Comparison of clinical and biochemical features of hospitalized COVID-19 and influenza pneumonia patients

Didem Görgün Hattatoğlu | Birsen P. Yıldız

Department of Pulmonology, University of Health Sciences, Yedikule Chest Disease and Surgery Training and Research Hospital, Pulmonology, Istanbul, Turkey

Correspondence
Didem Görgün Hattatoğlu, University of Health Sciences, Yedikule Chest Disease and Surgery Training and Research Hospital, Istanbul 34020, Zeytinburnu/Kazlıçeşme, Turkey. Email: didem.gorgun@yahoo.com

Abstract
Both severe acute respiratory syndrome coronavirus 2 and influenza viruses cause similar clinical presentations. It is essential to assess severely ill patients presenting with a viral syndrome for diagnostic and prognostic purposes. We aimed to compare clinical and biochemical features between pneumonia patients with coronavirus disease 2019 (COVID-19) and H1N1. Sixty patients diagnosed with COVID-19 pneumonia and 61 patients diagnosed with influenza pneumonia were hospitalized between October 2020–January 2021 and October 2017–December 2019, respectively. All the clinical data and laboratory results, chest computed tomography scans, intensive care unit admission, invasive mechanical ventilation, and outcomes were retrospectively evaluated. The median age was 65 (range 32–96) years for patients with a COVID-19 diagnosis and 58 (range 18–83) years for patients with influenza (p = 0.002). The comorbidity index was significantly higher in patients with COVID-19 (p = 0.010). Diabetes mellitus and hypertension were statistically significantly more common in patients with COVID-19 (p = 0.019, p = 0.008, respectively). The distribution of severe disease and mortality was not significantly different among patients with COVID-19 than influenza patients (p = 0.096, p = 0.049). In comparison with inflammation markers; C-reactive protein (CRP) levels were significantly higher in influenza patients than patients with COVID-19 (p = 0.033). The presence of sputum was predictive for influenza (odds ratio [OR] 0.342 [95% confidence interval [CI], 2.1130–0.899]). CRP and platelet were also predictive for COVID-19 (OR 4.764 [95% CI, 1.003–1.012] and OR 0.991 [95% CI 0.984–0.998], respectively. We conclude that sputum symptoms by itself are much more detected in influenza patients. Besides that, lower CRP and higher PLT count would be discriminative for COVID-19.

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19) first emerged in Wuhan, China, in December 2019 and spread to a worldwide pandemic by March 2020. In comparison, the pandemic A (H1N1) virus caused an estimated 151 700–575 500 respiratory and cardiovascular deaths during the first 12 months of the latest influenza pandemic of 2009–2010 while seasonal influenza is estimated to be responsible for 291 243–645 832 respiratory deaths annually. Both severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and influenza viruses cause similar clinical presentations such as fever, fatigue, myalgia, and respiratory symptoms that range from a mild form to severe acute respiratory distress syndrome (ARDS). It was shown that SARS-CoV-2 appears to cause higher morbidity and mortality rates than seasonal Influenza in previous studies. Older age, pregnant women, under 2-year-old children, and people with comorbidities are high-risk groups of influenza while older age, male sex, and comorbidities are established for COVID-19. In clinical practice, it is essential to distinguish these two respiratory viral infections via their differential clinical manifestations, because of their distinct treatments and prognosis. Specific nucleic acid detection for SARS-CoV-2 and influenza virus
detection is the main diagnostic tool, however, substantial false-negative results can be obtained.

Simple, low-cost, easily hematological and biochemical tests are always used in practice. There are limited and conflicting results from studies that compare laboratory tests including several models based on clinical, laboratory, and radiological parameters, which had moderate performance in differentiating influenza pneumonia from COVID-19 pneumonia.9,10 Thus, there is a need for other clinical, biochemical, and imaging characteristics to assess severely ill patients presenting with a viral syndrome at the Emergency Department (ED) for diagnostic and prognostic purposes. We aimed to compare clinical and biochemical features between pneumonia patients with COVID-19 and H1N1.

2 | METHODS

Sixty patients diagnosed with COVID-19 pneumonia and 61 patients diagnosed with influenza pneumonia hospitalized between October 2020–January 2021 and October 2017–December 2019, respectively, in Yedikule Chest Disease and Surgery Training and Research Hospital, İstanbul, Turkey were included in this retrospective study. All patients included in the study had been confirmed by real-time reverse transcriptase-polymerase chain reaction (RT-PCR). The RT-PCR test was performed using nasal and pharyngeal swab specimens. Patients were aged less than 18 years and the pregnant were excluded.

All the clinical data and symptoms, comorbidities, smoking status, laboratory results (blood routine test and blood chemistry), chest computed tomography (CT) scans, intensive care unit (ICU) admission, invasive mechanical ventilation (IMV), and outcomes were retrospectively extracted from electronic medical records. We obtained the baseline data from the patients after admission. Patients’ illness severity was defined according to World Health Organization: (1) Critical Defined by the criteria for ARDS, sepsis, septic shock, or other conditions that providing mechanical ventilation (invasive or noninvasive) or vasopressor therapy. (2) Severe defined as oxygen saturation less than 90% on room air, a respiratory rate more than 30 breaths/min with the signs of severe respiratory distress (accessory muscle use, inability to complete full sentences).3 Nonsevere, defined as the absence of any criteria for severe or critical COVID-19.11 Charlson Comorbidity Index (CCI) was calculated for each patient according to the original publication and included in the analyses.12

This study was approved by the University of Health Sciences, Hamidiye Ethics Committee (no:7/10) owing to the retrospective nature of the study with no available informed consent.

2.1 | Statistical analyses

Data were analyzed using the IBM SPSS Statistics 18 © Copyright SPSS Inc. 1989, 2010 software. The compliance of continuous variables to normal distribution was examined using the Shapiro–Wilk test. The categorical variables in the study are presented with frequency (n) and percentage (%), and among the continuous variables, those that provide parametric test assumptions are presented with mean ± standard deviation (SD), and those that do not are presented with median (minimum and largest) values. Pearson χ² and Fisher’s exact tests were used in the analysis of categorical variables. The independent samples T-test was used in the comparison of two groups that provided the parametric test assumptions, and the Mann–Whitney U test was used in the comparison of the two groups that did not provide the parametric test assumptions. In addition, possible factors determined by univariate analysis were then analyzed with a multiple logistic regression model. The statistical significance level was accepted as 0.05 in the study.

3 | RESULTS

A total of 60 COVID-19 and 61 influenza patients were included in the analyses. The median age was 65 (range 32–96) years for patients with a COVID-19 diagnosis and 58 (range 18–83) years for patients with influenza (p = 0.002). Thirty-seven (61.7%) of patients with COVID were male, 23 (38.3%) of patients were female likewise 36 (59.0%) of influenza patients were male and 25 (41.0%) were female.

Hypertension (HT), diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), ischemic heart disease, and heart failure are the most common comorbidities. DM and HT were statistically significantly more common in patients with COVID-19 (p = 0.019, p = 0.008, respectively). Also, the CCI index was significantly higher in patients with COVID-19 (p = 0.010).

There was no statistical difference in terms of smoking status or packet/year of the cigarette between the two groups (p = 0.160; p = 0.362, respectively).

Demographic characteristics of patients with patients are shown in Table 1.

Clinical characteristics of patients with patients were shown in Table 2.

At admission 93.3% of patients with COVID-19 reported dyspnea, 51.7% reported cough, 38.3% reported fever. The 86.9% of patients with influenza reported dyspnea, 57% reported cough and 38.8% reported fever. The proportion of sputum (17%) was higher in influenza patients (p: 0.025), myalgia (18.3%) and vomiting (11.7%) was higher in COVID-19. (p = 0.008; p = 0.032).

The distribution of severe disease was not significantly different among patients with COVID-19 than influenza patients (p = 0.096).

For the total population, the median length of hospital stay was 9 days. (8 days for COVID-19 and 10 days for influenza; p = 0.097). There was no statistical difference between hospitalization days. Thirteen of (21.7%) patients with COVID-19 needed mechanical ventilation in ICU, while 10 of (16.4%) influenza patients needed mechanical ventilation in the ICU (p: 0.46). Days from hospitalization to mechanical ventilation were longer in patients with COVID-19 than influenza patients (5.5 days, 1.5 days, respectively, p: 0.003).
The median age of patients with COVID-19 admitted to the ICU was higher significantly (71.00 ± 11.00) than influenza patients (56.20 ± 7.71) (p = 0.002).

The median age at death in the total COVID-19 and influenza population was 70.67 ± 10.26 and 61.06 ± 15.12 years, respectively. (p: 0.049). The in-hospital mortality rate was not statistically different for both diseases (p = 0.877).

For routine blood examination; the results showed that WBC, neutrophil, lymphocyte, eosinophil, basophil, monocyte counts, RBC, hemoglobin, hematocrit, MCH, MCV, PCT as well as the hematological index (i.e., NLR, PLR, and LMR) had no significant difference between COVID-19 and influenza (Table 3). Platelet count was lower in influenza patients than COVID-19. (p: 0.001). However; MPV levels and MPV/platelet ratio were higher in patients with COVID-19 (p: = 0.043; p = 0.001, respectively).

In comparison with inflammation markers; CRP levels were significantly higher in influenza patients than in patients with COVID-19 (136 (5–502) mg/dL, 102 (3–242) mg/dL, respectively; p: 0.033). There was no significant difference in terms of pro-calcitonin levels (p = .498).

Potassium levels (4.5 [3.20–6.00] mg/dL) in patients with COVID-19 were significantly higher than in patients with influenza. (p:0.001). Aspartate transaminase levels (45 [16–772] mg/dL) were significantly higher in influenza patients (p:0.04). Additionally, glomerular filtration rate (84 [17–121]) was lower in in patients with COVID-19 (p = 0.009).

In terms of imaging distribution on chest CT, no statistical difference was found between COVID-19 and influenza (p = 0.494).

3.1 | Multivariable analysis

All variables that were significant in the univariate analysis were included in the multivariable regression model, and a backward selection was performed. Prediction of COVID and influenza In Table 4, the multivariable logistic regression analysis of the association of clinical and laboratory characteristics with influenza or COVID-19 is presented. The presence of sputum was predictive for influenza (OR 0.342 [95% CI, 2.1.130–0.899]). CRP and platelet were also predictive for COVID-19 (OR 4.764 [95% CI, 1.003–1.012] and OR 0.991 [95% CI 0.984–0.998], respectively.

| Variables                  | COVID-19 (n: 60) | Influenza (n: 61) | Total (n: 121) | p  |
|----------------------------|------------------|-------------------|----------------|----|
| Age                        | 65 (32–96)       | 58 (18–83)        | 61 (18–96)     | 0.002 |
| Sex                        |                  |                   |                | 0.766 |
| Female                     | 23 (38.3)        | 25 (41.0)         | 48 (39.7)      |    |
| Male                       | 37 (61.7)        | 36 (59.0)         | 73 (60.3)      |    |
| Smoking History            |                  |                   |                | 0.160 |
| Never smoke                | 28 (46.7)        | 28 (46.7)         | 56 (46.7)      |    |
| Current smoker             | 6 (10.0)         | 13 (21.7)         | 19 (15.8)      |    |
| Ex smoker                  | 26 (43.3)        | 19 (31.7)         | 45 (37.5)      |    |
| Smoking (packet/year)      | 40 (0–150)       | 35 (0–120)        | 40 80–150)     | 0.362 |
| Comorbidities              |                  |                   |                |    |
| Hypertension               | 35 (58.3)        | 21 (34.4)         | 56 (46.3)      | 0.008 |
| Diabetes mellitus          | 21 (35.0)        | 10 (16.4)         | 31 (25.6)      | 0.019 |
| COPD                       | 13 (21.7)        | 20 (32.8)         | 33 (27.3)      | 0.170 |
| Ischemic heart diseases    | 18 (30.0)        | 11 (18.0)         | 29 (24.0)      | 0.123 |
| Asthma                     | 8 (13.3)         | 6 (9.8)           | 14 (11.6)      | 0.548 |
| Congestive heart diseases  | 8 (13.3)         | 8 (13.1)          | 16 (13.2)      | 0.972 |
| Chronic renal failure      | 2 (3.3)          | 2 (3.3)           | 4 (3.3)        | 0.999 |
| Malignancy                 | 5 (8.3)          | 3 (4.9)           | 8 (6.6)        | 0.491 |
| No comorbidity             | 17 (28.3)        | 23 (37.7)         | 40 (33.1)      | 0.273 |
| Comorbidity index          | 1.22 ± 1.02      | 0.85 ± 1.15       | 1.03 ± 1.01    | 0.010 |

Note: Continuous variables are shown with median (smallest-largest) values, and the Mann–Whitney U test was performed. Categorical variables were shown with frequency, column percentage values and χ² and Fisher’s exact tests were performed.

Abbreviations: COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019.
DISCUSSION

This retrospective study showed the distinctive clinical, biochemical features and outcomes of COVID-19 and influenza pneumonia.

In our study, we found the median age of COVID-19 is higher than that of influenza. However, most of the previous studies reported that there was no statistical difference in terms of age between COVID-19 and influenza.\textsuperscript{5,13} Our results were confirmed in a recently published cohort study that included 89,530 COVID-19 and 45,819 influenza patients that showed that patients with COVID-19 were more elderly.\textsuperscript{4} The relationship between age and disease severity was clearly demonstrated in both diseases.\textsuperscript{5,14} It seems that the relationship between age and disease severity is more notable in patients with COVID-19. Moreover, we did not show any difference between study groups according to sex distribution similar to previous studies.\textsuperscript{9,10,15}

But, it should also be taken into account that men have an increased risk of severe disease in COVID-19.\textsuperscript{4,5,15}

In our study group, the most frequent comorbidities were diabetes and hypertension as previously reported in COVID and COPD, and hypertension in influenza. CCI is higher in COVID-19 when compared with influenza which confirmed previous reports.\textsuperscript{6} Although a variety of the comorbidities have been linked with both COVID-19 and influenza previously, it is difficult to make a comparison according to adjacent

| Variables                      | COVID (n: 60) | INF (n: 61) | Toplam (n: 121) | p       |
|-------------------------------|--------------|-------------|-----------------|---------|
| Symptoms                      |              |             |                 |         |
| Dyspnea                       | 56 (93.3)    | 53 (86.9)   | 109 (90.1)      | 0.235   |
| Cough                         | 31 (51.7)    | 38 (62.3)   | 69 (57.0)       | 0.238   |
| Fever                         | 23 (38.3)    | 24 (39.3)   | 47 (38.8)       | 0.909   |
| Sputum                        | 7 (11.7)     | 17 (27.9)   | 24 (19.8)       | 0.025   |
| Hemoptetic sputum             | 1 (1.7)      | 2 (3.3)     | 3 (2.5)         | 0.999   |
| Fatigue                       | 12 (20.0)    | 6 (9.8)     | 18 (14.9)       | 0.116   |
| Anorexia                      | 5 (8.3)      | 4 (6.6)     | 9 (7.4)         | 0.743   |
| Chest pain                    | 8 (13.3)     | 5 (8.2)     | 13 (10.7)       | 0.362   |
| Myalgia                       | 11 (18.3)    | 2 (3.3)     | 13 (10.7)       | 0.008   |
| Diarrhea                      | 2 (3.3)      | 0 (0.0)     | 2 (1.7)         | 0.244   |
| Headache                      | 2 (3.3)      | 0 (0.0)     | 2 (1.7)         | 0.244   |
| Vomiting                      | 7 (11.7)     | 1 (1.6)     | 8 (6.6)         | 0.032   |
| Severity                      |              |             |                 |         |
| None_severe                   | 11 (18.3)    | 5 (8.2)     | 16 (13.2)       | 0.196   |
| Severe                        | 15 (25.0)    | 21 (34.4)   | 36 (29.8)       |         |
| Critical                      | 34 (56.7)    | 35 (57.4)   | 69 (57.0)       |         |
| Invasive mechanical ventilation (IMV) |          |             |                 |         |
| Need IMV                      | 13 (21.7)    | 10 (16.4)   | 23 (19.0)       | 0.460   |
| No IMV                        | 47 (78.3)    | 51 (83.6)   | 98 (81.0)       |         |
| Duration of hospitalization   |              |             |                 |         |
| Duration of hospitalization   | 8 (2–60)     | 10 (3–47)   | 9 (2–60)        | 0.097   |
| (days) (n: 121)               |             |             |                 |         |
| Duration from hospitalization to ICU | 5.5 (2–14) | 1.5 (1–16) | 3 (1–16)        | 0.003   |
| (days) (n: 40)                |             |             |                 |         |
| In hospital mortality         |              |             |                 |         |
| Exitus                        | 15 (25.0)    | 16 (26.2)   | 31 (25.6)       | 0.877   |
| Discharged                    | 45 (75.0)    | 45 (73.8)   | 90 (74.4)       |         |

Note: Continuous variables are shown with median (smallest-largest) values, and the Mann–Whitney U test was conducted. Categorical variables were shown with frequency, column percentage values, and $\chi^2$ and Fisher’s exact tests were performed.

4 | DISCUSSION
### TABLE 3 Laboratory findings of patients

| Variables       | COVID-19 (n: 60) | INF (n: 61) | Toplam (n: 121) | p     |
|-----------------|------------------|------------|----------------|-------|
| Saturation      | 88 (60–99)       | 88 (51–98) | 88 (51–99)     | 0.801 |
| Hemoglobin      | 12.97 ± 1.79     | 13.25 ± 1.80 | 13.11 ± 1.79 | 0.384 |
| Hematocrit      | 38.88 ± 5.01     | 37.14 ± 5.06 | 39.01 ± 5.02 | 0.782 |
| RBC             | 4.55 (2.99–5.86) | 4.58 (3.78–6.00) | 4.58 (2.99–6.00) | 0.313 |
| MCH             | 28.95 (21.10–32.70) | 28.80 (20.20–34.30) | 28.90 (20.20–34.30) | 0.604 |
| MCV             | 85.85 (63.90–96.10) | 85.00 (60.30–99.20) | 85.50 (60.30–99.20) | 0.381 |
| MPV             | 9.90 (7.10–12.80) | 10.00 (8.10–13.70) | 10.00 (7.10–13.70) | 0.043 |
| WBC             | 8.58 (2.25–24.81) | 7.60 (0.93–34.23) | 8.40 (0.93–34.23) | 0.977 |
| Basophil        | 0.01 (0.00–0.05) | 0.02 (0.00–0.18) | 0.02 (0.00–0.18) | 0.888 |
| Eosinophil      | 0.01 (0.00–0.50) | 0.01 (0.00–0.60) | 0.01 (0.00–0.60) | 0.418 |
| Lymphocyte      | 0.92 (0.18–3.58) | 1.03 (0.10–5.30) | 0.93 (0.10–5.30) | 0.996 |
| Monocyte        | 0.43 (0.10–1.37) | 0.54 (0.10–1.99) | 0.46 (0.01–1.99) | 0.172 |
| Neutrophil      | 6.57 (1.13–20.37) | 5.91 (0.25–30.42) | 6.39 (0.25–30.42) | 0.622 |
| Platelet        | 242.5 (97–487)   | 201 (78–376) | 221 (78–487) | 0.001 |
| PCT             | 0.24 (0.10–0.51) | 0.21 (0.09–0.40) | 0.22 (0.09–0.51) | 0.012 |
| PDW             | 15.75 (9.40–17.70) | 11.60 (8.00–20.00) | 12.90 (8.00–20.00) | <0.001 |
| RDW             | 13.40 (10.20–20.00) | 14.30 (12.20–22.90) | 13.90 (10.20–22.90) | 0.005 |
| MPV/Platelet    | 0.041 (0.02–0.11) | 0.049 (0.02–0.15) | 0.043 (0.02–0.15) | 0.001 |
| NLR             | 6.11 (1.22–39.45) | 6.29 (0.24–36.74) | 6.12 (0.24–39.45) | 0.697 |
| PLR             | 258.3 (65.1–1477.7) | 203.8 (42.1–850.0) | 224.5 (42.1–1477.7) | 0.142 |
| LMR             | 2.42 (0.49–6.60) | 2.14 (0.31–76.0) | 2.34 (0.31–76.0) | 0.476 |
| CRP             | 102 (3–242)      | 136 (5–502) | 121 (3–502) | 0.033 |
| Procalcitonin   | 0.16 (0.02–48.90) | 0.22 (0.01–37.61) | 0.19 (0.01–48.90) | 0.498 |
| ALT             | 29 (3–616)       | 28 (8–435) | 29 (3–616) | 0.836 |
| AST             | 33.5 (13–220)    | 45 (16–772) | 39 (13–772) | 0.004 |
| GGT             | 49 (14–579)      | 37 (10–408) | 45 (10–579) | 0.136 |
| LDH             | 376 (215–1374)   | 462 (192–1214) | 400 (192–1374) | 0.384 |
| Albumine        | 37.20 ± 4.53     | 35.70 ± 3.96 | 36.45 ± 4.30 | 0.056 |
| Sodium          | 135 (123–146)    | 135 (120–145) | 135 (120–146) | 0.347 |
| Calcium         | 8.80 (6.70–9.60) | 8.50 (7.10–11.40) | 8.70 (6.70–11.40) | 0.055 |
| Potassium       | 4.50 (3.20–6.00) | 4.10 (2.90–5.70) | 4.30 (2.90–6.00) | 0.001 |
| Clor            | 98.67 ± 5.00     | 99.40 ± 4.63 | 99.03 ± 4.81 | 0.423 |
| GFR             | 84 (17–121)      | 101 (31–151.8) | 90 (17–151.8) | 0.009 |
| Creatinin kinase| 66.5 (18–921)    | 63 (40–4746) | 65 (18–4746) | 0.635 |
| CK-MB           | 24.4 (14.8–66.9) | 25.4 (12.0–56.7) | 24.4 (12–66.9) | 0.949 |
| Glucose         | 146 (63–724)     | 139 (70–484) | 141 (63–724) | 0.224 |
| Urea            | 37 (17–124)      | 39 (15–123) | 38.5 (15–124) | 0.815 |
| Creatinine      | 0.89 (0.43–2.93) | 0.86 (0.08–2.10) | 0.88 (0.08–2.93) | 0.250 |
| Total Bilirubine| 0.45 (0.00–4.51) | 0.47 (0.10–1.91) | 0.46 (0.00–4.51) | 0.768 |

(Continues)
In our study, we showed that both hypertension and diabetes were statistically more prominent in COVID-19. The presence of lymphopenia has been noticed in COVID-19, which is a laboratory abnormality characteristic of the illness in the ambulatory population. There are studies showing that patients with COVID-19 have a worse prognosis, that is, increased in the use of mechanical ventilation, longer hospital and intensive care units duration, and higher mortality. Zayet et al. obtained similar results as our study. This difference can be attributed to the small number of patients included both in Zayed et al.’s study and in our study. Elderly age, obesity, and having more comorbidities have been risk factors for severe disease and ICU admission in both COVID-19 and influenza. In large cohort studies, it was shown that patients with COVID-19 had a worse prognosis, that is, increase in the use of mechanical ventilation, longer hospital and intensive care units duration, and higher mortality. In the comparison between COVID-19 and influenza, the mortality rate was similar in both diseases as well as hospital duration and need for mechanical ventilation in our study. In our study, the duration from admission to the intensive care unit was found to be shorter in patients with influenza compared with patients with COVID-19. We can conclude that patients with influenza became critical and needed ICU more rapidly. However, this result was not confirmed in all studies.

The presence of lymphopenia has been noticed in COVID-19 patients mostly associated with severity. This phenomenon was previously observed in severe acute respiratory syndrome and the Middle East respiratory syndrome patients. Lymphopenia also would be an important laboratory abnormality characteristic of comorbidities due to the heterogeneous populations included in the studies. In our study, we showed that both hypertension and diabetes mellitus were statistically more prominent in COVID-19, but differences were not shown in the multivariate analyses. Only less than a third of the patients with COVID-19 did not have any major comorbidities in our cohort. It can be concluded that hypertension would be an important risk for both viral diseases, but any of the comorbidities would be distinctive between the two diseases.

**TABLE 3** (Continued)

| Variables | COVID-19 (n: 60) | INF (n: 61) | Toplam (n: 121) | p |
|-----------|-----------------|-------------|-----------------|---|
| Total proteine | 68.55 ± 5.83 | 68.48 ± 6.62 | 68.51 ± 6.22 | 0.952 |
| Úric aside | 5.25 ± 1.48 | 4.43 ± 1.79 | 5.12 ± 1.54 | 0.171 |
| PT | 97.58 ± 14.32 | 102.98 ± 18.91 | 100.38 ± 17.00 | 0.093 |
| APTT | 29 (18.5–41.8) | 23.7 (17.4–38.1) | 26.25 (17.4–41.6) | 0.001 |
| INR | 1.00 (0.45–1.40) | 1.00 (0.90–1.400) | 1.00 (0.45–1.40) | 0.33 |

Chest Computed Tomography (CT)

| | Non-severe | Severe | Critical |
|---|-----------|--------|----------|
| | 15 (25.0) | 16 (26.2) | 31 (25.6) | 0.494 |
| | 15 (25.0) | 10 (16.4) | 25 (20.7) |
| | 30 (50.0) | 35 (57.4) | 65 (53.7) |

Note: Independent samples T-test was performed for parameters showing normal distribution, and the results are shown as mean ± SD. Mann–Whitney U test was performed for parameters that did not show a normal distribution, and the results were shown with median (smallest-largest) values.

**TABLE 4** Multivariate analysis

| Variable | Multivariate analysis | p value |
|----------|----------------------|---------|
| Age | 1.020 | 0.958–1.087 | 0.530 |
| Diabetes Mellitus | 1.776 | 0.341–9.259 | 0.495 |
| Hypertension | 2.448 | 0.473–12.664 | 0.286 |
| Comorbidite index | 0.740 | 0.397–1.381 | 0.345 |
| Sputum | 0.146 | 0.026–0.809 | 0.028 |
| Myalgia | 8.015 | 1.036–62.012 | 0.046 |
| CRP | 0.991 | 0.984–0.998 | 0.016 |
| MPV | 0.954 | 0.513–1.774 | 0.882 |
| Platelet | 1.011 | 1.003–1.019 | 0.008 |
| Potassium | 1.826 | 0.633–5.263 | 0.265 |
| GFR | 0.986 | 0.958–1.015 | 0.346 |
| Aptt | 1.220 | 1.070–1.392 | 0.003 |

Abbreviations: CI, confidence interval; CRP, C-reactive protein; GFR, glomerular filtration rate; OR, odds ratio.
influenza while viral infections can induce depletion of lymphocytes during the clinical course. Moreover, we confirmed the results of previous studies that both COVID-19 and influenza decreased the number of lymphocytes, but no statistically significant difference was found between study groups. However, a few studies showed that lymphopenia was deeper in the influenza group. 

Patients with COVID pneumonia had a greater decreased number of white blood cells including neutrophils, compared with patients with influenza pneumonia in previous studies. But even neutropenia associated with the disease or distinctive role for the two viral infections is not clearly detected. Therefore, it is not realistic to conclude as suggested by Luo et al. using decreased lymphocytes and neutrophils for differentiating COVID-19 from influenza due to the inconclusive results. Our results did supported that neither lymphopenia nor neutropenia would differentiate COVID-19 from influenza.

NLR has taken both the levels of neutrophils and lymphocytes into account and has been proposed as a new biomarker for systemic inflammation. The inflammatory response could stimulate the production of neutrophils and speed up the apoptosis of lymphocytes. High NLR levels have been shown in COVID-19 as well reflected in the severity of the disease. NLR was also found to be useful indicators for diagnosis and differentiation of influenza A infection. Lin et al. conducted a study including only nine patients with COVID-19, and revealed that NLR was higher in influenza than COVID-19, but the difference was not statistically different. However, Kazancioglu et al. showed that NLR was higher in the influenza group when compared with the COVID-19. We did not show any difference according to NLR levels between study groups.

MPV defines the size of the platelets which is a marker of inflammation. Excessive inflammation associated with the cytokine activity might be leading to the breakdown of these larger, young platelets at the inflammation site, then decreasing the MPV. In the literature, it has been observed that MPV levels decreased in viral diseases together with the increase of the platelet count. In our study, MPV levels and MPV/platelet ratio has been shown to decrease whereas the PLT count increased in the COVID-19 compared with the influenza group. Ozcelik et al. have been shown similar results with our study, but without any difference in PLT count. In previous studies, a relationship between platelet count at the time of hospitalization and the severity of the disease was observed for both influenza and COVID-19 diseases. Our study concluded that lower MPV and higher PLT count have been associated with COVID-19. But in the multivariate analysis, both MPV and PLT could not be independent factors to discriminate between two different viral diseases. There are limited data comparing coagulation parameters between COVID-19 and influenza. Similar to our study, Lou et al found that APTT, fibrinogen, and thrombin time were higher in COVID-19 patients, which may indicate that COVID-19 has a higher risk of abnormal coagulation than influenza. Furthermore, we showed APTT was an independent distinctive parameter, however, PT and INR were not.

Our study has been shown that CRP might have a distinctive role for COVID-19 and influenza. In large-scale studies, it has been shown that COVID-19 patients were associated with increased CRP levels. There are contradictory results available on the role of CRP for the differentiation of COVID-19 from influenza. Although the role of CRP was not evaluated in the multivariate analysis in previous studies, increased CRP might be potentially distinctive for influenza in the admission of the hospital.

In our study, we included the patients admitted to the hospital and hospitalized. Thus, our results represent severe disease status. Although both COVID-19 and influenza patients have the same inclusion criteria, we were able to analyze these two groups without any bias. Accordingly, due to the influenza group being a historic control, some of the biochemical data was not available and were not included in the analysis (D-dimer, ferritin, fibrinogen, etc.).

In conclusion, although there are many studies comparing COVID-19 and influenza, none of them could clearly determine the parameter that can be used as a differential marker. In multivariable regression models performed in previous studies, several complex combinations of biochemical and radiological parameters were used to distinguish between influenza and COVID-19, but none of them have been used in clinical practice. We conclude that sputum symptoms by itself are much more detected in influenza patients. Besides that, lower CRP and higher PLT count would be discriminative for COVID-19.

ACKNOWLEDGMENT
We thank Başak Gökttaş for statistical analyses.

CONFLICT OF INTERESTS
The authors declare that there are no conflict of interests.

REFERENCES
1. Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020; 579(7798):270-273. https://doi.org/10.1038/s41586-020-2012-7
2. Dawood FS, Iuliano AD, Reed C, et al. Estimated global mortality and illness from pandemic influenza A H1N1 virus circulation: a modelling study. Lancet Infect Dis. 2012 Sep;12(9):687-95. Erratum in. Lancet Infect Dis. 2012; 12(9):655. https://doi.org/10.1016/S1473-3099(12)70121-4
3. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China [published correction appears in Lancet. 2020 Jan 30]. Lancet. 2020; 395(10223):497-506. https://doi.org/10.1016/S0140-6736(20)30183-5
4. Pirolo 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(3):251-259. https://doi.org/10.1016/S2213-2600(20)30527-0
5. Ludwig M, Jacob J, Basedow F, Andersohn F, Walker J. Clinical outcomes and characteristics of patients hospitalized for influenza or COVID-19 in Germany. Int J Infect Dis. 2021;103:316-322. https://doi.org/10.1016/j.ijid.2020.11.204
6. Zhang J, Wang X, Jia X, et al. Risk factors for disease severity, improvement, and mortality in COVID-19 patients in Wuhan, China.
D’Onofrio V, Van Steenkiste E, Meersman A, et al. Differentiating influenzas from COVID-19 in patients presenting with suspected sepsis. *Eur J Clin Microbiol Infect Dis*. 2021;40(5):987-995. https://doi.org/10.1007/s10096-020-04109-x

Clinical management of COVID-19 patients: living guidance, January 25, 2021. https://www.who.int/publications/i/item/WHO-2019-nCoV-viral-infection-2021-1

Charlson ME, Pompei P, Alex KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373-383. https://doi.org/10.1016/0021-9681(87)90171-8

Levin AT, Hanage WP, Owusu-Boaitey N, Cochran KB, Walsh SP, Meyerowitz-Katz G. Assessing the age specificity of infection fatality rates for COVID-19: systematic review, meta-analysis, and public policy implications. *Eur J Epidemiol*. 2020;35(12):1123-1138. https://doi.org/10.1007/s10654-020-00698-1

Lin YH, Luo W, Wu DH, et al. Comparison of clinical, laboratory, and radiological characteristics between SARS-CoV-2 infection and community-acquired pneumonia caused by influenza virus: a cross-sectional retrospective study. *Medicine*. 2020;99(44):e23064. https://doi.org/10.1097/MD.00000000000023064

Deng LS, Yuan J, Ding L, et al. Comparison of patients hospitalized with COVID-19, H7N9 and H1N1. *Infect Dis Poverty*. 2020;9(1):163. https://doi.org/10.1186/s40249-020-00781-5

Pedersen CJ, Quinn JV, Ragan DT, Yang S. Factors associated with influenza in an emergency department setting. *J Emerg Med* 2019;56(5):478-483. https://doi.org/10.1016/j.jemermed.2018.12.012

Tang X, Du RH, Wang R, et al. Comparison of hospitalized patients with ARDS caused by COVID-19 and H1N1. *Chest*. 2020;158(1):195-205. https://doi.org/10.1016/j.chest.2020.03.032

Donnino MW, Moskowitz A, Thompson GS, et al. Comparison between patients hospitalized with influenza and COVID-19 at a tertiary care center. *J Gen Intern Med*. 2021;36:1-7. https://doi.org/10.1007/s11606-021-06647-2

Simonnet A, Chetboun M, Poissy J, et al. High prevalence of obesity in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation [published correction appears in Obesity (Silver Spring). 2020 Oct;28(10):1994]. *Obesity (Silver Spring)*. 2020;28(7):1195-1199. https://doi.org/10.1002/oby.22831

Hanley B, Lucas SB, Yould E, Swift B, Osborn M. Autopsy in suspected COVID-19 cases. *J Clin Pathol*. 2020;73(5):239-242. https://doi.org/10.1136/jclinpath-2020-206522

Alraddadi B, Bawareth N, Omar H, et al. 766 Clinical Features and Outcome of Patients with Middle East Respiratory Syndrome-Coronavirus (MERS-CoV) Infection. Open Forum Infect Dis. 2014;1(suppl 1):S216.

Jain S, Kamimoto L, Bramley AM, et al. Hospitalized patients with 2009 H1N1 influenza in the United States, April-June 2009. *N Engl J Med*. 2009;361(20):1935-1944. https://doi.org/10.1056/NEJMoai0906695

Cao B, Li XW, Mao Y, et al. Clinical features of the initial cases of 2009 pandemic influenza A (H1N1) virus infection in China. *N Engl J Med*. 2009;361(26):2507-2517. https://doi.org/10.1056/NEJMoai0906612

Sohn CH, Ryooy SM, Yoon YJ, et al. Comparison of clinical features and outcomes of hospitalized adult patients with novel influenza A (H1N1) pneumonia and other pneumonia. *Acad Emerg Med*. 2013;20(1):46-53. https://doi.org/10.1111/acem.12062

Han Q, Wen X, Wang L, et al. Role of hematological parameters in the diagnosis of influenza virus infection in patients with respiratory tract infection symptoms. *J Clin Lab Anal*. 2020;34(5):e23191. https://doi.org/10.1002/jcla.23191

Chen J, Pan Y, Li G, et al. Distinguishing between COVID-19 and influenza during the early stages by measurement of peripheral blood parameters. *J Med Virol*. 2021;93(2):1029-1037. https://doi.org/10.1002/jmv.26384

Ozcelik N, Ozurt S, Yilmaz Kara B, Gumus A, Sahin U. The value of the platelet count and platelet indices in differentiation of COVID-19 and influenza pneumonia. *J Med Virol*. 2021;93(4):2221-2226. https://doi.org/10.1002/jmv.26645

Tang X, Du RH, Wang R, et al. Comparison of hospitalized patients with ARDS caused by COVID-19 and H1N1. *Chest*. 2020;158(1):195-205. https://doi.org/10.1016/j.chest.2020.03.032

Kazancioglu S, Bastug A, Ozbay BO, Kemirtek N, Bodur H. The role of haematological parameters in patients with COVID-19 and influenza virus infection. *Epidemiol Infect*. 2020;148:e272. https://doi.org/10.1017/S095026882000271X

Channappanavar R, Perlman S. Pathogenic human coronavirus infections: causes and consequences of cytokine storm and immunopathology. *Semin Immunopathol*. 2017;39(5):529-539. https://doi.org/10.1007/s00281-017-0629-x

Liu Y, Du X, Chen J, et al. Neutrophil-to-lymphocyte ratio as an independent risk factor for mortality in hospitalized patients with COVID-19. *J Infect*. 2020;81(1):e6-e12. https://doi.org/10.1016/j.jinf.2020.04.002

Fei Y, Zhang H, Zhang C. The application of lymphocyte/platelet and mean platelet volume/platelet ratio in influenza A infection in children. *J Clin Lab Anal*. 2019;33(9):e22995. https://doi.org/10.1002/jcla.22995

Lin HA, Lin SF, Chang HW, Lee YJ, Chen RJ, Hou SK. Clinical impact of monocyte distribution width and neutrophil-to-lymphocyte ratio for distinguishing COVID-19 and influenza from other upper respiratory tract infections: a pilot study. *PLoS One*. 2020;15(11):e0241262. https://doi.org/10.1371/journal.pone.0241262

Mete E, Akelma AZ, Cizmeci MN, Bozkaya D, Kanburuglu MK. Decreased mean platelet volume in children with acute rotavirus gastroenteritis. *Platelets*. 2014;25(1):51-54. https://doi.org/10.3109/09537104.2013.764493

Korniluk A, Koper-Lenkiewicz OM, Kaminiska J, Kemonha H, Dymicka -Piekarska V. Mean platelet volume (MPV): new perspectives for an old marker in the course and prognosis of inflammatory conditions. *Mediators Inflamm*. 2019;2019:9213074. https://doi.org/10.1155/2019/9213074

Qadri S, Holman S, Dehovitz J, Crystal H, Minkoff H, Lazar JM. Mean platelet volume is decreased in HIV-infected women. *HIV Med*. 2013;14(9):549-555. https://doi.org/10.1111/hiv.12048

Renshaw AA, Drago B, Toraya N, Gould EW. Respiratory syncytial virus infection is strongly correlated with decreased mean platelet volume. *J Infect Dis*. 2013;179(6):e678-e680. https://doi.org/10.1016/j.ijd.2013.01.012
39. Lippi G, Plebani M, Henry BM. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A meta-analysis. *Clin Chim Acta*. 2020;506:145-148. https://doi.org/10.1016/j.cca.2020.03.022

40. Liu Y, Sun W, Guo Y, et al. Association between platelet parameters and mortality in coronavirus disease 2019: retrospective cohort study. *Platelets*. 2020;31(4):490-496. https://doi.org/10.1080/09537104.2020.1754383

41. Lopez-Delgado JC, Rovira A, Esteve F, et al. Thrombocytopenia as a mortality risk factor in acute respiratory failure in H1N1 influenza.

---

*How to cite this article:* Hattatoğlu DG, Yıldız BP. Comparison of clinical and biochemical features of hospitalized COVID-19 and influenza pneumonia patients. *J Med Virol*. 2021;93:6619-6627. https://doi.org/10.1002/jmv.27218