Content available at: https://www.ipinnovative.com/open-access-journals

IP Archives of Cytology and Histopathology Research

Journal homepage: https://www.achr.co.in/

Editorial

Predictive role of lymphocyte subsets in COVID-19 patients

Sunil Vitthalrao Jagtap[1,*], **Pranjal Setul Shah**[1]

[1] *Dept. of Pathology, Krishna Institute of Medical Sciences, Karad, Maharashtra, India*

ARTICLE INFO

Article history:
Received 22-05-2023
Accepted 01-07-2023
Available online 27-07-2023

Keywords:
Coronaviruses
COVID19 biomarkers
CD4+ and CD8+T cells
Prognostic role T lymphocytes

ABSTRACT

Coronaviruses: CoVs, is related to the family of Coronaviridae. The SARS-CoV-2: severe acute respiratory syndrome coronavirus 2, is unique strain of RNA viruses. The recent pandemic caused by coronavirus SARS-CoV-2 is threatening the human population worldwide. The patients with severe forms may develop severe pneumonia and may fatal. The COVID-19 range from a mild to severe form., SARS-CoV-2 infected patients shows severe lymphopenia in about 2/3 cases. In patients with severe disease lymphocyte subset counts in the peripheral blood owere significantly reduced. The predictor biomarker for assessing disease and monitoring with SARS-CoV-2 infection is done by peripheral blood CD4+ and CD8+ T cells' count. It is necessary to do more studies on larger populations and detail understanding of Tell immunity and for new treatment strategies.

1. Introduction

SARS-CoV-2, a RNA virus, member of B-CoV lineage B, and it is an etiological agent for pathogenesi of COVID-19, It give rise to mild clinical symptoms of common cold to the severe acute respiratory syndrome (SARS).[1]

Clinical manifestations of SARS-CoV-2 vary from mild to severe-critical symptom. These are mild fever, myelgia, chills, breathing difficulty, cough, alter sentation to taste or smell, diarrhea etc. Also respiratory disease with pneumonia as one of the most common form. In cases of severe SARS-CoV-2 form it may give rise to acute respiratory distress syndrome, respiratory failure and multiorgan failure. The polymerase chain reaction (PCR), qualitative test have the specificity of SARS-CoV-2 is nearly 100% in diagnosis. There are clinical and inflammatory biomarkers which play a significant role to detect the severity of disease. The serum biomarkers for renal functions are serum urea, creatinine, cystatin C are considered. The liver function of serum direct bilirubin, cholinesterase and lactate dehydrogenase values, coagulation panel etc are used to know the severity. The various inflammatory markers such as ESR, C-reactive protein, ferritin, D-dimer, IL-6 and procalcitonin were specifically higher in severe patients. However, their prognostic significance in COVID-19 is not clear. The virus-specific T lymphocytes, play a crucial role in clearing the virus and providing symptomatic relief. A biomarker, T-lymphocyte count is considered as a significant role in COVID-19 diagnosis and progress of disease to determine its severity and mortality.[2,3]

2. Immune Response Against COVID 19 Infection

After infection the innate immunity gives initial response for detection and clearance of viral infection by producing proinflammatory cytokines to inhibit viral replication, stimulates adaptive immune response and are important for primary defense system They recruits other immune cells to the site of infection. The innate immune cells consisted of macrophage, neutrophils, dendritic cells, mast cells,

* *Corresponding author*.
E-mail address: drsvjagtap@gmail.com (S. V. Jagtap).

https://doi.org/10.18231/j.achr.2023.018

basophil, eosinophil and natural killer cells. Lymphocyte is an adaptive immune cell which has a role in viral elimination. To develop antiviral immunity NK cells and T cells have important function. The pro-inflammatory cytokines are raised in patients with severe COVID-19 infection which leads to excessive inflammatory responses. In classical viral infection, proportion of lymphocyte usually increases. But in influenza viral infection such in HINI and severe acute respiratory syndrome lymphopenia occurs. Lymphocte T play a vital role in adaptive immune system against COVID 19 infection.[1] Decreased lymphocyte count or T cell subset (CD4 and CD8) indicate worsening of the patient's condition.

3. Role of CD4+ and CD8+ T-cell Absolute Counts to Disease Severity

The T cells are responsible for elimination of acute infection and reducing the viral load by its clearance. Also these cell have immunological memory, so when patient develops re- infection they provides immunity against infection. However as disease progress with severity with cvtokine storm, the COVID-19 patients shows lymphopenia (absolute lymphocyte count $< 1000/\mu$l), reduction in absolute number of $CD8^{+}$. cells, reduce CD4+ and CD8+T cells counts,alter platelet to lymphocyte ratio and IFN-γ production. The various mechanisms for lymphopenia are direct viral infection of lymphocytes, robust viral replication, cytokine storm, activation-induced apoptosis and inhibition of lymphocyte proliferation from lymphoid organs. It is observed that patients with cytokine storms shows rapid detoriation in critically ill COVID-19 patients .In SARS-CoV-2, severe lung infection leads to development of immune -mediated interstitial pneumonitis which is related to the depletion of CD4+T cells. The mortality in COVID-19 patients are related to cytokine storm and secondary infection and septicemia.. The IL-6 have unique role in the cytokine storm occurring in patients with COVID-19.[2]

Zhou Yonggang et al reported that after SARS-CoV-2 infection, CD4+ T lymphocytes are rapidly activated into pathogenic T helper (Th) 1 cells and secrete proinflammatory cytokines, such as IL-6. Inflammatory monocytes are activated and proliferate, and the activated immune cells enter the pulmonary circulation, leading to serious lung injury. The majority of infiltrative inflammatory cells in the pulmonary interstitium are CD8+ T cells that play an important role in virus clearance as well as in immune-mediated injury. Blocking GM-CSF or IL-6 may inhibit immunopathological injury.[3]

Munawaroh Fitriah et al observed a significant decrease in the number of CD3, CD4, CD8 and NK cells in COVID-19 patients with severe to critical and moderate symptoms associated with poor patient clinical outcome.[4] The important role of NK cells subset in contributing to the disease severity and the widespread inflammatory reaction which makes them a potential therapeutic target in complicated cases of COVID-19. Severe COVID 19 resulted in an increase in NK cells containing high levels of cytotoxic proteins such as perforin.[5] S It is observed that the lower T Ivmphocyte subsets were significantly associated with higher admission to I U, mechanical ventilation, patients associated with mucormycosis HIV infections and mortality in COVID-19 patients.[6,7] The number of CD4+ or CD8+ T-cells and CD4/CD8 ratio at tumor site have been studied. The high number of tumor-infiltrating CD8+ T lymphocytes is considered as a favorable prognostic value in some cancer such as endometrial cancer, ovarian cancer, breast cancer.[8]

The critically ill COVID-19 patients have significantly lower white blood cells, neutrophils, and lymphocytes, CD4 and CD8 counts was observed by by Zheng et al.[9]

Depending on the severity of infection the monitoring of peripheral blood CD4+ and CD8+ T cells count is useful as a predictor biomarker to know COVID- 19 course as noted by Hu D et al.[10] The disease severity and significantly poor outcome were associated with in COVID patients if CD 4 count $< 250/\mu$l and CD 8 count $< 100/\mu$l . The subset of CD3+ CD4+CD25+ T cells are found it to be significantly lower in patients with severe disease

It is recommended to detect lymphocyte subsets and IL-6 at least once every 3 days. If lymphocyte or CD4 T cell counts are reduced, patients can be treated with thymosin.[11]

The prognosis of COVID-19 is largely dependent on various factors .The higher mortality noted in elderly, diabetic, immunocompromised, associated infections, obesity, and severe ARDS patients. Lymphocyte subset counts are significant role to predict the prognosis, response to therapy, and outcome in COVID-19 patients. A larger populations studies would be beneficial for the design of vaccines and new treatment strategies.

4. Conclusion

In patients with COVID-19, the degree of lymphopenia correlates with illness severity. In the critically ill COVID-19 patients, the CD4+ helper T cells, CD8+ cytotoxic T cells, and memory T cells are significantly depleted. The peripheral blood CD4+ and CD8+ T cells' count could be a predictor biomarker for assessing severity, predict disease prognosis and monitoring with SARS-CoV-2 infection patients.

5. Clinical Message

1. The severity of COVID-19, SARS-CoV-2 infection induces lymphopenia, CD4+, CD8+ T cells correlates with disease progress.
2. The total number of T lymphocytes cell count, CD4+ T cells, CD8+ T cells could play a prognostic role in COVID-19 patients.

3. The correlation between numbers of lymphocyte subsets are significant for mortality assessments in COVID- 19 patients.
4. Suggestion is to provide more healthcare provisions for patients in critically ill patients due to low CD4+ T cell counts.

6. Conflicts of interest

There are no conflicts of interest.

7. Source of Funding

None.

References

1. Moss P. The T cell immune response against SARS-CoV-2. *Nat Immunol*. 2022;23:186–93. doi:10.1038/s41590-021-01122-w.
2. An update on the epidemiological characteristics of novel coronavirus pneumonia (COVID-19). *Zhonghua Liu Xing Bing Xue Za Zhi*. 2020;41(2):139–44. doi:10.3760/cma.j.issn.0254-6450.2020.02.002.
3. Zhou Y, Fu B, Zheng X, Wang D, Zhao C, qi Y, et al. Aberrant pathogenic GM-CSF+ T cells and inflammatory CD14+CD16+ monocytes in severe pulmonary syndrome patients of a new coronavirus. *medRxiv*. 2020;doi:10.1093/nsr/nwaa041.
4. Fitriah M, Betty AT, Hartono K, Jusak N, Fauqa A. Characteristics of Natural Killer (NK) Cell and T Lymphocyte in COVID-19 patients in Surabaya, Indonesia. *Res J Pharm Technol*. 2022;15(5):2198–203. doi:10.52711/0974-360X.2022.00365.
5. Maucourant C, Filipovic I, Ponzetta A, Aleman S, Cornillet M, Hertwig L, et al. Natural killer cell immunotypes related to COVID-19 disease severity. *Sci Immunol*. 2020;5(50):eabd6832. doi:10.1126/sciimmunol.abd6832.
6. Jagtap SV, Jagtap SS, Hulwan A, Vartak SA. COVID-19 Associated Mucormycosis (CAM) : A Clinico Histopathological Study of at a Tertiary Care Centre. *Indian J Pathol: Res Pract*. 2022;11(1):19–26. doi:10.21088/ijprp.2278.148D.11122.2.
7. Wang L, Chen J, Zhao J, Li F, Lu S, Liu P, et al. The predictive role of lymphocyte subsets and laboratory measurements in COVID-19 disease: a retrospective study. *Ther Adv Respir Dis*. 2021;p. 17534666211049739.
8. Jagtap SV. Evaluation of CD4+ T-cells and CD8+ T-cells in triple-negative invasive breast cancer. *Indian J Pathol Microbiol*. 2018;61:477–485.
9. Zheng Y, Xu H, Yang M, Zeng Y, Chen H, Liu R, et al. Epidemiological characteristics and clinical features of 32 critical and 67 noncritical cases of COVID-19 in Chengdu. *J Clin Virol*. 2020;127:104366. doi:10.1016/j.jcv.2020.104366.
10. Hu D, Li L, Shi W, Zhang L. Less expression of CD4+ and CD8+ T cells might reflect the severity of infection and predict worse prognosis in patients with COVID-19: Evidence from a pooled analysis. *Clin Chim Acta*. 2020;510:1–4. doi:10.1016/j.cca.2020.06.040.
11. Guirao JJ, Cabrera CM, Jiménez N, Rincón L, Urraa JM. High serum IL-6 values increase the risk of mortality and the severity of pneumonia in patients diagnosed with COVID-19. *Mol Immunol*. 2020;128:64–8. doi:10.1016/j.molimm.2020.10.006.

Author biography

Sunil Vitthalrao Jagtap, Professor https://orcid.org/0000-0002-4844-7624

Pranjal Setul Shah, Assistant Lecturer

Cite this article: Jagtap SV, Shah PS. Predictive role of lymphocyte subsets in COVID-19 patients. *IP Arch Cytol Histopathology Res* 2023;8(2):73-75.