ISSN NO: 2770-2936
Date of Publication:10-11-2023

Correlation Relationship of Interferons, Cytokines with Biochemical Mediators of Inflammation in The Blood in The Association of Covid-19 and Type 2 Diabetes

Aslonova Marjona Ramazonova
Bukhara State Medical Institute named after Abu Ali ibn Sino
aslonovam93@gmail.com

Resume: The study included 103 patients hospitalized for SARS-CoV-2 pneumonia at the Bukhara Regional Infectious Diseases Hospital, which was reorganized into the Covid Center. Immunological studies of the blood of sick children were carried out in the laboratory of immunomorphology of the Institute of Human Immunology and Genomics of the Academy of Sciences of the Republic of Uzbekistan. The indicators of interferon (INF-a, IFN-γ), cytokines (IL4, IL18) and biochemical tests in the blood were studied.

In patients with SARS-CoV-2 pneumonia and type 2 diabetes, total bilirubin has a high relationship with the diabetogenic cytokine IL-18 - r = 0.42, against the background of a noticeable negative relationship with IL-4 (r = -0.30) and INF γ -r=-0.34. At the same time, the free fraction of bilirubin, like total bilirubin, has noticeable negative connections with IL-4 (r = -0.22) and IFN-γ r = -0.34, and has a significant positive connection with IL-18 - r = 0.34

Key words: SARS CoV-2, pneumonia, type 2 diabetes mellitus, pneumonia, interferon, cytokine

Relevance

Coronavirus disease 2019 (COVID-19) is a newly recognized infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was recently declared a pandemic[13]. The number of deaths from COVID-19 is growing. As of April 21, 2020, 2,397,217 patients have been confirmed worldwide and 162,956 have died. A total of 84,250 cases have been diagnosed in China, of which 4,642 have died[14, 8]. COVID-19 in patients with diabetes: Diabetes is one of the most common comorbidities in patients with COVID-19 and was present in approximately 10% of the 7,162 patients with COVID-19 who had comorbidities according to data provided by the USDA CDC. Studies conducted in different parts of the world have shown varying prevalence of diabetes in patients with COVID-19. Prospective surveillance data from the UK showed uncomplicated diabetes in 19% of 16,749 cases of COVID-19. The largest study in primary care found that diabetes was present in 9.8% of 121,263 patients with COVID-19 [11,9] in Spain. The issue of an increased risk of SARS-CoV2 infection has not yet been resolved, since many studies have shown the same prevalence of diabetes in the general population and in patients with COVID-19. There are several specific factors and mechanisms by which diabetes predisposes to infections in general and may increase susceptibility or risk and severity of SARS-CoV-2 disease. Potential mechanisms that may increase susceptibility to COVID-19 in diabetics include the role of hyperglycemia, higher cell binding affinity and efficient viral entry, decreased viral clearance, decreased T-cell function, increased susceptibility to hyperinflammation, cytokine storm syndrome, and the presence of cardiovascular disease. vascular diseases[6]. In addition, the higher risk of progression to severe pneumonia caused by influenza and SARS-CoV-2 in individuals with T2DM [4, 1] is associated with increased viral entry, decreased viral clearance, and increased levels of circulating IL-6 and C-reactive protein (SRB) [3]. People with T2DM also have a higher incidence of severe metabolic complications [12], and viral infections worsen hyperglycemia in people with and without diabetes [2,10]. The infection also leads to profound changes in whole-body metabolism, with low-grade inflammation disrupting glucose homeostasis and insulin sensitivity. Thus, it is not surprising that hyperglycemia, a hallmark of T2DM, is associated with dysregulation of the innate and adaptive (humoral) immune responses. However, whether diabetes causes an exacerbation of the inflammatory response [7,13] or a decrease and failure of the inflammatory response [5,14], the immune cellular response remains poorly defined. Notably, the underlying reasons for the potential differential effects of the diabetic state on infection-induced inflammatory responses remain incomplete.

ISSN NO: 2770-2936
Date of Publication:10-11-2023

SARS-CoV-2 may cause exaggerated and aberrant ineffective host immune responses that are associated with acute respiratory distress syndrome. In these critically ill patients infected with COVID-19, cytokine storms mediated by overproduction of proinflammatory cytokines were observed in a large population. Exaggerated immune responses lead to long-term lung damage and fibrosis, causing functional disability, decreased quality of life, and even death [15].

Objective: Study of interferons, cytokines and biochemical mediators of inflammation in the blood in association with COVID-19 and type 2 diabetes.

Materials and methods

The study included 103 patients hospitalized for SARS-CoV-2 pneumonia in the Bukhara Regional Infectious Diseases Hospital, which was reorganized into the Covid Center. Of all those hospitalized for SARS-CoV-2 pneumonia against the background of type 2 diabetes, there were 35 patients with severe pneumonia (group 1), and 33 with moderate severity (group 2). The comparison group (group 3) consisted of 35 patients with SARS-CoV-2 pneumonia who did not suffer from diabetes. The control group consisted of 30 healthy people of the appropriate age.

The average age of patients in group 1 was 60.2 ± 2.2 years, in patients in group 2 it was 50.0 ± 2.0 years, and in the comparison group it was 52.4 ± 2.0 years. In the control group, the average age was 54.0 ± 2.0 years.

The average time of stay in the hospital was: group 1 - 8.7 ± 0.47 days, group 2 - 6.4 ± 0.26 days, group 3 - 10.6 ± 0.45 days.

Results

Correlation is a consistent change in variables. More precisely, correlation is the consistency of the distributions of observed variables. The main indicators of correlation are the strength, direction and reliability (validity) of the connection. The strength of the connection is determined by the absolute value of the correlation (varies from 0 to 1). The direction of the connection is determined by the sign of the correlation coefficient: positive coefficient – direct connection; negative – feedback. The reliability of the relationship is determined by the p-level of statistical significance (the lower the p-level, the higher the statistical significance or reliability of the relationship) [15].

To develop more informative clinical and laboratory blood parameters in patients with the association of SARS-CoV-2 pneumonia and type 2 diabetes, it is important to study their relationship, which determines the prognosis of the underlying disease.

In order to study the relationship of interferons and blood cytokines with indicators of general analysis and biochemical blood analysis in patients with the association of SARS-CoV-2 pneumonia and type 2 diabetes, their correlation was calculated.

As a result of the calculation, a very high negative relationship was revealed between:

- bound fraction of bilirubin and INF-a- (p = -0.95),
- bound fraction of bilirubin and IL-4 (p = -0.76), against the background of a high positive relationship between:
- bound fraction of bilirubin and INF-γ (p = 0.77), Fig. 1.

The data obtained show the effect of the SARS-CoV-2 virus on bilirubin metabolism in patients with type 2 diabetes.

In the study, in patients of this group, the average concentration of the bound bilirubin fraction averaged 6.22±0.34 mmol/l (min - 4.0 mmol/l; -max - 8.9 mmol/l).

The high positive dependence of the bound bilirubin fraction on IFN-γ allows us to conclude that the higher the level of bound bilirubin fraction in patients with SARS-CoV-2 pneumonia and type 2 diabetes, the more elevated the level of IFN-γ, and vice versa. The absence of the bound bilirubin fraction indicates low immunity, which was typical in our studies for patients in this group.

ISSN NO: 2770-2936
Date of Publication:10-11-2023

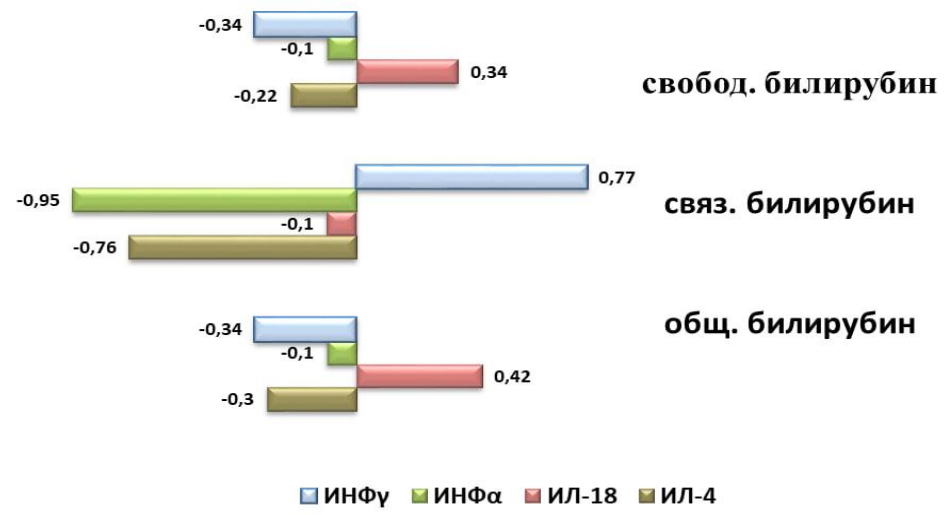

Figure 1. Correlation of bilirubin with interferons and cytokines in SARS-CoV-2 pneumonia in association with type 2 diabetes mellitus

In patients with SARS-CoV-2 pneumonia and type 2 diabetes, total bilirubin has a high relationship with the diabetogenic cytokine IL-18 - p = 0.42, against the background of a noticeable negative relationship with IL-4 (p = -0.30) and INFu-p=-0.34. At the same time, the free fraction of bilirubin, like total bilirubin, has noticeable negative connections with IL-4 (p = -0.22) and INF-γ p = -0.34, and has a significant positive connection with IL-18 - p = 0.34 .

It is important to note that INF-a is associated only with the bound fraction of bilirubin (p = -0.95), and its concentration does not depend on the level of total bilirubin and its free fraction.

Analysis of the correlation of INF-a showed a high negative relationship with the level of calcium in the blood (p = -0.40) and a noticeable negative relationship with potassium in the blood (p = -0.33).

ISSN NO: 2770-2936
Date of Publication:10-11-2023

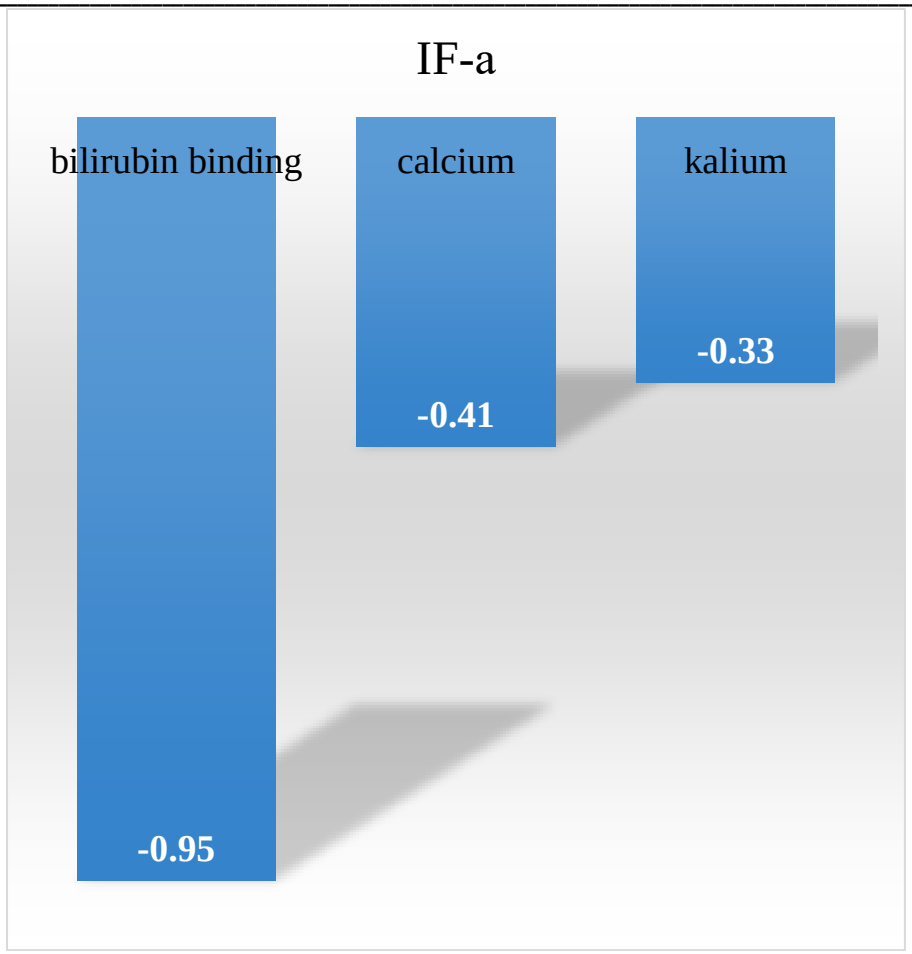

Figure 2. Correlations of interferon alpha in SARS-CoV-2 pneumonia in association with type 2 diabetes

At the same time, the question arose: what is the role of INF-a in the implementation of blood rheology in SARS-CoV-2 pneumonia in association with type 2 diabetes?

The established high negative relationship of INF-a with the level of calcium in the blood followed the study of its relationship with coagulogram parameters in this case. The correlation showed significant positive associations of INF-α with:

- platelet count - p=0.30;
- fibrinogen level-p=0.30;
- the beginning of VSC-p=0.30, against the background of a noticeable negative relationship between INF-α and INR-p=-0.30.

ISSN NO: 2770-2936
Date of Publication:10-11-2023

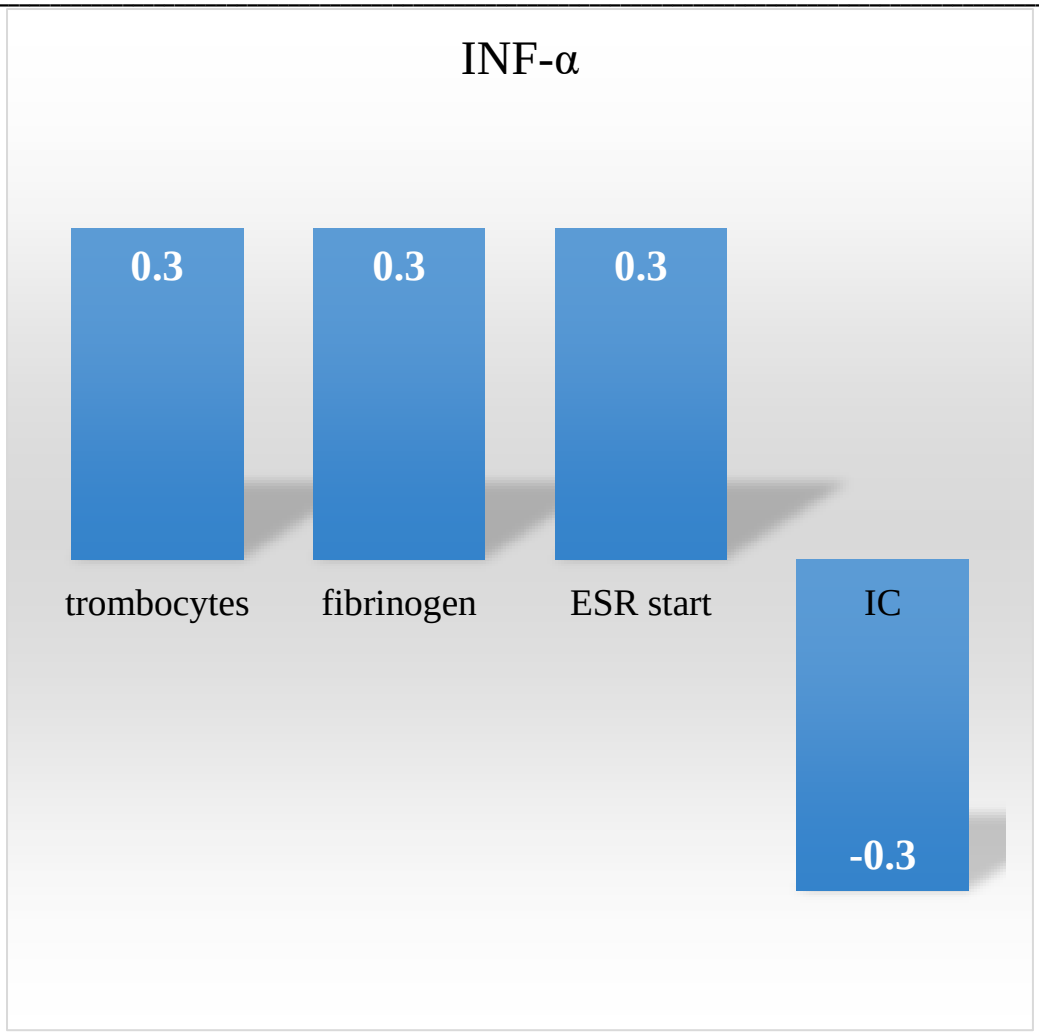

Figure 3. Correlations of interferon alpha in SARS-CoV-2 pneumonia in association with type 2 diabetes

Consequently, in case of SARS-COV-2 pneumonia in association with type 2 diabetes, for timely diagnosis and prognosis of the outcome of the condition, it becomes possible to use the INR as a guide, while an increase in INR is accompanied by a decrease in the level of IFN-α, and vice versa, a low level of IFN-α predicts an increase in INR .

Analysis of the correlation of IFN-γ levels with biochemical blood parameters showed the presence of noticeable negative relationships with:

- ESR- p=-0.30;
- total bilirubin - p=-0.33;
-free fraction of bilirubin - p=-0.33;
-procalcitonin - p=-0.30;
-beginning of VSC - p=-0.30 against the background of a high positive correlation with the bound fraction of bilirubin - p=0.77.

ISSN NO: 2770-2936
Date of Publication:10-11-2023

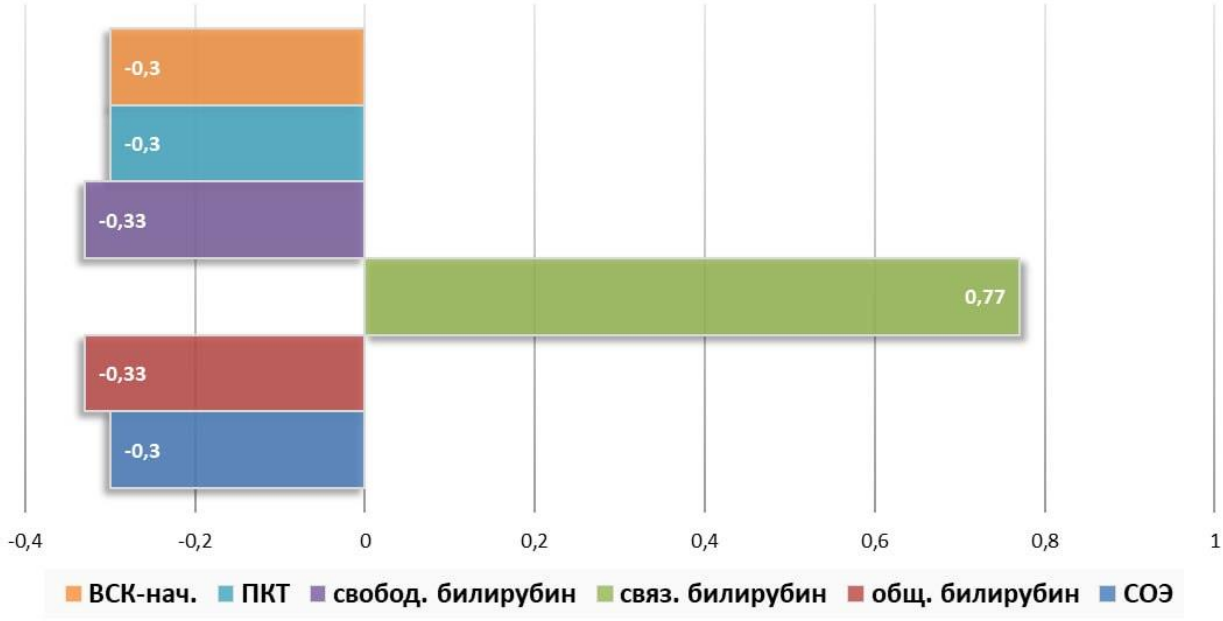

Figure 4. Correlations of interferon gamma in SARS-CoV-2 pneumonia in association with type 2 diabetes

The identified connections of INF-γ show its participation in the system of bilirubin metabolism and blood rheology. The higher the ESR and hyperbilirubinemia, the lower the level of IFN-γ, and vice versa. And also the time of onset of blood clotting noticeably negatively depends on the level of IFN-γ in the blood and vice versa.

Its noticeable negative relationship with PCT in the blood proves protection against secondary bacterial infection in patients with SARS-CoV-2 pneumonia in association with type 2 diabetes.

Thus, in case of SARS-CoV-2 pneumonia in association with type 2 diabetes, it is necessary to study interferon status, which allows predicting the outcome of the disease and choosing patient management tactics.

Analysis of the level of pro-inflammatory IL-4 and diabetogenic IL-18 in patients with SARS-CoV-2 pneumonia in association with type 2 diabetes showed the presence of significant positive relationships with INR and the onset of CVS, which is p = 0.3 and p = 0, 31 respectively.

IL-4 also has noticeable opposite connections with:

-level of total bilirubin - p=-0.3;

-D-dimer- p=-0.3;

-PCT- p=-0.33, against the background of a high negative correlation with the bound bilirubin fraction- p=-0.76.

Consequently, the data obtained led to the conclusion that in SARS-CoV-2 pneumonia in association with type 2 diabetes, a decrease and/or absence of the bound fraction of bilirubin in the blood indicates an increase in the proinflammatory cytokine IL-4 in the blood.

Analysis of the relationship of the diabetogenic cytokine in SARS-CoV-2 pneumonia in association with type 2 diabetes showed its noticeable positive relationship with:

- free fraction of bilirubin - p = 0.30;
-potassium concentration in the blood – p=0.30
-concentration of D-dimer - p=0.34, with a high positive correlation with the level of total bilirubin p=0.43.

ISSN NO: 2770-2936
Date of Publication:10-11-2023

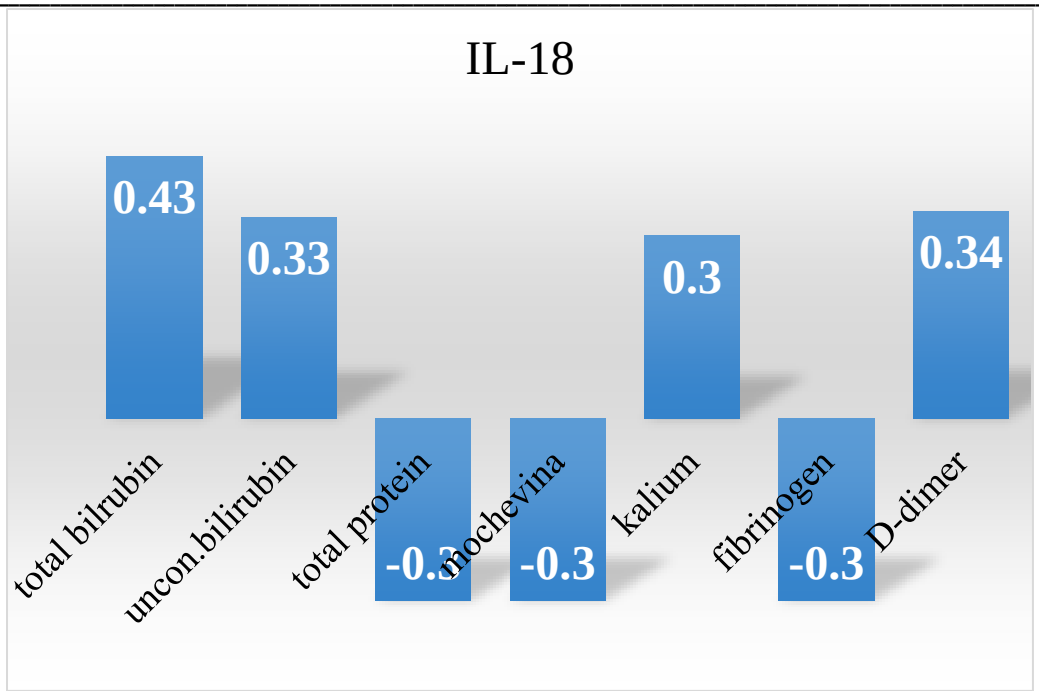

Figure 6. Correlation of IL-18 in SARS-CoV-2 pneumonia in association with type 2 diabetes

The diabetogenic cytokine in SARS-CoV-2 pneumonia in association with type 2 diabetes also has noticeable negative relationships with the level of:
-total blood protein-p=-0.30;
-urea in the blood - p=-0.30;
-fibrinogen--p=-0.30

Conclusion

The obtained connections show the influence of type 2 diabetes on the course of SARS-CoV-2 pneumonia in this way: a decrease in IL-18 contributes to the development of hypoproteinemia, uremia and hypercoagulation and vice versa. Therefore, when managing patients with SARS-CoV-2 pneumonia, it is important to take into account not only IL-6, but also IL-4 and IL-18.

Literature

1. Allard R, Leslers P, Tremblay C, Tannenbaum TN. Diabetes and the North of Pandemic Influenza A (H1H1) infection. Diabetes Sarah. 2010;33(7):1491–1493.
2. Chen Zh, Wu C, Wang H, Yu Zh, Sun Z. The impact of COVID-19 on blood glucose: a systematic review and meta-analysis. Front Endosrinol (Lausanne). 2020;11:574541.
3. Guo W, Li M, Dong Y, et al. Diabetes is a risk factor for the progression and prognosis of COVID-19. Diabetes Metab Res Rev. 2020;36(7):e3319. 10.1002/dmrr.3319
4. Gupta R, Ghosh A, Singh AK, Misra A. Clinical considerations for patients with diabetes in times of COVID-19 epidemic. Diabetes Metab Syndr. 2020;14(3):211–212.
5. Lee YH, Kim SR, Han DҲ, et al. Senescent T Cells predisposed the development of hyperglycemia in humans. Diabetes. 2019;68(1):156–162.
6. Muniyappa R, Gubbi S. COVID-19 pandemic, coronavirus, and diabetes mellitus. Am J Physiol Endosrinol Metab (2020) 318(5):E736–E41. 10.1152/azhpendo.00124.2020
7. Nyambuya TM, Dludla PV, Mhinwa V, Nkambule BB.T-cell activation and cardiovascular risk in adults with type 2 diabetes mellitus: a systematic review and meta-analysis.Clin Immunol. 2020;210:108313.
8. Облокулов, А. Р., & Ниёзов, Г. Е. (2020). Слинисал анд епидемиологисал чарастеристисс оф патиентс витҳ СОВИД-19. Интернатионал Жоурнал оф Пҳармасеутисал Ресеарч, 3749-3752.

ISSN NO: 2770-2936
Date of Publication:10-11-2023

9. Mukhammadieva M.I. (2022). Modern Clinical and Biochemical Characteristics of Liver Cirrhosis Patients of Viral Etiology with Spontaneous Bacterial Peritonitis //Texas Journal of Medical Science. – 2022.- P. 86-90.
10. Облоқулов, А. Р., Ниёзов, Г. Е., Елмуродова, А. А., & Орифов, Д. У. (2020). Слинисал чарастеристисс оф патиентс витҳ СОВИД-19.Интердиссиплинарй Аппроачес то Медисине,1(2), 40-43.
11. World Health Organization Coronavirus Disease 2019 (COVID-19) situation report – 92.
12. Ильин В.П. Корреляционный анализ количественных данных в медико-биологических исследованиях// Бюллетень ВСНЦ СО РАМН- 2013,-№4(92)-с.125-130]
13. Аслонова М.Р., (2023). Оценка интерферонового статуса у пациентов с сахарным диабетом 2 типа, инфицированных covid-19 // Журнал гуманитарных и естественных наук. – 2023. № 3 (09). С. 196-202.
14. Облокулов, А. Р., Ниезов, Г. Э., & Ражабов, А. Р. (2021). Совид-Ассоциированная Коагулопатия У Пациентов Новой Коронавирусной Инфекции. Сентрал асиан жоурнал оф медисал анд натурал ссиенсес, 124-130.
15. Mukhtorova Shokhida Abdulloevna. (2023). Microbiological Indicators of Patients Infected with SarsCov-2. Texas Journal of Medical Science, 21, 41–45.Retrieved from https://www.zienjournals.com/index.php/tjms/article/view/4116
16. Мухаммадиева М.И. (2023). Вирус этиологияли жигар циррози беморларида спонтан бактериал перитонит билан асоратланишнинг профилактикаси ва давосини такомиллаштириш//Oriental Renaissance: Innovative, educational, natural and social sciences. - 2023.-P.947-953.
17. Облоқулов А.Р., Холов Ў.А., Жалилова А.С. СОВИД-19 инфекцияси тасдиқланган беморларнинг микробиологик параметрлари. // Новый День в Медицине. 2022 -2 (40) 363-369 б.
18. Облоқулов, А., & Муҳаммадиева, М. (2022). КЛИНИКО-ЛАБОРАТОРНАЯ ХАРАКТЕРИСТИКА СПОНТАННОГО БАКТЕРИАЛЬНОГО ПЕРИТОНИТА ПРИ ЦИРРОЗЕ ПЕЧЕНИ ВИРУСНОЙ ЭТИОЛОГИИИ. Журнал вестник врача, 1(3), 66–69. извлечено от https://inlibrary.uz/index.php/doctors_herald/article/view/2016
19. Oblokulov. A.R., M.I. Mukhammadieva.(2022). Clinical and biochemical characteristics of liver cirrhosis patients of viral etiology with spontaneous bacterial peritonitis//ACADEMICIA GLOBE: INDERSCIENSE RESEARCH.-2022.- P. 210-216