Research Article

Laboratory Abnormalities in Patients with COVID-19 in Mazandaran Province, Iran

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Abstract

Background: Coronavirus is a single-stranded RNA virus, causing an epidemic of pneumonia and acute respiratory distress syndrome (ARDS) worldwide in late 2019.

Objectives: In addition to the clinical symptoms, laboratory diagnosis can greatly help diagnose the diseases; therefore, this study aimed to analyze laboratory parameters in patients with COVID-19.

Methods: In this cross-sectional study, the laboratory data of 2563 patients with COVID-19 admitted to hospitals affiliated with Mazandaran University of Medical Sciences were extracted from hospital information systems (HIS). The data were recorded on Excel and analyzed through t-test, chi-squared, and Fisher's exact tests in SPSS 19 at the significance level of $P < 0.05$.

Results: Out of 2563 patients with a mean age of 55.1 ± 16.7 years, 1409 (55%) were male, and 1154 (45%) were female with a mean age of 55.7 ± 16.8, and 54.3 ± 16.6 years, respectively. As the most frequent clinical findings, ESR, CRP, and LDH were increased by 83.5%, 71%, and 69.3% of the patients, respectively. Other research findings included lymphopenia, disturbed INR, abnormal SGOT, abnormal alkaline phosphatase (ALP), and increased lactate dehydrogenase (LDH), which were significantly higher in men than in women and was different between age groups.

Conclusions: Conducting simple, convenient, and inexpensive laboratory tests can be helpful in the diagnosis of COVID-19.

Keywords: Coronavirus, COVID-19, ARDS, Laboratory Test

1. Background

Coronavirus is the world's latest biological hazard, a mysterious threat, and a serious zoonotic pathogen. It was first identified on December 31, 2019, in Wuhan, Hubei, China, as the cause of a pneumonia epidemic. Since then, it has spread very fast, affecting an increased number of cases across the world. To date, there have been more than 200,000 definite cases worldwide (1, 2). Similar to the virus that caused the SARS epidemic in 2003, it harms the lower respiratory tract in humans (2, 3). It is a single-stranded RNA virus spreading wildly among humans. Normally, it causes cold symptoms, although it can result in the ARDS in people with weak immune systems (4). It is transmitted through respiratory particles and droplets in sneezes and coughs from an infected person to a healthy one. Old age and diseases such as diabetes, acute respiratory diseases, cancer, and hypertension are among the risk factors of COVID-19. The clinical symptoms of patients with COVID-19 include fever, cough, fatigue, muscle pain, diarrhea, and pneumonia, which can turn into the ARDS, metabolic acidosis, septic shock, coagulopathy, and failures in different organs, such as liver, kidneys, and heart. The most common laboratory findings of these patients include lymphopenia, increased LDH, and increased CRP (5, 6). Apart from clinical symptoms, laboratory diagnosis can be of great help in the definite diagnosis of sicknesses such as viral diseases (2).

2. Objectives

Since COVID-19 is now a novel pandemic with different indices reported by various studies (7), this study aims to analyze laboratory indices in patients with COVID-19 and their relationships with the disease in Mazandaran Province.

3. Methods

This cross-sectional study intended to analyze the laboratory parameters of hospitalized patients with COVID-19 at Imam Khomeini Hospital in Behshahr, Razi Hospital in Qaemshahr, Bou-Ali Sina Hospital in Sari, Rajaei Hospital in Tonekabon, Fereydunkenar Hospital, Nowshahr Hospital, Chalus Hospital, Imam Reza Hospital in Amol, Imam Ali Hospital in Amol, and 17 Shahrivar Hospital in Amol in March-April 2020. The statistical population included the suspected cases of COVID-19 showing the early symptoms such as fever, cough, dyspnea, and sometimes gastrointestinal symptoms in the 2020 epidemic at the abovementioned hospitals. By the standard protocol for the coronavirus confirmation, samples of respiratory secretions were taken from patients and sent to relevant laboratories for the RT-PCR test and other tests.

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Patients had signed a consent form during admission for diagnostic-therapeutic procedures and laboratory tests. Exclusion criteria were receiving medication before laboratory sampling. The results were recorded in the hospital information systems. Given the delay in the process of receiving the RT-PCR test results and the limited number of tests for all patients, The National Protocol suggests that patients with clinical symptoms whose suspected CT scan results (indicating complications within their lungs) should also be considered positive. Table 1 indicates the normal laboratory indices of this study (8-11).

3.1. Ethics

Having been approved by the Committee of Mazandaran University of Medical Sciences (code: IR.MAZUMS.REC.1399.7334), the relevant variables were coded and extracted from the HISs by maintaining information confidentiality. The data were recorded in Excel and analyzed through *t*-test, chi-squared, and Fisher's exact tests in SPSS 19 at the significance level of P < 0.05.

Table 1. Normal Laboratory Values

Lab Test	Normal Range
WBC, count/μL	4000 - 11000
Lymphocyte, count/μL	$\geq$ 1500
Hemoglobin, g/dL	
Male	$\leq$ 13.5
Female	$\leq$ 11.5
Platelet, $\times 10^3/\mu$L	$\geq$ 150
INR, s	$\leq$ 1.1
CRP, plus	
Normal	0
Abnormal	+1 plus and +2 plus
ESR, mm/h	
Age, y $\leq$ 50	
Male	$\leq$ 15
Female	$\leq$ 20
Age, y: 51 - 85	
Male	$\leq$ 20
Female	$\leq$ 30
Age, y > 85	
Male	$\leq$ 30
Female	$\leq$ 42
SGOT = AST, U/L	$\leq$ 40
SGPT= ALT, U/L	
Male	$\leq$ 45
Female	$\leq$ 34
Alkaline Phosphatase, U/L	
Male	$\leq$ 270
Female	$\leq$ 240
Bilirubin total, mg/dL	$\leq$ 1.2
Bilirubin direct, mg/dL	$\leq$ 0.3
Lactate dehydrogenase, U/L	$\leq$ 470

4. Results

This study was conducted on 2563 hospitalized patients, including 1409 (55%) men and 1154 (45%) women. The mean age of patients was 55.1 $\pm$ 16.7. The first and third age quarters were 43 and 67 years, respectively. Moreover, the mean age of men and women was 55.7 $\pm$ 16.8 and 54.3 $\pm$ 16.6 years, respectively (P = 0.029). Table 2 shows the central tendency and dispersion of laboratory parameters. The most frequent laboratory findings were increased ESR (83.5%), positive CRP (71%), and increased LDH (69.3%)

(Figure 1). Table 3 presents the distribution of laboratory test results among COVID-19 patients based on gender. The cases of lymphopenia, thrombocytopenia, disturbed INR, abnormal SGOT, total bilirubin, and increased direct bilirubin were significantly higher in men than in women. However, the cases of abnormal ALP were significantly higher in women (P < 0.001). The distribution of laboratory test values in COVID-19 patients based on age groups showed that the cases of lymphopenia, disturbed INR, abnormal SGOT, abnormal ALP, and increased LDH were significantly higher in the elder age groups (Table 4).

5. Discussion

COVID-19 emerged in China in late 2019 as a new beta-coronavirus-infected RNA virus and the leading cause of pneumonia. It has created a global panic, causing international concern on the part of the World Health Organization (11). The present cross-sectional study analyzed the laboratory specifications of hospitalized COVID-19 patients at the hospitals affiliated with Mazandaran University of Medical Sciences. The middle-aged men accounted for the majority of cases (men: 55%, women: 45%). The studies conducted by W. Guan and Ni. (11), Lippi and Plebani (12), Xu et al. (13), and Ng and Li (14) reported larger numbers of cases in men than in women, a fact which shows the higher infection rate of men than that of women in this disease. Accordingly, patients with COVID-19 experience a decreased number of lymphocytes (2, 7, 11, 15). In this regard, Wu J reported the rate of lymphocytopenia as 32.5% (10), whereas the present study reported that 21% of patients had lymphocytopenia, which was significantly associated with the age and gender of patients. In other words, lymphopenia was more prevalent in men (P = 0.002). Its prevalence also increased among elder patients (P < 0.001). Moreover, 44.8% of patients showed the disturbing rates of hemoglobin, which had no significant relationship with the disease (P = 0.142). This was consistent with the findings of Chen et al. (16) and Huang and Wang (17), who reported hemoglobin declines at 52% and 31%, respectively. In the present study, 23.7% of patients had abnormal numbers of platelets, which was significantly associated with the disease (P < 0.001). This finding was consistent with that of W. Guan and Ni. (11); however, Huang and Wang (17) reported that 5% of patients showed abnormal numbers of platelets. The inconsistency can be attributed to the difference in the research methodologies. It should also be mentioned that men showed higher rates of thrombocytopenia than women in the present study (P < 0.001),

which deteriorates with age (P = 0.003). Moreover, 83.5% of patients showed an increased ESR, a finding which was consistent with that of Chen et al. (16), who reported that 85% of patients indicated an increased ESR. Many studies have reported C reactive protein (CRP) in these patients, showing that CRP increased in 37% - 91% of patients (2, 7, 15, 16). In the present study, 71% of patients experienced increased CRP rates. Regarding the liver function indices, SGOT and SGPT were higher than normal in 33.3% and 24.9% patients in this study. This finding was consistent with the studies conducted by Arentz and Yim (8), Mardani et al. (7), and Chen et al. (16). In addition, ALP increased in 12.4% of patients in this study, a finding which was consistent with that of Arentz and Yim (8), who reported that ALP increased in 80% of patients. However, the abnormal level of ALP was significantly higher in women than in men (P < 0.001). Furthermore, LDH increased in 69.3% of patients, which is consistent with Huang et al. (6) and Lippi and Plebani (2). In the present study, total and direct bilirubin rates increased in 7.5% and 21.8% of patients, respectively. This is also consistent with W. Guan and Ni. (11), Huang and Wang (17), Chen et al. (16), and Lippi and Plebani (2, 12), according to whom 10.5% - 18% of patients showed increases in total and direct bilirubin levels. In brief, laboratory findings of this study demonstrated lymphopenia, thrombocytopenia, disturbed INR, abnormal SGOT, increased total bilirubin, increased direct bilirubin, increased ESR, increased CRP, and increased LDH. The most frequent laboratory findings of these parameters were increased ESR, increased CRP, and increased LDH. In addition, the percentages of lymphopenia, disturbed INR, abnormal SGOT, abnormal alkaline phosphatase, and lactate dehydrogenase increased more significantly in men than in women. The increasing trends in these parameters were also significantly higher in elder patients. Given the involvement of various organs in the disease, although several clinical signs have been defined for COVID-19, it is clear that laboratory diagnosis can effectively help diagnose viral diseases in addition to clinical symptoms. Considering the existing limitations and lack of 100% sensitive diagnostic devices, such as RT-PCR and CT scan, it would be helpful to conduct simpler, more convenient, and more inexpensive laboratory tests in the process of diagnosing COVID-19. Also, the difference between abnormal findings based on age groups and gender can be effective in monitoring high-risk patients.
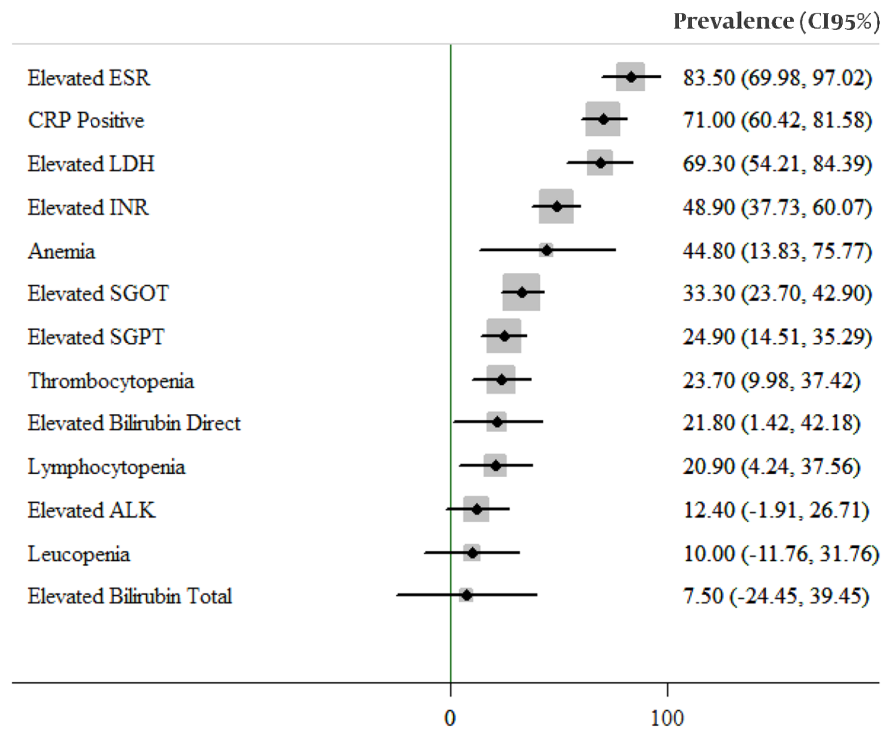
The present study has some limitations that should be addressed, RT-PCR was not performed for all, and the measurement was evaluated for one time. It is suggested that future examinations evaluate patient's clinical symptoms

Table 2. Central Tendency and Dispersion of Laboratory Parameters in COVID-19 Patients[a]

Lab Test	Numbers[b]	Values	Percentiles		
			25	50	75
WBC	900	7174.4 ± 3714.8	5100	6800	8100
Lymphocyte	845	2710.7 ± 1312.2	1800	2700	3500
Hemoglobin	163	12.9 ± 1.8	11.9	13	14.1
Platelet	1139	224803.3 ± 134385.3	150000	201000	271000
INR	1232	1.2 ± 0.5	1	1.19	1.36
ESR	1544	50 ± 27.6	28	47	70
SGOT (AST)	1877	40.6 ± 48.1	23	32	46
SGPT (ALT)	1882	37.1 ± 54.1	18	26	41
Alkaline phosphatase	1741	181.1 ± 121.5	124.5	156	204
Bilirubin total	545	0.7 ± 0.7	0.5	0.6	0.8
Bilirubin direct	542	0.3 ± 0.5	0.2	0.2	0.3
Lactate dehydrogenase	802	642 ± 387.6	438	570.5	753

[a] Values are expressed as mean ± SD.
[b] Since this is a multicenter study, all of the tests were not conducted in all of the centers.

Prevalence (CI95%)

Elevated ESR	83.50 (69.98, 97.02)
CRP Positive	71.00 (60.42, 81.58)
Elevated LDH	69.30 (54.21, 84.39)
Elevated INR	48.90 (37.73, 60.07)
Anemia	44.80 (13.83, 75.77)
Elevated SGOT	33.30 (23.70, 42.90)
Elevated SGPT	24.90 (14.51, 35.29)
Thrombocytopenia	23.70 (9.98, 37.42)
Elevated Bilirubin Direct	21.80 (1.42, 42.18)
Lymphocytopenia	20.90 (4.24, 37.56)
Elevated ALK	12.40 (-1.91, 26.71)
Leucopenia	10.00 (-11.76, 31.76)
Elevated Bilirubin Total	7.50 (-24.45, 39.45)

Figure 1. Distribution of abnormal laboratory values in COVID-19 patients

along with routine laboratory tests as well as inflammatory markers such as IL-6.

Footnotes

Authors' Contribution: All authors contributed equally.

Table 3. Distribution of Laboratory Values in COVID-19 Patients Based on Gender[a]

Parameter	Male		Female		P Value
	Normal Value	Abnormal Value	Normal Value	Abnormal Value	
Lymphocyte	389 (82.9)	80 (17.1)	331 (88)	45 (12)	0.041
Hemoglobin	52 (50.5)	51 (49.5)	38 (63.3)	22 (36.7)	0.142
Platelet	438 (70.9)	180 (29.1)	431 (82.7)	90 (17.3)	< 0.001
INR	336 (47.4)	373 (52.6)	294 (56.2)	229 (43.8)	0.002
ESR	133 (15.5)	726 (84.5)	121 (17.7)	564 (82.3)	0.269
CRP	260 (28.6)	650 (71.4)	216 (29.6)	514 (70.4)	0.662
SGOT (AST)	642 (61.4)	403 (38.6)	610 (73.3)	222 (26.7)	< 0.001
SGPT (ALT)	775 (73.8)	275 (26.2)	639 (76.8)	193 (23.2)	0.147
Alkaline phosphatase	879 (91.1)	86 (8.9)	646 (83.2)	130 (16.8)	< 0.001
Bilirubin total	255 (89.5)	30 (10.5)	249 (95.8)	11 (4.2)	0.006
Bilirubin direct	205 (72.4)	78 (27.6)	219 (84.6)	40 (15.4)	0.001
Lactate dehydrogenase	132 (29.8)	311 (70.2)	114 (31.8)	245 (68.2)	0.59

[a]Values are expressed as No. (%).

Table 4. Distribution of Laboratory Values in COVID-19 Patients Based on Age Group[a]

Parameter	≤ 44 Years		45 - 55 Years		56 - 67 Years		> 67 Years		P Value
	Normal	Abnormal	Normal	Abnormal	Normal	Abnormal	Normal	Abnormal	
Lymphocyte	184 (94.4)	11 (5.6)	190 (94.1)	12 (5.9)	175 (82.5)	37 (17.5)	171 (72.5)	65 (27.5)	< 0.001
Hemoglobin	18 (62.1)	11 (37.9)	19 (76)	6 (24)	24 (48)	26 (52)	29 (49.2)	30 (50.8)	0.077
Platelet	217 (77.8)	62 (22.2)	207 (77.5)	60 (22.5)	220 (76.9)	66 (23.1)	225 (73.3)	82 (26.7)	0.54
INR	183 (57)	138 (43)	161 (54.2)	136 (45.8)	145 (47.9)	158 (52.1)	141 (45.3)	170 (54.7)	0.011
ESR	75 (17.8)	346 (82.2)	65 (16.1)	339 (87.2)	48 (12.8)	327 (87.2)	66 (19.2)	278 (80.8)	0.106
CRP	139 (30.8)	312 (69.2)	114 (27.2)	305 (72.8)	104 (26.4)	290 (73.6)	119 (31.6)	257 (68.4)	0.266
SGOT (AST)	352 (70.5)	147 (29.5)	346 (73)	128 (27)	291 (62.9)	172 (37.1)	263 (59.6)	178 (40.4)	< 0.001
SGPT (ALT)	348 (69.3)	154 (30.7)	352 (74.4)	121 (25.6)	356 (76.6)	109 (23.4)	358 (81)	84 (19)	< 0.001
Alkaline phosphatase	422 (91.3)	40 (8.7)	391 (88.7)	50 (11.3)	370 (86)	60 (14)	342 (83.8)	60 (16.2)	0.005
Bilirubin total	153 (93.3)	11 (6.7)	134 (94.4)	8 (5.6)	115 (94.3)	7 (5.7)	102 (87.2)	7 (5.7)	0.104
Bilirubin direct	133 (82.1)	29 (17.9)	115 (81)	27 (19)	91 (75.2)	30 (24.8)	91 (75.2)	30 (24.8)	0.183
Lactate dehydrogenase	177 (38.7)	122 (61.3)	69 (34.2)	133 (65.8)	50 (26.9)	136 (73.1)	50 (23.3)	165 (76.7)	0.003

[a]Values are expressed as No. (%).

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