

Hematological Parameters as a Prognostic Biomarker in COVID-19 Patients

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Abstract - The onset of COVID-19 has brought the global healthcare system into jeopardy. The disease since its outburst has accounted for several lives and brought the entire global economy to a standstill. Meanwhile, the development of several new potent strains has put the entire scientific community at crossroads regarding its approach to curb the viral menace. Several vaccines have been developed and are being produced on a rapid scale; however, none of these guarantees complete protection against the viral pathogen. This makes the early detection of the disease quite important. Certain hematological parameters have been found to serve as an important biomarker for the prognosis of COVID-19. The current review discusses the role of hematological parameters like blood lymphocytes, Interleukin-6 (IL-6), C-reactive protein (CRP), Procalcitonin (PCT), and Ferritin in the prognosis of the deadly disease. The parameters serve as an important biomarker to COVID-19 related complications in patients.

Key Words: Blood lymphocytes, C-reactive protein, COVID-19, Cytokine storm, Ferritin, Hematological parameters, Procalcitonin.

1. INTRODUCTION

COVID-19 is a major respiratory infection that imparts a deleterious effect on the human hematopoietic system. Also known as SARS-CoV-2 coronavirus, the disease has quickly evolved from an epidemic in the Wuhan province of China [1] to a pandemic encompassing the entire global landscape. The disease has affected more than 150 million cases and has claimed approximately 3.5 million lives worldwide (Fig. 1). COVID-19 was initially considered to be a viral infection of the respiratory tract; however subsequent research on the topic has revealed it to be a multisystem systemic disease having an impact on several organs, tissues, and as well as immune systems [2]. People belonging to higher age groups and with certain comorbidities pose higher death risks from COVID-19, however, young persons without any significant underlying diseases may also experience complications and lethality.

Hematological parameters have been found to serve as an important factor for the prognosis of COVID-19. Keeping in mind the current global scenario of COVID-19, its complications, and aggravation, the current paper discusses the various hematological parameters in relation to the complications during COVID-19 (Fig. 2).

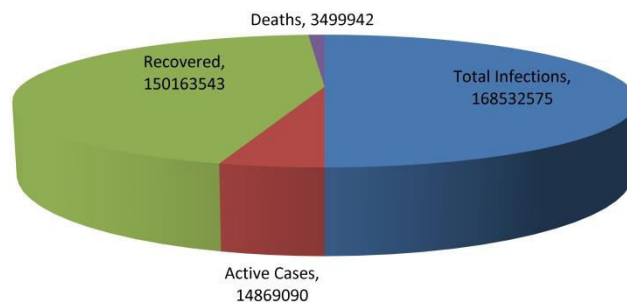


Fig-1: Global impact of COVID-19 (as of 26th May 2021, 6:05+GMT)

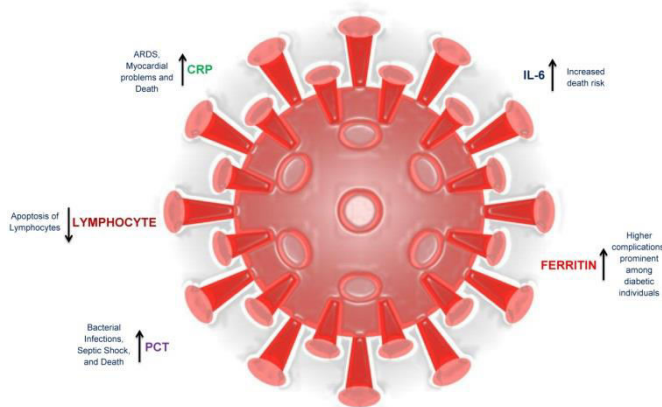


Fig-2: Role of hematological parameters in COVID-19 prognosis.

2. Blood Lymphocyte as a Prognostic marker in COVID19

During the viral incubation period and the subsequent early phase of viral growth, the peripheral blood lymphocytes count is either normal or displays a slight reduction. The SARS-CoV-2 enters into the human cells by binding to the receptor named angiotensin-converting enzyme 2 (ACE2) present on the cells and tissues. Lymphocytes are known to express the ACE2 receptor on the cell surfaces [3] and are more prone to attack by the virus, thus leading to lysis. Hence, after 7-14 days of the viral onset, a significant decrease in blood lymphocytes is found.

3. The Cytokine Storm and Increased Levels of Interleukins

Post 7 – 14 days of the onset of initial COVID symptoms, there is a rise in clinical signs of the disease along with a prominent increase in the inflammatory mediators and

cytokines. This surge in the clinical manifestations is often termed a cytokine storm. The cytokine storm is often characterized by lymphopenia or reduction in certain levels of blood cells. It is also marked with increased levels of interleukins (IL-6, IL-2, and IL-7) that promote apoptosis of lymphocytes [4]. The interleukins leads to continuous inflammation of the viral infection site by inviting T-cells, monocytes, and macrophages to act upon. In addition T-cells produce IFN γ thereby establishing a continuous inflammatory response loop. As a part of innate immunity response, there is a gradual increase in the accumulation of immune cells in the lungs, the first of the organs to get affected. This condition leads to an excessive production of pro-inflammatory cytokines, thus damaging the lungs [5]. The cytokine storm moves on to other organs leading to multiple organ failures. Interleukin-6 (IL-6) is an important biomarker for COVID-19. Increased viral load in COVID-19 patients has been associated with increased levels of IL-6 coupled with increased death risks. IL-6 levels in COVID-19 non-survivors have been found to increase even further during the course of hospitalization thus signifying its importance as an important biomarker. The interpretation is well supported by the findings of Chen et al. (2020) [6].

4. C-reactive protein (CRP), Procalcitonin (PCT), and Ferritin in the prognosis of COVID-19

C-reactive protein (CRP) is a liver protein that is produced in response to any kind of inflammation and thus released to the bloodstream. Being a marker of serious infections and disorders CRP remains elevated in COVID-19 patients. A study conducted by Guan (2020) [7] from December 2019 to January 2020 and comprising of 552 hospitals in mainland China with a sample size of 1099 revealed that CRP levels were elevated in COVID-19 cases. Elevated levels of CRP were observed in 81.5% of severe cases as compared to 56.4% in the case of non-severe ones. In another study higher level of hs-CRP was found to be associated with the development of acute respiratory distress syndrome (ARDS) [8]. Studies confirmed that elevation in CRP levels was higher in patients requiring oxygen supplementation as compared to those who did not require it [9]. Higher CRP levels were also evident in COVID-19 non-survivors and continued to remain high even after treatment [10]. High levels of CRP besides causing ARDS have also been linked with unfavorable outcomes in COVID-19 patients which include higher levels of Troponin-T, myocardial problems [11], and eventually death [10]. The above findings support the role of CRP as an important biomarker in COVID-19 prognosis.

Procalcitonin (PCT) is a peptide comprising 116 amino acids with a molecular weight of 14.5 kDa. PCT is an important marker of microbial sepsis in the human body. Significantly high levels of PCT have been observed in COVID-19 patients thereby suggesting secondary bacterial infections. These infections are mostly responsible for

complicating the clinical outcomes of the disease. COVID-19 patients in critical care units have been observed to demonstrate severe sepsis accompanied by multiple organ failures, a state termed as septic shock thus leading to death. Respiratory tract infections are the most common sites for sepsis [12] and are thus found to be frequent in critical COVID-19 patients. A study conducted by Huang et al (2020) [13] found out that in a cohort of 12 COVID-19 ICU patients, 25% demonstrated high levels of PCT while no elevation was found in the case of non-ICU patients. Similar results were obtained by a study conducted by Wang et al (2020) wherein 75% of ICU patients with COVID-19 demonstrated high levels of PCT as compared to only 21.6% in the case of non-ICU patients [14]. A meta-analysis of 4 published articles by Lippi et al (2020) revealed that high PCT values were associated with 5 times higher risk of severe infection [15].

Ferritin is an intracellular iron storage protein. Modifications in iron metabolism could be used for predicting mortality in COVID-19 patients [16]. Individuals with existing diabetic conditions exhibit high levels of ferritin in the serum and thus pose a higher risk of COVID-19 complications [17]. Ferritin levels are much higher in very severe COVID 19 cases as compared to the severe ones. A study by Fei et al (2020) [18] revealed that in the patients who died of COVID-19, the ferritin levels were much higher during hospitalization and increased continuously exceeding the upper detection limit during the period. It can be thus being concluded that serum ferritin levels are associated with the risk of COVID-19.

4. CONCLUSION

Hematological parameters are an important biomarker in the prognosis of deadly COVID-19. The parameters like blood lymphocyte, interleukins, C-reactive protein, procalcitonin, and ferritin are closely associated with clinical outcomes and complications of the viral disease. A more in-depth study on these parameters is required for a better understanding and prognosis of the disease which would help in better diagnosis.

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