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Clinical & Laboratory markers as predictors for severity and mortality in COVID-19

Asma Ameen Ghareeb
Department of Medical Laboratory Technology, Erbil Technical Health and Medical College, Erbil Polytechnic University, Erbil, 44001, IRAQ., asmaa.mhm20@epu.edu.iq

Sazan Moffaq Abdulaziz
Department of Medical Laboratory Technology, Erbil Technical Health and Medical College, Erbil Polytechnic University, Erbil, 44001, IRAQ., sazan.abdulaziz@epu.edu.iq

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Abstract

Backgrounds: COVID-19, a new health challenge, can be diagnosed by many laboratory biomarkers. Biomarkers became valuable for prognosis; identifying the severity and mortality of the disease in COVID-19 patients. This study aims to determine the association of clinical, demographics, and laboratory biomarkers (CRP, D-dimer, lymphocyte, and platelet) with the severity and mortality of COVID-19. Methods: Between June 1st and November 1st, 2020, 34 healthy controls and 104 COVID-19 cases were enrolled in this study. SARS-CoV-2 infection was confirmed using the real-time RT-PCR technique. All cases were analyzed for clinical, epidemiological, and laboratory biomarkers. COVID-19 cases were regrouped into mild (n=40), moderate (n=32), and severe (n=32) groups depending on the severity of the disease; it was also re-categorized into survivor (n=85) and non-survivor (n=19) groups depending on mortality. After collecting blood from participants, hematological parameters (lymphocyte and platelet) and other biomarkers (CRP and D-dimer) were measured by colter and Cobas c111, respectively. Results: For age categories and comorbidities, Statistical significance was found among COVID-19 groups. Regarding ABO, Rh, and gender, a non-significant difference was found among groups of COVID-19 patients. Cough and headache i the most common symptom in our population. SpO2 depressed more significantly in severe and moderate groups than in mild groups. Severe and moderate groups exhibit higher CRP, D-dimer, and lymphocyte percentages than control while there was a non-significant change for platelets and absolute lymphocyte counts among studies groups. All studied laboratory biomarkers were higher in non-survivors than in survivor COVID-19 groups. A significant correlation was found between D-dimer and other laboratory biomarkers. Conclusion: Gender, ABO, and Rh were not associated but age and comorbidities were associated with the severity of COVID-19. All studied laboratory biomarkers were associated with mortality.

Keywords

COVID-19, mortality, laboratory biomarkers, and SARS-CoV-2.

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RESEARCH ARTICLE

Clinical & Laboratory markers as predictors for severity and mortality in COVID-19

Asmaa Ameen Ghareeb[1], Sazan Moffaq Abdulaziz[2]
[1] *Department of Medical Laboratory Technology, Erbil Technical Health and Medical College, Erbil Polytechnic University, Erbil, 44001, IRAQ.*
[2] *Department of Medical Laboratory Technology, Erbil Technical Health and Medical College, Erbil Polytechnic University, Erbil, 44001, IRAQ.*

***Corresponding author: Asmaa Ameen Ghareeb, Department of Medical Laboratory Technology, Erbil Technical Health and Medical College, Erbil Polytechnic University, Erbil, 44001, IRAQ**

E-mail: asmaa.mhm20@epu.edu.iq

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ABSTRACT

Backgrounds: COVID-19, a new health challenge, can be diagnosed by many laboratory biomarkers. Biomarkers became valuable for prognosis; identifying the severity and mortality of the disease in COVID-19 patients. This study aimed to determine the association of clinical, demographics, and some laboratory biomarkers (CRP, D-dimer, lymphocyte, and platelet) with the severity and mortality of COVID-19.
Methods: 104 COVID-19 cases and 34 healthy controls were collected between the 1st of June and the 1st of November 2020. SARS-CoV-2 infection was confirmed using the real-time RT-PCR technique. All cases were analyzed for clinical, epidemiological, and laboratory biomarkers. COVID-19 cases were grouped into mild (n=40), moderate (n=32), and severe (n=32) depending on the severity of the disease. After collecting blood from participants, hematological parameters (lymphocyte and platelet) and other biomarkers (CRP and D-dimer) were measured by colter and Cobas c111, respectively.
Results: Age and comorbidities like DM, CVD and smoking showed a significant relation with COVID-19, while ABO, Rh, gender and other comorbidities showed a non-significant relation. Cough and headache were the most common symptoms expressed by the patients. SpO2 levels were significantly low in severe and moderate groups. Patients with severe and moderate infections significantly exhibited higher CRP, D-dimer, and lymphocyte percentage levels than the control group, whereas a non-significant difference was recorded for each of platelet and absolute lymphocyte counts among study groups. All studied laboratory biomarkers were significantly higher in non-survivors than in survivors. A significant correlation was found between D-dimer and other laboratory biomarkers.
Conclusion: Age and most of the studied comorbidities were associated with COVID-19. CRP, D-dimer, and lymphocyte percentage were markers of diseases severity and outcome. All the studied laboratory biomarkers were associated with mortality.
Keywords: COVID-19, mortality, laboratory biomarkers, and SARS-CoV-2.

INTRODUCTION

COVID-19, which is caused by SARS-CoV-2, created a worldwide health problem in late 2019 in Wuhan city in China (Guan et al., 2020, Wu and McGoogan, 2020). SARS-CoV-2 belongs to family of coronaviruses (WHO, 2020). The latter compromises a group of viruses including SARS-CoV-1, MERS-CoV, and SARS-CoV-2 (Peiris et al., 2003a, Zaki et al., 2012, Yin and Wunderink, 2018).
Early signs and symptoms of COVID-19 patients are typically relatively mild, and the infection may even be asymptomatic. However, the disease can quickly progress into acute respiratory distress syndrome (ARDS) and serious multi-organ issues because of rapid viral replication and cytokine storms (Chen et al., 2020). The clinical symptoms reported in SARS-CoV-2 were fever, cough, asthenia, dyspnea, sore throat, headache, arthromyalgia, and diarrhea (Young et al., 2020, Wang et al., 2020). However, as the infection spread and reached Europe, sudden changes in smell (anosmia/hyposmia) emerged as a new symptom (Gautier and Ravussin, 2020).
Acute lung inflammation is a complicated pathophysiological process that involves inflammatory mediators, such as cytokines and chemokines, which induce macrophages in the alveoli and disrupt the immune system (Nicholls et al., 2003). Cytokine storm, an inflammatory immune response that leads to organ failure, is thought to be the cause of the severity of COVID-19 disease (Wang and Ma, 2008, Ciceri et al., 2020). Severe cases of COVID-19 disease and cytokine storm have been associated with a high concentration of interleukin-6 (IL-6) (Hu et al., 2021), which induces the liver to release CRP (Sproston and Ashworth, 2018).
Several demographic factors associate with susceptibility

and severity of the disease. The association of ABO to the severity of the disease documented by some studies (Gérard et al., 2020, Zaidi et al., 2020) in which patients with blood group A have more susceptibility to infection than blood group O. Regarding gender, infection rate was higher among males than females due to hormonal differences. Testosterone in males increases the expression of ACE2 acting as a receptor for SARS-CoV-2. Moreover, smoking and drinking alcohol are more common in men (Taslem Mourosi et al., 2022). Old age is also regarded as a risk factor for SARS-CoV-2 infection due to the presence of comorbidities in elderly persons (Asai et al., 2022). In addition, a number of comorbidities have been well documented in this issue such as obesity, diabetes mellitus (DM), cardiovascular diseases (CVD), renal failure, pregnancy and smoking (Park, 2020, Bermejo-Martin et al., 2020, Zhou et al., 2020).

Retrospective studies revealed that the levels of the inflammatory proteins CRP, IL-6, ESR, D-dimer, ferritin, and LDH were higher in patients who passed away than in survivors (Ruan et al., 2020, Huang et al., 2020). Decreased lymphocytes and platelet can be also associated with the severity to SARS-CoV-2 infection (Palladino, 2021). These findings suggested that an overactive immunity, expressed primarily as increased inflammatory biomarkers, is likely to be associated with the intensity and outcomes of the COVID-19 disease. However, some demographic and laboratory biomarkers are expected to be altered in SARS-CoV-2 infections. As the results reported by many studies regarding lab parameters used to study the clinical state of COVID-19 were controversy and showed variable findings, this study was performed and aimed to investigate the association of a number of laboratory markers with disease severity and mortality rate in COVID-19 patients in Erbil city/Iraq.

SUBJECTS AND METHODS

Subjects

A case-control study that has been done in Erbil / Iraq from the 1st of November 2021 to the 28th of February 2022. The study included 104 COVID-19 patients who tested in Central Laboratory in Erbil or were admitted to the three COVID-19-specific hospitals; Al Emirati Hospital, Rozhawa Hospital, and Lalav Hospital in Erbil city/Iraq. According to the severity of the disease, COVID-19 patients were reclassified into mild (n=40), moderate (n=32), and severe (n=32) groups. The 34 healthy controls who were in this study had were totally negative for COVID-19 IgG/IgM rapid test (Inzek B.V./ Netherlands) demographic and clinical information regarding each subject were recorded. Subjects who accepted to participate in the study have been included.

Throat and nasal swab collection and processing

Sample collection was done using disposable virus sampling tubes specified for SARS-CoV-2. Nucleic acid extraction from nasopharyngeal and throat swab samples and detection of the virus were totally performed in the Central laboratory in Erbil/Iraq using specific kits (Zybio/China) (WHO, 2020).

Blood collection and processing

Seven ml of blood sample was taken by vein puncture using a disposable syringe from each individual enrolled in this study (both study and control groups), Blood samples were divided into 3 tubes, 2 ml of blood was added to tubes containing sodium citrate as an anticoagulant to obtain plasma which needed for determination of D-dimer. In the second part, 2 ml added EDTA tube was used within two hours after collection for assessing hematological parameters from the determination of CBC (Lymphocytes, platelets). The remaining blood was put into a serum separation tube and centrifuged for about a quarter-hour at 3000 rpm, it is used for measuring CRP. Hematological parameters (lymphocyte and platelet) and other biomarkers (CRP and D-dimer) were measured by Colter and Cobas c111 (Hitachi/Japan), respectively (Zeng et al., 2020).

Statistical analysis

SPSS 28 and Graph Pad Prism 9 were used to perform the statistical analysis of the collected data. Normality test was performed to select the correct test. Statistical significance has been considered if the *P value* was < 0.05.

RESULTS

Demographics and clinical characteristics among different groups of COVID-19 patients

All the clinically suspected cases for having COVID-19 were confirmed by Real-time PCR that specifically detected SARS CoV-2 in nasal and throat swab samples. Only samples which were positive for SARS-CoV-2 have been included in the study. The Demographics and clinical characteristics among different groups of COVID-19 patients are presented in table 1. the results indicate that most of the COVID-19 patients were located between the age interval of 42-65 years (42%). Young age groups; 18-29 and 30-41 years, mostly experienced mild infections (88.89% and 71.4%, respectively), whereas severe infection was mostly seen among old age groups; 54-65

and ≥ 66 years (54.5% and 50%, respectively. The relation between COVID-19 and age was statistically significant (*P* value= 0.000). The results showed no significant relation between COVID-19 and gender (*P* value= 0.96) although males had a higher rate of infection than females (57.7% and 42.3%, respectively), but no specific characterization has been seen regarding the severity of infection.

A non-significant relation between COVID-19 and ABO blood groups and Rh positivity (*P* value= 0.41 and 0.47, respectively) was detected. Blood groups A and O had the same distribution among the patients (35.6%) followed by group B (26%). No specific characterization regarding the severity of infection has been observed among ABO groups. Ninety-three patients were Rh+ and 11 were Rh-. Most of the Rh- patients showed mild infection (54.55%).

The history of patients with COVID-19 showed that 71 (68.3%) patients had single or multiple comorbidities. Mild patients showed the least comorbidities (25%) most of which were single factors such as obesity, type 2 diabetes mellitus (DM), smoking, and pregnancy. Complicated, serious and multiple comorbidities were common among hospitalized patients (90.6% of moderate and 100% of severe patients). Patients in the severe group were mostly admitted to the intensive care unit (ICU). Statistical analysis showed a significant relation between COVID-19 infection and disease comorbidities. Details on the type and rate of occurrence of each comorbidity are presented in table 1.

Several signs and symptoms have been related to COVID-19 and expressed and/or recorded relatively differently among different patient groups. Cough, headache, body aches, and fever were the most common symptoms recorded in all three patient groups. Shortness of breath (dyspnoea) was specifically observed in hospitalized patients (47.54% and 52.46% for moderate and severe infections, respectively) and was statistically significantly related to COVID-19 (*P* value 0.000). On the other hand, the loss of sense of smell (anosmia) *and* sense of taste (ageusia) were two symptoms specifically described by patients with mild infection both of which were significantly related to COVID-19 *(P* value= 0.002).

Death rate showed a significant relation with COVID-19 (*P* value 0.000). No death has been recorded among patients with a mild infection, but the death rate was high among severe patients (17(53.1%)) as a consequence of multiple comorbidities. The lowest mean±SD of PO_2 was recorded among patients with severe COVID-19 (67.94±13.35) that required an urgent need for an artificial oxygen supply. Patients with moderate infection required oxygen supply intermittently as the drop in PO_2 was not high and continuous (mean±SD: 85.91±6.35).

Table 1: Demographic and clinical characteristics among different groups of COVID-19 patients.

Character	Mild n(%)	Moderate n(%)	Severe n(%)	Total n(%)	Chi² *P value*
Age groups (years)					
18-29	16(88.89)	2(11.11)	0(0)	18 (100)	0.000
30-41	10(71.4)	4(28.6)	0(0)	14(100)	
42-53	10(45.4)	6(27.3)	6(27.3)	22(100)	
54-65	3(13.6)	7(31.9)	12(54.5)	22(100)	
≥66	1(3.6)	13(46.4)	14(50)	28(100)	
Total	40(38.46)	32(30.77)	32(30.77)	104(100)	
Gender					
Female	17(38.7)	13(29.5)	14(31.8)	44(100)	0.96
Male	23(38.3)	19(31.7)	18(30)	60(100)	
ABO &Rh					
A	14(37.84)	13(35.14)	10(27.02)	37(100)	0.41
AB	2(66.67)	1(33.33)	0(0)	3(100)	
B	9(33.33)	11(40.74)	7(25.93)	27(100)	
O	15(40.54)	7(18.92)	15(40.54)	37(100)	
Rh-	6(54.55)	2(18.2)	3(27.3)	11(100)	0.47
Rh+	34(36.6)	30(32.3)	29(31.2)	93(100)	
Comorbiditie	10 (25)	29 (90.6)	32 (100)	71 (68.3)	0.000
Obesity					
Underweight	4 (66.7)	1(16.7)	1(16.7)	6(100)	0.239
Normal	24(46.2)	14(26.9)	14(26.9)	52(100)	
Overweight	10(32.3)	11(35.5)	10(32.3)	31(100)	
Obese	2(13.11)	6(40)	7(46.7)	15(100)	
Smoking	2(11.8)	6(35.3)	9(52.9)	17(100)	0.028
Diabetes mellitus (DM)	3(12)	8(32)	14(56)	25(100)	0.002
Chronic renal Diseases	0(0)	2(13.33)	13(86.67)	15(100)	0.000
Respiratory Problems	0(0)	2(16.67)	10(83.33)	12(100)	0.000
Cerebrovas-cular diseases	0(0)	1(16.67)	5(83.33)	6(100)	0.014
Cardiovascular diseases	1(5.6)	3(16.7)	14(77.8)	18(10)	0.000
Pregnancy	1(33.33)	2(66.67)	0(0)	3(100)	0.322
Cancer	0(0)	2(66.67)	1(33.33)	3(100)	0.288
Thyroid Diseases	0(0)	1(50)	1(50)	2(100)	0.529
Autoimmune diseases	0(0)	1(100)	0(0)	1(100)	0.321
Mental illness	0(0)	1(50)	1(50)	2(100)	0.53
Liver diseases	0 (0)	0(0)	1(100)	1(100)	0.32
Signs and symptoms					
Cough	27(34.62)	26(33.33)	25(32.05)	78(100)	0.36
Headache	36(52.17)	19(27.5)	14(20.3)	69(100)	0.000
Body ache	24(39.3)	15(24.6)	22(36.1)	61(100)	0.201
Fever	20(35.71)	18(32.14)	18(32.14)	56(100)	0.82
Sneezing	13(61.90)	5(23.81)	3(14.3)	21(100)	0.039
Abdominal	1(100)	0(0)	0(0)	1(100)	0.446
Diarrhea	6(37.5)	4(25)	6(37.5)	16(100)	0.78
Vomiting	1(11.11)	4(44.44)	4(44.44)	9(100)	0.21
Dyspnea	0(0)	29(47.54)	32(52.46)	61(100)	0.000
Anosmia	7(100)	0(0)	0(0)	7(100)	0.002
Ageusia	7(100)	0(0)	0(0)	7(100)	0.002
Shivering	4(80)	1(20)	0(0)	5(100)	0.124
Mortality	0(0)	2(6.3)	17(53.1)	19(18.3)	0.000

SpO2 (mean±SD)	97.35±1.2	85.91±6.4	67.94±13.4		0.013

Laboratory parameters among COVIC-19 infection

The findings of the selected laboratory parameters among different patient groups and healthy controls are shown in table 2. There was a significant increase in CRP in moderate and severe patients compared to both the control group and patients with mild infection. D-dimer value was elevated among all patient groups compared to the control group. The increase in hospitalized patients was obvious and the statistical analysis showed a significant difference among all four groups. Regarding Platelet count, there was no significant distinction among all the groups despite the low platelet count recorded among severe patients compared to other groups. Both lymphocyte count and lymphocyte % decreased among hospitalized COVID-19 patients compared to the control group, in which the difference in lymphocyte count was not statistically significant among all the groups, but the difference in lymphocyte % was significant among hospitalized patients compared to both patients with mild infection and healthy controls.

Table 2: Laboratory parameters among COVID-19 patients.

Parameter	Control (34)	Mild (40)	Moderate (32)	Severe (32)
CRP (mg/L)	0.35 [a] (0.27-0.422)	0.168 [a] (0.05-0.37)	4.262 [b] (0.60-10.98)	7.114 [b] (3.83-9.92)
D-dimer (ng/ml)	28.5 [a] (6-37.2)	120 [b] (60-205)	1105 [c] (600-2428)	3193 [c] (1310-5000)
Platelet count (10^9/L)	228.5 [a] (147-260)	256 [a] (215-315)	249.5 [a] (193-324)	172 [a] (128.5-227)
Lympho-cyte count (10^9/L)	2.42± 0.53 [a]	2.26± 0.69 [a]	1.17± 1.0 [a]	0.91±0.81 [a]
Lympho-cyte %	31.41± 1.00 [a]	35.5± 9.33 [a]	13.65± 11.35 [b]	10.52± 12.94 [b]

The same letters mean no significant difference.
The different letters mean significant difference at $p<0.05$.
The data are expressed as mean ± SEM for parametric analysis using one-way ANOVA followed by Tukey's test, while for non-parametric analysis the data are expressed as median (interquartile range) and analyzed with Kruskal-Wallis followed by Dunne's test.

Laboratory parameters and COVID-19 outcome

Table 3 illustrates the difference in the measurements of selected laboratory parameters among patients with COVID-19 who survived following infection compared to those who died. Statistical analysis showed a high to very high significant difference between the mean measurements of all the laboratory tests among survivors compared to non-survivors (*P* value= 0.001, 0.001, 0.002, 0.009 and 0.000 for CRP, D-dimer, platelet count, lymphocyte count, and lymphocyte %, respectively).

Table 3: Laboratory parameters and COVID-19 outcome.

Parameter	Outcomes of COVID-19 infection	N	Median (IQR) Mean± SEM	*P value*
CRP (mg/dl)	Survivors	85	0.62 (0.17-5.84)	0.001
	Non-survivors	19	8.10 (4.89-10.28)	
D-dimer (ng/ml)	Survivors	85	483 (123-1272)	0.001
	Non-survivors	19	5000 (1310-5000)	
Platelets count(10^9/L)	Survivors	85	264 (192-306)	0.002
	Non-survivors	19	182 (127-227)	
Lymphocyte count (10^9/L)	Survivors	85	2.15±0.52	0.009
	Non-survivors	19	0.74±0.10	
Lymphocyte %	Survivors	85	24.3±1.73	0.000
	Non-survivors	19	6.19±0.74	

IQR: interquartile range, SEM: standard error of mean.
The data are expressed as mean ± SEM for parametric analysis using un- paired t-test, while for non-parametric analysis the data are expressed as median (interquartile range) and analyzed using *Mann–Whitney* test.
Significant difference at $p<0.05$, Highly significant difference at $p<0.01$, Very highly significant difference at $p<0.001$.

Correlation between D-dimer with each of the studied laboratory parameters in COVID-19 pateints

Table 4 and figures 1, 2, 3, and 4 illustrate the correlation between D-dimer with the other four lab parameters. It was found that there is a significant positive correlation between D-dimer and CRP (r= 0.69, *P* value= 0.000). On the other hand, a significant negative correlation was observed between D-dimer and each of platelet count (r= -0.28, *P* value= 0.004), lymphocyte count (r= -0.73, *P* value= 0.000), and lymphocyte % (r= -0.76, *P* value= 0.000).

Table 4: Correlation between D-dimer with each of CRP, Platelet count, Lymphocyte count, and Lymphocytes % among hospitalized COVID-19 patients.

Parameter	D-dimer	
	r	*P value*
CRP (mg/dl)	0.69	0.000
Platelets count (10^9/L)	-0.28	0.004
Lymphocyte count	-0.73	0.000
Lymphocyte %	-0.76	0.000

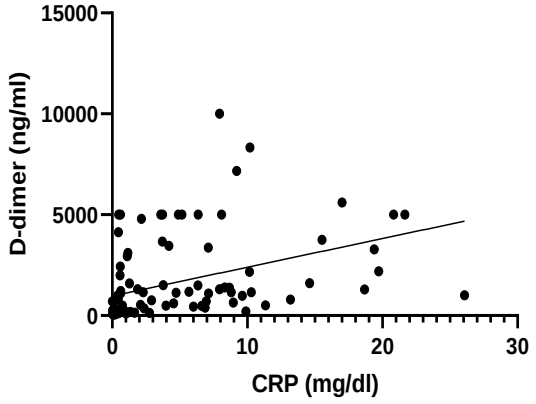

Figure 1: Correlation between D-dimer and CRP.

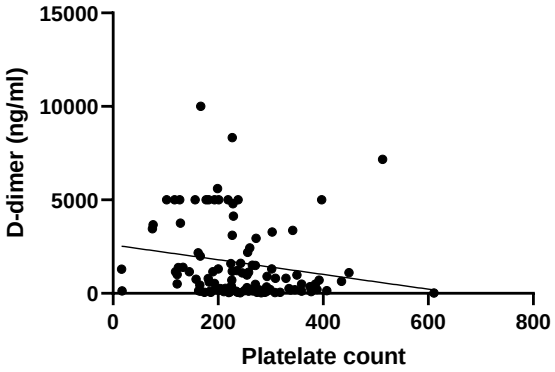

Figure 2: Correlation between D-dimer and platelet count.

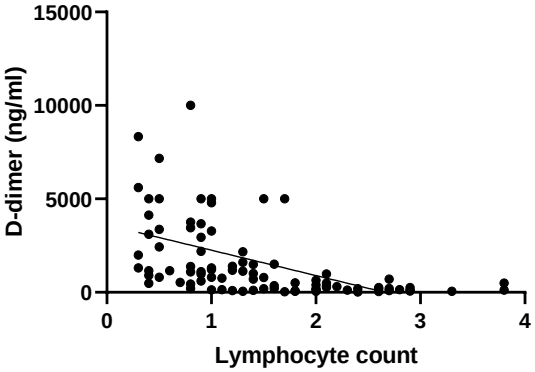

Figure 3: Correlation between D-dimer and lymphocyte count.

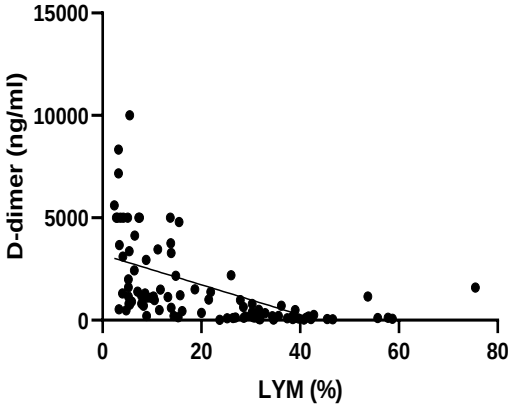

Figure 4: Correlation between D-dimer and lymphocyte %.

DISCUSSION

In the present study, the severe COVID-19 patients were older than those who were infected mildly. This agrees with other studies where age and severity are correlated with worse clinical outcomes (Ballaz et al., 2021). A possible explanation for the modifying effect of age is that elderly people are more susceptible to weight gain and other comorbidities (Barek et al., 2020). This study also shed the light on comorbidities that were associated with the severity of COVID-19. According to the present finding, obesity, diabetes, and cardiovascular diseases are among the comorbidities that imply the highest risk for a severe clinical presentation in patients with COVID-19. The association of comorbidities with the severity of the clinical presentation has also been reported for other human respiratory diseases caused by influenza (Mertz et al., 2013), SARS-CoV-1 (Peiris et al., 2003b), and MERS-CoV (Alraddadi et al., 2016). In particular, clarifying the link between comorbidities and the clinical severity of the disease has implications for the characterization of the pathophysiology of COVID-19 and the development of effective therapeutic strategies.

The present observational study found that Blood groups A and O had the same distribution among the patients. This finding is not in concordance with Wu et al. (2020) who found that patients in group A may be more susceptible to becoming infected with COVID-19 than those in group O. On the other hand, a meta-analysis has been published on the greater susceptibility of the ABO blood group, which does not necessarily coincide with greater mortality or severity (Golinelli et al., 2020). It has been found that ABO blood groups increased susceptibility to certain diseases, such as cancer, cardiovascular, and infectious diseases. The latter can be caused by parasites such as *Plasmodium falciparum* and *Plasmodium vivax*, bacterial infections such as those caused by *Escherichia coli*, *Helicobacter pylori*, and also viral infections by parvovirus B19, hepatitis B virus, chikungunya virus, and West Nile virus, and SARS-CoV-1 (Torres-Alarcón et al., 2021, Yaylacı et al., 2020). Regarding the Rh blood group, this study uncovered that a statistical relationship was not found between severity and the Rh blood group. This result is similar to the finding of Yaylacı et al. (2020) who documented Rh blood group did not link to the severity of the disease.

Present study show that the severity of SARS-CoV-2 infection was not related to gender. This result was similar to the finding of Ishaq et al. (2021) who showed that there were no significant differences in IgG levels in both genders. However, our finding was not parallel to Previous studies which have demonstrated that males are more susceptible to infection with SARS-CoV and MERS-CoV than females (Badawi and Ryoo, 2016, Channappanavar et al., 2017). This has been described by other studies where the prognosis has been worse among patients older than 60 and mainly males (Stokes et al., 2020). Jaillon and his colleagues found that females are less susceptible to viral infections, which may be due to X chromosome and sexual hormone defenses, both of which are essential in the innate and adaptive immune system (Jaillon et al., 2019). Our results proved that men were similar to women in susceptibility and severity of SARS-CoV-2 infection. Ishaq et al. (2021) proved the similarity in immune response items of immune response and antibody titers.

Likewise, in the present study, adequate prognostic performance of the biochemical markers (CRP and D-dimer) and the hematological markers (lymphocyte and platelet) has been demonstrated. In COVID-19, multiple studies have focused on measuring the response to inflammation through biomarkers. There is a variety of inflammatory markers including CRP, procalcitonin, interleukin-6, and, ferritin (Du et al., 2020). CRP was assessed in this study which was associated to the severity and mortality of COVID-19. Other papers support our finding, they found that measuring CRP is important for predicting severity and mortality (Liu et al., 2020, Zeng et al., 2020). The reason for increasing CRP is due to excessive immune response in COVID-19, called a cytokine storm, which arises from the overproduction of proinflammatory early-response cytokines such as TNF, IL-6, and IL-1β which stimulate hepatocytes to produce excessive CRP (Deb et al., 2022).

D-dimer was associated with severity and mortality in the current study. D-dimer is produced as a result of the breakdown of fibrin, it is used as a marker of thrombosis in COVID-19 (Thachil et al., 2017). The level of D-dimer also elevated in other pathological conditions (Jiang et al., 2021). The study by Lehmann et al. (2021) confirms that the D-dimer level may be an important predictor of thromboembolic events in patients with COVID-19, and may have an impact on the diagnostic and therapeutic approach of patients who recovered. It is evidenced in the study that, in non-surviving patients, the D-dimer increase; while the lymphocytes decrease (Wang et al., 2020). according to the work of Görlinger et al. (2020), deceased patients presented D-dimer values of ≥2.0 µg/ml. Therefore, for patients with markedly elevated D-dimers (cut-off: 2.0 µg/mL), hospital admission should be considered even in the absence of other serious symptoms. Similarly, it was found in the study by Mareev et al. (2020) at the time of admission, values higher than 2.0 µg/mL were reported, where the authors emphasize that D-dimer could effectively predict in-hospital mortality in patients with COVID-19.

In this study, lymphopenia was associated with mortality. Similar to our finding, Fajgenbaum and June (2020)

proved that in hospitalized patients with COVID-19, low lymphocyte counts were independently determined as predictors of mortality. Most of the patients with severe COVID-19 have lymphopenia (Yang et al., 2020). According to a study by Wang et al. (2020), lymphopenia was common in COVID-19 patients in the ICU and the persistence of lymphopenia is a sign of poor prognosis.
Our results indicate that, thrombocytopenia was also associated with mortality. The participation of platelets in the endothelial and thrombotic alterations of SARS-CoV-2 has been widely demonstrated, mainly their interaction with neutrophils that form extracellular neutrophil traps (NETs) in a deregulated way to trigger thrombosis and microcirculation disturbances (Gong et al., 2020, Xu et al., 2020). In COVID-19, platelets are activated and aggregate chaotically, are consumed, and their mean volume increases, and their absolute count decreases (Grommes et al., 2012, Wool and Miller, 2021).

CONCLUSION

Gender, ABO and Rh were not associated with COVID-19. Elder patients were found to be more susceptible to infection, ICU admition and death. People with multiple comorbidities were associated with the severity of COVID-19 and bad outcome. CRP, D-dimer, lymphocyte %, and platelet were excellent predictors of disease severity and outcome.

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