

Impact of Lymphopenia on COVID-19 Infection Severity

Dear Editor,

Coronavirus disease-2019 (COVID-19) is an infectious disease caused by a new coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). World Health Organization (WHO) first learned of this new virus on December 31, 2019, following a report of a cluster of cases of “viral pneumonia” in Wuhan, People’s Republic of China.

WHO declared the outbreak a public health emergency of international concern on January 30, 2020, and a pandemic on March 11, 2020. Globally according to WHO data, as of September 9, 2021 there were 4,592,934 deaths occurred due to this disease.

Complete blood count (CBC) as an effective, cheap, available lab test was frequently used to investigate and follow COVID-19 patients, and lymphopenia was an attractive finding associated with severity and poor outcome of these patients as our experience and as published global research papers concluded.

Lymphopenia, defined as a lymphocyte count less than 1×10^9 /L (normal range $1-4 \times 10^9$ /L), has been associated with severe COVID-19 illness and it is a poor predictor of outcomes.^[1-5]

Lymphopenia was reported in various types of virus-infected diseases, such as SARS, MERS, and respiratory syncytial virus. A previous study reported that lymphopenia in SARS may be due to enhanced vascular sequestration associated with increased soluble vascular cell adhesion molecule-1 levels, but the mechanism is not clear in patients with COVID-19. Glucocorticoid treatment results in lymphopenia because it induces the migration of lymphocytes from the peripheral blood. Viral infections inevitably lead to activation of the hypothalamic–pituitary–adrenal axis under stress, which results in the upregulation of endogenous corticosteroids.^[6]

A Chinese study^[7] speculated four mechanisms leading to potential lymphocyte deficiency: (1) the virus might directly infect lymphocytes, resulting in lymphocyte death. Lymphocytes express the coronavirus receptor angiotensin-converting enzyme 2 (ACE2) and may be a direct target of viruses. (2) The virus might directly destroy lymphatic organs such as thymus and spleen cannot be ruled out. (3) Inflammatory cytokines continued to be disordered, perhaps leading to lymphocyte apoptosis. (4) Inhibition of lymphocytes by metabolic molecules produced by metabolic disorders, such as hyperlactic acidemia. The severe type of patients with COVID-19 had elevated blood lactic acid levels, which might suppress the proliferation of lymphocytes.

We retrospect and observe data of 70 patients with COVID-19 who visited Merjan Teaching Hospital during July–August 2021. Thirty-five patients had lymphopenia according to their CBC at the time of hospital presentation and the other 35 had normal lymphocyte count at their initial CBC [Table 1].

The severity of their disease classified according to Iraqi ministry of Health national guide of COVID-19.

Data were analyzed by using the Statistical Package for the Social Sciences (SPSS) software program, version 24.0. Continuous variables were presented as mean with standard deviation and discrete variables were presented as numbers and percentages. T-test for two independent variables was used to test the significance of the observed difference in mean age between the two study groups. Chi-square test for independence was used as appropriate to test the significance of association between discrete variables. Level of significance was set at P value <0.05 .

The study did not find a significant association between lymphopenia and case fatality but found the relation significant with the need for advanced care (admission to ward/intensive care unit) in the lymphopenic group [Table 1 and Figure 1].

In conclusion, lymphopenia could act as a laboratory and clinical indicator of disease severity in patients with COVID-19.

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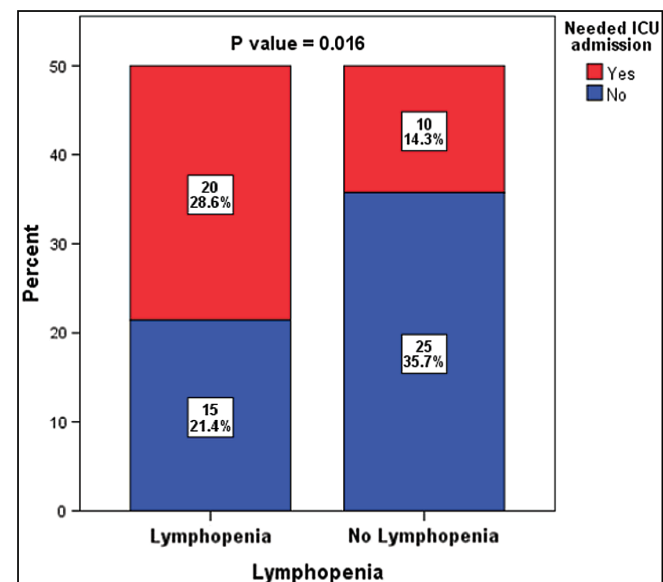


Figure 1: Distribution of enrolled patients with COVID-19 according to presence of lymphopenia and the need for admission into intensive care unit (ICU)

Table 1: Characteristics of enrolled COVID-19 patients according to presence or absence of lymphopenia and other studied factors

Studied factors	Lymphopenia		No lymphopenia		P Value
	N = 35	100%	N = 35	100%	
Age (years); mean $\pm$ SD	58.9 $\pm$ 14.0		52.1 $\pm$ 18.6		
Age group					0.065
20–40 years	4	11.4%	12	34.3%	
41–60 years	13	37.1%	8	22.9%	
$\geq$ 61	18	51.4%	15	42.9%	
Sex					0.615
Male	24	68.6%	22	62.9%	
Female	11	31.4%	13	37.1%	
Hypertension					0.101
Yes	12	34.3%	6	17.1%	
No	23	65.7%	29	82.9%	
Heart disease					1.000
Yes	7	20.0%	7	20.0%	
No	28	80.0%	28	80.0%	
Renal disease					0.393
Yes	2	5.7%	4	11.4%	
No	33	94.3%	31	88.6%	
Diabetes					0.806
Yes	14	40.0%	13	37.1%	
No	21	60.0%	22	62.9%	
Case severity					0.030
Moderate	11	31.4%	20	57.1%	
Sever/critical	24	68.6%	15	42.9%	
Outpatient treatment					<0.001
Yes	8	22.9%	35	100.0%	
No	27	77.1%	0	0.0%	
Ward admission					0.001
Yes	29	82.9%	15	42.9%	
No	6	17.1%	20	57.1%	
Needed ICU					0.016
Yes	20	57.1%	10	28.6%	
No	15	42.9%	25	71.4%	
Died					0.324
Yes	7	20.0%	4	11.4%	
No	28	80.0%	31	88.6%	

Bold values indicate significant at P value < 0.05 **Conflicts of interest**

There are no conflicts of interest.

Ethical approval

Not applicable.

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Letter to the Editor

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