

# Lymphocyte as A Predictive Marker for Seronegativity of COVID-19

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## ABSTRACT

**Background:** To use baseline lymphocyte as a predictive marker of covid 19 seronegativity.

**Method:** In this study, the baseline lymphocyte of every covid patient, diagnosed on basis PCR (nasopharyngeal swab) was done, and they were monitored. All patients in this study are aged between 20 to 84 years, and their PCRs are repeated after 7 days of 1<sup>st</sup> PCR as per guideline of WHO in April. A sum of 142 patients was observed for over 7 to 35 days.

**Result:** Lymphocyte count has a co-relation with seronegativity. It has been observed, patient with high or normal lymphocyte count are more likely to have a negative PCR test after 7 days of their initial test provided, they are asymptomatic, while those with low lymphocyte count are likely to have a negative conversion of their test in 14 to 35 days, depend on age and comorbid.

## Introduction

In the month of December 2019, in Wuhan Province of China, multiple cases of pneumonia with an unknown origin were reported. By PCR and bronchoalveolar lavage studies, it was confirmed that the causative microorganism belongs to virus family and name coronavirus/Novel Covid-19 (SARS-COV-2) AND DISEASES NAMED AS covid-19 [1]. The virus got international attention as it spreads to Japan, Korea, Iran, India and New Zealand. America and Italy were badly affected by this virus, and the mortality rate went beyond 8%. In March WHO declared Covid as the pandemic of 20th century. Pakistan is badly hit by covid 19, and in the first week of June the total number of confirmed cases was above 150 thousand and deaths were around 3000. While the world census is above 8 million total confirmed cases with 0.5million deaths.

Lymphocytes play a pivotal role in maintaining our immune system. The alteration in the total lymphocyte count after viral infection indicates a potential association between lymphocyte and viral pathogenic mechanism [2,3]. The studies Conducted after COVID 19 declared as a pandemic, indicated showed a low lymphocyte count, but its impact on seronegativity of COVID is still unknown [4]. In this article we aimed to establish a role of lymphocyte count and number of days taken for seroconversion of COVID 19.

## Patients and Methods

It is a longitudinal study in which a total of 142 patients have been monitored for 7 to 35 days admitted in a field hospital in Rawalpindi district. The research is conducted for 40 days from

the 20<sup>th</sup> of April to the 30<sup>th</sup> of May. All patients were male, and age ranges from 20 to 84 years. All patients were confirmed covid case diagnosed on nasopharyngeal sample PCR. The patients were further classified into two groups, those who stayed less than 8 days and those who stayed more than 8 days. Patient’s lymphocyte counts were monitored at the time of admission, and their outcome is monitored.

**Results**

142 patients of COVID-19 included in this study. The median age was years, and all were male. Most of the patients were asymptomatic or had mild symptoms of Covid. Three of the patients died during the treatment. Their stay in the hospital while the rest

of 139 was fully recovered. 07 of them were shifted to ICU based on symptoms and chest X-ray findings. It is seen that patients with low lymphocyte count have taken more than 2 weeks to have their PCR negative, while those with normal or high lymphocyte count have cleared the virus in a time span of a week (Tables 1 & 2). The mean age of patients was 37 years, while the average stays of patients 11 days with SD deviation .5.6. In addition, the mean lymphocytic count of 142 patients was 25% with SD 12.5, while the absolute lymphocytic count was 1.80 with SD 1.3. We analyze the level of lymphocytes and relate it with the number of days patients spent in a field hospital and days they have taken for seroconversion. 61 out of 142 patients have stayed more than 8 days, and their PCR was negative after more than 14 days. All of them have low lymphocyte count at the time of admission.

**Table 1:** Correlations.

		Number of days at hospital	White cell count	Absolute lymphocytic count	Percentage of lymphocyte
Number of days at hospital	Pearson Correlation	1	-.176*	-.530**	-.685**
	Sig. (2-tailed)		.039	.000	.000
	N	139	139	139	138
White Cell Count	Pearson Correlation	-.176*	1	.548**	.152
	Sig. (2-tailed)	.039		.000	.072
	N	139	142	142	141
Absolute lymphocytic count	Pearson Correlation	-.530**	.548**	1	.782**
	Sig. (2-tailed)	.000	.000		.000
	N	139	142	142	141
Percentage of lymphocyte	Pearson Correlation	-.685**	.152	.782**	1
	Sig. (2-tailed)	.000	.072	.000	
	N	138	141	141	141

\*Correlation is significant at the 0.05 level (2-tailed).

\*\*Correlation is significant at the 0.01 level (2-tailed).

**Table 2:** Descriptive Statistics.

	N	Range	Minimum	Maximum	Mean	Std. Deviation
age	142	53	16	69	37.11	10.473
percentage of lymphocyte	141	55	2	57	25.30	12.513
white cell count	142	23	1	24	7.46	3.620
Absolute lymphocytic count	142	6.58	.02	6.60	1.8675	1.31747
Number of days at hospital	139	28	8	36	11.75	5.681
Valid N (listwise)	138					

**Discussion**

Lymphocytes play an important role in our body defense system. Lymphocyte count is an index of disease progression and severity. Differential lymphocyte count is often employed to diagnose certain diseases [5,6]. Acute disease conditions are associated with raised macrophages and neutrophil count. In contrast, chronicity is associated with the prevalence of lymphocyte numbers. A rise in eosinophil count is frequently associated with underlying parasitic

and allergic aetiology [7,8]. Similarly, infection with Severe Acute Respiratory Syndrome Virus-2 (SARS-CoV-2) is associated with a change in leukocyte count [9]. A general trend seen in most of the COVID patients is the raise in lymphocyte count [10]. Looking at the usual trend of disease severity, most of the patients develop a milder form of the disease with benign signs and symptoms. Many of the diagnosed patients tested with Rt-PCR were asymptomatic. This is attributed to natural immunity of the host to SARS-CoV-2 [11].

Similarly, low lymphocyte count against viral infection is associated with poor defense against the invading pathogen [12]. A number of research studies have been conducted on the role of baseline lymphocyte as a marker of severity, but none of them to date have focused on seroconversion. Seroconversion forms a valuable basis for prediction of host response against SARS-CoV-2 [13]. Low lymphocyte count is investigated for its possible association with severe disease outcomes.

As 98% of COVID patients have a mild course of illness. Out of several ways to label a patient to have a milder course of the disease, the number of hospital days or number of quarantine days is one of the crucial factors. Lymphocyte count forms a baseline marker which can predict the number of days [14]. Recently, a study was conducted in Hong Kong, in which the patterns of lymphocyte counts were discussed in critically ill patients [15].

This study demonstrated that out of 142 patients, 3 individuals who died had very low lymphocyte count, and those who were shifted to the intensive care unit had similar findings on Complete Blood Count (CBC). Several systematic review and meta-analysis studies support the notion of the study. A review study, including 24 clinical trials with a total of 3099 patient showed a significant relationship of low lymphocyte count with poor outcome of COVID patients. In comparison, the age of the patient is the predictive factor of severe outcome in patients with poor outcomes [16]. Moreover, low lymphocytes are associated with greater odds of COVID patients leading to an Intensive Care Unit (ICU) admission. ICU admission is characterized by poor compliance to usual treatment strategies, and the patient is shifted to advanced therapies to save the life of the patient. Lymphopenia is an established predictor of ICU admission. Low blood lymphocyte counts among COVID patients reflect disease severity. Acute organ failure and Acute Kidney Injury (AKI) frequently occur in COVID patients with low lymphocyte counts [17].

## Conclusion

The finding of studies showed a clear association between lymphocyte count and seroconversion, as those patients with low lymphocyte count have a longer duration of stay and adverse outcomes, and 7 of them shifted to ICU and 3 of them died. There are a few other factors that contributed to ICU and deaths, but lymphocyte is the only marker that determines seroconversion.

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