ORIGINAL ARTICLE

Demographics, laboratory parameters and outcomes of 1061 patients with coronavirus disease 2019: a report from Tehran, Iran

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Abstract

We aimed to determine the characteristics of coronavirus disease 2019 (COVID-2019) among the Iranian population. In this study, we collected and analysed the demographics, laboratory findings and outcomes of patients with COVID-19 who were admitted to Masih Daneshvari Hospital in Tehran, Iran between 20 February 2020 and 2 April 2020. Among 1061 patients, 692 (65.2%) were male and the median age was 55 years (interquartile range (IQR), 44–66 years). Totally, 129 (12.2%) patients died during hospitalization in the ward or intensive care unit. From the remaining 932 individuals, 46 (5.0%) were admitted to the intensive care unit and 886 (95.0%) were hospitalized in the ward. Those patients who died were significantly older than those hospitalized in the ward ($p < 0.001$). The median absolute number of lymphocytes was 1.2×10^3/μL (IQR 0.9×10^3 to 1.6×10^3/μL) and 708 (66.7%) patients had lymphopenia (absolute lymphocyte count <1500/μL). Among the laboratory tests, D-dimer, serum ferritin and albumin had the strongest correlations with mortality ($r = 0.455$, $r = 0.412$, $r = -0.406$, respectively; $p < 0.001$ for each one). In conclusion, laboratory findings could provide useful information with regard to the management of individuals with COVID-19.

Keywords: Coronavirus disease 2019, D-dimer, Iran, Laboratory, Lymphocyte
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Introduction

In December 2019, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified in Wuhan City, Hubei province, China [1]. The disease caused by this highly contagious viral pathogen, which was later named as the novel coronavirus disease 2019 (COVID-19) by the WHO, spread rapidly to other countries, including Iran, South Korea, and Italy. As of 13 May 2020, 188 countries have reported confirmed cases of COVID-19 with more than 293 241 deaths having occurred worldwide [2]. Patients infected with this novel beta-coronavirus mostly manifest with fever, cough, dyspnoea, headache and fatigue [3,4]. In a minority of patients, SARS-CoV-2-associated pneumonia can lead to severe complications such as, acute respiratory distress syndrome, multiple organ failure and even death [2–5].

According to the literature, individuals with COVID-19 are prone to developing lymphopenia, increased neutrophil count and thrombocytopenia [4,6,7]. More recently, neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were proposed as potential predictors of mortality in indivudals

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with confirmed COVID-19 [8–10]. Higher levels of infection-related markers, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), D-dimer, serum ferritin and pro-inflammatory cytokines (interleukin-6 (IL-6), IL-1β, interferon-γ, tumour necrosis factor-α) have also been suggested as markers of disease progression in several studies [11–13].

The vast majority of studies describing the demographics and clinical characteristics, as well as the laboratory findings, of individuals with COVID-19 are from mainland China [2–5]. Although Iran is one of the countries greatly affected by this novel coronavirus, to date information on the laboratory findings of COVID-19 infection among Iranian patients is scarce. Herein, we report the demographic and laboratory data of 1061 individuals who were admitted to a specifically designated hospital for COVID-19 in Tehran, Iran.

Materials and methods

Study design and participants

This retrospective study was conducted on 1061 individuals with suspected COVID-19 who were admitted to Masih Daneshvari Hospital, Tehran, Iran between 20 February and 2 April 2020. This hospital was the first and largest hospital that was specifically designated for the hospitalization of individuals with suspected COVID-19 in Tehran. All individuals who tested positive for SARS-CoV-2 by real-time RT-PCR or those suspected of having COVID-19 based on characteristic clinical symptoms and chest CT findings, were included in this study. Demographic data including age, sex, date of admission and laboratory findings were collected from patients' electronic medical records. One researcher reviewed the data collection forms for quality control. No age limitation was considered in our study; however, almost all the included patients were adults. Final follow-up date was 1 May 2020. Individuals were divided into three main groups: patients who were admitted to the ward, patients who were admitted to the intensive care unit (ICU) and those who died before follow up. It should be noted that patients who had died by the end of final follow up but who had also received care in the ICU/ward during hospitalization were included in the 'expired' group, and all the patients in the 'ward' and 'ICU' groups had survived until the final follow-up date. This study was approved by the ethics committee of Shahid Beheshti University of Medical Sciences and written informed consent was obtained from all patients before enrolment in the study.

Laboratory tests

Laboratory tests were taken based on the hospital protocol for COVID-19 management. These assessments included complete blood count, coagulation tests (prothrombin time (PT), international normalized ratio (INR), partial thromboplastin time (PTT)), serum total protein, serum albumin, lactate dehydrogenase (LDH), CRP, serum ferritin (measured by ELISA), cardiac troponin I, ESR, D-dimer, 25-hydroxyvitamin D_3 (25-OH-D_3), IL-6, blood urea, creatinine, aspartate aminotransferase (AST) and alanine aminotransferase (ALT). In addition, an RT-PCR assay was performed on nasopharyngeal specimens for SARS-CoV-2 detection in all patients using Taqman® Premix TAKARA (TaKaRa, Dalian, China) considering the protocols provided by the manufacturer. In patients with laboratory examinations at multiple time-points during the study period, only the initial tests were evaluated. According to our clinical experience, we also investigated whether a decreasing trend in the absolute number of lymphocytes was correlated with mortality. This was defined as at least two consecutive decreases in the lymphocyte count during the study period.

Statistical analysis

Categorical variables were expressed as frequency (%), and continuous variables were presented as mean (SD) or median (interquartile range (IQR)) for normally distributed and non-normally distributed variables, respectively. The Kolmogorov–Smirnov test was conducted to assess the distribution normality. To compare the continuous variables between the groups, one-way analysis of variance and Kruskal–Wallis tests were used for parametric and non-parametric data, respectively. Chi-square test was used for comparing categorical data between groups. Subgroup analysis was also performed for patients who had a positive RT-PCR test. Pearson's correlation test was used for assessing the correlation between mortality and variables. Patients were divided into two categories for this analysis; those who were admitted to the ICU or ward were grouped as survivors and those patients who died during the study period formed the non-survivors group. All statistical analyses were performed with SPSS software version 23.0 (IBM Corp., Chicago, IL, USA). Values of $p < 0.05$ were considered statistically significant. Three age groups were defined: patients <21 years old, patients aged 21–64 years, and those ≥65 years.

Results

Total study population

A total of 1061 hospitalized individuals were included in this study. Among them, 129 (12.2%) died during hospitalization in the ward or ICU. From the remaining 932 individuals, 46 (5.0%) were admitted to the ICU and 886 (95.0%) were hospitalized in the ward. The median age of all patients was 55 (IQR 44–66)

years, and 65.2% of the patients were males. Median age of those who died was 65 years and no significant difference in age was seen between patients who died and those who received ICU care (p 0.064); however, patients who died were significantly older than those hospitalized in the ward (p < 0.001). Although all patients were considered to be COVID-19-positive, only 53.6% had a positive RT-PCR test. The laboratory findings of patients within each group are shown in Table 1. At baseline, 126 (12.3%) patients had leukopenia and 708 (66.7%) had lymphopenia. The median absolute number of lymphocytes was 1.2 × 10^3/μL (IQR 0.9 × to 1.6 × 10^3/μL). Among laboratory tests, only haemoglobin level, platelet count, PTT, 25-OH-D_3 level, IL-6 and quantitative CRP level were not statistically significant between groups. Compared with patients who died by the end of final follow up, those admitted to the ward were significantly younger (p < 0.001), had significantly lower blood urea (p < 0.001), creatinine (p < 0.001), AST (p < 0.001), ALT (p 0.027), LDH (p < 0.001), serum ferritin (p 0.001), cardiac troponin I (p < 0.001), white blood cell count (p < 0.001), neutrophil count (p < 0.001), neutrophil percentage (p < 0.001), NLR (p < 0.001), PLR (p < 0.001), ESR (p 0.001), PT (p 0.006), INR (p 0.002), D-dimer level (p < 0.001), and significantly higher albumin (p < 0.001), total protein (p < 0.001), lymphocyte count (p < 0.001) and lymphocyte percentage (p < 0.001). Moreover, individuals who were admitted to the ICU also had significantly lower LDH (p 0.009), ESR (p 0.007), neutrophil percentage (p 0.001), NLR (p 0.026) and serum ferritin (p < 0.001), and statistically higher lymphocyte count (p 0.006) than those who had a final outcome of death. Among survivors, when comparing patients admitted to the ward with those admitted to the ICU,

TABLE 1. Demographics and baseline laboratory findings of all included patients (*n* = 1061)

Variable	Ward	ICU	Died	Total	p value
Age (years)	54 (43–65)	56 (44–70)	65 (54.5–72)	55 (44–66)	<0.001
Age groups					
≤20	9 (1.0)	2 (4.3)	—	11 (1.0)	<0.001
21–64	653 (73.7)	29 (63.0)	64 (49.6)	746 (70.3)	—
≥65	224 (25.3)	15 (32.6)	65 (50.4)	304 (28.7)	—
PCR assay positivity	456 (51.5)	25 (54.3)	89 (69.0)	570 (53.7)	0.001
Sex					
Male	563 (63.5)	32 (69.6)	97 (75.2)	692 (65.2)	0.028
Female	323 (36.5)	14 (30.4)	32 (24.8)	369 (34.8)	
Blood routine					
WBC (× 10^3/μL)	6.0 (4.7–7.9)	7.8 (6.2–12.0)	8.5 (6.1–11.5)	6.3 (4.9–8.4)	<0.001
≤4.0	117 (13.7)	2 (4.3)	7 (5.5)	126 (12.3)	<0.001
4.0–10.0	629 (73.7)	28 (60.9)	75 (58.6)	732 (71.3)	—
≥10.0	107 (12.5)	16 (34.8)	64 (35.9)	169 (16.5)	—
Haemoglobin (g/dL)	13.9 (12.7–14.9)	13.3 (11.8–14.7)	13.7 (12.4–14.9)	13.8 (12.7–14.9)	0.121
PLT (× 10^3/μL)	180 (144–230)	185.5 (138–233.5)	184 (147–236)	180.5 (144–230)	0.822
Neutrophil					
Percentage	71.0 (63.5–79.0)	78.8 (65.5–84.5)	83.7 (78.0–87.5)	73.0 (65.0–81.0)	<0.001
Count (× 10^3/μL)	4.2 (3.1–5.9)	6.2 (4.6–9.1)	6.9 (4.7–9.8)	4.5 (3.2–6.5)	<0.001
Lymphocyte					
Percentage	21.2 (15.0–28.0)	15.0 (9.6–20.0)	11.2 (7.3–16.3)	20.0 (13.0–27.0)	<0.001
Count (× 10^3/μL)	1.2 (0.9–1.7)	1.2 (0.9–1.7)	0.9 (0.6–1.2)	1.2 (0.9–1.6)	<0.001
<1.5	577 (67.6)	28 (62.2)	103 (81.7)	708 (66.7)	0.004
NLR	3.36 (2.26–5.30)	5.33 (3.30–8.63)	7.24 (4.86–11.87)	3.71 (2.43–6.15)	<0.001
PLR	0.14 (0.11–0.20)	0.15 (0.11–0.24)	0.21 (0.13–0.31)	0.15 (0.11–0.22)	<0.001
Blood chemistry					
Urea (mg/dL)	31 (24–40)	42 (28–54.5)	44 (34–62.8)	32 (25–42)	<0.001
Creatinine (mg/dL)	1.1 (1.0–1.3)	1.2 (1.1–1.4)	1.2 (1.0–1.5)	1.1 (1.0–1.3)	<0.001
AST (U/L)	36 (27–49)	40 (32–66)	49.5 (35–86.5)	37 (28–51)	<0.001
ALT (U/L)	28 (19–44)	25 (18–46)	33 (22–59)	28 (19–45)	0.025
LDH (U/L)	472 (380.5–614.5)	585 (451.5–805)	762.5 (570.8–992.3)	500 (399.8–669.5)	<0.001
25-OH-D_3 (ng/mL)	23.0 (17.0–41.0)	19.0 (13.0–55.0)	27.5 (14.5–36.0)	23.0 (15.8–39.0)	0.931
Albumin (g/dL)	3.5 (3.2–3.8)	3.1 (2.6–3.5)	3.0 (2.6–3.2)	3.4 (3.0–3.7)	<0.001
Total protein (g/dL)	6.3 (5.9–6.7)	6.1 (5.6–6.4)	5.7 (5.3–6.1)	6.1 (5.7–6.6)	<0.001
Troponin I (ng/mL)	0.01 (0.01–0.01)	0.01 (0.01–0.01)	0.04 (0.01–0.12)	0.01 (0.01–0.01)	<0.001
Coagulation function					
PT (s)	13.1 (12.6–13.8)	13.5 (12.8–15.6)	13.3 (12.8–14.1)	13.2 (12.6–13.9)	<0.001
INR	1.19 (1.10–1.32)	1.25 (1.12–1.68)	1.22 (1.14–1.39)	1.19 (1.10–1.34)	<0.001
PTT (s)	40.0 (36.0–45.0)	39.0 (35.0–46.8)	42.0 (38.0–47.0)	41.0 (36.3–46.0)	0.061
D-dimer (ng/mL)	1206 (717.5–1954)	6071.5 (1497–10 000)	8465.5 (2206.3–10 000)	1752 (920–7070)	<0.001
Infection-related markers					
ESR (mm/h)	50.0 (27.5–83.0)	45.0 (23.0–69.8)	64.0 (44.0–94.0)	52.0 (28.0–85.0)	0.001
≥100	86 (11.3)	5 (12.5)	15 (15.8)	106 (11.8)	0.438
IL-6 (pg/mL)	4.3 (2.4–10.7)	4.8 (2.6–11.5)	10.1 (3.0–28.6)	4.5 (2.6–14.9)	0.088
Ferritin (ng/mL)	614.5 (223.0–1270.0)	1440.5 (485.5–2000.0)	2000.0 (1306.8–2000.0)	772.0 (243.8–1749.3)	0.001
CRP, *n* (%)					
Positive	443 (85.9)	11 (26.8)	51 (67.1)	505 (79.8)	<0.001
Weakly positive	28 (5.4)	3 (7.3)	5 (6.6)	36 (5.7)	
Negative	45 (8.7)	27 (65.9)	20 (26.3)	92 (14.5)	
Quantitative CRP (mg/L)	50.0 (30.0–57.0)	55.0 (52.0–57.0)	53.0 (33.0–58.0)	51.0 (31.0–57.0)	0.163

Abbreviations: 25-OH-D_3, 25-hydroxyvitamin D_3; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; ICU, intensive care unit; IL-6, interleukin-6; INR, international normalized ratio; LDH, lactate dehydrogenase; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; PLT, platelet; PT, prothrombin time; PTT, partial thromboplastin time; WBC, white blood cell.
Data are reported as median (interquartile range) or *n* (%).

significant differences were found in the following variables: urea (p 0.001), LDH (p 0.001), albumin (p < 0.001), white blood cell count (p < 0.001), lymphocyte percentage (p < 0.001), neutrophil count (p < 0.001), neutrophil percentage (p 0.023), NLR (p 0.001), PT (p 0.006), INR (p 0.024) and D-dimer (p 0.008).

Individuals with laboratory-confirmed COVID-19

As mentioned earlier, 570 patients had RT-PCR-confirmed COVID-19 infection. Among this subpopulation, 89 (15.6%) patients died, 25 (4.4%) were admitted to the ICU, and the remaining (80%) received care in the ward. The median (IQR) age of these patients was 56.5 (45–66) years and approximately 65% were male. Also, the median age of those who died was 64 years. At baseline, 81 (14.6%) patients had leukopenia and 410 (74.1%) had lymphopenia. After performing a subgroup analysis, we found that results were similar to that of the total population except for ALT and serum ferritin, which did not vary significantly between the three groups (p 0.307 and p 0.135, respectively), and PTT, which was found to be statistically different across groups (p 0.047) (Table 2).

Correlation between mortality and study variables

As shown in Table 3, the variables that had the greatest correlation with mortality were D-dimer (r = 0.455, p < 0.001), serum ferritin (r = 0.412, p < 0.001) and albumin (*r* = −0.406, p < 0.001) in descending order. Although a statistically significant positive correlation was observed between decreasing lymphocytes and mortality (r = 0.254, p < 0.001), it was not as strong as variables such as, D-dimer, serum ferritin, albumin, LDH, total protein and NLR. Moreover, PLT (p 0.431), 25-OH-

TABLE 2. Demographics and baseline laboratory findings among laboratory-confirmed patients with coronavirus disease 2019 (*n* = 570)

Variable	Ward (*n* = 456)	ICU (*n* = 25)	Died (*n* = 89)	Total	p value
Age (years)	55 (44–64)	63 (55–77)	64 (55–72)	56.5 (45–66)	<0.001
Age groups					
≤20	5 (1.1)	—	—	5 (0.9)	<0.001
21–64	338 (74.1)	13 (52)	45 (50.6)	396 (69.5)	—
≥65	113 (24.8)	12 (48)	44 (49.4)	169 (29.6)	—
Sex					
Male	282 (61.8)	19 (76.0)	68 (76.4)	369 (64.7)	0.015
Female	174 (38.2)	6 (24.0)	21 (23.6)	201 (35.3)	
Blood routine					
WBC (× 10^3/μL)	5.7 (4.5–7.4)	7.3 (6.1–9.9)	8.5 (6.0–11.0)	6.0 (4.7–8.0)	<0.001
≤4.0	74 (16.7)	2 (8.0)	5 (5.7)	81 (14.6)	<0.001
4.0–10.0	332 (74.9)	17 (68.0)	56 (63.6)	405 (72.8)	—
≥10.0	37 (8.4)	6 (24.0)	27 (30.7)	70 (12.6)	—
Haemoglobin (g/dL)	13.9 (12.6–15.1)	13.5 (11.9–14.6)	13.9 (13.0–15.0)	13.9 (12.7–15.0)	0.32
PLT (× 10^3/μL)	171 (139–214)	173 (110–209)	184 (150–224)	175 (140–214)	0.10
Neutrophil					
Percentage	83 (78.0–87.1)	80.5 (67.3–86.8)	83 (78.0–87.1)	74 (64.8–81.8)	<0.001
Count (× 10^3/μL)	3.9 (2.9–5.5)	5.9 (4.7–6.9)	6.8 (4.6–9.0)	4.3 (3.1–6.2)	<0.001
Lymphocyte					
Percentage	21 (15.0–28.6)	14 (8.5–19.8)	12 (8.0–16.3)	20 (13–27)	<0.001
Count (× 10^3/μL)	1.2 (0.9–1.6)	1.0 (0.7–1.4)	0.9 (0.7–1.2)	1.1 (0.8–1.5)	<0.001
<1.5	320 (72.2)	19 (79.2)	71 (82.6)	410 (74.1)	0.115
NLR	3.36 (2.18–5.20)	5.86 (3.42–10.36)	6.71 (4.83–10.97)	3.80 (2.41–6152)	<0.001
PLR	0.14 (0.11–0.20)	0.15 (0.12–0.25)	0.21 (0.14–0.30)	0.15 (0.11–0.22)	<0.001
Blood chemistry					
Urea (mg/dL)	31 (24–39)	39 (27.5–55)	44 (34.5–58.5)	32 (26–43)	<0.001
Creatinine (mg/dL)	1.1 (1.0–1.3)	1.2 (1.1–1.3)	1.2 (1.0–1.5)	1.1 (1.0–1.3)	<0.001
AST (U/L)	37 (29–49)	40 (32–63)	48 (35–86.5)	38 (29–53)	<0.001
ALT (U/L)	29 (19–44)	26 (18–50)	32 (21.3–58.3)	29.5 (19–45)	0.307
LDH (U/L)	472 (390.3–621.8)	642.5 (490.8–783.5)	705.5 (570–992.8)	514.5 (409–686)	<0.001
25–OH-D_3 (ng/mL)	23 (17–37)	21 (13.8–69.5)	22 (11.5–33.5)	23 (16–35)	0.852
Albumin (g/dL)	3.5 (±0.4)	3.0 (±0.5)	3.0 (±0.4)	3.3 (±0.5)	<0.001
Total protein (g/dL)	6.2 (5.9–6.7)	5.7 (5.1–6.3)	5.9 (5.5–6.2)	6.1 (5.7–6.5)	<0.001
Troponin I (ng/mL)	0.01 (0.01–0.01)	0.01 (0.01–0.01)	0.04 (0.01–0.2)	0.01 (0.01–0.01)	<0.001
Coagulation function					
PT (s)	13.1 (12.6–13.8)	13.4 (12.7–15.4)	13.2 (12.9–14.0)	13.1 (12.6–13.9)	0.005
INR	1.18 (1.08–1.32)	1.24 (1.12–1.63)	1.21 (1.15–1.35)	1.19 (1.10–1.34)	0.003
PTT (s)	41.8 (±8.3)	44.3 (±11.6)	44.4 (±10.0)	42.4 (±8.9)	0.047
D-dimer (ng/mL)	1420 (746–1888)	6182 (1353–10 000)	8731 (2338–10 000)	2075 (1185–10 000)	0.002
Infection-related markers					
ESR (mm/h)	47 (26–78)	45 (35.3–65)	69 (51.5–94)	51 (28.5–81)	<0.001
≥100	38 (9.4)	3 (15)	12 (18.2)	53 (10.8)	0.088
IL-6 (pg/mL)	4.5 (2.5–10.2)	4.8 (2.6–11.5)	6.6 (3.4–25.4)	5.1 (2.8–11.2)	0.209
Ferritin (ng/mL)	639 (228–1323)	1352 (376–1765)	1358 (1031–1727)	714 (250–1510)	0.135
CRP, *n* (%)					
Positive	240 (87.6)	8 (38.1)	38 (73.1)	286 (82.4)	<0.001
Weakly positive	16 (5.8)	1 (4.8)	2 (3.8)	19 (5.5)	
Negative	18 (6.6)	12 (57.1)	12 (23.1)	42 (12.1)	
Quantitative CRP (mg/L)	50 (33–57)	56 (54–57)	53 (40–58)	52 (34–57)	0.121

Abbreviations: 25-OH-D_3, 25-hydroxyvitamin D_3; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; ICU, intensive care unit; IL-6, interleukin-6; INR, international normalized ratio; LDH, lactate dehydrogenase; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; PLT, platelet; PT, prothrombin time; PTT, partial thromboplastin time; WBC, white blood cell.
Data are reported as median (interquartile range) or *n* (%).

TABLE 3. Correlation between mortality and study variables among patients

Variable	Total population (n = 1061)		RT-PCR-confirmed patients (n = 570)	
	r	p-value	r	p-value
Age	0.189	<0.001	0.204	<0.001
Sex (male)	0.078	0.011	0.105	0.012
Urea	0.274	<0.001	0.281	<0.001
Creatinine	0.137	<0.001	0.141	0.001
AST	0.094	0.003	0.268	<0.001
ALT	0.025	0.428	0.102	0.017
LDH	0.355	<0.001	0.381	<0.001
Albumin	−0.406	<0.001	−0.404	<0.001
Total protein	−0.366	<0.001	−0.254	0.001
Serum ferritin	0.412	<0.001	0.233	0.111
Troponin I	0.288	<0.001	0.338	<0.001
WBC	0.161	<0.001	0.167	<0.001
Haemoglobin	−0.062	0.048	−0.012	0.776
PLT	0.025	0.431	0.090	0.033
Neutrophil				
Percentage	0.299	<0.001	0.315	<0.001
Count	0.260	<0.001	0.341	<0.001
Lymphocyte				
Percentage	−0.291	<0.001	−0.300	<0.001
Count	−0.084	0.007	−0.064	0.136
NLR	0.328	<0.001	0.308	<0.001
PLR	0.187	<0.001	0.219	<0.001
Decreasing lymphocyte trend	0.254	<0.001	0.266	<0.001
ESR	0.114	0.001	0.192	<0.001
PT	0.106	0.001	0.129	0.004
INR	0.137	<0.001	0.150	0.001
PTT	0.085	0.011	0.107	0.017
D-dimer	0.455	<0.001	0.456	0.001
25-hydroxyvitamin-D_3	−0.050	0.697	−0.090	0.567
IL-6	0.235	0.006	0.041	0.692
C-reactive protein				
Quantitative	0.025	0.684	0.046	0.561
Qualitative	0.121	0.002	0.127	0.018

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; ESR, erythrocyte sedimentation rate; IL-6, interleukin-6; INR, international normalized ratio; LDH, lactate dehydrogenase; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; PLT, platelet; PT, prothrombin time; PTT, partial thromboplastin time; WBC, white blood cell.

D_3 (p 0.697), ALT (p 0.428) and quantitative CRP (p 0.684) did not show a significant correlation with mortality. We also found that ESR levels had a significant negative correlation with albumin levels ($r = -0.301$, $p < 0.001$). Among patients with RT-PCR-confirmed COVID-19, D-dimer ($r = 0.456$, p 0.001), albumin ($r = -0.404$, $p < 0.001$) and LDH ($r = 0.381$, $p < 0.001$) had the strongest correlation with mortality (Table 3).

Discussion

In the COVID-19 pandemic, identifying risk factors that are associated with a poor outcome will help in appropriate resource allocation and patient management. Initially, clinical characteristics such as increased age and the presence of comorbidities were suggested as predictive factors of outcome [2,14,15]; however, more recently, studies have addressed the prognostic value of laboratory parameters. In this study, we investigated the demographic and laboratory findings of COVID-19 infection among the Iranian population. Our results showed that the median age of patients with COVID-19 was 55 years. This finding is similar to studies from China in which the median age of infected patients ranged between 55.5 and 57 years [2,5,16]. Male patients represented 65% of all patients; similarly, Wu et al. observed that 63.7% of the patients with COVID-19 were male [17]. Also, the median age of patients who experienced COVID-19-related mortality in our study was 65 years, and approximately 75% of these patients were male. Wang et al. evaluated the characteristics of 77 individuals who died from COVID-19 in Wuhan [18]. They reported an average age of 71 years at death and male patients constituted a greater percentage compared with female patients (66% versus 34%) [18]. In another study from China, the median age of individuals who had died of COVID-19 was also 71 years, and male patients were more likely to die than females [19]. In a systematic review by Rodriguez-Morales et al., 13.9% of the hospitalized patients with confirmed COVID-19 had fatal outcomes [20]; our study found that 12.2% of the hospitalized patients died during the study period. In addition, a relatively small percentage of patients who survived (5.0%) required ICU care, whereas other studies have reported higher percentages [2,5,21,22]. However, as stated earlier, those who died by the final follow-up date but had received ICU care before death were not included in the 'ICU' group.

Many studies have investigated laboratory findings in COVID-19 that are associated with disease severity. Generally, patients with COVID-19 tend to have abnormal blood counts, coagulopathy, and liver and kidney dysfunction [4,7]. Higher serum CRP, D-dimer, LDH, creatine kinase and procalcitonin levels have been found among patients with severe disease [16,17,23,24]. In this study, D-dimer, serum ferritin and albumin had the strongest correlations with mortality. Although albumin has a half-life of 15–19 days, it is more rapidly decreased than expected during the course of COVID-19 infection. Elevated levels of inflammatory cytokines, particularly IL-6, increase vascular permeability during an acute-phase response and result in the redistribution of albumin into the interstitial space [25]. In addition, increased IL-6 may induce apoptosis in lymphocytes, leading to lymphopenia in individuals with COVID-19 [26]. Our study failed to show a significant difference in IL-6 levels between the three groups; however, in contrast to patients admitted to the ward or ICU, the median IL-6 level (10.1 pg/mL) was higher than the upper limit of normal (5.9 pg/mL) in individuals who died. Another finding of this study was that patients who died had significantly increased ESR and serum ferritin levels and a higher proportion of positive CRP compared with those admitted to the ward. These results suggest that patients with severe disease have an increased activity of the innate immune system. As mentioned by Shi et al., individuals with an impaired adaptive immune

response progress to the severe stage of disease, which is marked by pulmonary inflammation [27]. Stimulation of the innate immune system also leads to cytokine release storm. The non-significant difference in IL-6 levels between the three groups in our study could be because we assessed the initial laboratory findings of the individuals included, so the cytokine release storm might have occurred at a later stage of disease in critical patients. About 10% of the patients in our study had an ESR value of greater than 100 mm/h. Although the main reason for enhanced ESR in inflammatory conditions is increased fibrinogen, an acute-phase reactant, albumin, also has a suppressive effect on sedimentation; this was confirmed by the significant negative correlation between ESR and albumin levels in this study. From the clinical perspective, COVID-19 could be considered in the differential diagnosis of markedly increased ESR of over 100 mm/h.

As mentioned earlier, COVID-19-associated coagulopathy is a common finding among hospitalized patients [28,29]. In this study, coagulopathy was characterized by elevated D-dimer levels and prolonged PT, INR and PTT. Individuals with COVID-19 suffer from a hypercoagulable state for several reasons. SARS-CoV-2 can directly cause injury to the endothelial cells, which along with systemic inflammation activates the coagulation cascade [30,31]. Besides, patients with hypoxia are more prone to thrombosis due to increased blood viscosity and stimulation of hypoxia-inducible factors [32].

Among all patients, approximately 67% had lymphopenia; this is in accordance with previous reports that have indicated a diagnostic value for lymphopenia in patients with COVID-19 on admission [11,16,28,33,34]. According to our results, patients who died were more likely to have a white blood cell count of more than 10.0 × 10^3/μL compared with patients who received care in the ward. In a single-centre study by Qu et al., a higher PLR was proposed as a prognostic indicator of prolonged hospitalization in individuals with confirmed COVID-19. They also found that patients with a peak in the absolute count of platelets during the disease course had poor outcomes [10]. Likewise, in our study, PLR values were markedly lower in the ward patients compared with those who died. Interestingly, only lymphocyte percentages were significantly lower in patients admitted to the ICU compared with those hospitalized in the ward. Zhang et al. have also reported lower lymphocyte percentages, but not lymphocyte counts, in severe patients in comparison to non-severe patients [16]. On the other hand, neutrophil counts were significantly higher in patients admitted to the ICU and those who died compared with patients in the ward. We observed statistically lower values of NLR in patients hospitalized in the ward compared with both those admitted to the ICU and those who died, and also in patients admitted to the ICU compared with patients who died.

Regarding haemoglobin, a decreased haemoglobin level was an uncommon finding in this study. One possible explanation is haemoconcentration, caused by the leakage of plasma from blood vessels in response to increased pro-inflammatory markers. Dehydration also plays a role in increased haemoglobin levels, although to a lesser extent.

In this study, we included 1061 individuals who were treated as COVID-19 patients; however, nearly half of these patients had a positive RT-PCR test while the remaining patients tested negative. As the current reference standard test for the diagnosis of COVID-19 is RT-PCR, we performed a subgroup analysis among individuals with laboratory-confirmed COVID-19. Notwithstanding, the results were relatively similar to those of the total population.

Our study has several limitations. First, we did not report the detailed clinical and radiological manifestations of the included population due to lack of access to data. Hence, we were not able to evaluate the severity of disease based on predefined classifications by international agencies. Second, we did not consider the co-morbidities of patients, a factor that may have an important role in the mortality of patients with COVID-19 [2]. In addition, due to the retrospective nature of the study, we did not have access to complete laboratory data for all patients, which might potentially reduce the strength of the reported findings.

In conclusion, the results of this study suggest that laboratory abnormalities are seen in patients with COVID-19. These alterations may be due to the induction of inflammatory response, cytokine storm or the direct invasion of SARS-CoV-2. Specific haematological markers could help to predict the prognosis of individuals with COVID-19.

Conflicts of interest

The authors have stated that there are no conflicts of interest in relation to this article.

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