Although, nausea, a body temperature greater than 38.1°C, and a WBC count greater than 9000/L were more frequent in people with flu than in those with COVID-19.

REFERENCES

1. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China. *Zhonghua Liu Xing Bing Xue Za Zhi* 2020; 41: 145–151. doi: 10.3760/cma.j.issn.0254-6450.2020.02.003.
2. Wu JT, Leung K and Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. *Lancet* 2020; 395: 689–697. doi: 10.1016/S0140-6736(20)30260-9.
3. Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med* 2020; 382: 1199–1207. doi: 10.1056/NEJMoa2001316.
4. Wu Z and McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020; 323: 1239–1242. doi: 10.1001/jama.2020.2648.
5. Pongpirul WA, Pongpirul K, Ratnarathon AC, et al. Journey of a Thai taxi driver and novel coronavirus. *N Engl J Med* 2020; 382:1067–1068. doi: 10.1056/NEJMoa2001621.
6. Chang C, Lin M, Wei L, et al. Epidemiologic and clinical characteristics of novel coronavirus infections involving 13 patients outside Wuhan, China. *JAMA* 2020; 323: 1092–1093. doi:10.1001/jama.2020.1623.
7. Liu YC, Liao CH, Chang CF, et al. A locally transmitted case of SARS-CoV-2 infection in Taiwan. *N Engl J Med* 2020; 382: 1070–1072. doi: 10.1056/NEJMoa2001573.
8. Spinato G, Fabbri C, Polesel J, et al. Alterations in smell or taste in mildly symptomatic outpatients with SARS-CoV-2 infection. *JAMA* 2020; 323: 2089–2090. doi: 10.1001/jama.2020.6771.
9. Giacomelli A, Pezzati L, Conti F, et al. Self-reported olfactory and taste disorders in patients with severe acute respiratory coronavirus 2 infection: a cross-sectional study. *Clin Infect Dis* 2020; 71: 889–890. doi: 10.1093/cid/ciaa330.
10. Wu P, Duan F, Luo C, et al. Characteristics of ocular findings of patients with coronavirus disease 2019 (COVID-19) in Hubei Province, China. *JAMA Ophthalmol* 2020; 138: 575–578. doi: 10.1001/jamaophth.2020.1291.
11. Burn E, You SC, Sena AG, et al. Deep phenotyping of 34,128 patients hospitalised with COVID-19 and a comparison with 81,596 influenza patients in America, Europe and Asia: an international network study. *medRxiv* 2020; 2020: 20074336. doi: 10.1101/2020.04.22.20074336.
12. Verity R, Okell LC, Dorigatti I, et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. *Lancet Infect Dis* 2020; 20: 669–677. doi: 10.1016/S1473-3099(20)30243-7.
13. Zayet S, Kadiane-Oussou NJ, Lepiller Q, et al. Clinical features of COVID-19 and influenza: a comparative study on Nord Franche-comte cluster. *Microbes Infect* 2020; 22: 481–488. doi: 10.1016/j.micinf.2020.05.016.
14. Piroth L, Cottenet J, Mariet AS, et al. Comparison of the characteristics, morbidity, and mortality of COVID-19 and seasonal influenza: a nationwide, population-based retrospective cohort study. *Lancet Respir Med* 2021; 9: 251–259. doi: 10.1016/S2213-2600(20)30527-0.
15. Foy BH, Carlson JCT, Reinertsen E, et al. Association of red blood cell distribution width with mortality risk in hospitalized adults with SARS-CoV-2 infection. *JAMA Netw Open* 2020; 3: e2022058. doi: 10.1001/jamanetworkopen.2020.22058.
16. Bi X, Su Z, Yan Haixi, et al. Prediction of severe illness due to COVID-19 based on an analysis of initial fibrinogen to albumin ratio and platelet count. *Platelets* 2020; 31: 674–679. doi: 10.1080/09537104.2020.1760230.
17. Tomoda Y, Toya M, Kagawa S, et al. Influenza follicles. *Intern Med* 2019; 58: 2269. doi: 10.2169/internalmedicine.2573-18.
18. Kenzaka T, Kyotani M, Goda K, et al. Reply to 'Influenza follicles and their buds as early diagnostic markers of influenza: typical images' and demonstration of lymphoid follicles in the posterior pharyngeal walls of patients with mycoplasmal pneumonia. *Postgrad Med J* 2018; 94: 311–312. doi: 10.1136/postgradmedj-2017-135540.
19. Kanda Y. Investigation of the freely available easy-to-use software 'EZ' for medical statistics. *Bone Marrow Transplant* 2013; 48: 452–458. doi: 10.1038/bmt.2012.244.
20. Von Elm E, Altman DG, Egger M, et al. The Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Ann Intern Med* 2007; 147: 573–577.
21. Auvinen R, Nohynek H, Syrjänen R, et al. Comparison of the clinical characteristics and outcomes of hospitalized adult COVID-19 and influenza patients – a prospective observational study. *Infect Dis (Lond)* 2021; 53: 111–121. doi: 10.1080/23744235.2020.1840623.
22. Nouri-Vaskeh M, Sharifi A, Khalili N, et al. Dyspneic and non-dyspneic (silent) hypoxemia in COVID-19: possible neurological mechanism. *Clin Neurol Neurosurg* 2020; 198: 106217. doi: 10.1016/j.clineuro.2020.106217.
23. Tostmann A, Bradley J, Bousema T, et al. Strong associations and moderate predictive value of early symptoms for SARS-CoV-2 test positivity among healthcare workers, the Netherlands, March 2020. *Euro Surveill* 2020; 25: 2000508. doi: 10.2807/1560-7917.ES.2020.25.16.2000508.
24. Brann DH, Tsukahara T, Weinreb C, et al. Non-neural expression of SARS-CoV-2 entry genes in the olfactory epithelium suggests mechanisms underlying anosmia in COVID-19 patients. *Sci Adv* 2020; 6: eabc5801. doi: 10.1126/sciadv.abc5801.
25. Recalcati S. Cutaneous manifestations in COVID-19: a first perspective. *J Eur Acad Dermatol Venereol* 2020; 34: e212-3. doi: 10.1111/jdv.16387.
26. D'Onofrio V, Steenkiste E, Meersman A, et al. Differentiating influenza from COVID-19 in patients presenting with suspected sepsis. *Eur J Clin Microbiol Infect Dis* 2021; 40: 987–995.
27. Pormohammad A, Ghorbani S, Khatami A, et al. Comparison of influenza type A and B with COVID-19: A global systematic review and meta-analysis on clinical, laboratory and radiographic findings. *Rev Med Virol* 2021; 31: e2179. doi: 10.1002/rmv.2179.
28. Henry BM. COVID-19, ECMO, and lymphopenia: a word of caution. *Lancet Respir Med* 2020; 8: e24. doi: 10.1016/S2213-2600(20)30119-3.
29. Soraya GV and Ulhaq ZS. Crucial laboratory parameters in COVID-19 diagnosis and prognosis: an updated meta-analysis. *Med Clin (Engl Ed)* 2020; 155: 143–151. doi: 10.1016/j.medcle.2020.05.004.
30. Lo IL, Lio CF, Cheong HH, et al. Evaluation of SARS-CoV-2 RNA shedding in clinical specimens and clinical characteristics of 10 patients with COVID-19 in Macau. *Int J Biol Sci* 2020; 16: 1698–1707. doi: 10.7150/ijbs.45357.
31. Ruan Q, Yang K, Wang W, et al. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intens Care Med* 2020; 46: 846–848. doi: 10.1007/s00134-020-05991-x.
32. Lippi G and Plebani M. Procalcitonin in patients with severe coronavirus disease 2019 (COVID-19): a meta-analysis. *Clin Chim Acta* 2020; 505: 190–191. doi: 10.1016/j.cca.2020.03.004.
33. Gao Z, Xu Y, Sun C, et al. A systematic review of asymptomatic infections with COVID-19. *J Microbiol Immunol Infect* 2021; 54: 12–16. doi: 10.1016/j.jmii.2020.05.001.
34. Stadler RN, Maurer L, Aguilar-Bultet L, et al. Systematic screening on admission for SARS-CoV-2 to detect asymptomatic infections. *Antimicrob Resist Infect Control* 2021; 10: 44. doi: 10.1186/s13756-021-00912-z.
35. Kinoshita T, Watanabe K, Sakurai Y, et al. Co-infection of SARS-CoV-2 and influenza virus causes more severe and prolonged pneumonia in hamsters. *Sci Rep* 2021; 11: 21259. doi: 10.1038/s41598-021-00809-2.