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EVALUATION OF THE EFFECTIVENESS OF THE EFFECT OF ACETYLCYSTEINE ON INTRARENAL HEMODYNAMICS IN PATIENTS WITH CORONAVIRUS ASSOCIATED NEPHROPATHY

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ABSTRACT: This article discusses the assessment of kidney function in patients with coronavirus-associated nephropathy through Doppler ultrasound of renal vessels. The study focuses on research groups comprising individuals affected by this nephropathy. Dopplerography studies aim to evaluate the effectiveness of N-acetylcysteine in treating coronavirus-associated nephropathy. Doppler ultrasound helps assess renal blood flow and vascular parameters, providing insights into the functional state of the kidneys. The evaluation of N-acetylcysteine's effectiveness suggests an exploration of its potential as a therapeutic intervention for coronavirus-associated nephropathy. This research contributes to understanding the renal implications of COVID-19 and potential treatment avenues through the application of Doppler ultrasound techniques.

INTRODUCTION: With the help of dopplerography, it is possible to obtain information about the morphofunctional state of these organs, especially the kidney, based on the assessment of blood circulation changes, intrarenal hemodynamics and vascular resistance, as well as diagnose nephropathies [10, 11]. It describes in detail the mechanisms of damage to the heart, lungs, brain and other vital organs caused by infection, clinical-pathogenetic aspects, and morpho-functional changes occurring in them.

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At the same time, we nephrologists are monitoring in our clinical practice that these changes do not bypass the kidney parenchyma. In this case, the infection of COVID-19 deepens the existing SBK in patients or causes new kidney pathology in patients without kidney disease - Coronavirus-associated nephropathies [1, 7]. Coronavirus-associated nephropathies range from asymptomatic patients with limited urinary syndrome to severe, life-threatening acute kidney injury [2, 7]. Therefore, in our research, we found it necessary to carry out scientific research on the analysis of spectral Doppler data in the assessment of the morphofunctional state of the kidney in patients experiencing coronavirus-associated nephropathy.

The Purpose of the Study: Study of intrarenal hemodynamics and vascular resistance by

conducting renal vascular dopplerography in research groups consisting of patients with coronavirus-associated nephropathy and evaluating the effect of N-acetylcysteine on it.

MATERIALS AND METHODS: 101 patients with coronavirus-associated nephropathy treated at the Tashkent Medical Academy multidisciplinary clinic and RINvaBTIATM nephrology departments were selected for the study. They were randomly divided into two study groups. Group 1 was treated only with standard treatment (antiviral, anticoagulant, antiaggregant, glucocorticosteroids, antibiotic drugs) recommended for the disease of COVID-19. Group 2 was given N-acetylcysteine (NAS) in addition to the standard-recommended routine treatment for COVID-19. In the beginning, the drug was recommended to be injected in the amount of 1200-1800 mg for 5-7 days and then orally in the amount of 600-1200 mg for another 20 days. The patients included in the study underwent inpatient treatment in nephrology departments for 7-10 days and then were under outpatient supervision for up to 1 month. The age of patients ranges from 19 to 65 years, the average age of patients in group 1 is 48.7±2.89; In group 2, it is 49.4±2.97 years.

At the beginning and 30 days after the treatment, all patients underwent a dopplerographic examination of the renal vessels to determine the resistance of the renal arteries and the blood flow rate in the vessels. This examination was performed in the reception department of the TMA multidisciplinary clinic on the "Sonoscape S20 Color Doppler diagnostic" device. Through this examination, the blood flow rate and vascular resistance in the main, circular, interlobular vessels of the kidney are studied by the spectral analysis method. Intrarenal hemodynamics was studied using the spectral analysis method with the help of ultrasound dopplerography.

The right and left renal arteries are evaluated in the entry field as follows:

Maximum systolic velocity of arterial blood flow (Vs max), final diastolic speed (Vd);

In Intrarenal Arteries: Segmental – V max, Vd; intersegmental – V max, Vd.

Resistance index (RI) and pulse index (PI) were calculated to characterize renal vascular resistance. The average value of the results obtained from the examination of the right and left kidney vessels was used in the statistical analysis of the data.

RESULTS AND DISCUSSION: The results of the research conducted during one month showed the following. In this case, Vs max in the main renal arteries was 55.4±1.74 at the beginning of treatment in patients of the 1st group; after one month it increased to 63.1±2.11 cm/s. This indicator was 55.2±1.72 at the beginning of treatment in the 2nd group of patients receiving N-acetylcysteine (NAS); after one month it was observed that it increased by 66.7±1.23 cm/s. The results were statistically significant (R<0.001) in both study groups compared to the control group, and moderately significant (R<0.01) in group 1 and significant (R<0.001) in group 2 compared to baseline. The end-diastolic velocity in these main renal arteries was 19.5±1.23 at the beginning of treatment in group 1 patients, and after one month it increased to 22.0±1.25 cm/s. In group 2, which received NAS drug for one month, it was equal to 19.4 ± 1.22 values at the beginning of the treatment, and after one month it significantly increased to 23.6 ± 0.89 cm/s. Statistical analysis showed that the results increased reliably (R<0.001) in both study groups compared to the control group but less reliable (R<0.05) in group 1 and more reliable (R<0.01) in group 2 compared to the beginning of treatment it happened **Table 1.**

TABLE 1: HEMODYNAMICS OF MAIN AND INTRARENAL ARTERIES CHANGE OF INDICATORS AGAINST THE BACKGROUND OF TREATMENT

Indicators	Control n=20	Group 1 n = 50		Group 2 n = 50	
		At the beginning of treatment	After 30 days	At the beginning of treatment	After 30 days
Main renal artery					
Vs max, cm/s	87,98±0,91	55,4±1,74***	63,1±2,11***^^	55,2±1,72***	66,7±1,23***^^^
cm/s	28,98±0,64	19,5±1,23***	22,0±1,25***^	19,4±1,22***	23,6±0,89***^^
S/D	3,03±0,28	2,84±0,27	2,87±0,24	2,84±0,25	2,83±0,26
Segmental artery					

V_s max, cm/s	58,38±0,82	42,1±1,44***	47,2±1,78***^	42,0±1,46***	49,6±0,97***^^^
V_d, cm/s	23,11±0,32	16,5±1,23***	18,6±1,43**	16,4±1,22***	19,8±0,85***^^
S/D	2,52±0,41	2,56±0,21	2,54±0,44	2,56±0,42	2,51±0,41
Interlobular artery					
V_s max, cm/s	37,74±0,88	25,6±1,32***	27,4±1,18***	25,5±1,30***	29,8±0,83***^^
V_d, см/с	15,41±0,60	11,1±0,63***	11,6±0,68***	11,0±0,54***	13,4±0,57***^^
S/D	2,44±0,21	2,31±0,17	2,36±0,19	2,32±0,18	2,23±0,17

Note: * - differences are significant compared to the indicators of the control group (*- R<0.05, **- R<0.01, ***- R<0.001); ^ - differences are significant compared to the indicators at the beginning of treatment (^ - R<0.05, ^^ - R<0.01, ^^^ - R<0.001).

In Segmental Renal Arteries, Vs max Increased from 42.1±1.44 at the beginning of treatment to 47.2±1.78 cm/s after one Month: In group 2 patients who received additional NAS to the planned treatment, it was shown that Vs max increased from 42.0±1.46 cm/s at the beginning of treatment to 49.6±0.97 cm/s after one month.Values increased reliably (R<0.001) compared to the control group in both study groups, and Vs max increased less reliably (R<0.05) in group 1 and significantly (R<0.01) in group 2 compared to baseline. found its confirmation in statistical analysis.

The end-diastolic velocity in group 1 was 16.5±1.23 at the beginning of treatment and after one month it increased to 18.6±1.43 cm/s. In group 2, which received NAS drug, Vd increased from 16.4±1.22 cm/s at the beginning of treatment to 19.8±0.85 cm/s after treatment. Statistical analysis showed that the results showed a reliable (R<0.001) increase in both study groups compared to the control group but an unreliable (R<0.01) increase in group 1 and a reliable (R<0.01) increase in group 2 compared to baseline **Table 1.**

Vs max in interlobular renal arteries was 25.6±1.32 at the beginning of treatment and increased to 27.4±1.18 cm/s after one month. In group 2 patients who received additional NAS drug to the planned treatment, Vs max increased from 25.5±1.3 cm/s at the beginning of the treatment to 29.8±0.83 cm/s one month after the treatment we were. When we statistically analyzed the results, it was observed that the values changed reliably (R<0.001) in both study groups compared to the control group. However, statistical analysis showed that Vs max was unreliable in group 1 and reliable (R<0.01) in group 2 compared to the beginning of treatment. Vd in group 1 was 11.1±0.63 at the beginning of treatment, and after one month it increased slightly to 11.6±0.68 cm/s. In group 2, Vd, which was 11.0±0.54 cm/s at the beginning of treatment, significantly increased to 13.4±0.57 cm/s one month after treatment. Statistical analysis showed that the results changed reliably (R<0.001) in both study groups compared to the control group, but were unreliable in group 1 and reliable (R<0.01) in group 2 compared to the beginning of treatment **Table 1.** Analyzing the results of the study in a diagram, it was found that vs max values were unreliable or less reliable (R<0.05) after one month in the 1st group consisting of patients who were satisfied with only scheduled treatment after experiencing COVID-19 associated nephropathy, and additional NAS drugs were given to scheduled treatment for one month.

In patients of the 2nd group, almost reliable (R<0.01; R<0.001) changes were observed in all main and intrarenal blood vessels of the kidney. NAC is known to suppress oxidative stress by acting as a cell-permeable amino acid precursor of glutathione, angiotensin-converting enzyme 2, the cellular receptor for SARS-CoV-2, by breaking disulfide bonds [13, 15]. Also, NAC reduces the occurrence of inflammatory cytokines such as IL-8 and FNO-α [16].

The indirect antioxidant property of the drug is explained by increasing the activity of enzymes such as glutathione-S-transferase, glutathione peroxidase, and glutathione reductase, which are the basis of the balance of the "oxidation-reduction" system [11]. Of course, this coordination has the effect of improving and accelerating blood flow in all renal arteries. This picture is clearly reflected in the indicators' dynamics columns in the diagram **Fig. 1.** According to the results of the study, the end-diastolic velocity changed unreliable or less reliably (R<0.05) in almost all blood vessels of all sizes after one month in group 1, which consisted of patients who experienced COVID-19-associated nephropathy and were satisfied with

only scheduled treatment. and in group 2 patients who received it during the month, a positive (R<0.01) increase in Vd was observed in all arteries of the kidney. This is interpreted as an effect of the NAS drug. This effect was also reflected in the improvement of end-diastolic velocity in all renal arteries. This picture is also clearly reflected in the indicators' dynamics columns in the chart **Fig. 2.**

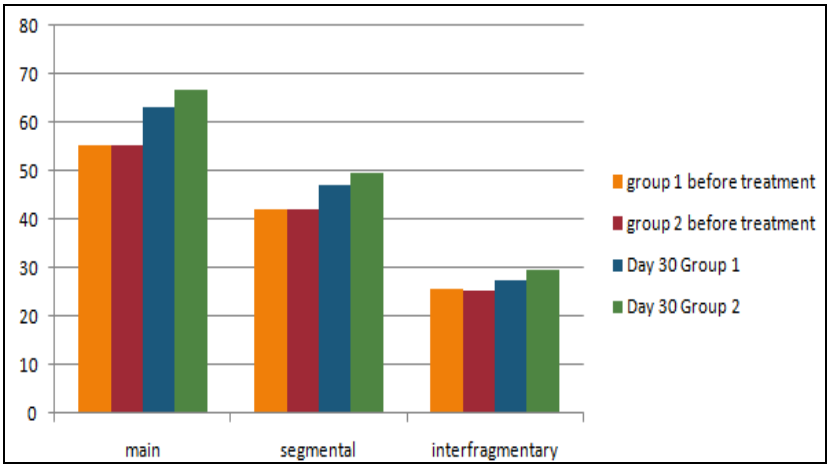

FIG. 1: CHANGES IN THE MAXIMUM SYSTOLIC VELOCITY (VS MAX) OF THE RENAL ARTERIES AGAINST THE BACKGROUND OF TREATMENT

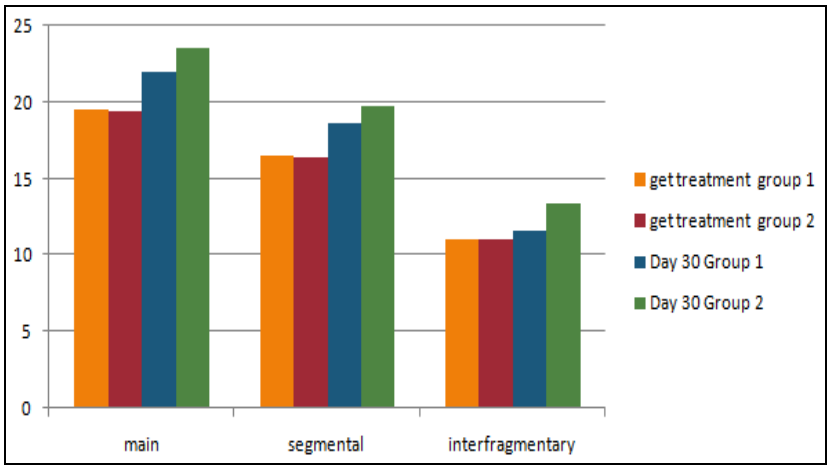

FIG. 2: END-DIASTOLIC VELOCITY OF RENAL ARTERIES (VD) CHANGE OF INDICATORS AGAINST THE BACKGROUND OF TREATMENT

The calculated resistance index (RI) and pulse index (PI), which determine the level of renal vascular resistance, showed the following picture during one month of treatment in patients with coronavirus-associated nephropathy, which is the basis of our research.

According to the results, the resistance index in the main renal arteries was 0.74±0.01 at the beginning of treatment in group 1, and after one month this value was 0.71±0.01.In group 2 patients who received additional NAS drugs to the scheduled treatment for one month, this indicator was 0.73±0.01 at the beginning of the treatment, and after one month it significantly decreased to 0.68±0.01. The results showed that the values in both study groups changed reliably (R<0.001) compared to the control group, and compared to the beginning of treatment, it was observed in the statistical analysis that the values changed reliably (R<0.001) in both groups. The pulse index in group 1 was 1.26±0.01 at the beginning of treatment, and after one month this value decreased to 1.19±0.01.

In group 2, which received NAS drugs for one month, this indicator, which was equal to 1.26±0.01 at the beginning of treatment, changed to 1.17±0.01 one month after treatment. The results showed that in both study groups the values changed reliably (R<0.001) compared to the

control group, and compared to the beginning of the treatment they changed reliably (R<0.001) in all groups, as reflected in the statistical analysis **Table 2.**

TABLE 2: CHANGES IN VASCULAR RESISTANCE INDICATORS IN THE MAIN AND INTRARENAL ARTERIES AGAINST THE BACKGROUND OF TREATMENT

Indicators	Control n=20	Group 1 n = 50		Group 2 n = 50	
		At the beginning of treatment	After 30 days	At the beginning of treatment	After 30 days
Main renal artery					
RI	0,65±0,01	0,74±0,01***	0,71±0,01***^^^	0,73±0,01***	0,68±0,01***^^^
PI	1,10±0,03	1,26±0,01***	1,19±0,01***^^^	1,26±0,01***	1,17±0,01***^^^
Segmental artery					
RI	0,63±0,02	0,71±0,01***	0,69±0,01**^	0,71±0,01***	0,67±0,01*^^^
PI	1,02±0,02	1,21±0,01***	1,17±0,01***^^^	1,22±0,01***	1,14±0,01***^^^
Interlobular artery					
RI	0,59±0,01	0,67±0,01***	0,65±0,01***^	0,68±0,01***	0,63±0,01***^^^
PI	0,98±0,01	1,13±0,01***	1,1±0,01***^^	1,14±0,01***	1,08±0,01***^^^

Note: * - differences are significant compared to the indicators of the control group (*- R<0.05, **- R<0.01, ***- R<0.001); ^ - differences are significant compared to the indicators at the beginning of treatment (^ - R<0.05, ^^ - R<0.01, ^^^ - R<0.001).

Resistance index in segmental renal arteries was equal to 0.71±0.01 value at the beginning of treatment in group 1 of patients with coronavirus-associated nephropathy treated only with scheduled recommendations, and after one month RI decreased to 0.69±0.01 value. In patients of the 2nd group, who received additional NAS drugs to the planned treatment for one month, the RI index was 0.71±0.01 at the beginning of the treatment, and after the treatment, it significantly decreased to 0.67±0.01.

The results showed that the values at the beginning of the treatment in both research groups changed reliably (R<0.001) compared to the control group, while the results after one month compared to the control group were observed to be moderate (R<0.01) and less reliable (R<0.05). Compared to the beginning of treatment, RI changed less reliably (R<0.05) in group 1 after one month, and more reliably (R<0.001) in group 2, which received NAS drugs for one month, was reflected in the statistical analysis.

If it is significant, the results after one month of treatment are less reliable (R<0.05) compared to the control group, i.e., healthy individuals; this indicates the effectiveness of our drug. The pulse index in group 1 was 1.21±0.01 at the beginning of treatment, and after one month, this value decreased to 1.17±0.01. In the 2nd group, which received NAS drugs for one month, this index, which was equal to 1.22±0.01 at the beginning of the treatment, decreased to 1.14±0.01 one month after the treatment, and it was observed that the results moved in a positive direction. The results were confirmed by statistical analysis that values in both study groups changed significantly (R<0.001) compared to the control group and significantly (R<0.001) compared to the beginning of treatment in all groups **Table 2.**

The resistance index in interlobular renal arteries was 0.67±0.01 at the beginning of treatment in group 1 of patients with coronavirus-associated nephropathy treated only according to the standard recommendations for COVID-19 disease. After one month, the RI decreased to 0.65±0.01.

In group 2 patients who received additional NAS drugs to the scheduled treatment for one month, the RI index was 0.68±0.01 at the beginning of treatment and significantly decreased to 0.63±0.01 after treatment. We observed that the results changed reliably (R<0.001) in both study groups compared to the control group. Still, the RI value after one month compared to the beginning of treatment was less reliable (R<0.05) in group 1. In group 2, who received NAS drugs for one month reliable (R<0.001) decrease was reflected in statistical analysis. The pulse index in group 1 was 1.13±0.01 at the beginning of treatment, and after one month, it decreased to 1.10±0.01. In the 2nd group that received NAS drugs, this indicator, which was equal to 1.14±0.01 at the beginning of the treatment, decreased to 1.08±0.01 one month after the treatment, and it was observed that the results moved in a positive direction. The results

showed that in both study groups, the values changed reliably (R<0.001) compared to the control group, and compared to the beginning of treatment, it was observed that the values changed reliably (R<0.01, R<0.001) in all groups **Table 2.** Visualizing the results in diagrams also directs the conclusions based on the statistical analysis (Fig. 3)**.**

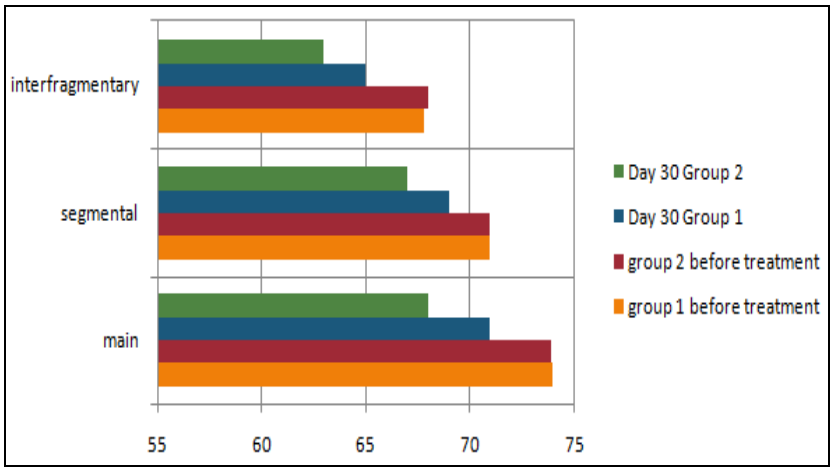

FIG. 3: VASCULAR RESISTANCE IN THE MAIN AND INTRARENAL ARTERIES CHANGES IN RESISTANCE INDEX (RI) AGAINST THE BACKGROUND OF TREATMENT

According to it, resistance and pulse indices in our studies were equal in both groups before treatment. The results obtained after one month revealed a different picture in certain groups. It was shown to be as effective as the standard treatment for COVID-19 and, in addition, the NAS drug **Fig. 3.**

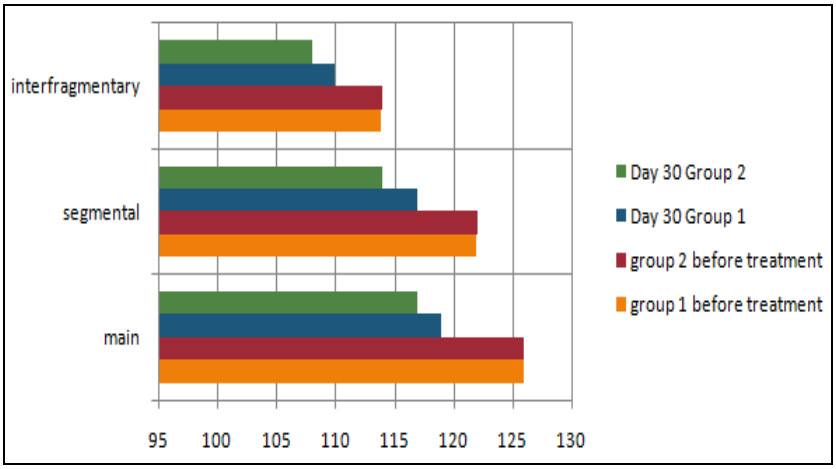

FIG. 4: VASCULAR RESISTANCE IN THE MAIN AND INTRARENAL ARTERIES CHANGES IN PULSE INDEX (PI) INDICATORS AGAINST THE BACKGROUND OF TREATMENT

RI and PI values were unreliable or less reliable (R<0.05) after one month in group 1, which consisted of patients who were satisfied with standard treatment after experiencing coronavirus-associated nephropathy. In group 2, who received NAS drugs in addition to standard treatment for one month, all values have a reliable (R<0.001) change, which is reflected in the diagram. However, compared to group 1, which was satisfied only with standard treatment, in group 2, which received NAS drugs in addition to standard treatment, a reliable (R<0.001) change in dopplerographic indicators was observed in all blood vessels of the main and intrarenal kidneys, so we recognize positive conclusions about NAC drug. In addition, in the studies carried out until now, A.M. Kelly and co-authors recognized in their study that among drugs with renoprotective effects, only NAC reliably reduced the risk of developing nephropathies with X-ray contrast [14]. Thus, Vs. Max and Vd, which indicate the blood flow in the kidney vessels, and RI and PI, which determine the level of resistance, are related to the rheology, volume (quantity) of blood, hemodynamic

disturbances in the cardiovascular system, and a chain of neuroendocrine control mechanisms, such as the renin-angiotensin system.In any kidney disease, this chain creates a number of imbalances in accordance with pathological processes.

Therefore, the study of intrarenal hemodynamics and vascular resistance by conducting dopplerography of renal blood vessels in research groups consisting of patients with coronavirus-associated nephropathy, as well as substantiating the positive effect of the drug N-acetylcysteine in our studies with specific laboratory analyzes as well as special instrumental examinations, is the real essence of our ongoing research.

CONCLUSION: Maximum systolic velocity and end-diastolic velocity indicators have changed negatively in patients who have experienced coronavirus-associated nephropathy. Resistance and pulse index increase in patients who have experienced coronavirus-associated nephropathy. Use of N-acetylcysteine drug leads to acceleration of Vs max and Vd and reduction of RI and PI in coronavirus-associated nephropathy. The use of N-acetylcysteine drug in coronavirus-associated nephropathy reduces the risk of severe renal complications, that is, acute kidney injury, caused by the cytopathic effect of SARS-CoV 2 infection on the kidneys.

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REFERENCES:

1. Abdullaev, Sh.S., Igamberdieva, R.Sh., Sharapov, O.N. "Renal Involvement in COVID-19: Clinical and Pathogenetic Aspects and Management of Patients with Chronic Kidney Disease." Clinical Nephrology 2021; 1: 63-67.
2. Vykhristenko LR, Schastlivenko AI, Bondareva LI, Sidorenko EV and Muzykova OG: "Renal Manifestations in COVID-19 Infection." Bulletin of VGMU 2021; 1: 7-23.
3. Treatment of Acute Kidney Injury in Patients with COVID-19.https://stopcovid19.com.ru/wp-content/uploads/2020/09/628_RUS_COVID19_Acute_Kidney_Injury_in_patients_with_COVID-19.pdf
4. Tomilina, N.A., Volgina, G.V. "Mechanisms of Kidney Damage in COVID-19." Copyright 2012–2022.
5. Cao M., Zhang D., Wang Y. *et al.* Clinical features of patients infected with the 2019 novel coronavirus (COVID-19) in Shanghai, China MedRxiv 06, 2020.
6. Cheng Y., Luo R., Wang K. *et al.* kidney disease is associated with in-hospital death of patients with COVID-19. KidneyInt 2020; 97: 829-38. https://pubmed.ncbi.nlm.nih.gov/32247631/
7. Ibrahim H., Perl A., Smith D et al. Therapeutic blockade of inflammation in severe COVID-19 infection with intravenous N-acetylcysteine Clin Immunol 2020; 219: 108544.
8. Luo P., Liu Y., Dong Liu D., Li J. Perspectives for the Use of N-acetylcysteine as a Candidate Drug to Treat COVID-19. Mini Rev Med Chem. 2020 Oct 27. DOI: 10.2174/1389557520666201027160833.
9. Jabbarov, O. O., Tursunova, L. D., Tashpulatova, M. X., Daminov, B. T., Boboev, K. T., & Maksudova, L. I. (2020). Associations of polymorphic markers aluins/deli> D Ace T-786C gene Enos3 in diabetic nefropate progressing for type 2 diabetes mellitus. International J of Research in Pharmaceutical Sciences, 11(4), 6028-6032.
10. Sultonov, N. N., Sabirov, M. O., Tashpulatova, M. H., & Maksudova, LI: Evaluating the effectiveness of antiplatelet therapy of the patients with kidney disease. European Journal of Molecular and Clinical Medicine, 2020; 7(8), 1500-1505.

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