To investigate the relation between LDH and CRP levels and mortality of COVID-19 (SARS-CoV-2) patients admitted in SURGERY ICU at Shariati Hospital from 19 February 2020 till 19 February 2021

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Abstract

Background: The aim of this study is to investigate the relationship between LDH and CRP levels and the mortality of COVID-19 (SARS-CoV-2) patients admitted to the SURGERY ICU at Shariati Hospital from 19 February 2020 to 19 February 2021.

Methods: Our study is a cross-sectional descriptive study. A total of 81 patients were enrolled in this study. We examined lab reports, including CBC parameters (WBC, neutrophil count, neutrophil percentage), other inflammatory markers ESR and CRP, and also studied the medical records of cases to collect details about age, gender, length of stay in SURGERY ICU, BMI, fever, survival status, comorbidity, intubation, and NIV. These patients were referred to Shariati Hospital, Tehran, from 19 February 2020 to 19 February 2021, regarding the relationship between LDH and CRP levels and the mortality of COVID-19 (SARS-CoV-2) patients admitted to the SURGERY ICU. The data obtained was analyzed using SPSS software, and a significance value of < 0.05 was considered.

Results: In this study, the data of 81 patients were considered. The data were obtained from the medical records of Shariati Hospital, Tehran. We used 11 variables to compare data from different patients that were recorded in the registry and system of medical records in Shariati Hospital, Tehran. The study population included 81 patients, of which 41 were female and 40 were male, ranging in age from 25 to 89. In total, 80.2% had mild disease versus 18.5% who had severe disease. Sixty-five patients survived, and 16 were admitted to the SURGERY ICU with endotracheal intubation and later died. The length of stay in the SURGERY ICU ranged from 1 to 25 days. Out of 81 patients, 52 (62.4%) had comorbidity, and 29 (35.8%) did not have comorbidity. Twelve patients (14.8%) received NIV, and 69 patients (85.2%) did not receive NIV. Most of the patients did not have a fever. The minimum and maximum levels of CRP were 4 and 416, respectively, and for LDH were 9 and 2401, respectively. The prognostic factors for the severity of COVID-19 infection identified in this study (CRP and LDH) help predict the course of the disease at an early stage. Elevated concentrations of CRP and LDH at admission were found to be associated with a higher risk for COVID-19 severity as they were significant (p-value =0.049 and 0.048, respectively).

Conclusions: This study's laboratory investigation showed that the SURGERY ICU patients had significantly higher values of inflammatory markers CRP and LDH than the non-SURGERY ICU patients. LDH and CRP were superior and effective biomarkers in predicting the severity of COVID-19.

Keywords: SARS-CoV-2, Lab Results, LDH, CRP, Lung Lesions

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Introduction

At the end of 2019, an outbreak of atypical pneumonia of unknown cause was detected in Wuhan, China [1, 2]. The etiological agent of this disease was identified to be a novel coronavirus, named "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2) [3]. The disease caused by SARS-CoV-2, named COVID-19, has since spread worldwide, hence warranting recognition as a pandemic by the WHO [4]. It is characterized by the presence of fever, cough, and dyspnea, and about 5% of COVID-19 subjects ultimately develop full-on acute respiratory distress syndrome, requiring admittance to an intensive care unit (SURGERY ICU) to administer invasive mechanical ventilatory support [5]. Given the elevated risk of death, it is vital to ascertain the patient's risk for poor outcome, and many laboratory tests have been proposed for this purpose [6].

For this purpose, many biomarkers were studied to have played a role in detecting the mortality rate. However, experts, after going through all the studies, concluded that there are two main biomarkers that predict the mortality of individual patients more than 10 days in advance with more than 90% accuracy: lactic dehydrogenase (LDH), lymphocyte, and high-sensitivity C-reactive protein (hs-CRP) [7,16]. Lactate dehydrogenase (LDH) is a hydrogen transfer enzyme that catalyzes the oxidation of l-lactate to pyruvate with the mediation of NAD+ as a hydrogen acceptor, with the reaction being reversible [8]. In particular, relatively high levels of LDH alone seem to play a crucial role in distinguishing the vast majority of cases that require immediate medical attention [8]. This finding is consistent with current medical knowledge that high LDH levels are associated with tissue breakdown occurring in various diseases, including pulmonary disorders such as pneumonia [8].

The increase in LDH reflects tissue/cell destruction and is regarded as a common sign of tissue/cell damage [9]. Serum LDH has been identified as an important biomarker for the activity and severity of idiopathic pulmonary fibrosis [10]. For critically ill patients with COVID-19, the rise in LDH level indicates an increase in the activity and extent of lung injury [11].

The increase in hs-CRP, an important marker for poor prognosis in acute respiratory distress syndrome, reflects a persistent state of inflammation [12]. The result of this persistent inflammatory response is large grey-white lesions in the lungs of patients with COVID-19, as seen in autopsies [13]. In tissue sections, a large amount of sticky secretion is also seen overflowing from the alveoli [14]. At the early stage of COVID-19, CRP levels were positively correlated with lung lesions. C-reactive protein levels could reflect disease severity and should be used as a key indicator for disease monitoring [15].

Material and methods

This was a cross-sectional study that included COVID-19 patients admitted to the SURGERY ICU

Table 1. Distribution of demographic variables among all patients under study

Variables	Mean	Standard deviation	Min	Max
Age (year)	55.93	19.23	25	89
Length of stay in SURGERY ICU(DAYS)	5.41	4.23	1	25
CRP	97.31	74.70	4	416
LDH	792.98	443.66	9	2401
FEVER	37.07	0.615	34	39
BMI	28.10	6.94	18	42

Table 2. Distribution of demographic and clinical characteristics among all patients under study

variables		Number	%
Sex	female	41	50.6
	male	40	49.4
survival status	alive	65	80.2
	died	15	18.5
comorbidity	yes	52	62.4
	no	29	35.8
Intubation	yes	16	19.8
	no	65	80.2
NIV	yes	12	14.8
	no	69	85.2

Table 3. Association between CRP and LDH levels in total and based on other factors

		Spearman's correlation	P-value
Total (n=81)		+0.31	**0.014**
Age	<=50 yr	0.483	**0.011**
	>50 yr	0.146	0.394
sex	female	0.430	0.014
	male	0.173	0.351
Length of stay in SURGERY ICU	<=5 days	0.338	0.054
	>5 days	0.238	0.205
survival status	alive	0.270	0.048
	died	-0.469	0.203
comorbidity	yes	0.197	0.211
	no	0.638	0.002
Intubation	yes	-0.321	0.365
	no	0.375	0.009
NIV	yes	-0.145	0.784
	no	0.331	0.012
Fever	<= 37.2	0.368	0.009
	>37.2	0.110	0.721

Table 4. Comparison CRP and LDH levels among groups

Variables		CRP	P-Value	LDH	P-Value
Age	<=50 yr	72.25±41.71	**0.015**	741.64±446.84	**0.327**
	>50 yr	114.43±87.02		832.92±443.32	
sex	female	81.61±60.31	**0.076**	752.53±458.39	**0.289**
	male	112.75±84.51		833.44±431.88	
Length of stay in SURGERY ICU	<=5 days	106.26±86.80	**0.415**	745.59±413.866	**0.711**
	>5 days	86.34±55.94		846.70±476.54	
survival status	alive	92.12±74.97	**0.049**	758.09±444.58	**0.048**
	died	124.70±70.13		981.50±408.84	
comorbidity	yes	104.82±81.12	**0.027**	776.38±472.44	**0.437**
	no	81.27±57.06		824.68±391.33	
Intubation	yes	115.97±84.74	**0.273**	886.80±238.48	**0.092**
	no	92.98±72.32		775.61±471.54	
NIV	yes	100.33±32.57	**0.344**	1091.00±511.18	**0.069**
	no	96.92±78.73		762.16±429.33	
Fever	<= 37.2	93.36±69.67	**0.657**	814.62±472.49	**0.974**
	>37.2	111.53±91.92		715.71±322.84	

in Shariati Hospital from 19 February 2020 (13-11-1398) to 19 February 2021 (1-12-1399). To execute the sampling, medical records for the study were collected from the archives of Shariati Hospital. After implementing the inclusion and exclusion criteria, a total of 80 records were consecutively selected by the convenient sampling method.

Inclusion criteria

All patients with severe illness, aged >16 years, and COVID-19 positive, admitted to the SURGERY ICU in Shariati Hospital from 19 February 2020 (30-11-1398) till 19 February 2021 (1-12-1399).

Exclusion criteria

Patients who died in less than 5 days.

Statistical analysis

To describe categorical (nominal) variables with two or more categories, we used frequency and percent. We evaluated the normality of continuous variables by the Kolmogorov-Smirnov test and P-P and Q-Q plots.

To describe the continuous variable with a normal distribution, we used the mean and standard deviation (SD), and for non-normally distributed continuous variables, we used the median and inter-quartile range (IQR).

To assess the relationship between two categorical variables with two or more categories, we used the Chi-square test, and if necessary, we used the Fisher's exact test.

To evaluate the relationship between normally distributed continuous variables with a categorical variable with two categories, we used the independent sample T-test. Otherwise, we used the non-parametric Mann-Whitney U test.

Statistical Analysis

Continuous variables will be described as mean

(SD) or median (IQR). Categorical variables will be reported as number (%). The normality assumption will be checked by the Kolmogorov-Smirnov test, and parametric (independent t-test, etc.) or nonparametric tests (Mann-Whitney test, etc.) will be used to assess the aims of the study. A p-value of <0.05 will be considered statistically significant. All analyses will be performed using SPSS version 27.

Results

In this study, the data of 81 patients were considered. The data were obtained from the medical records of Shariati Hospital, Tehran. We used 11 variables to compare data from different patients that were recorded in the registry and system of medical records in Shariati Hospital, Tehran.

The study population included 81 patients, of which 41 were female and 40 were male, ranging in age from 25 to 89. In total, 80.2% had mild disease versus 18.5% who had severe disease. Sixty-five patients survived, and 16 were admitted to the SURGERY ICU with endotracheal intubation and later died. The length of stay in the SURGERY ICU ranged from 1 to 25 days. Out of 81 patients, 52 (62.4%) had comorbidity, and 29 (35.8%) did not have comorbidity. Twelve patients (14.8%) received NIV, and 69 patients (85.2%) did not receive NIV. Most of the patients did not have a fever.

The minimum and maximum levels of CRP were 4 and 416, respectively, and for LDH were 9 and 2401, respectively.

The prognostic factors for the severity of COVID-19 infection identified in this study (CRP and LDH) help predict the course of the disease at an early stage. Elevated concentrations of CRP and LDH at admission were found to be associated with a higher risk for COVID-19 severity as they were significant (p-value =0.049 and 0.048, respectively).

Discussion

In one study examining the relationship between lactate dehydrogenase (LDH) levels and COVID-19 mortality, it was shown that LDH levels are associated with COVID-19 mortality rates, with elevated LDH levels significantly impacting patient mortality [16].

Consistent with these findings, our study also demonstrated that LDH levels are correlated with mortality in COVID-19 patients. Additionally, in another study that examined various laboratory findings in COVID-19 patients and their relationship with mortality rates, similar results were obtained. This study, like ours, found that levels of lactate dehydrogenase (LDH) and C-reactive protein (CRP) are significantly associated with mortality in these patients [17].

In another study examining the relationship between laboratory findings and mortality rates in COVID-19 patients, similar results were obtained. This study, like ours, found that lactate dehydrogenase (LDH) levels are significantly associated with mortality in these patients [18].

In another study, similar to ours, it was found that lactate dehydrogenase (LDH) and C-reactive protein (CRP) can serve as predictive markers for mortality in COVID-19 patients [19].

In conclusion, CRP and lactate dehydrogenase (LDH) can generally be considered as predictors of mortality in COVID-19 patients admitted to intensive care units

References

1. World Health Organization. Coronavirus Disease 2019 (COVID-19) Situation Report 46, 6 March 2020.
2. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, Ren R, Leung KS, Lau EH, Wong JY, Xing X. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med. 2020 Jan 29. https://doi.org/10.1056/NEJMoa2001316
3. World Health Organization. Coronavirus Disease 2019 (COVID-19) Situation Report 46, 6 March 2020.
4. World Health Organization. Coronavirus Disease 2019 (COVID-19) Situation Report 68, 28 March 2020.
5. World Health Organization. Coronavirus Disease 2019 (COVID-19) Situation Report 68, 28 March 2020.
6. C, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395:497-506. https://doi.org/10.1016/S0140-6736(20)30183-5
7. Panteghini M, Bais R. Serum enzymes. In: Rifai N, Horvath AR, Wittwer CT, editors. Tietz textbook of clinical chemistry and molecular diagnostics, 6th ed. St. Louis: Elsevier Saunders; 2018:404-34 pp.
8. Huijgen HJ, Sanders GT, Koster RW, Vreeken J, Bossuyt PM. The clinical value of lactate dehydrogenase in serum: a quantitative review. Eur J Clin Chem Clin Biochem. 1997;35:569-
9. Kishaba T, Tamaki H, Shimaoka Y, Fukuyama H, Yamashiro S. Staging of acute exacerbation in patients with idiopathic pulmonary fibrosis. Lung. 2014;192:141-149. https://doi.org/10.1007/s00408-013-9530-0
10. Shi J, Li Y, Zhou X, Zhang Q, Ye X, Wu Z, et al. Lactate dehydrogenase and susceptibility to deterioration of mild COVID-19 patients: A multicenter nested case-control study. BMC Med. 2020;18(1):168. doi: 10.1186/s12916-020-01680-9. https://doi.org/10.1186/s12916-020-01633-7
11. Ridker PM, Danielson E, Fonseca FA, Genest J, Gotto AM Jr, Kastelein JJ, et al. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. N Engl J Med. 2008;359(21):2195-207. https://doi.org/10.1056/NEJMoa0807646

12. Sharma SK, Agarwal S, Gupta D, Joshi K, Mishra HK. Aetiology, outcomes & predictors of mortality in acute respiratory distress syndrome from a tertiary care centre in North India. Indian J Med Res. 2016;143(6):782-92. https://doi.org/10.4103/0971-5916.192063
13. Bajwa EK, Januzzi JL, Gong MN, Thompson BT, Christiani DC. Plasma C-reactive protein levels are associated with improved outcome in ARDS. Chest. 2009;136(2):471-80. https://doi.org/10.1378/chest.08-2413
14. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 2020;46(5):846-8. https://doi.org/10.1007/s00134-020-05991-x
15. Fajgenbaum DC, June CH. Cytokine storm. N Engl J Med. 2020;383(23):2255-73. https://doi.org/10.1056/NEJMra2026131
16. Li C, Ye J, Chen Q, Hu W, Wang L, Fan Y, et al. Elevated Lactate Dehydrogenase (LDH) level as an independent risk factor for the severity and mortality of COVID-19. Aging (Albany NY). 2020;12(15):15670-81. https://doi.org/10.18632/aging.103770
17. Bilgir F, Çalık Ş, Demir İ, Bilgir O. Roles of certain biochemical and hematological parameters in predicting mortality and ICU admission in COVID-19 patients. Rev Assoc Med Bras. 2021;67:67-73. https://doi.org/10.1590/1806-9282.67.suppl1.20200788
18. Muhammad R, Ogunti R, Ahmed B, Munawar M, Donaldson S, Sumon M, et al. Clinical characteristics and predictors of mortality in minority patients hospitalized with COVID-19 infection. J Racial Ethn Health Disparities. 2022;1-11. https://doi.org/10.1007/s40615-020-00961-x
19. Akdogan D, Guzel M, Tosun D, Akpinar O. Diagnostic and early prognostic value of serum CRP and LDH levels in patients with possible COVID-19 at the first admission. J Infect Dev Ctries. 2021;15(6):766-72. https://doi.org/10.3855/jidc.14072