Laboratory Findings and Outcomes of Critically Ill COVID-19 Patients

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ABSTRACT

Background: COVID-19 patients have various laboratory findings associated with severe conditions and higher mortality rates. We conducted this study to evaluate the laboratory changes and their effect on the mortality of critically ill patients with COVID 19.

Methods: This cohort study evaluated the laboratory changes in 192 patients admitted to intensive care units of Imam Khomeini hospital complex, Tehran, Iran. The patients with manifestations of severe COVID-19 of both sexes and older than 16 years were enrolled in the study. The primary outcome was the laboratory changes, and the secondary outcome was the death or survival of the patients. The laboratory data were recorded on the admission day, followed daily by the changes and the neutrophil-lymphocyte ratio (NLR). The laboratory changes of two groups of survived or non-survived patients were compared by chi-square for categorical variables. An independent sample t-test was applied to study the differences between the two groups' continuous variables. Values are shown as mean±SD.

Results: Of all the 192 patients, 123 (64.06%) were male, and 69 (35.93%) were female. The survived group was 86 (44.79%), and the non-survived group was 106 (55.20%). Age (62.31±13.77), sex, and BMI (27.34±4.63) were not significantly different in the two groups (P value= .248, .368, and .444, respectively). NLR, lactate dehydrogenase/lymphocyte (LDH/LYM) ratio were significantly different in the two groups (P value= .000, .004, respectively).

Conclusion: COVID-19 patients have a variety of laboratory findings. NLR and LDH/LYM ratios have a prognostic value in severe COVID-19 patients.

Since December 2019, coronavirus disease (COVID-19) has spread rapidly worldwide and became pandemic [1]. There have been over 500,000,000 confirmed cases worldwide up to this point [2]. COVID-19 patients have various clinical presentations, from mild to critical cases. The most common symptoms are fever, cough, and myalgia [3]. COVID-19 is not the first and will not be the last pandemic disease described as a global health emergency. Numerous methods for diagnosing and treating the illness during these pandemics are suggested. Assessing factors that influence the prognosis and outcomes of these pandemic diseases is very important. Besides that, understanding and distinguishing the

mortality factors of the conditions will significantly help us control and manage the patients. Nowadays, laboratory medicine, parallel to clinical medicine, guides us in the management and progress of diseases [4]. SARS-CoV-2 pathogenesis is not fully understood. Viruses may invade many organs, particularly the respiratory and immune systems, such as lymph nodes, tonsils, and bone marrow, resulting in viral pneumonia, immunodeficiency, liver damage, myocardial injury, and other complications. These laboratory results demonstrate that the virus may injure multiple organs [5]. COVID-19 patients have various laboratory findings; some of them, such as lymphopenia, increased CRP, and increased LDH, are associated with severe conditions and

higher mortality rates [5]. Leukopenia may be because of a cytokine storm caused by SARS-CoV2 that influences the peripheral white blood cells and immune cells [6]. Some research showed that patients admitted to the intensive care units had higher white blood cells, neutrophil counts, and prothrombin time. Also, severe lymphopenia was associated with an increased mortality rate [6]. According to these researches, more attention is needed to COVID-19 laboratory findings [4-6]. We conducted this study to evaluate the laboratory changes and their ratio to the mortality of critically ill patients with COVID 19.

Methods

The study was reviewed and approved by the Tehran University of Medical Sciences ethics committee (IR.TUMS.VCR.REC. 1399. 192). This cohort study evaluated the laboratory changes in 192 patients admitted to intensive care units (ICU) tertiary Imam Khomeini hospital complex, Tehran university of medical sciences, Tehran, Iran. SARS-CoV2 was confirmed for all the participants with the RT-PCR test. The patients with manifestations of severe COVID-19 of both sexes and older than 16 years were enrolled in the study. The criteria for severe COVID-19 are defined as: Shortness of breath, tachypnea (RR ≥ 30 times/min), hypoxia (Oxygen saturation ≤ 93%), Oxygenation index ≤ 300 mmHg, Chest radiographic images showed more than 50% of affected tissue within 24–48 h.

Data collections and outcome

Demographic data, co-morbidities, vital signs of admission, and laboratory values were collected by the intensivist who visited the patient immediately after entry into the ICU. Acute Physiology and Chronic Health Evaluation (APACHE) II and Sequential Organ Failure Assessment (SOFA) scoring were performed and recorded in the first 24 hours and daily for SOFA score.

The primary outcome was the laboratory changes, and the secondary outcome was the death or survival of the patients. The laboratory data were recorded at admission and daily, and we followed the changes in the findings and the neutrophil-lymphocyte ratio (NLR). Also, the progress of the COVID-19 and the patient's need for non-invasive or invasive mechanical ventilation was recorded.

Statistical analysis

The laboratory changes of two groups of survived or non- survived patients were compared by chi-square or Fisher exact test for categorical variables. An independent sample t-test was applied to study the differences between the two groups' continuous variables. Normality assumption was checked using the Kolmogorov-Simonov test. Values are shown as mean±SD or as number and percentage for continuous and categorical variables, respectively. In this study P value of less than 0.05 was considered statistically significant. Statistical analyses were carried out by SPSS version 26.0 for Windows.

Results

Of 270 ICU patients, 192 patients with severe confirmed COVID-19 were enrolled in the study. Of all the 192 patients, 123 (64.06%) were male, and 69 (35.93%) were female. The survived group was 86 (44.79%), and the non-survived group was 106 (55.20%). The mean age was 62.31±13.77, and the mean body mass index (BMI) was 27.34±4.63. Age, sex, and BMI were not significantly different in the two groups (P value= .248, .368, and .444, respectively).

The mean APACHE II score (P value= .000, 95% CI: 3.324_ 6.514) and mean SOFA score on the first day of admission (P value= .000, 95% CI: 1.479_ 2.979) were significantly different in the two groups. (Table 1) Neutrophil/ lymphocyte ratio (NLR), lactate dehydrogenase/lymphocyte LDH/LYM ratio were significantly different in the two groups (P value= .000, .004, respectively) (Table 2).

Table 1- Demographic characteristics of survived and non-survived group

Variable	Outcome		P value	95% CI	
	Non-survived	Survived		Lower	Upper
Age,n (%)					
≥60	63 (59.43)	46 (53.48)	.248	---	---
<60	43 (40.56)	40 (45.51)			
Sex,n (%)					
Male	71 (66.98)	52 (60.46)	.368	---	---
Female	35 (33.01)	34 (39.53)			
BMI,n (%)					
≥30	21 (22.82)	13 (17.56)	.444	---	---
<30	71 (77.17)	61 (82.43)			
APACHE II, mean±SD	14.38±5.694	9.47±5.233	.000	3.324	6.514
SOFA 1st day, mean±SD	5.4±3.276	3.18±1.003	.000	1.479	2.979
SOFA at admission,	7.271±3.048	3.04±1.008	.000	3.527	4.931

mean±SD					
Comorbidities,n (%)					
Diabetes	42 (25.60)	33 (26.61)	.883		
Cancer	20 (12.19)	7 (5.64)	.038		
Respiratory	15 (9.14)	3 (2.41)	.013		
HTN	35 (21.34)	39 (31.45)	.101		
Cardiac	28 (17.07)	25 (20.16)	.746	---	---
GI	0	1 (.80)	.448		
Hepatic	3 (1.82)	0	.254		
Kidney	9 (5.48)	2 (1.61)	.115		
Endocrine	12 (7.31)	11 (8.87)	.825		

BMI: Body Mass Index, APACHE II: Acute Physiology and Chronic Health Evaluation (APACHE) II, SOFA: Sequential Organ Failure Assessment, HTN: Hypertension, GI: Gastrointestinal

Table 2- Comparison of laboratory findings and mechanical ventilation in the non-survived and survived groups.

Variable	Outcome		P	95% CI	
	Non-survived, mean±SD	Survived, mean±SD	value	Lower	Upper
WBC	9233.02±4371.5	9444.19±13181.1	.877	-2900.988	2478.653
Neutrophil	84.529±7.9	78.629±7.9	.000	3.603	8.197
Lymphocyte	10.921±8.07	15.604±6.96	.000	-6.877	-2.486
Platelets	258066.04±137995.1	258895.35±130018.4	.966	-39327.994	37669.372
Hemoglobin	12.52±2.32	12.43±1.91	.773	-.526	.706
NLR	12.666±10.693	6.507±4.314	.000	3.720	8.598
1st day LDH	774.54±394.957	581.58±211.616	.034	14.730	371.200
1st day CPK	241.333±279.073	189.095±160.023	.440	-82.402	186.878
CRP	129.491803±64.164	89.352±61.478	.001	16.465	63.812
LDH/LYM ratio	154.548±109.964	39.094±33.082	.004	37.855	193.051
MV,n (%)					
Yes	89(83.96)	12(13.95)	.000	---	---
No	17(16.03)	74(86.04)			

NLR: neutrophil/ lymphocyte ratio, LDH: Lactate dehydrogenase, CPK: Creatine phosphokinase, CRP: C-reactive Protein, LDH/LYM ratio: lactate dehydrogenase/lymphocyte ratio, MV: Mechanical Ventilation

Discussion

Of all 192 patients enrolled in the study, 156 (81.25%) had at least one co-morbidity. The most common co-morbidity was diabetes (DM) (39.06%), and the second one was malignancies (14.06%). In a review by Khamis et al. [7], the prevalence of co-morbidities was 17%, with the most common for DM (13.8%), cardiovascular diseases (9.7%), and chronic obstructive pulmonary disease (COPD) (3.9%). As a result, DM is the most common co-morbidity in severe COVID-19 patients.

Lippie et al. [8] demonstrated that the most predictive and prevalent parameters for severe COVID-19 are respectively lymphopenia (96.1%), thrombocytopenia (57.7%), and leukocytosis (11.4%). In our study, 56 (29.5%) patients had leukocytosis, 44 (23.3%) were thrombocytopenic, and the prevalence of lymphopenia was 121 (64.4%). Despite the study of Lippie et al., leukocytosis was higher, and lymphopenia and thrombocytopenia were lower in our study. Lymphopenia is considered an immunity response for SARS-CoV2, especially in severe forms of the disease. All of our COVID-19 patients were in the intensive care unit, and in comparison, to Haung et al. [9] findings, the rate of lymphopenia was lower in our critically ill patients. (85% vs. 64.4%)

Another important value for COVID-19 patients is the neutrophil-lymphocyte ratio (NLR). Lagadinou et al. [10] demonstrated that NLR is significantly higher in more severe COVID-19 patients. NLR is a well-known marker of systematic inflammation; since inflammation in COVID-19 patients is a significant condition, NLR can guide us in detecting the inflammatory phase. Several patients with SARS-CoV2 had a rising neutrophil count and a low lymphocyte count during the severe phase so that the NLR would be elevated. We also detected that this ratio is significantly higher in the non-survived group. This condition may be due to the inflammatory phase they turn in, and this inflammation and cytokine storm lead them to death.

In a review from Martha et al. [11] increased level of lactate dehydrogenase (LDH) was detected in 44% of patients. This elevation was correlated with DM and poor outcomes. There was no relation between elevated LDH and age, sex, and HTN. Of our critically ill patients, 48% of them with increased LDH were in the non-survived group. This finding may show us that an increased level

of LDH is associated with a poor prognosis and a high mortality rate.

Another parameter is LDH/lymphocyte ratio in COVID-19 patients. Serin et al. [12] announce that LDH/Lymph ratio can be a diagnostic marker in COVID-19 patients. This ratio was significantly higher in the non-survived group, and the mortality rate may be associated with this ratio. LDH/lymph ratio in COVID-19 patients can be detected quickly and early, so it can alert the physicians that the patients' condition is getting worse.

Conclusion

COVID-19 patients have a variety of clinical presentations, symptoms, and laboratory findings. NLR and LDH/LYM ratios have a prognostic value in severe COVID-19 patients. But, further research in laboratory tests for predicting the mortality and outcome of critically ill COVID-19 patients seems to be needed.

Acknowledgements

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