



## The Relationship between Severity of Lung Involvement Based on High-Resolution Computed Tomography (HRCT) Findings and Lymphopenia in Patients with COVID-19

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### Abstract

**Background:** Lymphopenia may reflect the degree of lung injury in patients with coronavirus disease 2019 (COVID-19). Given that few studies have been conducted in this regard, this study aimed to evaluate the association between severity of lung involvement based on high-resolution computed tomography (HRCT) findings and lymphocyte count in patients with COVID-19.

**Materials and Methods:** This descriptive-analytical study was conducted on 123 patients with COVID-19 from March 2020 to April 2020 in Shahid Sadoughi hospital, Yazd, Iran. Data including age, gender, hospitalization ward, lymphocyte count, and computed tomography (CT) scan findings were extracted from medical records.

**Results:** The mean lung involvement score was  $36.8 \pm 22.34$ . The mean lymphocyte count in these patients was  $1229.25 \pm 536.80 \mu\text{L}$ . Lymphopenia was observed in 79 patients (64%). No relationship was seen between HRCT findings and lymphopenia in patients with COVID-19 ( $P=0.31$ ). Although a significant relationship was seen between HRCT findings and lymphopenia in females ( $P<0.05$ ), there was no relationship between HRCT findings and lymphopenia, regarding age, male gender, and hospitalization wards ( $P>0.05$ ).

**Conclusion:** There was no significant relationship between HRCT and lymphopenia findings, and parameters such as age and inpatient ward in patients with Covid-19. However, there was an interesting relationship between lymphopenia and lung involvement in women; therefore, more studies are needed to prove this hypothesis.

**Keywords:** High-resolution computed tomography, Lymphocyte count, COVID-19

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### Introduction

Coronavirus disease 2019 (COVID-19) emerged in late 2019 in Wuhan, China, and quickly became a global pandemic (1). Most patients with COVID-19 infection experience mild cold symptoms, including cough, fever, and fatigue (2). In cases with severe infection, the disease rapidly leads to acute respiratory distress syndrome, coagulopathy, septic shock, and death (2).

Considering the high transmission rate of this disease and high rate of asymptomatic infection, performing rapid, cost-effective, and efficient diagnostic tests in both clinical and non-clinical settings is of great importance. Currently, reverse-transcription polymerase chain reaction (RT-PCR) is used for the early detection of viral RNA in patients with COVID-19. However, this

test is time-consuming (3) and many countries may face shortages. In addition, diagnostic tests of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the early stage may be associated with false-negative results (4, 5).

Low lymphocyte count is one of the markers of interest and diagnostic criteria for a suspected COVID-19 case (5). Many studies have shown a correlation between the severity of COVID-19 and abnormally low counts of lymphocytes or lymphopenia (6). The pathogenesis of lymphocyte reduction in COVID-19 may be similar to beta-CoV infections, including the Middle East respiratory syndrome (MERS) as well as the severe acute respiratory syndrome (SARS) (7). Peripheral T lymphocytes such as CD8<sup>+</sup> and CD4<sup>+</sup> are rapidly decreased in acute SARS-CoV

infection due to lymphocyte sequestration in particular target organs (8).

High-resolution computed tomography (HRCT) is a practical imaging method that plays a major role in the diagnosis, treatment, and monitoring prognosis of COVID-19 (9). According to imaging characteristics, COVID-19 can be classified into different scores. Computed tomography (CT) severity scores are used to evaluate the degree of lung injury (9, 10). Most radiology societies do not recommend routine CT scan to assess COVID-19 pneumonia; however, the frequency of CT scan in patients under investigation for COVID-19 is increasing (10).

Given that lymphocyte count and neutrophil to lymphocyte ratio may reflect the degree of lung injury (11) and that few studies have been conducted regarding the relationship between severity of lung involvement and lymphocyte count in these patients (12, 13), we evaluated the relationship between severity of lung involvement based on HRCT findings and lymphocyte count in patients with COVID-19.

### Materials and Methods

This descriptive-analytical study was conducted on 123 patients with COVID-19 from March 2020 to April 2020 in Shahid Sadoughi Hospital, Yazd, Iran.

The inclusion criterion to enter the study was the definitive diagnosis of COVID-19 based on PCR test findings. Moreover, patients who did not give written consent or did not complete the treatment process were excluded from the study. Data including age, gender, and hospitalization ward were extracted from medical records. When patients were admitted to the hospital, their lymphocyte count and CT scan findings were assessed.

Table 1 shows the scope scoring system of COVID-19 based on CT scan findings.

### Statistical Analysis

Data were entered into SPSS version 23.0. The Chi-square test was used for the analysis of data.  $P$  value  $< 0.05$  was considered significant.

### Results

The current study was conducted on 77 males and 46 females. Among these patients, 16 (13%) and 107 patients (97%) were hospitalized in the ICU and non-ICU wards, respectively. The mean age of men and women was  $54.32 \pm 17.68$  and  $57.39 \pm 19.96$  years old, respectively ( $P=0.327$ ). In addition, no mortality was observed in patients. The frequency of patients based on age is shown in Table 2.

The frequency of patients with COVID-19 based on HRCT findings and lymphocyte count is shown in Table 3.

In most patients (42.3%), lung involvement was mild. The mean score of lung involvement in these patients

was  $36.8 \pm 22.34$ . The mean lymphocyte count was  $1229.25 \pm 536.80 \mu\text{L}$ . No relationship was seen between the severity of lung involvement based on HRCT findings and lymphocyte count ( $P=0.31$ ). Moreover, the mean score of lung involvement based on HRCT findings in men and women was  $38.79 \pm 21.95$  and  $33.48 \pm 22.83$ , respectively ( $P=0.203$ ). The mean lymphocyte count in males and females was  $1209.29 \pm 526.75$  and  $1262.67 \pm 526.66$ , respectively ( $P=0.597$ ).

According Table 4 there was no relationship between HRCT findings and lymphopenia, regarding age, male gender, and hospitalization wards ( $P>0.05$ ), but a significant relationship was seen between HRCT findings and lymphopenia in females ( $P<0.05$ ).

### Discussion

Lymphocytes play an important role in inflammatory response and maintaining immune homeostasis. The mechanism of lymphocyte reduction is expected to provide a new strategy for the COVID-19 treatment (6). According to the results of this study, men are more likely to be infected with this disease than women. Previous studies have demonstrated that men are more prone to SARS-COV-2 infection (13). Our study demonstrated that the mean age of men and women was  $54.32 \pm 17.68$

**Table 1.** Scope Scoring System of COVID-19 Based on CT Scan Findings

Severity of involvement	Percentage	Score
None	0	0
Minimal	1-25	1
Mild	26-50	2
Moderate	51-75	3
Severe	76-100	4

**Table 2.** Frequency of Patients Based on Age Group

Age Group (y)	Frequency (%)
< 40	28 (22.8)
40-69	64 (52)
> 70	31 (25.2)
Total	123 (100)

**Table 3.** Frequency of Patients with COVID-19 Based on HRCT Findings and Lymphocyte Count

	No. (%)	
HRCT findings	Minimal	42 (34.1)
	Mild	52 (42.3)
	Moderate	22 (17.9)
	Severe	7 (5.7)
Lymphocyte	Grade 4	31 (25.2)
	Grade 3	5 (4.1)
	Grade 2	43 (35)
	Grade 1	44 (35.8)

**Table 4.** Relationship Between HRCT Findings and Lymphocytopenia in Patients With COVID-19

Parameters	HRCT Findings	Lymphocytopenia				P Value	
		Grade 1	Grade 2	Grade 3	Grade 4		
Age	Under 40 years	Minimal	6	3	0	5	0.419
		Mild	3	3	0	1	
		Moderate	2	0	0	1	
		Severe	1	1	1	1	
	40-69 years	Minimal	3	4	1	8	0.466
		Mild	11	12	1	7	
		Moderate	8	4	0	3	
		Severe	1	1	0	0	
	Over 70 years	Minimal	4	5	0	3	0.493
		Mild	4	8	1	1	
		Moderate	0	2	1	1	
		Severe	1	0	0	0	
	Total	Minimal	13	12	1	16	0.372
		Mild	18	23	2	9	
		Moderate	10	6	1	5	
		Severe	3	2	1	1	
Gender	Male	Minimal	10	5	1	9	0.771
		Mild	13	14	1	5	
		Moderate	5	4	1	4	
		Severe	2	2	0	1	
	Female	Minimal	3	7	0	7	0.025
		Mild	5	9	1	4	
		Moderate	5	2	0	1	
		Severe	1	0	1	0	
	Total	Minimal	13	12	1	16	0.372
		Mild	18	23	2	9	
		Moderate	10	6	1	5	
		Severe	3	2	1	1	
Ward	ICU	Minimal	2	5	0	2	0.165
		Mild	1	2	0	0	
		Moderate	0	0	1	2	
		Severe	1	0	0	0	
	Non-ICU wards	Minimal	11	7	1	14	0.149
		Mild	17	21	2	9	
		Moderate	10	6	0	3	
		Severe	2	2	1	1	
Total	Minimal	13	12	1	16	0.372	
	Mild	18	23	2	9		
	Moderate	10	6	1	5		
	Severe	3	2	1	1		

\* The Chi-square test was used to analyze the data.

and  $57.39 \pm 19.96$  years old, respectively. Li et al reported that the mean age of all patients with Covid-19 was 46.7 years (15). Chen et al also noted that the mean age of hospitalized patients was 55 years (16). The results of this study showed that lymphopenia was observed in

approximately 64% of patients. In a study, Zhang et al reported that lymphopenia was observed in 89.2% of patients with COVID-19 at the time of admission (11). COVID-19 could mainly affect lymphocytes, especially T lymphocytes. Abbasi-Oshaghi et al reported that

COVID-19 via stimulation of inflammation induces a cytokine storm, leading to the change of immune cells such as WBCs and lymphocytes (17). Zhao et al reported that lymphopenia is a reliable indicator and an effective diagnostic tool for predicting disease severity in patients with COVID-19 (18). In addition, lymphopenia is the most common laboratory finding for determining the severity of disease in pneumonia patients with abnormal chest CT scan findings or lung lesions (19-22). Therefore, according to these studies, we assessed the relationship between lung involvement findings and lymphocyte count in patients with COVID-19 and found that there was no significant relationship between severity of lung involvement and lymphocyte count. According to these findings, it seems that lymphopenia cannot be a predictor of HCRT findings.

Few studies have been conducted regarding the relationship between lymphocyte count and lung involvement based on HRCT findings. Ruch et al assessed CT scan images and laboratory findings in patients with COVID-19 and reported that patients with lung involvement > 50% had lower lymphocyte count and more consolidations on CT than those with lung involvement ≤ 25% (13). One difference between our study and that of Ruch was the use of different sample sizes. We conducted this study on 123 patients, whereas Roche et al selected 572 patients. Moreover, another reason for the difference between the two studies is that we assessed the relationship between lymphocyte count and lung involvement in all patients, while Ruch et al evaluated the relationship between lung involvement > 50% and lymphocyte count. Luo et al evaluated the association between chest CT features and the clinical course of coronavirus disease. In this regard, patients with positive image findings showed higher levels of lymphocytes and lower levels of white blood cells. It seems that image alteration along the disease progression may be helpful in early recognition and differential diagnosis of COVID-19 (12). In addition, there was a significant relationship between severity of lung involvement and lymphocyte count in women participated in our study. It indicates that the female gender could affect the relationship between lung involvement and lymphocyte count; however, the relationship between HRCT findings and lymphocytopenia was not affected by age, male gender, and hospitalization wards. In addition to the limited sample size, the second limitation of this study was that no causal relationship can be clearly asserted for any factor based on a cross-sectional study. Finally, prospective and longitudinal studies are required to provide additional information.

### Conclusion

In the current study, no significant relationship was seen between HRCT findings and lymphocytopenia in patients with COVID-19. According to this finding, lymphopenia

cannot be a predictor of HCRT findings. Therefore, it seems that lymphopenia cannot be an alternative to the chest CT scan for predicting the severity of lung injury. In addition, the relationship between HRCT findings and lymphocytopenia was not affected by age, male gender, and hospitalization wards; however, the female gender could influence the relationship between HRCT findings and lymphocytopenia.

### Authors' Contribution

All authors contributed to the study conception and design. Material preparation, data collection, and data analysis were performed by FK, NN, and MM. The first draft of the manuscript was written by AI and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

### Conflict of Interests Disclosures

The authors have no conflict of interests to declare that are relevant to the content of this article.

### Ethics Statement

The current study was approved by the Ethics Committee of Islamic Azad University, Yazd Branch, Yazd, Iran (IR.IAU.YAZD.REC.1399.037).

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### Informed Consent

Informed consent was obtained from all individual participants included in the study.

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