



CHANGES IN CYTOKINE SPECTRA AND THEIR SIGNIFICANCE IN COVID-19 VIRAL INFECTION COMPLICATED WITH PNEUMONIA

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Abstract

Currently, COVID-19 disease is widespread in the world after infection with which patients begin to change in the spectra of cytokines in patients with pneumonia. The article discusses the role of cytokines in this disease.

Keywords: In Covid -19, pro-inflammatory TNF, MSCT, About EFINITIONS , immunoregulatory

Introduction

Relevance: Studying the role of cytokines in C ovid -19 is one of the fundamental points for understanding the pathogenesis of viral infections in general and, in particular, the nature of the pathogenicity of coronavirus [1]. The high incidence of lung damage in C ovid -19 is explained by the tropism of the virus to epithelial cells, including the endothelium, which determines the characteristic clinical picture of C ovid -19 and pneumonia against this background [6]. Problems in the fight against coronavirus infections is by far the most relevant not only in medicine but also in the whole of humanity [7]. The role of cytokines is of great importance for a more detailed understanding of the mechanisms of immunopathological changes in the body [3 , 9]. For clinical practice, the study of the role of the cytokine status can hardly be overestimated, since it reflects an individual, primary response to a viral agent, makes it possible to assess the nature of the process and predict the outcome of the disease in many viral infections , including coronavirus , as well as to objectively assess the effectiveness of therapy [5]. Also, one of the promising areas of study of the systemic inflammatory response is the determination in the blood of soluble forms of adhesion molecules that characterize the processes of activation of endothelial cells and promote the interaction of leukocytes and endothelial cells [4 , 8]. Increased permeability of lung capillaries, as well as excessive induction of cytokines , endothelial damage are the main mechanisms of development of ARDS [2]. The data of various authors indicate that an important pathogenetic link in the unfavorable course and prognosis in pneumonia is early





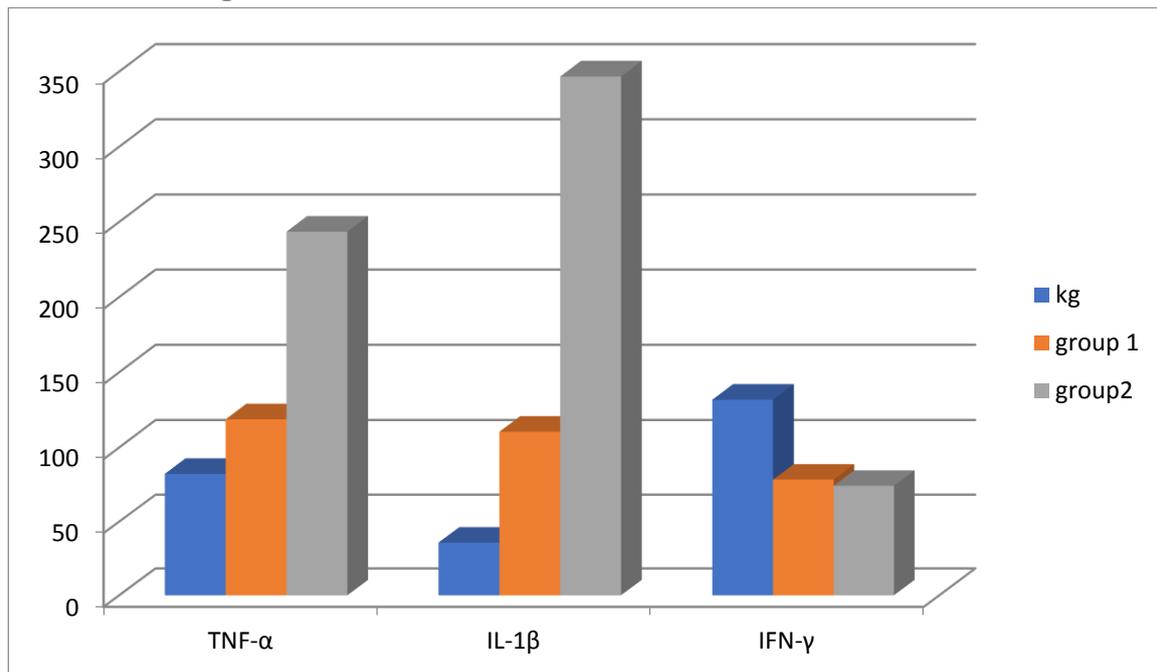
hyperactivation of cytokine production (pro-inflammatory TNF α , and anti-inflammatory IL-10) against the background of depression of markers of cell-mediated immune defense (IL-2, IFN γ) [10]. However, the peculiarities of the cytokine profile and the level of intercellular adhesion molecules in pneumonia against the background of C ovid -19 have not been practically studied [5].

Objective of the research : To study the role of cytokines in the pathogenesis of coronavirus infection.

Material and methods: The study is based on clinical and laboratory examination of 75 patients with coronavirus infection complicated by pneumonia who were admitted to the infectious diseases hospital of the Samarkand region from July to September 2020. All examined patients were divided according to the severity of the course of the disease into 2 groups. Group 1 included 22 patients with a severe form of the disease, group 2 - 53 patients with moderate severity of the disease. In addition to general clinical , laboratory and instrumental research methods, all patients underwent MSCT research, which confirmed the presence of pneumonia, i.e. symptoms of frosted glass. At the same time, saturation in group 1 was on average $88 \pm 1.4\%$. And in the second group $94 \pm 1.8\%$. In addition, the percentage of lung damage in group 1 was on average $64.2 \pm 2.8\%$, which corresponds to CT- III - stage , and in group 2, $38.8 \pm 3.4\%$ corresponds to CT- II- stage. As a control group, peripheral blood of 20 healthy individuals was examined . All immunopatologicakie blood parameters of patients including interferon : level protivovi -tier (alpha-IFN) and proinflammatory (gamma-IFN) in serum interferon peripheral blood were examined by ELISA using test systems "Vector-Best" (Novosibirsk, Russia) . To establish the role of the cytokine link in the pathogenesis of coronavirus infection, we determined the level of interferons IFN - α and IFN - γ , the level of IL- 4 and the level of pro-inflammatory cytokines IL- 1 β , IL- 6. Our data demonstrate a significant dependence of the concentration of the level of pro - inflammatory cytokines in blood serum from the form of the disease. Especially expressed disturbances observed in patients with severe disease CT III of - Art lung damage . Revealing changes significantly differed from the values obtained in the group of patients with moderate severity of pneumonia. In the control group, immunopathological parameters remained normal.

Fig. one.





Our data demonstrate a significant dependence of the concentration of the level of proinflammatory cytokines in the blood serum on the severity of the course of coronavirus infection. Particularly pronounced disorders were noted in patients with a severe course of coronavirus infection. The revealed changes significantly differed from the values obtained in the group of patients with moderate severity. So, if, in severe cases, the level of serum TNF- α in the examined patients was significantly exceeded (243.5 ± 23.9 pg / ml compared with the data of the control group - 82.4 ± 7.0 pg / ml, $P < 0.001$), then with an average severity of the course, only a moderate increase in this cytokine was noted (118.7 ± 9.3 pg / ml, compared with the control $P < 0.05$). When analyzing the results of the study of the level of IL- 1β in the blood serum, it was revealed that in patients with severe course there is an almost tenfold increase in its level compared to the control - 346.7 ± 36.6 pg / ml, versus 35.8 ± 3.9 pg / ml ($P < 0.001$). In patients with moderate severity, an increase in the level of IL- 1β was observed by more than 3 times compared with the control group of individuals - 110.4 ± 8.3 pg / ml ($P < 0.001$). All this found its confirmation in the clinical picture of the course of the disease, indicators of blood oxygenation by MSCT studies, as well as other clinical laboratory and instrumental indicators. As is known, IFN - γ is produced by activated Th 1 cells and NK cells. In our studies, a lower level of IFN - γ was noted in comparison with the control group. Moreover, this decrease is observed: in severe form 74.3 ± 4.9 pg / ml ($P < 0.001$), with an average severity of 78.5 ± 7.3 pg / ml ($P < 0.001$). The level of IFN - γ , while in the control group of individuals was on average 131.7 ± 11.0 pg / ml. When analyzing the level



of a number of inflammatory cytokines in the blood serum of patients with coronavirus infection, compared with the control, we noted a significant increase in the level of TNF - α and IL- 1β in severe disease and a moderate increase in their serum content with moderate severity. Syvorotochy level of IFN - γ at koronavirusnoy infection was significantly lower than in the control group and did not depend on its shape .About EFINITIONS interest was the study in patients with koronavirusnoy infection level Ig E in the blood and the concentration of IL - 4 in various biological fluids like activity markers inflammation.

Results of the study: In serum and smear levels of IL- 4, as well as the level of total Ig E in the blood serum of all examined patients, are presented in Table 1. As can be seen from the table, increased levels of total Ig E are detected in the peripheral blood of patients . The highest level is observed in the group of patients with a severe form of the disease (362.0 ± 19.5 IU / l), which significantly exceeds the value of this indicator in patients with moderate severity (308.0 ± 13.5 IU / l) and indicators of the control group (103.0 ± 6.12 IU / l) ($P < 0.001$). Thus, in severe cases, there is a higher content of Ig E in the blood serum compared to patients with moderate severity.

Table 1 The content of IL- 4 and Ig E in biological fluids of patients

Indicators	Control group (n = 40)	1st group (n = 22)	Group 2 (n = 53)
IL- 4 (smear), pg / ml	0	310.0 ± 13.5 ***	76.0 ± 3.6 *** ^^^
IL- 4 blood serum, pg / ml	$2, 85 0 \pm 0, 19$	$12, 0 \pm 0, 38$ ***	$15, 1 \pm 0, 6 3$ *** ^^^
Ig E in serum, IU / l	$103, 0 \pm 6, 12$	$308, 0 \pm 13, 5$ ***	362.0 ± 19.5 *** ^

Note: * - differences relative to the data of the control group are significant (* - $P < 0.05$, ** - $P < 0.01$, *** - $P < 0.001$); ^ - differences between the data of groups 1 and 2 are significant (^ - $P < 0.05$, ^^ - $P < 0.001$).

When studying the level of IL- 4 in the blood serum of patients, a similar pattern was revealed: the highest level of IL- 4 is characteristic of patients with a severe course (15.1 ± 0.63 pg / ml), which significantly ($P < 0.001$) exceeds this value. indicator in patients with moderate severity (12.0 ± 0.38 pg / ml). As mentioned above, in patients with a severe course of the disease, the cytokine values were higher than in patients with a moderate form of the disease. This has been observed for all types of cytokines . The difference is that mild forms of the disease usually did not cause an increase in serum levels of IL- 1α and TNF α . Based on the foregoing, we found it interesting to conduct a correlation study between the



concentrations of these cytokines, depending on the severity of the course of coronavirus pneumonia. The performed correlation analysis made it possible to establish the presence of a direct relationship between the content of IFN- γ and IL- 1β in the blood serum. We found that the strength of this connection is inversely proportional to the course of the coronavirus infection. So, if in the control group the correlation coefficient was close to one ($r = 0.95$), then in groups 1 and 2, the values of the correlation coefficient were 0.59 and 0.37, respectively. Significant correlation coefficients between other pairs of indicators of cytokine content were not obtained in either group. The results of the study confirm the existence of a relationship between the concentrations of IFN- γ and IL- 1β , and this dependence is direct and decreases depending on the severity of the course of the disease, which indicates impaired immunoregulatory mechanisms, and a reduced concentration of serum IFN- γ indicates a violation of IL- 1β mediated production of IFN- γ Th-1 cells.

Fig. 2.

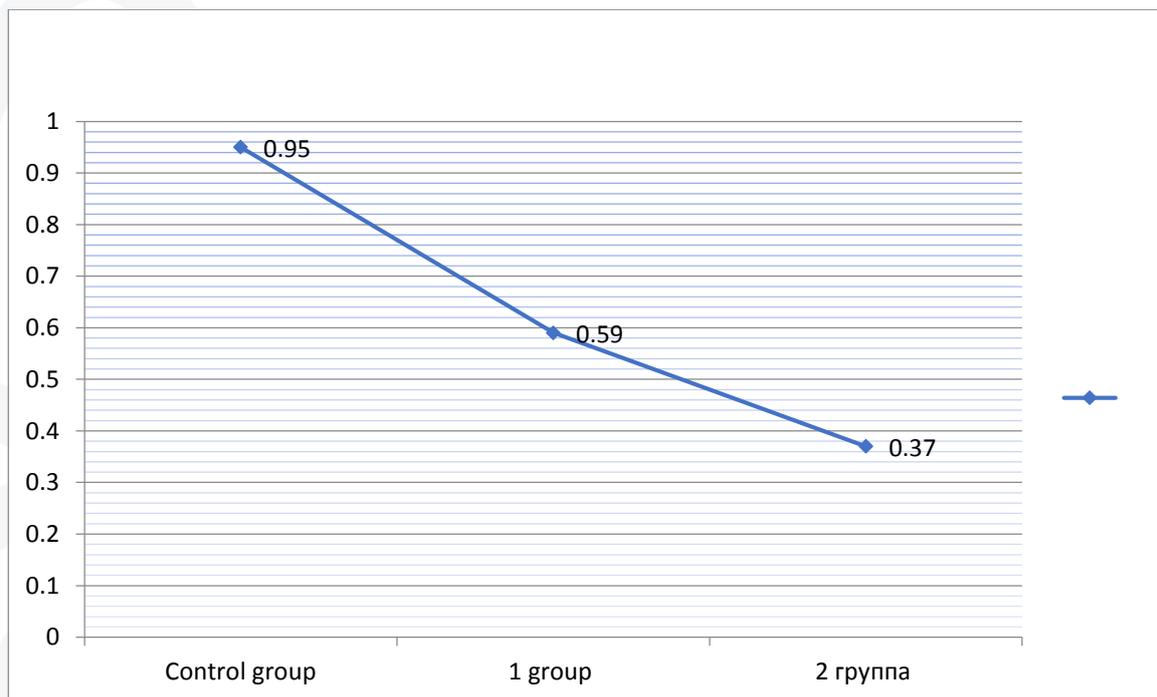


Fig. 2. Values of the correlation coefficient (r) between the serum levels of IFN- γ and IL- 1β in different forms of coronavirus infection.

At the same time, it is possible that the activation of the macrophage link of immunity, which occurs at COVID-19, can contribute to an increase in the production of substances by macrophages that inhibit the synthesis of IFN- γ . Thus, we found that in most patients with coronavirus infection





complicated by pneumonia, a reduced content of T cells is observed. A low content of CD 3+ cells indicates a reduction in the reserves of the pool of circulating T-lymphocytes and, therefore, a possible risk of their deficiency if an intensive immune response is required. A decrease in the content of functionally active T-cells naturally affects the content of specialized phenotypes that perform helper and suppressor functions. There is no doubt that a decrease or increase in their number can have a negative effect and, in all likelihood, is one of the pathogenetic factors of the inflammatory process. As you know, NK cells play an important role in anti-infectious protection, and their changes in one direction or the other, apparently, are explained by several reasons: partial immunodeficiency, insufficient production of non-toxic antibodies that block the activity of immunocompetent cells. As can be seen from the results of the study, a relationship is revealed between the concentrations of IF H- γ and IL- 1β , and this relationship is direct and decreases depending on the severity of the course of coronavirus pneumonia.

Conclusions

P Acquiring Our results show accurate dependence of the concentration levels of pro-inflammatory cytokines in the blood serum of the form koronavirusnoyinfektsi .

The results of the study confirm the existence of a relationship between the concentrations of IF H- γ and IL- 1β , and this dependence is direct and decreases depending on the severity of the course of coronavirus pneumonia, which indicates violations of the immunoregulatory mechanisms.

Thus, our results indicate a violation of metabolic processes and pronounced immunological changes, which contribute to the development of complications of this disease.

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