UDK 616.379-008.64:616.33-089.87:612.017.11

THE NATURE AND ANALYSIS OF CHANGES IN THE DYNAMICS OF HUMORAL IMMUNITY INDICATORS IN KIDNEY DAMAGE IN PATIENTS WHO HAVE UNDERGONE SARS-COV2.

Khursandov Ilyos Akhmedovich
Faculty of Medicine of the Termez University of Economics and Service

Resume. With kidney damage after SARS-CoV 2, there is an increase in all the studied indicators of humoral immunity, with the exception of IgM and IgG, the decrease of which was more pronounced in patients with a chronic course of the pathological process. At the same time, substitution therapy affects the structure of these transformations in the form of a decrease in the concentration of all studied cytokines in the blood against the background of an increase in SHPA and IgG immunoglobulins. The continued growth of IdM, cytokines IL-1β and IFN-γ in patients with a chronic course of the pathological process is manifested even after therapy.
Keywords: kidneys, humoral immunity, SARS-COV 2.

Relevance. The first statistical data on the frequency of PP in patients who have undergone SARS-CoV-2 were presented by scientists from the Yale University School of Medicine based on a study of 1.6 clinical cases. According to their data, 24-57% of hospitalized patients have kidney complications after coronavirus and during the course of the disease. Further studies showed that even 3 weeks after achieving negative results for SARS-CoV-2, kidney function still did not recover and rehabilitation measures were required, and sometimes even hemodialysis (1,3,5,7,9). The structure of the list of PP in patients who have undergone SARS-CoV-2 is diverse and to this day there is no consensus on the specificity of the lesion. In the pathogenesis of PP in patients who have undergone SARS-CoV-2, the leading role is assigned to damage to the renal tubules and the capillary system of the organ (2,4,6,8). The causes of such changes can be both direct damage to the anatomical structures of the kidneys, and the consequences of systemic disorders. Among patients with SARS-CoV-2, 27% and 34% of patients who died from SARS-CoV-2 had high blood urea levels during treatment. The autopsy of deceased patients revealed inflammatory changes in the kidneys, a decrease in the density of the organ parenchyma and the presence of massive tissue edema (11,13,15,17,30,31,32,33.34).

In a recent study conducted by Y. Cheng, et al. (2020), 44% of 710 hospitalized patients with SARS-CoV-2 had clinical manifestations of the disease expressed by the presence of hematuria and proteinuria, while 27% of them had hematuria already upon admission. This, in turn, may indicate that PP appears to be a common disease in SARS-CoV-2 infection, and PP is an independent prognostic factor (10,12,14,16,18,35,36,37,38,39,40,41,42,43).

Cell death and tissue damage can occur due to the presence of high levels of circulating cytokines. In addition, erythrocyte hemolysis and anemia are observed, since cytokines can activate macrophages; together (vascular hemostasis disorders, anemia and injuries caused by cytokines) lead to multiple organ failure, including the kidneys. It is the hemolysis of erythrocytes, which develops as a result of a cytokine storm and causes disorders in the kidneys (19,21,23,25,27,29).

Such a high frequency of PP interest in patients with SARS-CoV-2 indicates the relevance of this problem.

At the same time, such aspects as the peculiarities of the clinical manifestations of PP in patients who have undergone SARS-CoV2 (20,22,24,26,28,30) remain far from certain to date. Information on changes in the dynamics of humoral immunity in PP in patients who have undergone SARS-CoV2 remains far from being studied. Solving these aspects of this urgent problem would make it possible to substantiate the importance of immunological changes in the pathogenesis of PP development, as well as to identify their clinical significance in the diagnosis and prognosis of the outcome of PP in patients who have undergone SARS-CoV2.

The purpose of the study. To study the nature and analysis of changes in the dynamics of humoral immunity indicators in kidney damage in patients who have undergone SARS-COV2.

Research materials and methods: The paper presents information on the comprehensive examination and treatment of 62 patients with kidney damage who underwent SARS-CoV-2. The distribution of patients was carried out on the basis of a prospective targeted open randomized trial.

The period of research and collection of clinical material began in the second quarter of 2020 and ended in December 2023. At the same time, during the period from April to August 2020, the clinic also functioned as a specialized covid center, with the involvement of specialists from all directions in accordance with quarantine requirements. All patients were grouped into one main group.

The criteria for inclusion of patients in the main group were: the age of patients not younger than 20 and not older than 75 years; the presence of a history of coronavirus

infection, with severe course, with signs of kidney damage during treatment; preservation of signs of kidney disease (proteinuria, albuminuria, micro- or macrohematuria, decreased glomerular filtration rate, high creatinine values and urea in the blood, etc.); the presence of a negative result of a PCR test for SARS-CoV-2 during hospitalization in our clinic; availability of the patient's voluntary informed consent to participate in a clinical trial.

In a comparative assessment of clinical and immunological changes, data from 20 healthy individuals recognized by the medical commission as absolutely healthy were used. All of them were combined into a control (reference) group.

All patients in the main group were divided by stages of kidney damage after suffering SARS-CoV-2, which were also recommended by KDIGO.

Kidney damage was typical mainly for mature and elderly patients, while acute kidney damage after SARS-CoV-2 was typical for younger age.

Male patients prevailed (67.7%), and among both patients of the first and second subgroups.

Immunological studies were performed at the Bukhara branch of the Institute of Human Immunology and Genomics

Results and their discussion. The IgG reference value was distinguished by the widest range of the confidence interval [CI: 7.06; 15.92]. In this regard, it seems that the average IgG value in patients with kidney damage after SARS-CoV 2 showed relatively high values of the content of this immunoglobulin (12.84±3.22 g/l).

At the same time, the minimum value of IgG in peripheral blood was noted by us in patients with kidney damage after undergoing SARS-CoV2 before treatment (12.48±3.19 g/l), and the maximum after replacement therapy (13.2±3.24 g/l).

The average IgG value in patients of the first subgroup was 13.27±3.43 g/l [CI: 9.84; 16.69], whereas in patients of the second subgroup it was lower and amounted to 12.41±3.01 g/l [CI: 9.41; 15.42]. In patients of the first subgroup, relative low IgG values when patients came to our clinic [CI: 7.67; 13.03], after treatment significantly increased [CI: 12.01; 20.35] - $p<0.05$, whereas in patients of the second subgroup there was an inverse pattern of changes – a decrease in initially high IgG values [CI: 10.91; 18.31] to the minimum level [CI: 7.9; 12.52] - $p<0.05$.

Kidney damage after SARS-CoV2 was accompanied by an increase in the concentration of IdA by more than 2 times (from 1.02±0.15 g/l to 2.09±0.23 g/l) in patients already upon admission to the clinic ($p<0.05$). The minimum value of the confidence interval could be noted in the control group - [CI: 0.87; 1.17], while in patients of the main group before the start of treatment, it was higher - [CI: 1.86;

2.32]. At the same time, we noted higher ID values in patients of the main group after replacement therapy of kidney damage (2.23±0.49 g/l; [CI: 1.74; 2.72]. The level of IdA concentration in peripheral blood at this stage of the study in patients of the main group exceeded the reference value by 2.2 times ($p<0.05$), and the values before the start of treatment by 1.1 times. In other words, changes in the concentration of IdA in the blood are more related to the pathological process than to the therapeutic measures carried out. This can be confirmed by the average values of IdA in patients of the main group (2.16±0.36 g/l; [CI: 1.8; 2.52]), regardless of the stage of the study (before and after substitution therapy). It can also be noted that not only the presence of kidney damage after suffering SARS-CoV2 affects the level of IdA formation, but also the intensity of its manifestation (acute or chronic process).

The average level of IdA in patients of the first subgroup was equal to 1.72±0.23 g/l [CI: 1.49; 1.95], which was 1.7 times higher than the reference values ($p<0.05$), that is, there is an influence of the pathological process on IdA production. In comparison with the average value of the concentration of IdA in peripheral blood in patients of the second subgroup, one can once again verify the significance of the intensity of the course of the pathological process associated with kidney damage after suffering SARS-CoV2. This indicator was higher (2.6±0.49 g/l) than in patients of the first subgroup (1.72±0.23 g/l) by 1.5 times with a more significant confidence interval [CI: 2.11; 3.09].

The following analysis of changes in the concentration of IdA in peripheral blood was based on an assessment of the dynamics after the therapy. Relatively high concentrations of IdA in the blood were in patients of the first subgroup, noted before the therapy [CI: 1.7; 1.98], which exceeded the reference value by 1.8 times ($p<0.05$). At the same time, this indicator was 1.3 times lower than in patients of the second subgroup at this time of the study.

After the treatment, the concentration of IdA in patients of the first subgroup decreased by only 1.2 times compared to the previous study period [CI: 1.27; 1.91], although it was 1.6 times higher than the reference values ($p<0.05$). When compared with patients of the second subgroup, the IdA level after treatment was 1.8 times lower ($p<0.05$).

In patients of the second subgroup, the concentration of IdA in peripheral blood during the initial study was 2.3 times higher than the reference values ($p<0.05$) [CI: 2.01; 2.65], and after replacement therapy continued to grow, reaching its maximum peak by the end of our study [CI: 2.21; 3.53]. The excess of the reference values was 2.8 times ($p<0.05$).

Thus, the study of the dynamics of changes in the concentration of IdA in peripheral blood in patients with kidney damage after undergoing SARS-CoV2 can indicate the dependence of the formation of this immunoglobulin not only with the phase of the pathological process, but also with the treatment method used.

The concentration of IdM in peripheral blood in the control group averaged 5.76±1.2 g/l [CI: 4.56; 6.96].

At the same time, the average value of the IdM content in patients of the main group was 1.87±0.39 g/l [CI: 1.48; 2.26], which was 3.1 times less than the reference values ($p<0.05$). Relatively minimal values of IdM in peripheral blood were noted in patients of the island group before the treatment of kidney damage, after undergoing SARS-CoV2 - 1.81±0.49 g/l [CI: 1.33; 2.3], which was 3.2 times less than the reference values ($p<0.05$). Completion of replacement therapy for kidney damage after SARS-CoV2 led to an increase in the concentration of IdM in the peripheral blood of patients in the main group to 1.93±0.29 g/l [CI: 1.93; 2.22], however, it was still 3 times less than the reference values ($p<0.05$).

The average concentration of IdM in patients of the first subgroup, which was 1.84±0.35 g/l [CI: 1.49; 2.19], was 3.13 times lower than the reference values ($p<0.05$). The average level of IdM concentration in patients of the second subgroup was unreliably higher - 1.9±0.43 g/l [CI: 1.47; 2.32], which was 3 times less than the reference values ($p<0.05$). Thus, taking into account the comparative analysis of changes in the production of IdM, it can be noted that it is not associated with the phase of kidney damage after undergoing SARS-CoV2.

After the therapy, in patients of the first subgroup, the concentration of IdM decreased [CI: 1.14; 1.44] by 1.85 times ($p<0.05$) compared to the previous study period, and by 4.47 times ($p<0.05$) in relation to the reference values. At the same time, the reverse dynamics occurs in patients of the second subgroup, characterized by an increase in the concentration of IdM in the peripheral blood of patients after replacement therapy. The level of increase was 2.1 times ($p<0.05$) compared to the previous period of the study within the subgroup. Nevertheless, this indicator was 2.25 times lower than the reference values ($p<0.05$) and was 1.98 times higher than in patients of the first subgroup ($p<0.05$).

Thus, a comparative analysis of the dynamics of changes in the concentration of IdM showed a significant decrease in this immunoglobulin in the blood of patients with kidney damage after undergoing SARS-CoV2. At the same time, the therapeutic measures carried out increase the production of IdM, but these changes are not

reliable. In this regard, it is important to consider this issue in patients depending on the phase of kidney damage after undergoing SARS-CoV2.

When studying the concentration of cytokines in the blood of patients with kidney damage after undergoing SARS-CoV2, it was revealed that all manifest themselves with a certain pattern in the correlation of the dynamics of the course of the pathological process.

The proinflammatory cytokine IL-1β in patients of the main group exceeded the reference value by an average of 52.87 times ($p<0.001$). This gap is due to the fact that the average value of IL-1β in the control group in healthy people averaged 0.42±0.09 pg/ml [CI: 0.33; 0.51], in patients with kidney damage after SARS-CoV2, the average level of IL-1β increased to 22.21±3.23 pg/ml [CI: 18.98; 25.44] ($p<0.05$). In the main group of patients, high average values of the proinflammatory cytokine IL-1β were noted during the period of treatment of patients in our clinic and amounted to 29.53±4.44 pg/ml [CI: 25.09; 33.96]. High values of IL-1β in patients with kidney damage after SARS-CoV2 at this time were 70.3 times higher ($p<0.001$) than in healthy individuals. After the treatment, the average concentration of the proinflammatory cytokine IL-1β in the blood decreased to 14.89±2.03 pg/ml [CI: 12.86; 16.91], which was 35.44 times higher than the reference values ($p<0.001$), but 1.98 times less than in patients in previous study periods ($p<0.05$).

Thus, a general comparative assessment of the dynamics of changes in the concentration of proinflammatory cytokine IL-1β showed a significant increase in the indicator in patients with kidney damage after SARS-CoV2 and their reduction as a result of substitution therapy.

In patients of the first group, the average concentration of the proinflammatory cytokine IL-1β in the blood was higher (23.46±3.61 pg/ml [CI: 19.86; 27.07]) than among patients of the second subgroup (20.95±2.86 pg/ml [CI: 18.1; 23.81]).

Upon admission of patients to the clinic with acute kidney injury after SARS-CoV2, the concentration level of the proinflammatory cytokine IL-1β [CI: 37.49; 50.87] was 105.19 times higher than the reference values ($p<0.001$), in relation to the average value of patients of the first subgroup by 1.88 times ($p<0.001$) and compared to with indicators of the same period, the second subgroup of patients was 2.97 times higher ($p<0.001$). At the same time, after treatment, the concentration of proinflammatory cytokine IL-1β in the blood of patients with acute kidney injury after SARS-CoV2 decreased sharply by 16.12 times ($p<0.05$) compared with the day of admission of patients of the first subgroup to the clinic, by 5.43 times ($p<0.05$) compared with the

day of admission of patients of the second subgroup and 9.86 times ($p<0.05$) compared to patients of the second subgroup after treatment.

It should be noted that, unlike patients of the first subgroup, patients of the second subgroup had an inverse dynamics in the form of an increase in the concentration of the proinflammatory cytokine IL-1β in blood samples after treatment [CI: 23.5; 30.56]. Its concentration exceeded the reference value by 64.36 times ($p<0.05$) and the previous study period by 1.82 times ($p<0.05$).

The concentration of TNF-α in the blood of healthy individuals ranged in the confidence range from 1.45 pg/ml to 2.01 pg/ml and averaged 1.73±0.28 pg/ml. In patients with kidney damage after SARS-CoV2, the concentration of TNF-α cytokine increased 13.28 times ($p<0.05$) and averaged 22.97±3.77 pg/ml [CI: 19.2; 26.74]. At the same time, the leading role in increasing the concentration of TNF-α in patients of the main group was assigned to the first phase of research, that is, when patients were admitted to the clinic. The average concentration of TNF-α in peripheral blood was 27.06±4.42 pg/ml [CI: 22.64; 31.48], which was 15.64 times higher ($p<0.05$) than the reference value. Subsequently, after replacement therapy, the concentration of TNF-α in the blood of patients in the main group relatively decreased to 18.89±3.12 pg/ml [CI: 15.77; 22.01], it was 10.92 times higher ($p<0.05$) than the reference value and less than 1.43 times less ($p<0.05$) the previous period of the study, that is, before the treatment.

A separate analysis, depending on the timing of the course of kidney damage, revealed a predominance of TNF-α concentration among patients with acute kidney injury after SARS-CoV2, which amounted to 25.58±4.64 pg/ml [CI: 20.94; 30.21], which was 1.26 times higher ($p<0.05$) than in patients the second subgroup. In patients of the second subgroup, the average TNF-α value in the blood was 20.37±2.91 pg/ml [CI: 17.47; 23.28], which was 11.77 times higher than the reference values ($p<0.05$).

Upon admission to the clinic, that is, before the start of substitution therapy, higher concentrations of TNF-α were noted among patients of the first subgroup [CI: 27.32; 37.94]. They exceeded the reference value [CI: 1.45; 2.01] by 18.86 times ($p<0.05$) and the cross-indicators among patients of the second subgroup [CI: 17.96; 25.02] by 1.52 times ($p<0.05$).

After completion of the replacement therapy session, the concentration of TNF-α in the blood of patients of the first subgroup decreased by 1.76 times ($p<0.05$) [CI: 14.56; 22.48] compared with the previous study period, but remained high relative to the reference value by 1.76 times ($p<0.05$).

Unlike the dynamics of patients of the first subgroup, in patients of the second subgroup, there was also a marked tendency to decrease the concentration of TNF-α in the blood after replacement therapy [CI: 16.97; 21.53], was not significant.

The concentration of another proinflammatory cytokine IL-8 in healthy individuals was 23.38±3.01 pg/ml [CI: 20.37; 26.39], however, in patients of the main group, the level of this indicator increased, reaching 166.07±21.33 pg/ml [CI: 144.74; 187.4], which was 7.1 times higher than the reference values ($p<0.05$).

The maximum value of IL-8 was noted by us among patients before replacement therapy (196.84±23.44 pg/ml [CI: 173.4; 220.27]), which exceeded the reference value by 8.42 times ($p<0.05$). In patients with kidney damage after SARS-CoV2, substitution therapy led to a decrease in IL-8 concentration to (135.31±19.23 pg/ml [CI: 116.09; 154.54]), which was 1.45 times less than the previous study period ($p<0.05$), but 5.79 times higher than the reference value ($p<0.05$).

Higher IL-8 values were found among patients of the second subgroup, where they averaged 220.12±23.06 pg/ml [CI: 197.06; 243.17] and exceeded the reference value by 9.41 times ($p<0.05$). In patients of the first subgroup, this indicator was 112.03±19.61 pg/ml [CI: 92.43; 131.64] and exceeded the reference value by 4.79 times ($p<0.05$), then by half than in patients of the second subgroup.

Within the studied subgroups, when patients were admitted to the clinic, the concentration of IL-8 was higher in the second subgroup (1.39 times; $p<0.05$). At the same time, after the treatment, the concentration of IL-8 decreases in both subgroups of patients. In patients of the first subgroup, it decreases by 2.78 times ($p<0.05$), and in patients of the second subgroup – by 1.08 times.

Thus, the change in the concentration of IL-8 in patients with kidney damage after SARS-CoV2 is characterized by the presence of high values, which after replacement therapy in patients with acute kidney damage significantly decrease, whereas in patients with chronic process, we did not find significant differences in the change in the concentration of IL–8 in the blood.

The concentration of IL-10 in healthy individuals ranged in the confidence range from 3.06 pg/ml to 3.24 pg/ml and averaged 3.15±0.09 pg/ml, In patients of the main group this indicator increased by 2.83 times ($p<0.05$) and reached from 7.35 pg/ml to 10.51 pg/ml, averaging 8.93±1.58 pg/ml. At the same time, in patients at the initial value, this indicator ranged from 9.16 pg/ml to 13.03 pg/ml, averaging 11.1±1.94 pg/ml. After replacement therapy, the average concentration of IL-10 decreased to 6.77±1.23 pg/ml, varying from 5.54 pg/ml to 7.99 pg/ml.

We noted higher values of IL-10 among patients of the second subgroup, amounting to 10.34±1.56 pg/ml [CI: 8.78; 11.89], whereas in patients of the first subgroup, the concentration of IL-10 in the blood ranged from 5.92 pg/ml to 9.13 pg/ml and averaged 7.53±1.61 pg/ml (1.37 times less).

The excess of the reference values of IL-10 concentration in the blood in patients of the first subgroup was 2.39 times ($p<0.05$), and in patients of the second subgroup – 3.28 times ($p<0.05$).

It should be noted that the level of IL-10 in both patients of the first and second subgroups after replacement therapy decreased by 1.35 times ($p<0.05$) and 1.9 times ($p<0.05$), respectively.

Thus, kidney damage after SARS-CoV2 is characterized by an increase in IL-10 concentration in the long term of the disease (the second subgroup). As replacement therapy was carried out, we noted a decrease in IL-10 in the blood, to a greater extent in patients with chronic kidney damage after undergoing SARS-CoV2.

As for the change in the level of IFN-γ in patients with kidney damage after SARS-CoV2, a moderate increase in its concentration from 6.23±1.74 pg/ml [CI: 4.49; 7.97] to 10.56±1.98 pg/ml [CI: 8.56; 12.54] (1.69 times; $p<0.05$).

The maximum peak of the increase was in patients with kidney damage after undergoing SARS-CoV2 at hospital admission - 12.67±2.44 pg/ml [CI: 10.24; 15.11]. After replacement therapy, there was a decrease to 8.44±1.53 pg/ml [CI: 6.92; 9.97].

Higher values of IFN-γ were among patients of the second subgroup, amounting to 12.95±2.36 pg/ml [CI: 10.6; 15.31], whereas in patients of the first subgroup they equated to 8.16±1.61 pg/ml [CI: 6.56; 9.77].

After substitution therapy, there was a decrease in the concentration of IFN-γ by 4.73 times ($p<0.05$), whereas in patients of the second subgroup, we noted an increase in the concentration of IFN-γ by 1.18 times ($p<0.05$).

Conclusion.

1. In patients with kidney damage after SARS-CoV2, there is an increase in IFN-γ, which decreases in the acute process, whereas in the chronic process it increases. Such an opposite effect of the therapy is explained by the small role of the treatment used, rather than the pathological process itself and its severity of manifestation.
2. In case of kidney damage after SARS-CoV 2, there is an increase in all the studied indicators of humoral immunity, with the exception of IgM and IgG, the decrease of which was more pronounced in patients with a chronic course of the pathological process. At the same time, substitution therapy affects the structure of these transformations in the form of a decrease in the concentration of all studied

cytokines in the blood against the background of an increase in SHPA and IgG immunoglobulins. The continued growth of IdM, cytokines IL-1β and IFN-γ in patients with a chronic course of the pathological process is manifested even after therapy.

LITERATURE

1. Associated aposateddingmember S.-19 vasculitis, sub-vasculitis, sub-vasculitis, sub-vasculature TCP in real time cut: report O case / K series. Well. Belozerov, I. S. Avrusin, A. A. Yakovlev et al. // Treatment and Prevention. – 2023. - T. 13, № 1. - S. 71-81.
2. Atypical hemolytic-uremic syndrome associated with COVID-19 and the use of eculizumab therapy / A.V. Khomyakov, L. Y. Zhuravleva, A. E. Romanova [et al.] // Bulletin of the Chelyabinsk Regional Clinical Hospital. – 2023. – № 2(56). – Pp. 8-15.
3. Vorobyov P. A. Recommendations for the diagnosis and intensive therapy of disseminated intravascular coagulation syndrome in viral lung damage // Problems of standardization in healthcare. – 2020. – № 5-6. – pp. 71-94.
4. Clinical and prognostic criteria for the complicated course of a new coronavirus infection (COVID-19) / A. S. Sycheva, A. L. Kebina, A. L. Vertkin, et al. // Medico-pharmaceutical journal Pulse. – 2021. – Vol. 23, No. 9. – pp. 147-153.
5. Covid-19: connection with kidney pathology. Literature review / N. A. Tomilina, N. F. Frolova, L. Yu. Artyukhina et al./ / Nephrology and dialysis. – 2021. – Vol. 1. 23, No. 2. – pp. 147-159.
6. Confirmation of the high cumulative incidence of thrombotic complications in critically ill ICU patients with COVID-19 / F.A. Klok, M.J.H.A. Kruip, N.J.M. van der Meer, et al. // Thrombosis Research. – 2020. – Vol. 191 – P. 148–150.
7. Pathophysiology of COVID-19-associated acute kidney injury / M. Legrand, S. Bell, L. Forni, et al. // Nature Review Nephrology. – 2021. – Vol. 17 - No11 – P. 751-764.
8. Khamdamov B.Z. Comparative evaluation of methods of amputation related to tidiotarus witn severe forms of diadetic foot syndrome. European Science Review. Austria, Vienna 2014 Septemba-October №9-10. - C. 58-60.
9. Khamdamov B.Z. Changes in the quality of life after high amputations in patients with diabetic foot syndrome. Samarkand. Problems of biology and medicine. №1, 2019., (107) - S. 115-117.

10. Khamdamov B.Z. Complex treatment of diabetic foot syndrome with critical ischemia of the lower extremities. Journal of Biomedicine and Practice. Tashkent 2020, Special issue. Part 5. – pp. 801-814.
11. Khamdamov B.Z. Method of laser photodynamic therapy in the treatment of wound infection in diabetic foot syndrome. Biology and problems of medicine No.1 (116) 2020. – pp. 142-148
12. Khamdamov B.Z. Morphological changes in the application of photodynamic therapy in the treatment of wound infection in an experiment. Journal of Morphology. St. Petersburg. 2020. Volume 157 (2-3). – pp. 223-224.
13. Khamdamov B.Z. Optimization of methods of local treatment of purulent-necrotic lesions of the foot in diabetes mellitus. Journal. New day in medicine. 2018, No.4 (24) - pp. 112-115.
14. Khamdamov B. Z., Akhmedov R. M., Khamdamov A. B. The use of laser photodynamic therapy in the prevention of purulent-necrotic complications after high amputations of the lower limbs at the level of the lower leg in patients with diabetes mellitus. Scopus Preview. International journal of Pharmaceutical Research. Volume 11, Issue 3, July-Sept, 2019
15. Khamdamov B. Z., Nuraliev N.A. Pathogenetic approach in complex treatment of diabetic foot syndrome with critical lower limb ischemia. American Journal of Medicine and Medical Sciences, 2020 10 (1) 17-24 DOI: 10.5923/j.20201001.05.
16. Khamdamov B.Z. Indicators of immunocitocine status in purulent-necrotic lesions of the lover extremities in patients with diabetes mellitus. American Journal of Medicine and Medical Sciences, 2020 10 (7): 473-478 DOI: 10.5923/j.20201001.08
17. Khamdamov, B., & Dekhkonov, A. (2022). Clinical and laboratory parameters of the wound process complicated by the systemic inflammatory response syndrome in patients with diabetes mellitus. Journal of education and scientific medicine, 2(3), 25-29. Retrieved from https://journals.tma.uz/index.php/jesm/article/view/349
18. Khamroev, U., & Khamdamov, B. (2022). Features of changes in endothelial system parameters in patients with diffuse toxic goiter. Journal of education and scientific medicine, 2(3), 62-67. Retrieved from https://journals.tma.uz/index.php/jesm/article/view/358
19. Eshbekov M.A., Khamdamov B.Z. Indicators of the thyroid profile in various clinical forms of glomerulonephritis and correlations with the cytokine system // Journal of Theoretical and clinical Medicine. Tashkent, 2023- No.6.- pp.175-185.
20. Khamdamov B.Z., Nabieva U.P., Eshbekov M.A., Agzamova T.A. Cytokine

profile in patients with glomerulonephritis depending on the clinical course// Journal of Theoretical and clinical Medicine. Tashkent, 2023- No.4.- pp.112-116.

21. Khamdamov B.Z., Eshbekov M.A. Interrelations between cytokine and immune status indicators in patients with glomerulonephritis //Biology and problems of medicine. Samarkand, 2023- No.6. -pp.274-278.

22. Khamdamov B.Z., Nabieva U.P., Eshbekov M.A., Clinical and epidemiological characteristics and correlations with the cytokine system in patients with glomerulonephritis // Journal of Theoretical and Clinical Medicine. Tashkent, 2024- №1.- S.*175-185*.

23. Khamdamov B.Z.,Eshbekov M.A., Khamdamov A.B. Sharacteristics of the thyroid profile in various clinical forms of glomerulonephritis and correlations with the cytokine system //American Journal of Medicine and Medical Sciences 2024, *14(2):* 458-465.

24. Khamdamov B.Z.,Eshbekov M.A., Khamdamov A.B., Askarov T.A. Cytokine profile in patients with glomerulonepfritis depending on the clinical course //American Jornal of pediatric medicine and health science, 2024- Volume 2, Issue 2.- P.174-180.

25. Khamdamov B.Z.1, Eshbekov M.A. Immuno-endocrine markers of the course of chronic glomerulonephritis// XI International Scientific and Practical Conference "Topical Issues of Medicine" and "V Satellite Forum on Public Health and Health Policy", Baku, March 2024.- S.234-235.

26. Khamdamov B.Z., Nabieva U.P., Eshbekov M.A. The level of immunocomposite reactions in chronic glomerulonephritis // Proceedings of the international scientific and practical conference "Education, science, medicine" dedicated to the 80th anniversary of the Academy of Sciences of the Republic of Uzbekistan, Tashkent, June 22, 2023. Journal of Theoretical and Clinical Medicine. Tashkent, 2023- № 3.-C.184.

27. Eshbekov M.A.. Cytokine profile in patients with glomerulonepfritis depending on the clinical course // International scientific-online conference “Development of pedagogical thechnologies in modern sciences”, Turkish, 2023- doi.org/10.5281/zenodo/10653893.

28. Eshbekov M.A., Boimatov F.H. Immunocomplex mechanisms during chronic glomerulonephritis. // International bulletin of Applied science and technology, April 2023, Volume 3, Issue 4.-P.168-172.

29. Khamdamova M.T. Ultrasound features of three-dimensional echography in assessing the condition of the endometrium and uterine cavity in women of the first

period of middle age using intrauterine contraceptives // Biology va tibbyot muammolari. - Samarkand, 2020. - No. 2 (118). - P.127-131.
30. Khamdamova M. T. Ultrasound assessment of changes in the endometrium of the uterus in women of the first and second period of middle age when using intrauterine and oral contraceptives // Biomedicine va amaliyot journals. – Tashkent, 2020. - No. 2. - Part 8.- P.79-85.
31. Khamdamova M.T. Features of ultrasound parameters of the uterus in women of the first and second period of middle age using injection contraceptives // New day in medicine. Bukhara, 2020. - No. 2/1 (29/1). - P.154-156.
32. Khamdamova M.T. Features of ultrasound images of the uterus and ovaries in women of the second period of middle age using combined oral contraceptives // New day in medicine. Bukhara, 2020. - No. 2 (30). - P. 258-261.
33. Khamdamova M.T. Individual variability of the uterus and ovaries in women who use and do not use various types of contraceptives // New day in medicine. Bukhara, 2020. - No. 3 (31). - pp. 519-526.
34. Khamdamova M. T. Echographic features variability in the size and shape of the uterus and ovaries in women of the second period of adulthood using various contraceptives // Asian Journal of Multidimensional Research - 2020. – N9 (5). - P.259-263.
35. Khamdamova M. T. Somatometric characteristics of women of the first and second period of adulthood using different contraceptives with different body types // The american journal of medical sciences and pharmaceutical research - 2020. – N8 (2). - P.69-76.
36. Khamdamova M.T., Zhaloldinova M.M., Khamdamov I.B. The state of nitric oxide in blood serum in patients with cutaneous leishmaniasis // New day in medicine. Bukhara, 2023. - No. 5 (55). - P. 638-643.
37. Khamdamova M.T., Zhaloldinova M.M., Khamdamov I.B. The value of ceruloplasmin and copper in blood serum in women wearing copper-containing intrauterine device // New day in medicine. Bukhara, 2023. - No. 6 (56). - pp. 2-7.
37.Khamdamova M. T. Bleeding when wearing intrauterine contraceptives and their relationship with the nitric oxide system // American journal of pediatric medicine and health sciences Volume 01, Issue 07, 2023 ISSN (E): 2993-2149. P.58-62
38. Khamdamova M. T. The state of local immunity in background diseases of the cervix // Eurasian journal of medical and natural sciences Innovative Academy Research Support Center.Volume 3 Issue 1, January 2023 ISSN 2181-287X P.171-175.

39. Khamdamova M.T., Khasanova M.T. Various mechanisms of pathogenesis of endometrial hyperplasia in postmenopausal women (literature review) // New day in medicine. Bukhara. 2023. - No. 8 (58). - P. 103-107.
40. Khamdamova M.T. Reproductive Health of Women Using Copper-Containing Intrauterine Contraception // Eurasian Medical Research Periodical Volume 28 January 2024, ISSN: 2795-7624 .www.geniusjournals.org P. 39-45.
41. Khamdamov I.B. Advantages Of Laparoscopic Hernioplasty in Obesity Women of Fertile Age // Eurasian Medical Research Periodical Volume 28 January 2024, ISSN: 2795-7624 .www.geniusjournals.org P. 33-38.
42. Eshbekov M.A., Khamdamov B.Z., Usmanova N.U. Immunocomplex mechanisms during chronical glomerulonephritis // International conference on Advance research in humanities, science and education, London, April 2023- P.504-513.
43. Eshbekov M.A., Khamdamov B.Z., Usmanova N.U. The significance of immunocomplex mechanisms during chronical glomerulonephritis // International conference on Advance research in humanities, science and education, Germany, May 2023- P.89-98.