



ORIGINAL ARTICLE

Lymphocytopenia delays recovery in COVID-19 infected patients.

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ABSTRACT... Objective: To observe the effect of reduced lymphocyte count on the recovery of Covid 19 infected patients. **Study Design:** Observational study. **Setting:** Rawal Institute of Health Sciences Islamabad, Pakistan Institute of Medical Sciences, Islamabad. **Period:** March 2021 till June 2021. **Material & Methods:** One hundred adult humans suffering from COVID-19 infection. Hundred adult patients with positive PCR test for corona virus were selected. Adult patients belonging to both genders with reduced lymphocyte count and no immunological and blood disorder were included and those below the age of 18 years with any disorder related to immune system or blood were excluded. Adult patients were divided in two groups A and B with 50 patients in each group. Lymphocyte count of all the patients was noted from the record in the laboratory of Rawal institute of health sciences and Pakistan institute of Medical sciences Islamabad. Group A were those whose lymphocyte count was close to reference range and group B were those whose lymphocyte count was very low. Follow up of all the patients was done. Reduction and disappearance of symptoms like fever and cough were considered as recovery symptoms. The comparison in the days of recovery with the lymphocyte count showed a significant difference of P value of 0.00. **Results:** Group A patients had mean lymphocyte count $0.87 \times 10^9 / L$ and Group B had mean lymphocyte count of $0.45 \times 10^9 / L$. The average recovery time for corona virus infected patients with marked reduction in lymphocyte count is 19 days and those with mild reduction in lymphocyte count the average recovery time is 12 days. **Conclusion:** Patients suffering from COVID-19 infection with less lymphocytopenia showed early recovery and disappearance of symptoms as compared to those with more lymphocytopenia.

Key words: Corona Virus, Lymphocytopenia, Recovery Time, Reduction, Symptoms.

INTRODUCTION

Coronavirus disease (COVID-19) is an infectious disease caused by the SARS-CoV-2 virus. It has large RNA genome with club like spikes.¹ COVID-19 infected patients experiences mild to moderate symptoms like cough, fever, myalgia sore throat and symptoms like viral pneumonia. The virus spreads from an infected person's cough, sneeze, speak, sing or breathe. By touching a contaminated surface, eyes, nose or mouth. More easily spreads in indoors and in crowded settings. The particles size range from larger respiratory droplets to smaller aerosols. The minimum size calculated is about $4.7 \mu m$.² There is variation in recovery time depending on the age, immunity and severity of symptoms.³ According to WHO it takes more than forty days for critical

cases to recover and almost two weeks for mild cases to recover. Latest research suggest that 2 weeks are required for a body to recover from mild COVID-19 infection and severely infected critical cases can take more than six weeks to recover.³ One type of white blood cells that are related to immune response is lymphocytes. On stimulation by foreign antigen lymphocytes differentiate into T and B lymphocytes T cells are converted to three types helper, cytotoxic T cells and memory T cells. On stimulation by antigen, helper T cells secrete chemical messengers called cytokines, which causes differentiation of B cells into plasma cells producing antibody which bind to target and causes destruction, some are converted to memory B cells. Cytotoxic T cells bind and kill infected cells. Normal lymphocyte count for

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adults is between 1000 and 4800 lymphocytes per microliter of blood or $1.0-4.8 \times 10^9/\text{litre}$.⁴ there is variation in recovery time of covid 19 infected patients depending on their immunity, health and age. The recovery symptoms taken in our study are cough and fever One study suggested that it took more than 19 days for patients to recover from cough and almost 12 days to recover from fever, the percentage of cough and fever in these patient was 50 % and 99% respectively.⁵ in corona virus infected patients initially there is increase in lymphocyte count but as the duration of infection increases leading to chronic condition there is exhaustion of lymphocyte leading to impaired function and reduction in their count causing lymphocytopenia.⁶

To compensate this and to fight against the infection there is excessive production of pro-inflammatory cytokines from neutrophils, macrophages and monocytes leading to increase granulopoiesis and reduced lymphopoiesis making the condition more worse and marked reduction of lymphocytes.⁶ There was suggestion that corona virus attacks the lymphocyte because they have ACE receptors the target point of virus and also caused damage to lymphoid organs.⁶ Some studies suggested that coronavirus consumes many immune cells, including lymphocytes leading to reduction in their count.⁷ The present study is conducted to see the correlation of recovery time with low lymphocyte count in corona virus infected patients.

Data was entered using SPSS version 25. Data was checked for normality by using shapiro-wilk Test. The comparison between the days of recovery with lymphocyte count showed a significant difference of P value of 0.00.

MATERIAL & METHODS

This Observational study was conducted at Rawal Institute of Health Sciences from March 2021 to June 2021 after approval from ethical committee (IRHS/REC/062/21). We selected hundred patients with positive corona test, patients belonged to both genders with age above 18 years and without any immunological and blood disorders. Their blood records were

checked from the laboratory of Rawal Institute of Health sciences and Pakistan institute of medical sciences. Lymphocyte count was noted, based on that lymphocyte count we divided the patients into two groups. Group A had lymphocyte count close to reference range $1.0-4.8 \times 10^9/\text{liter}$ and group B had a very low lymphocyte count. We followed the patients for their recovery time by taking their contact numbers and home address. We took two recovery symptoms fever and cough because they were present in 99% corona positive patients. Improvement in these symptoms was noted.

RESULTS

The comparison in the days of recovery depending upon the lymphocyte count showed a significant difference of P value of 0.00. as shown in Table-I.

	Group A	Group B	P-Value
Days of recovery	12 (10-13)	19 (16-24)	0.00
Lymphocyte count per microliter of blood	0.87 (0.78-0.93)	0.45 (0.29-0.57)	0.00

Table-I. Comparison of days of recovery and lymphocyte count

A significant correlation of 0.00 was seen when the days of recovery were correlated with lymphocyte count. (Table-II)

Parameter	P-Value
Lymphocyte count	0.00
Days of recovery	

Table-II. Correlation of lymphocyte count with the days of recovery

From the above result it is seen that group A had the mean lymphocyte count of $0.87 \times 10^9/\text{l}$ with the average range was between $(0.78-0.93) \times 10^9/\text{l}$ and group B had the mean lymphocyte count of $0.45 \times 10^9/\text{l}$ with average of lymphocyte count was between $(0.29-0.57) \times 10^9/\text{l}$. The recovery time for group B with marked reduction in lymphocyte count was between 16-24 days. Group A with less reduction in lymphocyte count their recovery time was between 10-13 days.

Correlation of lymphocyte count with recovery shows p-value of 0.00 indicating that the group with less reduction in lymphocyte count showed early recovery from symptoms of corona virus as compared to the group with marked reduction in lymphocyte count.

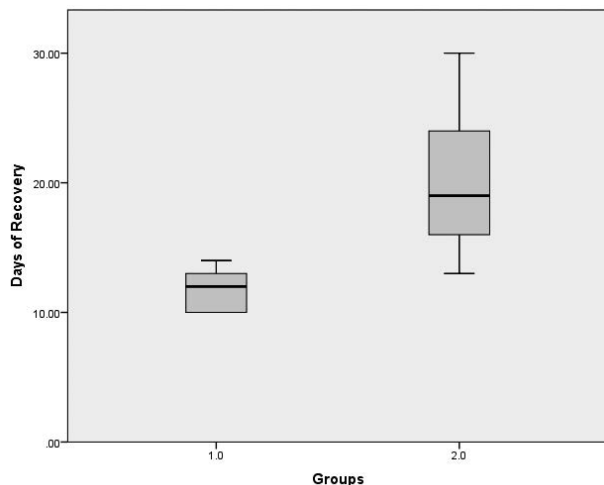


Figure-1

From the above graph it is clear that group A with less reduction in lymphocyte count recovered between 10-13 days and group B with marked reduction in lymphocyte count recovered between 16-24 days, indicating there is delay in recovery period with more lymphocytopenia.

DISCUSSION

We have conducted this study to see the effect of lymphocytopenia in corona virus infected patients and its relation with recovery time of patients. From the above result it is clear that patients with marked reduction in lymphocyte count their recovery time is delayed. Normal level of lymphocyte in the blood is 20-40 %.⁸ In our study we have seen that there is $0.13 \times 10^9/l$ difference of lymphocyte count in group A and $0.55 \times 10^9/l$ difference in lymphocyte count of group B indicating 17.4 % level of lymphocyte count in group A and 9 % level of lymphocyte count in group B. The group with marked reduction in lymphocyte count took more than 7 days to recover from the disease. Jiheng Liu, et.al 2020 in one of his research said that reduced lymphocyte count detects the severity of corona virus disease and lymphocyte count should be monitored.⁹ Corona virus causes lowering of lymphocyte count. LiTan et.al 2020

in one of his study suggested that lymphocytes have ACE2 receptors the target site for corona, virus attacks them and lead to destruction of lymphocytes, there is a possibility that this virus has damaged the lymphatic organs including thymus and spleen.¹⁰ He further suggested there is production of inflammatory cytokines specially interleukin (IL)-6 and tumor necrosis factor (TNF) α , leading to apoptosis of lymphocytes leading to further reduction in lymphocyte count.¹⁰ There was another suggestion by the author that patients with metabolic disorder leading to increased level of lactic acid have reduction in their lymphocyte count because there is a possibility that this increased level of lactic acid may be suppressing the proliferation of lymphocytes.¹⁰ All the above are just suggestions and further research work is needed to confirm them. Yangli Liu, et.al 2021 in one of his study said when there is reduction in lymphocyte count there is increased pro-inflammatory cytokines this leads to worsening of corona virus condition.¹¹ Hameed Akbari et.al 2020 in one of his study on doing meta-analysis of lymphocyte with cytokine overproduction suggested that Covid-19 infected patients showing reduced lymphocyte count with increase in cytokine storm indicates the severity of disease. More lymphocytopenia and elevated cytokines more severe is the disease.¹²

Al Ozaibi et.al 2020 in one of his research said that corona virus directly infect and damages the spleen leading to splenic abscess and also causes damage to other lymphoid tissues.¹³ The cytokines are produced in response to infection by covid 19, there is excessive production of cytokines having antiviral action, the lymphocytes produce lymphokines. Jun-Ming Zhang, et.al 2007 in one of his research said that Cytokines may act on the cells that secrete them and have autocrine action.¹⁴ Keeping in view we can say that increased cytokine storm is causing destruction of lymphocytes leading to lymphocytopenia which is worsening the condition. Increase in cytokines also causes the influx of other immune cells to the inflammatory site leading to destruction of lungs tissues and organs of covid 19 infected patients.¹⁵

Dina Ragab et.al 2020 in one of her articles has

written that cytokine storm further causes influx of other immune cells to reach the target site (inflammatory site) and causes damage to tissues leading to further worsening of condition.¹⁵ it was also seen in our study that the recovery time of patients was delayed in group B having marked reduction in lymphocyte count. In one study it was seen that reduced lymphocytes also causes immunosuppression leading to further production of cytokines, this further leads to virus replication and persistence of virus, this leads to worsening of condition and may cause death.¹⁶ in one study it was suggested that duration from infection to appearance of symptoms is 5 days and after 8 days there is disappearance of symptoms and patient shows recovery sign.¹⁷ We can say that patients without any hematological disorder are symptom free after 8 days but patients with lymphocytopenia shows delay in recovery due to weak immune response and need more care.

CONCLUSION

We come to the conclusion that lymphocytopenia prolongs recovery time, this may be due to increase cytokine production leading to destruction of lymphoid organs and autocrine action on the lymphokines causing their destruction. Corona virus also attacks and destroy lymphocytes leading to lymphocytopenia which further worsen the condition and delays recovery.






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2	Zunnera Rashid	Drafting the work, Statistical analysis, interpretation of data of work.	
3	Sana Rasheed	Design, Analysis and drafting the work.	
4	Sabeen Shakir	Drafting and design of work, Critical evaluation.	
5	Faiza Rasheed	Design and drafting the work.	
6	Aenza Asif	Design of work.	