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Relationship between Severity of Primary Lung Involvement with Erythrocyte Sedimentation Rate and Lactate Dehydrogenase in Patients with COVID-19 in Yazd

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ABSTRACT

Background & Objective: Measurement of inflammatory markers and lactate dehydrogenase (LDH) may contribute to the evaluation of lung involvement severity. This study aimed to evaluate relationship between severity of primary lung involvement with highest level of erythrocyte sedimentation rate (ESR) and LDH in patients with COVID-19.

Materials & Methods: This descriptive-analytical study was conducted on 123 patients with COVID-19 in Shahid Sadoughi Hospital**.** Data including age, gender, ESR (mm/h), LDH (U/L), and high-resolution Computed Tomography scan (HRCT) findings and hospitalization ward were extracted from medical records**.** The regression model was used to determine the relation between HRCT findings with LDH and ESR.

Results: Mean LDH, ESR, and HRCT findings were 508.41±224.65, 52.23±29.56, and 37.17± 22.18 respectively. A significant relation was seen between HRCT findings with highest level of LDH and ESR (P=0.001). A significant relation was observed between the highest levels of ESR and HRCT findings, regarding age, gender, and hospitalization wards (P<0.01). There was a significant relation between the highest level of LDH and HRCT findings regarding age group and hospitalization wards (P<0.01).

Conclusion: A significant relation was seen between HRCT findings and highest levels of ESR and LDH in patients with COVID-19. Therefore, it seems that assessment of laboratory findings such as LDH and ESR can be helpful as cost-effective markers instead of chest CT scan for predicting the severity of lung injury when the CT scan report is controversial. The relation between HRCT findings with LDH and ESR were affected by age and hospitalization ward. However, more studies should be conducted in this regard.

Keywords: COVID-19, Erythrocyte sedimentation rate, High-resolution computed tomography, Lactate dehydrogenase

Introduction

COVID19 virus spread rapidly from China to other countries and quickly became a global epidemic (1). In severe infection cases, the disease quickly becomes acute respiratory distress syndrome and septic shock, leading to death (2). The high rate of this transmission has led to widespread need worldwide for fast, efficient, and cost-effective diagnostic tests. Currently, reverse-transcription polymerase chain reaction (RT-PCR) is applied for the diagnosis of viral RNA. However, short supply of this test in many countries and being time-consuming have led to considering other techniques (3, 4).

High-resolution Computed Tomography scan (HRCT) is an essential and main technique in the diagnosis and treatment of COVID-19 (5). Kashyape et al., evaluated 1,499 confirmed and suspected COVID-19 patients and reported that in both symptomatic and asymptomatic patients, HRCT was an excellent adjunct for the initial diagnosis of COVID-19 (6). Although most radiologists do not recommend routine CT scan to evaluate COVID-19 pneumonia, the frequency of this technique is increasing in patients under investigation for COVID-19 (7). Besides, a reduction in CT scan availability in critical cases has also been reported. Thus, other specific and

sensitive biomarkers for the diagnosis of COVID-19 pneumonia are needed.

Studies have shown that different biomarkers are under investigation for determining the prognosis of patients with COVID-19 (8). Lactate dehydrogenase (LDH) is an enzyme that plays a key role in the conversion of lactate to pyruvate in the cells of most tissues. Increased level of serum LDH is seen in numerous clinical situations, including cancer, hemolysis, hematologic malignancies, severe infections, liver disease, sepsis, and many others. Nowadays, the serum level of LDH is considered a non-specific indicator of cellular death in some studies (9-11). It seems that the change of LDH may be correlated to the time course of COVID-19 pneumonia (9).

Erythrocyte sedimentation rate (ESR) is a common hematology test that indicates and monitors the increase in inflammatory activity within the body caused by one or more conditions such as infections (12). Moreover, the role of ESR as an inflammatory biomarker in the development of severe COVID-19 has been reported in some studies (13). Since Covid 19 causes inflammation in the body, and severe cases of inflammation lead to respiratory failure and decreased blood oxygen levels, therefore, the assessment of ESR may help with detection of the severity and prognosis of COVID-19 (13).

Sobhani et al., by evaluating laboratory findings in patients with covid-19 in Northeast Iran showed that ESR level was higher in non- survivors compared to survived patients (14). Another study by Ghahramani et al., reported ESR and LDH levels increase in the severe COVID-19 patients compared with the non-severe group among Asian populations (15).

Given that association between severity of lung involvement with ESR and LDH in patients with COVID-19 is not clear and few studies have been conducted in this regard, this study aimed to evaluate the relationship between severity of lung involvement with the highest level of ESR and LDH in patients with COVID-19.

Materials and Methods

Data selection

The current study was approved by the ethical committee of Islamic Azad University, Yazd Branch, and Yazd, Iran with the number IR.IAU.YAZD.REC.1399.036. This descriptive-analytical study was conducted on patients with COVID-19 in Shahid Sadoughi Hospital, Yazd, Iran from March 2020 to April 2020. 123 patients with COVID 19 were selected and data including age, gender, ESR (mm/h), LDH (U/L), and hospitalization ward were extracted from medical records. When the patients were admitted to the hospital their LDH, ESR, and computed tomography (CT) scan findings were assessed. LDH was measured by the commercial kit (Pars Azmoon, Iran) according to the manufacturer's instructions (16). ESR was assessed according to the Westergren method (17). HRCT was assessed in Shahid Sadoughi Hospital. Inclusion criteria were the diagnosis of COVID-19 based on PCR findings and participants who did not complete the treatment process and participants who did not consent to proceed with the study were excluded from the study.

The Scoring system of COVID-19 on CT scan findings were None (0%), Minimal (1-25%), Mild (26-50%), Moderate (51-75%), and Severe (76-100%) with scores of 0, 1, 2, 3, and 4 respectively.

Statistical analysis

Data were entered into SPSS, version 23. The t-test and ANOVA were used for statistical analysis. The regression model was used to determine the relation between HRCT findings with LDH and ESR. $P<0.05$ was assumed significant.

Results

The current study was conducted on 123 patients with COVID-19. Among them, 78 (63.4%) and 45 patients (36.5%) were male and female, respectively. Moreover, 17 (13.8%) and 106 (86.2%) patients were hospitalized in ICU and non-ICU wards. The mean ages of patients in the male and female groups were 54.32±17.68 and 57.39±19.96, respectively (p=0.256). Mean LDH, ESR, and HRCT findings were 508.41±224.65, 52.23±29.56, and 37.17± 22.18 respectively.

A significant relation was seen between HRCT findings and LDH (P=0.001). Moreover, a significant relation was observed between HRCT findings and ESR (P=0.001).

Table 1. Frequency of patients in different age groups

Age group (year)	Frequency (percent)
< 40	28 (22.764)
40-69	64 (52.033)
>70	31 (25.203)
Total	123 (100)

As shown in Table 1, most patients are in the age range of 40-69 years.

Table 2. Mean LDH, ESR, and HRCT findings in male and female groups

Variables	Male Mean± SD	Female Mean± SD	*P-value*
LDH	512.13± 239.83	501.13±197.98	0.786
ESR	51.53±30.10	53.44± 28.90	0.730
HRCT	38.55±21.91	34.78±22.69	0.366

LDH: lactate dehydrogenase. ESR: erythrocyte sedimentation rate. HRCT: high-resolution Computed Tomography scan. SD: Standard deviation.

In Table 2, no significant difference was seen between the two groups, regarding LDH, ESR, and HRCT findings (p>0.05).

Table 3. Frequency of patients in terms of HRCT findings

HRCT	Frequency (percent)
0-25	42 (34.147)
26-50	52 (42.276)
51-75	22 (17.886)
76-100	7 (5.691)

HRCT: high-resolution Computed Tomography scan.

As shown in Table 3, most patients (42.276 %) had a score of 26-50.

Table 4. The relation between HRCT and ESR considering age, gender, and hospitalization ward

Variables		Grade of HRCT	ESR rate			*P-value*
			< 28	**28-72**	**≥ 73**	
Age	**< 40 years**	1	0	5	9	0.000
		2	1	3	3	
		3	0	2	1	
		4	0	3	1	
	40-69 years	1	0	7	9	
		2	9	21	1	
		3	7	7	1	
		4	2	0	0	
	≥ 70 years	1	5	2	4	
		2	4	11	0	
		3	2	1	0	
		4	1	1	0	
Gender	**Male**	1	2	10	13	0.000
		2	9	21	4	
		3	4	7	2	
		4	2	3	1	
	Female	1	3	4	9	

Variables		Grade of HRCT	ESR rate			*P-value*
			< 28	28-72	≥ 73	
Ward	ICU	2	5	14	0	0.000
		3	5	3	0	
		4	1	1	0	
	Non-ICU	1	3	1	4	
		2	1	3	0	
		3	2	1	0	
		4	0	1	1	
		1	2	13	18	
		2	13	32	4	
		3	7	9	2	
		4	**3**	**3**	**0**	

HRCT: high-resolution Computed Tomography scan, ESR: erythrocyte sedimentation rate.

As shown in Table 4, a significant relation was seen between the highest level of ESR and HRCT findings, regarding age, gender, and hospitalization ward (p<0.05).

In Table 5, a significant relation was seen between HRCT findings and LDH in patients with COVID-19 in terms of age and hospitalization wards (p<0.05).

Table 5. The relation between HRCT and LDH regarding age, gender, and hospitalization ward.

Variable		Grade of HRCT	LDH			*P-value*
			349<	349-619	620>	
Age	< 40 years	1	0	9	5	0.002
		2	3	1	3	
		3	1	0	2	
		4	1	2	1	
	40-69 years	1	1	9	6	
		2	7	18	6	
		3	8	6	1	
		4	2	0	0	
	≥ 70 years	1	1	8	2	
		2	4	8	3	
		3	1	1	1	
		4	2	0	0	
Gender	Male	1	1	17	7	0.002
		2	9	18	7	
		3	6	5	2	
		4	3	2	1	
	Female	1	1	9	1	
		2	5	9	5	
		3	4	2	4	

Variable		Grade of HRCT	LDH			*P-value*
			349<	349-619	620>	
Ward	ICU	4	2	0	2	0.002
		1	0	6	2	
		2	0	3	1	
		3	2	1	0	
		4	0	1	1	
	Non-ICU	1	11	20	2	
		2	11	24	14	
		3	4	6	8	
		4	0	1	5	

HRCT: high-resolution Computed Tomography scan, LDH: lactate dehydrogenase.

The study of the relationship between LDH level with age, sex, and HRCT based on regression analysis showed HRCT was the only significant variable that predicts LDH level (P-Value = 0.001, B= 4.46) and the regression model based on the formula will be as follows:

LDH = 275.16 + 4.46. HRCT (%)

Evaluation of the relationship between ESR level with age, sex, and HRCT based on regression analysis showed that among the variables HRCT (P-Value = 0.001, B = 0.493) and age (P-Value = 0.001, B = 0.511)) predicted ESR level significantly and the regression model will be based on the following formula:

ESR=3.97 + 0.493. HRCT (%)

ESR=3.97 + 0.520. age

Discussion

COVID-19 is a viral disease that has rapidly been transmitted throughout the world. Clinically, some patients with COVID-19 show progressive symptoms during hospitalization. Identification of the progression of the disease is the main concern regarding decision making for therapies **(9)**. The laboratory findings have been emphasized in patients with COVID-19 pneumonia. LDH is released during tissue damage and is involved in various pathophysiological processes. Various studies have reported that LDH can be a predictor of worse outcomes **(18, 19)** and poor prognosis in malignancies **(20, 21)**. Aggrawel et al., assessed laboratory findings and clinical features of hospitalized patients with COVID-19 and reported elevated LDH in 80% of patients. It seems that LDH can be used as a biomarker for monitoring patients with severe COVID-19 **(22)**. In our study, there was a significant relationship between the highest level of LDH and HRCT findings in patients with COVID-19. It seems that LDH may be used for predicting lung involvement in patients with COVID-19. Parvizpour et al., conducted a study in Imam Khomeini Hospital (Tehran, Iran) and reported elevated levels of ESR and LDH in the COVID-19 patients compared with the control group **(23)**. Given that LDH is present in lung tissues, patients with severe COVID-19 infection release greater LDH to circulation indicating a severe form of interstitial pneumonia **(8)**. Therefore, it seems that the LDH level is associated with a worse outcome in patients with the viral infection and predicts COVID-19 severity and mortality **(8)**. Wu et al., reported that the increase or decrease in LDH levels are an index of radiographic progression or improvement **(9)**. Therefore, they concluded that serum LDH is a marker for assessing severity of treatment response and disease progression in COVID-19 pneumonia **(9)**. Assiri et al., reported that LDH level is increased in patients with Middle East Respiratory Syndrome **(24)**. These findings were consistent with our study. Luo et al., compared the LDH levels in patients with positive and negative CT scan and found higher levels of LDH in patients with positive CT scan compared to negative CT scan **(25)**. Wu et al., reported that reduction in the cut-off value of LDH is associated with poor sensitivity and specificity for predicting of image improvement, which may be due to dysfunction of a secondary organ in late diseases **(9)**.

In addition, the relation between inflammatory markers and severity of COVID-19 was reported in some studies **(26)**. In our study, we observed a significant relation between the highest level of ESR and HRCT findings. According to these findings, the ESR level can be applied for predicting HRCT findings. Few studies have been conducted regarding the association between ESR and lung involvement based on HRCT findings. The ESR level was significantly higher in the positive CT scan group than in the negative CT scan group **(25)**. Go et al., reported that increased ESR rate is associated with respiratory failure and its measurement can be used for predicting interstitial lung disease and mortality in dermatomyositis **(27)**. Therefore, according to the findings of current study and other studies, the ESR level was related to lung involvement.

In addition, we observed a significant relationship between the highest level of LDH and HRCT findings in terms of age range of patients. In this regard, there was a significant relationship between the patients in the age range of 40-69 years. Perhaps, this relation was due to higher number of patients in this age range. Regarding ESR, this significant relation was seen in age groups of 40- 69 years and > 70 years. In addition, a significant relation was seen between HRCT findings with LDH and ESR in patients with COVID-19 hospitalized in the non-ICU wards. It seems that this relation was also due to the higher number of patients in the non-ICU wards. However, the relation between HRCT findings and ESR was significant in male and female groups. Therefore, it seems that the relation between HRCT findings and ESR was significant, regardless of gender.

One of the limitations of the study is the number of samples. With more studies on a larger number of patients, more accurate results can be achieved.

Conclusion

In the current study, a significant relation was seen between HRCT findings with ESR and LDH level in patients with COVID-19. Therefore, it seems that the assessment of laboratory findings such as LDH and ESR can predict the severity of lung injury. In addition, the relation between HRCT findings with LDH and ESR was affected by the age range of patients and hospitalization wards. However, more studies should be conducted in this regard.

Acknowledgments

The current study was approved by the ethical committee of Islamic Azad University, Yazd Branch, and Yazd, Iran with the number IR.IAU.YAZD.REC.1399.036.

Conflict of Interest

Authors declare no conflict of interest.

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