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A comparative study of laboratory findings in PCR-positive and PCR-negative COVID-19 hospitalized patients

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Abstract

Introduction Given the many misconceptions in terms of both diagnosis and treatment, SARS-CoV-2 continues to infect and victimize. Notwithstanding molecular testing is the gold standard method of in vitro diagnostic, the often long-waiting time, as well as false-negative results are daunting challenges facing us. In this study, we aimed to report the diagnostic value of laboratory findings in COVID-19 patients, with an extensive focus on the differences between PCR-positive and PCR-negative cases.

Patients and methods We did a retrospective single-centre study on a large cohort of 1546 COVID-19 patients in Tehran, Iran. Based on clinical symptoms, chest CTs were performed for all the patients. Also, molecular testing of swab specimens was also performed for 1450 cases.

Results All the data on laboratory results were retrospectively extracted from medical records. Of the 1546 patients, 1040 (67.5%) were male and 506 (32.5%) were female with the mean age of 55.67. On admission, 31.4% of the whole study population displayed lymphopenia and 38.9% showed neutrophilia. Decreased hemoglobin and mild thrombocytopenia were also found in 40% and 18.6% of cases, respectively. Elevated lactate dehydrogenase in nearly 75% of COVID-19 cases was the most common alteration amongst biochemical parameters which together with increased ESR and CRP could serve as diagnostic markers in SARS-CoV-2 infection. Of the 1450 patients with a PCR result, 439 (28.3%) were PCR-negative and 1011 (65.3%) were PCR-positive. Notably, lymphopenia and increased AST were higher in the PCR-positive group than their negative counterparts. Albeit being in the normal range, a significant decrease in the number of monocytes was also evident in the PCR-positive cases.

Conclusions As far we are aware, this is the first time that we reported a comprehensive exploration of laboratory characteristics of a large cohort of hospitalized COVID-19 patients from Iran, hoping that these data will cast more light on the diagnostic significance of these parameters.

Keywords COVID-19 · Diagnosis · Iran · Laboratory · PCR · Polymerase chain reaction · SARS-CoV-2

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Abbreviations

WBC	White blood cell
RBC	Red blood cell
Plt	Platelet
ESR	Erythrocyte sedimentation rate
Cr	Creatinine
BUN	Blood urea nitrogen
CPK	Creatinine phosphokinase
LDH	Lactate dehydrogenase
AST	Aspartate transaminase
ALT	Alanine transaminase
Na+	Natrium (Sodium)
K+	Kalium (Potassium)
HCO3-	Bicarbonate

Introduction

Undoubtedly, the end of 2019 will be recorded as one of the most sinister times in the history of medicine, when an outbreak of fatal pneumonia caused by a novel coronavirus (later designated as SARS-CoV-2 [1, 2]) hits the headlines. In fact, the original heartfelt belief of the world that the disease—reported from Wuhan [3, 4]—is nothing more than a common cold was disappeared in the blink of an eye when the World Health Organization (WHO) issued a public health emergency on 30 January 2020 [3], followed by the declaration of a viral pandemic on 11 March [5]. Although the containment measures executed in the virus-originating country have, at least for the meantime, decreased the risk of contagion profoundly; needless to say, it is not the case in most countries of the world, including the USA, Spain, Italy, France, the UK, and Iran. Even though the general belief— by matching the number of deaths to the total number of infected cases—is that most patients with coronavirus disease 2019 (abbreviated to COVID-19) are recovering, stealing a glance at the outrageous statistics of deaths increasing day after day recaps that SARS-CoV-2 still is taking toll [6]. In Iran, where the virus was transmitted probably by a merchant who had traveled to China (Fig. 1), infection of over 1,000,000 people with more than 51,000 deaths ranked this country as the 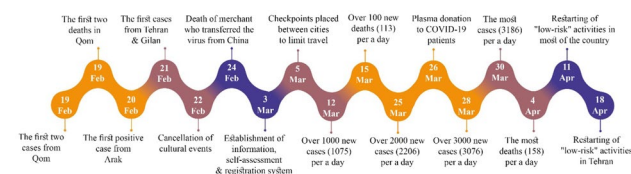15th highest number of SARS-CoV-2 cases as of 13 December 2020 (https://www.worldometers.info/coronavirus/country/iran).

Timely identification of COVID-19 carriers is critical not only to mitigate viral spread but also to alleviate disease progression in a well-controlled manner. Notwithstanding the fact that the nucleic acid test serves as the gold standard method for the etiological detection of SARS-CoV-2 infection, the existence of the false-negative results is the main challenge [7, 8]. Also, variable distribution of virus across the respiratory tract between patients, missing patients who have recovered from the disease, and the prerequisite of certified laboratories, expensive equipment and skilled personnel denote other limitations to PCR-based diagnostic methods [9]. Recitation of this concern from the fact that such limitations are even more highlighted in countries with restricted assets further uncovers the urgent necessity for alternative tests to timely detect COVID-19 patients. In this study, we aimed to report a comprehensive exploration of laboratory characteristics of a large cohort of 1546 hospitalized patients with COVID-19 of Baqiyatallah Hospital of Tehran, Iran, from February 30 to April 10, 2020, with an extensive focus on the differences between PCR-positive and PCR-negative cases.

Patients and methods

Participants

This retrospective single-center study, conducted on a large cohort of 1546 COVID-19 patients recruited at Baqiyatallah Hospital in Tehran, Iran, from February 30 to April 10, 2020, was approved by Baqiyatallah Hospital Ethics Committee, and written informed consent was waived from patients. Based on clinical symptoms including cough, sputum, fever, dyspnea, and pleuritic chest pain as well as coarse crackles on auscultation, chest CT was requested for all the patients admitted to the hospital. All the cases with a positive chest CT were defined as COVID-19 patients and entered into this study.

Procedures

All imaging features including pure ground-glass opacity (GGO), pure consolidation, mixed GGO and consolidation, reversed halo, interalesional traction bronchiectasis, crazy-paving, intralesional vascular enlargement, linear opacities, lymph node enlargement, pleural effusion, and pericardial effusion were reviewed and evaluated by an expert radiologist. In detail, a thin-section CT involvement score was assigned on the basis of all abnormal areas involved. Each lobe was assigned a score that was based on the following: score 0, 0% involvement; score 1, less than

Fig. 1 A timeline of SARS-CoV-2 outbreak in Iran (https://en.wikipedia.org/wiki/COVID-19_pandemic_in_Iran)

5% involvement; score 2, 5 to 25% involvement; score 3, 26 to 49% involvement; score 4, 50 to 75% involvement; and score 5, greater than 75% involvement. There was a score of 0 to 5 for each lobe, with a total possible score of 0 to 25. Next, a total pulmonary infiltration score was calculated; that is to say, the sum of scores of all the five pulmonary lobes was used. The number of affected lung lobes was also counted. The location of the lesion was considered as peripheral if it was in the outer one-third of the lung; otherwise, it was considered as central. Other radiological patterns were also evaluated.

In addition, throat swab specimens from the upper respiratory tract were obtained and maintained in the virus-transport medium. The presence of SARS-CoV-2 in pharyngeal swab specimens was detected by RT-PCR analysis for 1450 cases (of 1546 cases, 96 patients did not have a PCR test). The sequences of the primers targeting envelope gene of CoV were as follows: forward primer 5′-ACTTCTTTTTCTTGCTTTCGTGGT-3′; reverse primer 5′-GCAGCAGTACGCACACAATC-3′. Conditions for the amplifications were 50 °C for 15 min, 95 °C for 3 min, followed by 45 cycles of 95 °C for 15s and 60 °C for 30s. All the data on laboratory results were retrospectively extracted from patients' electronic medical records. Values of the hematological parameters (WBC-, RBC-, and Plt-related indices), inflammation-related factors (ESR and CRP), biochemical parameters (Cr, BUN, CPK, LDH, AST, ALT, Na^+, K^+), and blood gas analysis (pH, PO_2, PCO_2, O_2 saturation, HCO_3^-, and lactate) of COVID-19 patients were analyzed and related to their corresponding RT-PCR.

Statistical analysis

The continuous variables were examined to determine the normality of the distribution using histograms, measures of skewness and kurtosis, and Kolmogorov–Smirnov test. The normally distributed variables were described as the means ± standard deviation (SD), and the skewed distributed variables were expressed as the median and interquartile range (25–75%). Categorical variables were summarized as frequencies (percentages). The normally distributed continuous variables were compared between positive and negative PCR groups using the two independent sample *t*-test and non-normally distributed variables with the Mann–Whitney *U* test. Comparisons of categorical variables between groups were conducted using the chi-square test of independence. All tests were two-sided, and a *P* value of less than 0.05 was considered to indicate a statistically significant difference. All the statistical analyses were performed using the IBM SPSS version 24.0 (IBM Corp., Armonk, NY, USA).

Results

The main characteristics of the patients

Out of 1546 COVID-19 patients (based on the results of a positive chest CT), 1040 (67.5%) were male and 506 (32.5%) were female. The mean age was 55.67 (±14.22). While 29% of the patients were between 50 and 59 years, cases under the age of 40 were the least studied population with an approximate estimate of 15%. After removing 96 patients who did not have a PCR test, we sub-grouped patients to PCR-negative (*N* = 439; 28.3%) and PCR-positive (*N* = 1011; 65.3%) cases. We found almost the same trend in the percentage of males and females between these two groups (34.4% vs 31.7% female in PCR-negative and -positive cases, respectively). The age distribution pattern was also the same, just noting that the percentage of patients in the age range of 60–70 years was slightly higher in the PCR-positive group (24.1% vs 19.8%). A list of requested tests along with the number of each of these tests performed in different groups is summarized in Table 1.

Hematologic findings in COVID-19 patients

The complete blood count (CBC) test was performed nearly for all the patients (99.4%), and the results were presented in Table 2. Although we found that WBC counts of approximately 94% of patients were within the normal range, 31.4% of the whole study population displayed lymphopenia (lymphocyte count $< 1.1 \times 10^9$/L). Increased number of neutrophils ($> 6.3 \times 10^9$/L), on the other hand, was also observed in 38.9% of cases, highlighting the fact that lymphopenia along with neutrophilia may seemingly be appropriate items that should be taken into account in COVID-19 diagnosis. Decreased levels of hemoglobin (Hb) and mild thrombocytopenia—which were present in 40% and 18.6% of cases, respectively—may also contribute to the diagnosis of the disease. With respect to the information of CBC tests relevant to PCR results, we found that the percentage of COVID-19 cases with lymphopenia was higher in the PCR-positive group than their negative counterparts (33.1% vs 28.5%; *P* = 0.08). Even though being in the normal range, a significant decrease in the number of monocytes was also evident in the PCR-positive cases (*P* = 0.005). While values of RBC, hemoglobin (Hb), hematocrit (Hct), and MCHC were lower in cases with negative PCR results, there was no significant difference relevant to platelet-related parameters between these groups (Table 2).

Biochemical and blood gas findings in COVID-19 patients

As expected, 82% and 87% of the whole study population showed elevated ESR and CRP values, respectively;

Table 1 Demographic feature of COVID-19 cases and list of tests applied for these patients

	Total N (%)	PCR negative N (%)	PCR positive N (%)
Features			
Sample size	1546	439 (28.3%)	1011 (65.3%)
Age (year)	55.67 (±14.22)	55.45 (±13.94)	55.79 (±14.25)
≤39	235 (15.2)	62 (14.1)	159 (15.7)
40–49	256 (16.6)	76 (17.3)	162 (16.0)
50–59	447 (28.9)	144 (32.8)	273 (27.0)
60–69	349 (22.6)	87 (19.8)	244 (24.1)
≥70	259 (16.8)	70 (15.9)	173 (17.1)
Sex			
Female	506 (32.5%)	151 (34.4)	320 (31.7)
Male	1040 (67.5%)	285 (65.6)	691 (68.3)
Hematological			
CBC	1537 (99.4%)	436 (99.3%)	1006 (99.5%)
Inflammation			
ESR	1482 (95.8%)	420 (95.6%)	967 (95.6%)
CRP	1486 (96.1%)	415 (94.5%)	977 (96.6%)
Biochemical			
Cr	1540 (99.6%)	436 (99.3%)	1008 (99.7%)
BUN	1540 (99.6%)	436 (99.3%)	1008 (99.7%)
CPK	1101 (71.2%)	314 (71.5%)	727 (71.9%)
LDH	1258 (81.3%)	349 (79.4%)	845 (83.5%)
AST	1290 (83.4%)	357 (81.3%)	851 (84.1%)
ALT	1290 (83.4%)	357 (81.3%)	851 (84.1%)
Na	1539 (99.6%)	436 (99.3%)	1007 (99.6%)
K	1539 (99.6%)	436 (99.3%)	1007 (99.6%)
Blood gas			
ABG	418 (27.0%)	112 (25.5%)	292 (28.8%)
Lactate	395 (25.5%)	109 (24.8%)	273 (27.0%)

CBC complete blood count, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein, *Cr* creatinine, *BUN* blood urea nitrogen, *CPK* creatine phosphokinase, *LDH* lactate dehydrogenase, *AST* aspartate transaminase, *ALT* alanine transaminase, *ABG* arterial blood gas

suggesting that CRP may provide more valuable information than ESR (Table 3). Nonetheless, knowing that increased values of these parameters could serve as non-specific factors alarming the wide range of inflammatory conditions may reduce the diagnostic value of these parameters to some extent. Analysis of biochemical parameters also revealed an increased level of creatinine and BUN in 47% and 28% of COVID-19 cases, respectively. Elevated AST and ALT (nearly in 33% of all patients) also mirror an unfavorable clinical picture of the disease related to virus-mediated liver injury. Of particular importance, the change in biochemical parameters was not limited only to these factors, as an increase in CPK and especially in LDH values was eye-catching in the disease. As represented in Table 3, elevated LDH in nearly 75% of COVID-19 cases was the most common alteration amongst biochemical parameters which together with increased ESR and CRP could serve as invaluable diagnostic markers in SARS-CoV-2 infection. Albeit

AST level was significantly higher in PCR-positive cases compared to those with negative results, alterations of other factors were within a close range and actually represented no significant change between these two groups. Change in pH was observed in 18% of the patients, of which 7.8% experienced acidosis and the remaining displayed alkalosis. Decreased PO_2 and O_2 saturation were also reported in 23% of the whole study population (Table 3). However, since only 418 out of 1546 cases (27%) had the ABG test, it should be considered as a limitation to interpreting the results of the ABG test.

Discussion

In this retrospective single-center study which reflects laboratory findings of a large cohort of 1546 COVID-19 patients from Tehran, Iran, 439 cases (28.3%) had negative

Table 2 Values of hematological parameters in COVID-19 patients

		All Patients (N = 1546)	PCR Negative (N = 439)	PCR Positive (N = 1011)	*P* Value
WBC-related	**Normal ranges**				
*WBC count**	3.5–11 (×10⁹/L)	7.33 (5.70–8.90)	7.6 (5.7–9.1)	7.3 (5.7–8.85)	0.118
< 3.5		2.3%	1.6%	2.6%	0.008
3.5–11		93.7%	92.9%	94.4%	
> 11		3.3%	5.5%	2.5%	
*Lymphocyte count**	1·1–3.2 (×10⁹/L)	1.58 (0.91–2.26)	1.77 (0.98–2.45)	1.53 (0.89–2.21)	0.004
< 1.1		31.4%	28.5%	33.1%	0.08
*Neutrophil count**	1·8–6·3 (×10⁹/L)	5.68 (4.12–7.29)	5.81 (4.23–7.22)	5.68 (4.13–7.42)	0.691
< 1.8		0.7%	0.2%	0.9%	0.333
> 6.3		38.9%	41%	39.4%	
*Monocyte count**	0.1–0.7 (×10⁹/L)	0.49 (0.36–0.65)	0.53 (0.39–0.67)	0.47 (0.36–0.63)	0.005
*Eosinophil count**	0.06–0.46 (×10⁹/L)	0.09 (0.03–0.21)	0.09 (0.04–0.23)	0.09 (0.03–0.20)	0.164
*Basophil count**	0.01–0.3 (×10⁹/L)	0.04 (0.03–0.07)	0.04 (0.03–0.08)	0.05 (0.03–0.07)	0.711
RBC-related					
RBC count⁺	Female: 3.7–5.2 (×10¹²/L) Male: 4–5.7 (×10¹²/L)	4.94 (±0.63)	4.83 (±0.61)	4.99 (±0.64)	0.000
< 3.7 (Female)		2.8%	5%	2.1%	0.002
< 4 (Male)		6.1%	8.7%	5%	0.008
*Hemoglobin**	Female: 12–15.5 g/dL Male: 13–17.5 g/dL	14.40 (13.10–15.60)	14.2 (12.82–15.3)	14.5 (13.3–15.7)	0.005
< 12 (Female)		14.7%	18.5%	13.1%	0.008
< 13 (Male)		24.3%	27.3%	22.3%	0.037
Hematocrit⁺	Female: 36–46% Male: 39–51%	42.17 (±4.82)	41.45 (±4.95)	42.59 (±4.74)	0.000
< 36 (Female)		8.7%	13.7%	6.4%	0.000
< 39 (Male)		22.6%	26.2%	19.9%	0.007
*MCV**	81–96 FL	87.72 (84.55–90.93)	87.79 (84.74–90.83)	87.78 (84.66–91.05)	0.936
< 81		10%	8.4%	9.9%	0.509
> 96		4.5%	4.1%	4.9%	
*MCH**	27–33 pg	30.14 (28.76–31.23)	30.18 (28.77–31.18)	30.19 (28.81–31.3)	0.462
< 27		9.6%	8.9%	9.2%	0.848
*MCHC**	32–36 g/dL	34.70 (33.97–35.51)	34.63 (33.87–35–43)	34.81 (34.08–35.57)	0.013
< 32		3.4%	3.6%	2.9%	0.434
*RDW-CV**	11–14%	13.4 (12.7–14.3)	13.3 (12.7–14.3)	13.4 (12.8–14.4)	0.117
> 14		32.5%	29.8%	34.1%	0.11
*RDW-SD**	35–56 FL	43.95 (41.37–46.70)	43.9 (41.6–45.9)	44.1 (41.4–47)	0.263
> 56		1.9%	1.6%	2.1%	0.539
Plt-related					
*Platelet**	150–400 (×10⁹/L)	238 (168–325)	245 (172–339.75)	237 (166.5–325)	0.202
< 150		18.6%	16.6%	19.6%	0.185
*PDW**	12–20%	16.2 (15.7–16.6)	16.1 (15.6–16.6)	16.2 (15.8–16.6)	0.112
*MPV**	8.0–12.7 FL	9.7 (9.3–9.9)	9.7 (9.2–9.9)	9.7 (9.3–9.9)	0.994
P-LCR⁺	11.9–66.9	31.18 (±4.88)	30.04 (±8.36)	31.56 (±7.78)	0.113

*The skewed distributed variables were expressed as the median and interquartile range (25–75%) and the Mann–Whitney *U* test was used

⁺The normally distributed variables were described as the means ± standard deviation (SD), and two independent sample *t*-test was used. Comparisons of categorical variables between groups were conducted using the chi-square test

Table 3 Values of laboratory parameters in COVID-19 patients

		All patients (N = 1546)	PCR negative (N = 439)	PCR positive (N = 1011)	P value
Inflammation-related	**Normal ranges**				
ESR*	Up to 20	42 (26–61)	45 (26–69)	41 (26–60)	0.009
> 20		82.5%	81.8%	82.2%	0.848
CRP*	Up to 5	21.55 (8.87–51.52)	23.4 (7.8–60.7)	21.2 (9–50.8)	0.862
> 5		87.3%	83.4%	88.8%	0.004
Biochemical					
Cr*	0.7–1.2 mg/dL	1.10 (1.00–1.30)	1.1 (1.0–1.3)	1.1 (1.0–1.4)	0.074
> 1.2		46.9%	46%	49.6%	0.215
BUN*	7–19 mg/dL	14 (9–20)	15 (9–20)	14 (9.0–20)	0.326
> 19		28%	29.6%	28.4%	0.636
CPK*	Female: 26–140 U/L Male: 38 –174 U/L	137 (83.5–274)	141 (85–271.75)	133 (80–268)	0.381
< 140 (Female)		36%	35.3%	37.8%	0.37
< 175 (Male)		43%	43.5%	44.4%	0.75
LDH*	207–414 U/L	618 (509–780.25)	616 (512–759.5)	624 (508.5–803.5)	0.386
> 415		74.8%	72.7%	76.9%	0.088
AST*	10–40 U/L	35 (25–51)	32.5 (24–49)	36 (26–52)	0.01
> 40		33.4%	30.1%	35.2%	0.057
ALT*	10–45 U/L	37 (22–64)	35 (23–59)	39 (23–66.25)	0.232
> 45		33.2%	30.5%	36.2%	0.037
Electrolytes					
$Na^{+\#}$	136 – 145	141.13 (±4.88)	140.85 (±4.75)	141.35 (±4.98)	0.073
$K^{+\#}$	3.5 – 5.0	4.59 (±0.6)	4.59 (±0.6)	4.62 (±0.61)	0.49
Blood gas–related					
pH*	7.35–7.45	7.42 (7.33–7.47)	7.42 (7.33–7.47)	7.41 (7.32–7.47)	0.585
< 7.35		7.8%	7.7%	8.4%	0.908
> 7.45		10.2%	10.3%	10.4%	
$PO_2^{\#}$	75–100	46.37 (±19.16)	46.04 (±18.21)	46.59 (±79.59)	0.8
< 75		23.9%	23.5%	25.1%	0.5
$PCO_2^{\#}$	35–45	49.65 (±15.87)	49.08 (±15.33)	50.41 (±16.13)	0.46
> 45		15.1%	14.8%	16.5%	0.414
$O_2 Sat.^{\#}$	> 95	71.64 (±20.67)	71.97 (±19.44)	71.45 (±21.1)	0.822
< 94		23%	22.8%	24.3%	0.524
$HCO_3^{-\#}$	22–26	25.45 (±6.55)	25.35 (±5.35)	25.6 (±7.03)	0.7
Lactate*	0.3–0.8 mmol	1.8 (1.2–2.7)	1.6 (1.05–2.6)	1.9 (1.25–2.8)	0.049
> 0.8		23%	22.1%	24.7%	0.28

*The skewed distributed variables were expressed as the median and interquartile range (25–75%) and the Mann–Whitney U test was used

#The normally distributed variables were described as the means ± standard deviation (SD), and two independent sample t-test was used. Comparisons of categorical variables between groups were conducted using the chi-square test

PCR results, further emphasizing the fact that getting negative molecular testing is not usually as reliable as a positive result is. Albeit molecular testing is the gold standard method of in vitro diagnostic, the often long-waiting time to receive results, as well as the alarming rate of false negatives (30–50%), is daunting challenges facing us [10]. Considering the fact that diagnostic limitations are even more underscored in countries with restricted resources further discloses the necessity to apply simple alternative methods to diagnose COVID-19 patients. According to the results of CBC tests applied for 1537 (99.4%) patients, decreased number of lymphocytes (observed in 31.4% cases) along with increased neutrophil count (displayed in 38.9% cases) are seemingly appropriate items that should be taken into account in the identification of COVID-19. In agreement, decreased number of lymphocytes was reported in studies conducted on 207 and 149 COVID-19 patients [11, 12]; however, and inconsistent with our results, they

Table 4 Alteration rate of laboratory parameters in our study and several pertinent literatures

	Present Study	Chen et al. [14]	Yang et al. [12]	Liu et al. [19]	Cao et al. [21]	Chen et al. [16]	Guan et al. [20]	Wan et al. [22]	Xu et al. [23]
CBC									
Lymphocytes	↓31.4%	↓35%	↓35.5%	↓55%	↓8.9%	↓69%	↓83.2%	↓50%	↓42%
Neutrophils	↑38.9%	↑38%	↑4%	↑17%	↑6.2%				
Platelets	↓18.6%	↓12%	↓13.4%	↓8%	↓17.6%	↓17%	↓36.2%	↓17%	↓5%
Inflammation									
CRP	↑87.3%	↑86%	↑55%	↑83%	↑78.4%	↑93%	↑60.7%		
ESR	↑82.5%	↑85%			↑86.8%				
Biochemical									
Cr	↑46.9%	↑3%	↑28.8%	↑17%	↑5.3%	↑7%		↑4.4%	↑5%
LDH	↑74.8%	↑76%	↑30%	↑92%		↑69%	↑41%	↑43%	↑27%
ALT	↑33.2%	↑28%	↑12%	↑17%	↑10.8%	↑17%	↑21.3%		
AST	↑33.4%	↑35%	↑18%	↑8%	↑17.4%	↑24%	↑22.2%	↑22%	↑16%

demonstrated that neutrophil count is lower in SARS-CoV-2 infection than normal counterparts. Decreased levels of hemoglobin and mild thrombocytopenia, which were present respectively in 40% and 18.6% of our cases, may probably work hand in hand with the altered number of lymphocytes and neutrophils, and will all work together to better identify COVID-19 patients. While no significant association was found between platelets and the disease in a study by Ferrari et al. [11], Cheng et al. [13] revealed a significant correlation between the low number of platelets and COVID-19. There are also several studies representing that decreased levels of hemoglobin and platelet may contribute to facilitating the diagnosis of patients with COVID-19 [14–16].

Given the fact that the primary site of the SARS-CoV-2 attack is the lower respiratory tracts together with knowing LDH as an important marker of lung damage [17] may explain, at least partly, the elevated levels of this enzyme in the majority of COVID-19 patients [15, 18, 19]. Consistently, we found that approximately 75% of 1258 COVID-19 cases who had an LDH result displayed an increased level of LDH with the median value of 618 U/L. Notwithstanding atypical pneumonia being the primary symptom, the emergence of severe disease mainly resulting from the injury of non-pulmonary organs may also explicate abnormal values of kidney- and liver-related biochemical parameters. Analysis of creatinine and BUN in 1540 cases revealed that 50% and 28% of COVID-19 patients display increased levels of the aforementioned factors, which may effectively contribute to mirror virus-mediated kidney impairment. In addition, elevations in the enzymatic levels of AST and ALT nearly in 33% of 1290 patients (who had AST and ALT results)

may also reflect the deteriorating ability of SARS-CoV-2 in induction of liver injury. In a study conducted by Guan et al., it has been reported that ALT and AST levels of COVID-19 patients were elevated in 21.3% and 22.2% of cases, respectively [20]. Albeit ESR and CRP were elevated in 82% and 87% of COVID-19 cases in our study, non-specific alteration in the wide range of infectious conditions, thus including SARS-CoV-2 infection, may profoundly diminish the diagnostic value of these factors in discriminating between patients with or without COVID-19. Given this, even though they still retain specific diagnostic value, it is important to note that the increased amounts of these factors may be beneficial only when they are taking into account in combination with the aforementioned laboratory abnormalities. On the whole and to provide a well-organized viewpoint representing the importance of routine blood tests as a potential diagnostic tool for COVID-19, we summarized alteration rate of the indicated parameters which have been previously reported in several pertinent literature (Table 4).

Albeit the results of this study declared the potential diagnostic value of routine laboratory parameters in SARS-CoV-2 infection, several limitations may adversely affect our analysis. Actually, this study was a retrospective study and 96 cases had no PCR results. Moreover, all the listed parameters did not perform for all the studied cases. The absence of recorded patients' clinical signs also denotes a major limitation to the current study; however, we hope that the results of our study will shed more light on the diagnostic significance of these parameters in COVID-19, as the latest biological hazard to assume a sinister worldwide threat.

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