

CHANGES IN CLINICAL AND IMMUNOLOGICAL PARAMETERS DEPENDING
ON THE SEVERITY OF COVID-19

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ABSTRACT: Coronavirus infection (COVID-19) is an acute infectious disease caused by a new strain of the SARS CoV-2 coronavirus with an aerosol droplet and contact-household transmission mechanism. Pathogenetically, COVID-19 is characterized by viremia, local and systemic immune-inflammatory processes, endotheliopathy, hyperactivity of the coagulation cascade, which can lead to the development of micro-macrothrombosis and hypoxia.

In this study, we examined 141 patients diagnosed with Covid-19 with moderate and severe course and checked immunological tests and laboratory tests as a coagulogram, a general blood test. The results obtained were processed by a statistical method. And revealed by interleukins and laboratory data correlations in various forms.

KEYWORDS: COVID-19, cytokines, immunology, stages of COVID-19

BACKGROUND: The recently emerging COVID-19 continues to challenge health systems around the world and the scenario is still getting worse. COVID-19 is a growing threat to humans, with the death rate currently at 6.4% (2). COVID-19 infection is accompanied by an aggressive inflammatory response with the release of large amounts of pro-inflammatory cytokines in an event known as a cytokine storm. The host's immune response to the SARS-CoV-2 virus is overactive, resulting in an excessive inflammatory response. Several studies analyzing cytokine profiles in COVID-19 patients have shown that cytokine storms are directly correlated with lung damage, multiple organ failure, and poor prognosis for severe COVID-19 (1).

MATERIALS AND METHODS: The study included 141 patients, of which 80 patients were with moderate Covid-19, 29 patients with severe Covid-19, and 32 patients were in our control group, who were practically healthy at that time.

RESULTS AND DISCUSSION: Accumulating evidence suggests that some patients with severe COVID-19 are suffering from a cytokine storm. Analysis of plasma cytokine levels of 41 confirmed cases of COVID-19 in China revealed elevated levels of IL-1 β , IL-7, IL-8, IL-9, IL-10, FGF, G-CSF, GM-CSF, IFN- γ , IP-10, MCP-1, MIP-1A, MIP1-B, PDGF, TNF- α and VEGF in both ICU and non-ICU patients compared to healthy adults. All patients included in the study had pneumonia, 1/3 of patients were admitted to the intensive care unit, and six of these patients died (Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. (2020) 395: 497-506. doi: 10.1016 / S0140-67362030183-5). A multicenter retrospective study of 150 COVID-19 patients in China assessed predictors of COVID-19 mortality. The study analyzed data from 82 COVID-19 cured cases and 68 COVID-19 deaths, and reported significantly higher IL-6 levels in deaths than in cured cases (Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Med*. (2020) 46: 846-8. Doi: 10.1007 / s00134-020-06028-z). Another study, which analyzed data from 21 patients in China, reported elevated levels of IL-10, IL-6 and TNF- α in severe cases (n = 11 patients) compared with moderate cases (n = 10 patients) (Chen G, Wu D, Guo W, Cao Y, Huang D, Wang H, et al. Clinical and immunologic features in severe and moderate Coronavirus Disease 2019. *J Clin Invest*. (2020) 130: 2620-9. Doi: 10.1101 / 2020.02 .16.20023903). A similar study by Gao et al. evaluated 43 patients in China and reported that IL-6 levels were significantly higher in severe cases (n = 15) than in mild cases (n = 28) (Gao Y, Li T, Han M, Li X, Wu D, Xu Y, et al. Diagnostic utility of clinical laboratory data determinations for patients with the severe COVID-19. *J Med Virol*. (2020) 92: 791-6. Doi: 10.1002 / jmv.25770). Likewise, Chen et al. studied a total of 29 COVID-19 patients, divided into three groups according to appropriate diagnostic criteria, and found that IL-6 levels were higher in critical cases (n = 5 patients) than in severe cases (n = 9 patients), and that IL-6 was higher in severe cases than in mild cases (n = 15 cases) (Chen L, Liu H, Liu W, Liu J, Liu K, Shang J, et al. Analysis of clinical features of 29 patients with 2019 novel coronavirus pneumonia. *Zhonghua Jie He He Hu Xi Za Zhi*. (2020) 43: 203–8. doi: 10.3760 / cma.j.issn.1001-0939.2020.0005). There is no data yet on severe pediatric patients with COVID-19. In a study that evaluated eight critically ill

Chinese pediatric patients with COVID-19 in intensive care, aged 2 months to 15 years, elevated levels of IL-6, IL-10, and IFN were reported among other laboratory findings. -γ (Sun D, Li H, Lu X, Xiao H, Ren J, Zhang FR, et al. Clinical features of severe pediatric patients with coronavirus disease 2019 in Wuhan: a single center's observational study. *World J Pediatr.* (2020) 19: 1-9 .doi: 10.1007 / s12519-020-00354-4)

From all the listed data, we selected those interleukins that provide significant information during Covid-19. Therefore, based on the literature data, we studied immunological studies (IL-1 β , IL-2, IL-6, TNF- α), as well as laboratory instrumental studies (OAC, OAM, Coagulogram, biochemical blood tests, chest X-ray).

According to foreign literature, IL-1 is directly correlated with IL-2, IL-6, TNF- α , as well as with CRP. But the correlation with CRP was greater than the rest of the interleukins. This shows that when the level of IL-1 rises, then the level of CRP rises first of all, based on this, CRP is associated with D-dimer and fibrinogen. In addition, we observed that only platelets are incorrectly correlated with the rest of the laboratory parameters, as well as with interleukins. And it was clear that the more IL-1, CRP, D-dimer was increased, the disease progressed more severely.

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