Comparison of laboratory results and chest CT findings in COVID-19 patients

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Ertugrul Altinbilek[1], Derya Ozturk[1], Huseyin Ozkurt[2], Ahsen Oncul[3], Murat Ocal[4], Miray Tumer[5], Abdullah Algin[6]

[1] Department of Emergency Medicine, University of Health Sciences, Sisli Hamidiye Etfal Education and Research Hospital, Istanbul

[2] Department of Radiology, University of Health Sciences Sisli Hamidiye Etfal Education and Research Hospital, Istanbul

[3] Department of Infectious Diseases, University of Health Sciences, Sisli Hamidiye Etfal Education and Research Hospital, Istanbul

[4] Department of Microbiology, University of Health Sciences, Sisli Hamidiye Etfal Education and Research Hospital, Istanbul

[5] Department of Emergency Medicine, Ankara City Hospital, Ankara

[6] Department of Emergency Medicine, University of Health Sciences, Istanbul Umraniye Training and Research Hospital, Istanbul, Turkey

Abstract

Aim: COVID-19 has emerged in China and quickly spread around the world. Efficient screening of patients for the disease is crucial in the diagnosis and determination of the severity of the disease. However, the diagnostic methods performed are not optimal when applied alone. In this study, we aimed to investigate whether CT together with laboratory test results can provide insight for the prognosis of COVID-19 for patients admitted to the emergency room (ER) and investigate possible factors affecting the mortality.

Material and Methods: This retrospective study was conducted on 313 patients older than 18 years who had COVID-19 presentations and admitted to the ER. Patients' demographic data (age, gender, and comorbidities), complete blood counts, biochemistry parameters (d-dimer, ferritin, CRP, troponin, and lactate), chest CT and qRT-PCR-based SARS-CoV-2 test results were evaluated.

Results: The mean age of the patients was 58.7 ± 16.2 years (male = 58.7%). One hundred eighty-one patients had comorbidities and the most common comorbidity was hypertension (HT), followed by coronary artery disease (CAD). Ferritin and CRP levels were significantly higher in patients with severe CT findings compared to the patients with mild and moderate CT findings ($p < 0.05$). Interestingly, patients with severe CT findings were significantly younger than patients in other groups ($p < 0.05$). The number of patients with HT and CAD was significantly higher among patients with severe CT findings than among patients with mild and moderate CT findings ($p < 0.05$). Patients with moderate and severe findings had a higher mortality rate compared to patients with mild CT findings ($p < 0.05$).

Discussion: Despite inconsistencies between clinical findings, radiological features, and blood biochemistry results among COVID-19 patients, CRP and ferritin levels, together with HT and CAD, may be prognostic for disease severity, suggesting that the integration of CT assessments and laboratory results may be essential for predicting disease severity.

Keywords

Blood biochemistry; Chest CT; COVID-19; Complete blood counts; Pneumonia

Introduction

The two recent coronavirus (CoV) outbreaks, a severe acute respiratory syndrome coronavirus (SARS-CoV) emerged in China in 2002 and spread rapidly worldwide had an 11% mortality rate [1] and Middle East respiratory syndrome coronavirus (MERS-CoV) firstly identified in Saudi Araba in 2012 and subsequently reported in other countries had a mortality rate of 37% [2]. Both SARS-CoV and MERS-CoV were transmitted to humans from infected civets found in markets in China [3] and dromedary camels in Saudi Arabia [4], respectively, and they likely originated in bats [5,6].

In December 2019, several pneumonia cases with unknown etiology surfaced in Wuhan City, Hubei Province, China. The taxonomic and full genome sequencing analyses of the first isolated samples revealed that this virus is closely related to SARS-CoV and was named as SARS-CoV-2, and the disease was named as Coronavirus Disease 19 (COVID-19) [7]. On January 30, 2020, World Health Organization (WHO) declared the COVID-19 a "Public health emergency of international concern" [8], and on March 11, 2020, WHO declared a pandemic due to 13-fold increase in the number of cases outside of China [9].

The most common symptoms of COVID-19 were fever, sore throat, cough, and dyspnea [10]. Although some patients may present very mild symptoms or may be asymptomatic [11], the prognosis of the disease is unfavorable in elderly patients and those with background comorbidities, and in severe cases, infections may cause viral pneumonia leading to severe acute respiratory distress syndrome (ARDS) or end-organ failure and consequently death [12]. Close contact with an infected individual and being exposed to coughing, sneezing and respiratory droplets or aerosols leading to penetration of the viral particles into the body is the main human-to-human transmission route [13].

Alterations in the laboratory parameters such as elevated levels of cytokine, lymphopenia, thrombocytopenia, leukocytosis, elevated levels of C-reactive protein (CRP), lactate dehydrogenase (LDH), ferritin, troponin, and d-dimers were reported in the literature [14]. The diagnosis tests for COVID-19, on the other hand, include real-time reverse transcription-polymerase chain reaction (qRT-PCR) and chest computed tomography (CT) [15]. Moreover, thorax CT has been used for diagnosis, as it may reveal the positivity of SARS-CoV2 infection earlier than the positivity of viral infection is detected by RT-PCR. CT examinations are now used both for diagnosis and for detecting the severity of the disease [16].

In this retrospective, single-centered study, the primary aim was to investigate whether CT and laboratory test results are predictive for COVID-19 prognosis in the patients admitted to emergency service and hospitalized with the diagnosis of COVID-19. The secondary aim of the study was to examine the factors that likely contribute to the mortality of these patients.

Material and Methods

Patients and Study Design

The study complied with the international guidelines, the "Regulations on Pharmaceutical Research," enforced by the Ministry of Health of Turkey, published in the 27089 numbered Official Journal dated 23 December 2008 and also with other regulations published later. Moreover, this single-center study was approved by the local clinical research ethics committee. The study was conducted on 313 patients who admitted to the emergency room (ER) of our hospital with complaints of fever and acute respiratory problems (cough and dyspnea) and with suspected SARS-CoV-2 infection, diagnosed with COVID-19 and hospitalized in the clinics or intensive care unit (ICU) from April 1, 2020 to April 30, 2020. Medical records (date of admission to ER, place of hospitalization (service or ICU), comorbidity, laboratory parameters, CT results, SARS-COV-2 qRT-PCR results), and demographical characteristics (age and gender) of the patients were retrospectively investigated. Patients who were younger than 18 years old, those who were not diagnosed with or had the presentations of COVID-19, those with incomplete medical records, who were referred to another health institution and were not hospitalized were excluded from the study.

Upon admission, complete blood counts and blood biochemistry parameters d-dimer, ferritin, CRP, troponin, as well as nasopharyngeal swab samples for qRT-PCR based SARS-CoV-2 test were requested and patients were referred to the ER for thorax CT examinations. The reference values for the parameters investigated were as follows: neutrophils = 1.56 - 6.13 (x 109/L), lymphocytes = 1.18 - 3.74 (x 109/L), d-dimer = 0-500 (μg/L), ferritin = 23.9 - 336.2 (μg/L), troponin = < 19.8 ng/L, CRP = <5 mg/L and lactate = 0.0 - 2.0 mmol. If patient's neutrophil/lymphocyte ratio (NLR) was lower than 3, the decision to hospitalize the patient was made in conjunction with the Infectious Diseases Department.

Statistical Analysis

Statistical analyses were conducted using descriptive statistics, mean, standard deviation (SD), median, minimum and maximum values, frequency, and ratio. The normal distribution of data was analyzed using the Kolmogorov-Smirnov test. Quantitative independent data were analyzed using either one-way analysis of variance (ANOVA) followed by Tukey's multiple comparison tests, Kruskal-Wallis test or Mann-Whitney U test. Qualitative independent data were analyzed using the Chi-square test, and when the conditions for the Chi-square test were not met, the Fischer's exact test was used.

Results

The mean age of the patients was 58.7 ± 16.2 years (min-max = 22.0 - 97.0) and 182 patients were male (Table 1). Among the patients, 181 had comorbid diseases (Table 1), of which, hypertension (HT) was the major comorbidity, followed by chronic obstructive pulmonary disorder (COPD) (Table 1). Levels of d-dimer, ferritin, and CRP, as well as NLR, were above the reference limits while troponin and lactate levels were within the limits (Table 1). Most of the patients (274 (87.5%)) were discharged after recovery.

The mean age of the patients with severe CT findings was significantly lower than the patients with mild and moderate CT findings (p < 0.05; Table 2). On the other hand, the ages of the patients with moderate and mild CT findings did not differ significantly (p > 0.05).

The proportion of male patients with severe CT findings was significantly higher than those with moderate and mild CT

findings (p < 0.05; Table 2); however, there were no significant differences in gender ratio between the patient groups with mild and moderate CT findings (p > 0.05).

There were no differences between the patient groups with mild, moderate, and severe CT findings in terms of the presence of comorbid diseases (p > 0.05). The number of patients with hypertension (HT) and coronary artery disease (CAD) was significantly lower in the patient group with severe CT findings than the patient groups with mild and moderate CT findings (p < 0.05; Table 2), while the number of patients with HT and CAD did not differ between the groups with mild and moderate CT findings (p > 0.05). The number of patients with other comorbid diseases did not differ among the patient groups with different severity of CT findings (p > 0.05).

NLR value, d-dimer levels, troponin levels, and lactate levels did not differ significantly between the groups with severe, moderate, and mild CT findings (p > 0.05; Table 2). In the group with severe CT findings, the ferritin levels were significantly higher than the group with mild CT findings (p < 0.05) while there was no significant difference in ferritin levels between the patient group with moderate CT findings and with either severe or mild CT findings (p > 0.05; Table 2). There were no significant differences in the CRP levels between the patient groups with mild and moderate CT findings (p > 0.05), however, it was significant in the group of patients with severe CT findings, which were significantly higher than the group with moderate and mild CT findings (p < 0.05; Table 2).

The mortality rate was higher in patients with severe and moderate CT findings than patients with mild CT findings (p < 0.05; Table 2). On the other hand, there was no significant difference between the patient groups with moderate and severe CT findings in terms of mortality (p > 0.05).
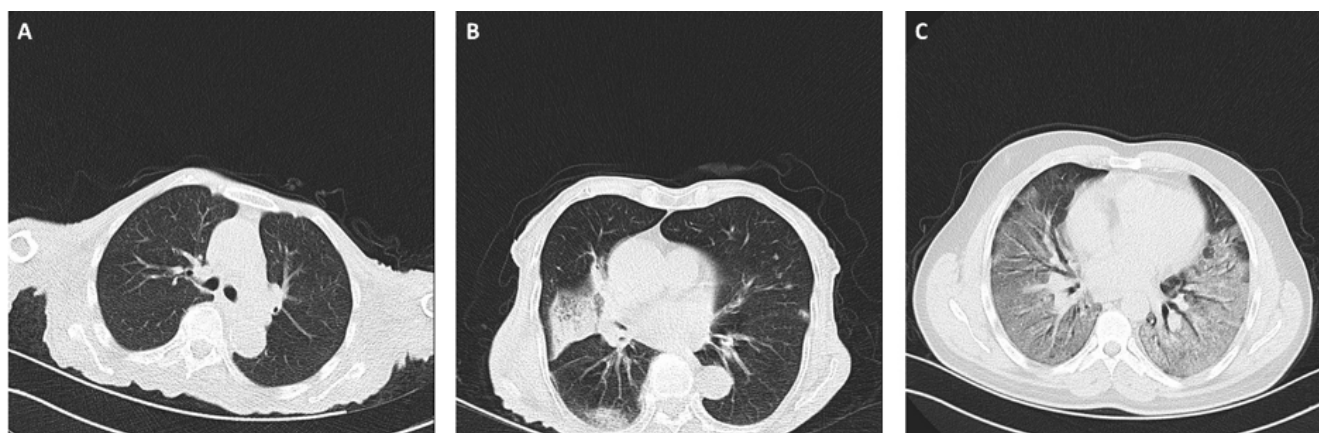
Representative chest CT images of mild, moderate, and severe COVID cases are given in Figure 1. Minimal central ground-glass opacity was observed in the CT images of a 78-year-old male patient who admitted to the ER with five days history of complaints of fever, fatigue, and dyspnea (Figure 1A). The qRT-PCR results of the case were positive, NLR, d-dimer, ferritin, troponin, CRP, and lactate levels were 4.17, 238 µg/L, 85 µg/L, 0.65 ng/L, 11 mg/L, and 0.65 mmol/L, respectively. The patient was discharged after five days of treatment. In the upper posterior lobe and segment and the upper inferior lobe of the right lung, on CT scans of an 86-year-old male patient admitted to the RP with a five-day history of complaints of fever, fatigue

Table 1. Demographical and clinical characteristics of the patients (Data are presented either as mean ± SD and median or n (%))

	Min - Max	Median	Mean ± SD / n (%)
Age (years)	22 - 97	59	58.7 ± 16.2
Gender			
Male			182 (58.1)
Female			131 (41.9)
Comorbid diseases			
Yes			181 (57.8)
HT			129 (41.2)
CAD			53 (16.9)
DM			68 (21.7)
COPD			25 (8.0)
CRF			14 (4.5)
Thyroid			7 (2.2)
Cancer			8 (2.6)
Other			23 (7.3)
No			132 (42.2)
Laboratory results			
NLR	0.55 - 43.94	3.16	4.82 ± 5.08
D-dimer (µg/L)	2.2 - 21200	565.0	921 ± 1724
Ferritin (µg/L)	4.0 - 138132	184.4	798 ± 7824
Troponin (ng/L)	2.30 - 1191	5.10	18.8 ± 76.3
CRP (mg/L)	0.50 - 417	39.00	62.6 ± 67.3
Lactate (mmol/L)	0.50 - 11	1.46	1.60 ± 0.90
Reason for hospitalization termination			
Discharged			274 (87.5)
Died			39 (12.5)

CAD: coronary artery disease; COPD: chronic obstructive pulmonary disorder; CRF: chronic renal failure; CRP: C-reactive protein; DM: diabetes mellitus; HT: hypertension; NLR: neutrophil-lymphocyte ratio.

and dyspnea, there were intense ground-glass opacities, and in the inferior upper lobe of the left lung, mild ground-glass opacity and infiltrative areas were observed (Figure 1B). The qRT-PCR results of the case were positive, NLR, d-dimer, ferritin, troponin, CRP, and lactate levels were 8.26, 425 µg/L, 130 µg/L, 0.9 ng/L, 95.2 mg/L, and 1.12 mmol/L, respectively. The patient was discharged after 14 days of treatment. Peripheral and central ground-glass opacity was observed in the CT images of a 38-year-old female patient who admitted to the ER with complaints of fever, coughing, and dyspnea (Figure 1C). The qRT-PCR results of the case were positive, NLR, d-dimer, ferritin, troponin, CRP, and lactate levels were 1.44, 977 µg/L, 518 µg/L, 12.2 ng/L, 95.2 mg/L, and 0.75 mmol/L, respectively.

Figure 1. Representative CT images of (A) mild, (B) moderate, and (C) severe CT findings

Table 2. Demographical and clinical characteristics of the patients according to the severity of CT findings (Data are presented either as mean ± SD and median or n (%). The statistically significant p-value is indicated in bold)

	Severity of CT findings						
	Severe		Moderate		Mild		p-value
	Mean ± SD / n (%)	Median	Mean ± SD / n (%)	Median	Mean ± SD / n (%)	Median	
Age (years)	56.6 ± 14.8	57	62.6 ± 18.4	64	65.6 ± 18.2	65	0.002 A
Gender							
Male	143 (64.4)		27 (45.0)		12 (38.7)		0.002 X²
Female	79 (35.6)		33 (55.0)		19 (61.3)		
Comorbid diseases							
Yes	102 (45.9)		21 (35.0)		9 (29.0)		0.093 X²
No	120 (54.1)		39 (65.0)		22 (71.0)		
HT	80 (36.0)		30 (50.0)		19 (61.3)		0.009 X²
CAD	27 (12.2)		16 (26.7)		10 (32.3)		0.002 X²
DM	47 (21.2)		13 (21.7)		8 (25.8)		0.842 X²
COPD	16 (7.2)		6 (10.0)		3 (9.7)		0.728 X²
CRF	8 (3.6)		3 (5.0)		3 (9.7)		0.302 X²
Thyroid	6 (2.7)		0 (0.0)		1 (3.2)		> 0.05 X²
Cancer	4 (1.8)		3 (5.0)		1 (3.2)		> 0.05 X²
Other	12 (5.4)		7 (11.7)		4 (12.9)		0.118 X²
Laboratory results							
NLR	4.8 ± 5.1	3.2	5.56 ± 6.00	3.39	3.14 ± 1.78	2.84	0.180 K
D-dimer (µg/L)	941.9 ± 2002.8	543	921 ± 739	631	774 ± 526	715	0.251 K
Ferritin (µg/L)	1008 ± 9285	196	319 ± 383	174	224 ± 380	106	0.035 K
Troponin (ng/L)	18.8 ± 87.6	4.7	15.1 ± 20.8	6.7	25.7 ± 55.0	5.5	0.296 K
CRP (mg/L)	66.8 ± 67.6	47.3	60.7 ± 75.8	22.7	35.9 ± 36.9	19.6	0.004 K
Lactate (mmol/L)	1.6 ± 1.0	1.5	1.6 ± 0.7	1.5	1.4 ± 0.5	1.4	0.583 K
Reason for hospitalization termination							
Discharged	194 (87.4)		49 (81.7)		31 (100.0)		0.043 X²
Died	28 (12.6)		11 (18.3)		0 (0.0)		

CAD: coronary artery disease; COPD: chronic obstructive pulmonary disorder; CRF: chronic renal failure; CRP: C-reactive protein; DM: diabetes mellitus; HT: hypertension; NLR: neutrophil-lymphocyte ratio. (Statistical analyses: A: ANOVA followed by Tukey's multiple comparison test; K: Kruskal-Wallis (Mann-Whitney U test); X²: Chi-Square test)

Discussion

In this study, all patients were COVID-19 positive that was detected with RT-PCR results. In our study, we observed that patients with severe CT findings were significantly younger than patients with mild and moderate CT findings. Similarly, ferritin and CRP levels were significantly higher in patients with severe CT findings compared to patients with mild and moderate CT findings.

The risk factors for the disease severity have been reported as age, high levels of lactate dehydrogenase, high levels of d-dimer [14]. Previous studies have indicated that elevated NLR is observed in the severe cases of COVID-19 [17] and is an independent risk factor for mortality [18]. Although levels of d-dimer, ferritin, and CRP, as well as NLR, were above the reference limits, we did not find an association between d-dimer levels, NLR and the severity of the disease. Elevated ferritin levels were suggested to represent the severity of COVID-19 [19]. In our study, we observed significantly higher ferritin levels in severe cases compared to mild and moderate cases. CRP levels, on the other hand, were found to be significant in severe cases compared to mild and moderate cases. A previous study indicated that the CRP levels with a cut-off value of 26.9 mg/L may predict the progression of COVID-19 in non-severe cases [20]. However, mean CRP levels were 35.9 ± 36.9 and 60.7 ± 75.8 mg/mL in mild and moderate cases that were grouped

according to CT findings. Moreover, in our cases, all of the mild cases and 81.7% of the moderate cases were discharged from the hospital after recovery. CRP levels were found to correlate with the severity of the disease [21], and CRP levels correlated with CT severity scores and may be implemented in early detection of severe COVID-19 [22].

In contrast to other studies, our study showed that the mean age was lower in severe cases than mild and moderate cases. This might be due to the fact that the frequency of CAD and HT was higher in our cases at a young age, and they were in a significant association with increased severity of the disease. The reason of the higher frequency of CAD and HT in cases with severe CT findings, and they were significantly younger, might be the lifestyle and other concomitant factors that may lead to CAD and HT development. In previous literature, chronic health problems including CAD and HT have been implicated to be associated with high mortality and morbidity [23,24]. However, in our study, we did not observe any significant association between the disease severity and other chronic health conditions. There was also a significant relationship between disease severity and mortality. These results suggest that the presence of HT and CAD may be a predictor of the severity and mortality of COVID-19.

This study has some limitations.. First of all, we only included cases with positive RT-PCR test results. However, it might have

been relevant to include cases with negative RT-PCR test results and positive CT findings and investigate the abovementioned parameters. Another limitation was that we needed to transfer some of the patients who had positive RT-PCR test results to another institution due to the fully occupied capacity of the intensive care unit.

Conclusions

Inconsistencies in the clinical condition, radiological features, and biochemical parameters of COVID-19 patients are not rare. CRP and ferritin levels, as well as accompanying HT and CAD, may be used to distinguish patients with severe disease from those with mild and moderate disease. In conclusion, for the detection of the disease severity and prediction of the progression, it is necessary to integrate CT assessments, complete blood counts and blood biochemistry is necessary.

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