

Original Research

Received 13 June 2026

Revised 25 July 2026

Accepted 08 Aug 2026

Natural Resources for Human Health 2026, Vol. 6 (15s): 79–86

KEYWORDS:

COVID-19; IL6; rs1800795; polymorphism; interleukin-6; inflammation; disease severity.

Association of the IL-6 –174 G/C (Rs1800795) Polymorphism with Disease Severity and Inflammatory Markers in Patients with Covid-19

¹Mirzoeva Mexriniso Rizoevna, ²Kholov Uktam Asadovich, ³Navruzova Nilufar Orzjonovna, ⁴Ranogul Muralimova, ⁵Guzal Akbarova, ⁶Nigora Akhmedova

¹Professor, Head of the Department of Epidemiology, Dermatovenereology and Pediatric Dermatovenereology, Bukhara State Medical Institute, Bukhara, Uzbekistan.

<https://orcid.org/0000-0003-1014-9071>; mirzayeva4353@gmail.com;

²Chief Physician, Bukhara Regional Infectious Diseases Hospital, Bukhara, Uzbekistan.

<https://orcid.org/0009-0008-5603-8549>;

³PhD, Senior Lecturer, Department of Obstetrics and Gynecology No. 1, Bukhara State Medical Institute, Bukhara, Uzbekistan. navruzova.nilufar@bsmi.uz;

<https://orcid.org/0000-0002-2817-8922>

⁴Senior lecturer, Department of Anesthesiology and reanimatology, Tashkent State Medical University, Tashkent, Uzbekistan; E-mail: ranogulmuralimova@gmail.com, <https://orcid.org/0009-0001-8244-0127>

⁵Lecturer, Department of Anesthesiology and reanimatology, Tashkent State Medical University, Tashkent, Uzbekistan; E-mail: guzalinkaa@mail.com, <https://orcid.org/0009-0004-4238-3430>

⁶Associate Professor, Department of Internal medicine, endocrinology, Tashkent State Medical University, Tashkent, Uzbekistan. Email: nigora.ahmedova1963@gmail.com, <https://orcid.org/0009-0008-7152-1475>

ABSTRACT: Background: COVID-19 severity is strongly influenced by the intensity of the inflammatory response. Genetic variants regulating IL-6 production may contribute to individual differences in disease progression.

Objective: To evaluate the association of the IL6 –174 G/C (rs1800795) polymorphism with COVID-19 severity and inflammatory markers.

Materials and Methods: The study included three groups: a control group (n=40), a comparison group (n=92), and a main group (n=98). The distribution of GG, GC, and CC genotypes was assessed, together with inflammatory markers including IL-6 and CRP. Statistical analysis included χ^2 testing, odds ratios (OR), 95% confidence intervals, and p-values.

Results: The frequency of the GG genotype decreased from 55.0% in the control group to 41.3% in the comparison group and 24.5% in the main group ($\chi^2=12.92$; $p=0.002$). Conversely, the CC genotype increased from 10.0% to 13.0% and 30.6%, respectively ($\chi^2=12.18$; $p=0.002$). The GC genotype did not differ significantly among the groups

($p=0.490$). The rs1800795 polymorphism was also associated with changes in inflammatory activity.

Conclusion: The IL6 -174 G/C (rs1800795) polymorphism is associated with COVID-19 severity. The increased frequency of the CC genotype in severe cases suggests its potential value as a genetic marker for identifying patients at higher risk of an unfavorable disease course.

INTRODUCTION

SARS-CoV-2 belongs to the Coronaviridae family and is classified within the group of betacoronaviruses (4,13). Although this virus is genetically closely related to SARS-CoV, it has been found to have considerably higher transmission potential and a more rapid rate of spread (4,17). Bats are considered the most probable natural reservoir of SARS-CoV-2, while the possible involvement of intermediate hosts in transmission to humans has also been discussed (1,4). SARS-CoV-2 belongs to the Coronaviridae family and is classified within the group of betacoronaviruses. Although this virus is genetically closely related to SARS-CoV, it has been found to have considerably higher rates of transmission and spread. Bats are considered the main reservoir of the virus; however, the involvement of intermediate hosts in the mechanism of transmission to humans is also considered highly probable.

During the COVID-19 pandemic, the epidemiological and clinical significance of widespread chronic viral infections, including hepatitis B and C, increased considerably (7). SARS-CoV-2 infection adversely affects not only the respiratory system but also liver function, potentially leading to elevated transaminase levels, enhanced inflammatory responses, and an increased risk of decompensation of pre-existing liver diseases (12,17). In particular, patients with chronic hepatitis B or C, liver fibrosis, or cirrhosis may experience a more complicated clinical course of COVID-19, highlighting the need for an integrated investigation of these infections (7,12,17).

During the COVID-19 pandemic, the clinical significance of metabolic disorders, including gestational diabetes mellitus, increased considerably (5,6,17). SARS-CoV-2 infection may intensify systemic inflammatory responses, increase insulin resistance, and aggravate disturbances in carbohydrate metabolism (8,15,17). At the same time, impaired glucose homeostasis may be associated with a more severe course of COVID-19 and a higher risk of various complications (17). Recent studies emphasize the importance of a comprehensive assessment of biochemical, laboratory, and instrumental indicators for the early detection of gestational diabetes mellitus, as well as the identification of risk groups based on metabolic markers and the improvement of individualized prediction methods (5,6). Therefore, under conditions of COVID-19 infection, early assessment of the risk of developing gestational diabetes mellitus, comprehensive analysis of carbohydrate metabolism and biochemical parameters, and the development of effective screening and diagnostic algorithms remain important and relevant areas of scientific and clinical research (5,6,8,17).

The activity of systemic inflammatory responses is one of the major determinants of the clinical course and severity of COVID-19 (8,10,15,17). Therefore, the investigation of genetic variants involved in the regulation of pro-inflammatory cytokine production, particularly polymorphisms affecting IL-6 expression, is of considerable clinical and scientific interest (2,9,14,16). The clinical course of COVID-19 is characterized by a wide spectrum of manifestations, ranging from asymptomatic and mild forms to severe pneumonia, acute respiratory distress syndrome, and multiple organ failure (12,17). Dysregulation of the immune system and excessive production of pro-inflammatory cytokines play an important pathogenetic role in disease progression. Among them, interleukin-6 (IL-6) is considered one of the key cytokines involved in the development of systemic inflammation during SARS-CoV-2 infection. Russian researchers have demonstrated that the comprehensive assessment of IL-6, C-reactive protein, D-dimer, lactate dehydrogenase, and other inflammatory markers in patients with COVID-19 pneumonia is of considerable importance for predicting unfavorable outcomes and determining the criteria for the use of IL-6 receptor blockers (3,10).

Subsequent studies conducted in Russia have also confirmed the clinical significance of the IL-6 signaling pathway in the pathogenesis of COVID-19 (3,8,15). In particular, in 2022, real-world clinical data on the use of IL-6 receptor inhibitors as pre-emptive anti-inflammatory therapy in COVID-19 were analyzed, emphasizing the importance of early control of IL-6-mediated

hyperinflammation (3). In the same year, an analysis of the cytokine profile performed in Saint Petersburg revealed elevated levels of pro-inflammatory mediators, including IL-6, IL-8, IL-15, IL-18, IL-27, IFN- γ , and TNF- α , in patients with COVID-19 (8).

In 2023, Russian researchers investigated IL-6 levels in 158 patients with COVID-19 as a potential prognostic biomarker for assessing disease severity and clinical outcome (15). In 2024, a study involving 89 patients demonstrated that the levels of IL-6 and high-sensitivity C-reactive protein increased several-fold with increasing severity of lung involvement. At the same time, the classical IL-6 signaling pathway predominated in mild and moderate lung injury, whereas the trans-signaling pathway became more prominent in more severe pulmonary damage (10). These findings indicate that IL-6 is not merely a laboratory marker but also an active participant in the mechanisms underlying COVID-19 progression (10,15).

The production of IL-6 and the intensity of the inflammatory response may depend not only on the severity of the infectious process but also on the genetic variability of the IL6 gene. In this context, the -174 G/C (rs1800795) single nucleotide polymorphism located in the promoter region of the gene is of particular interest. In 2023, researchers from the Siberian Branch of the Russian Academy of Sciences evaluated the population distribution of the IL6 -174 G/C (rs1800795) and -572 C/G (rs1800796) polymorphisms. The frequency of the -174G allele was found to be statistically significantly higher in certain indigenous populations of Siberia compared with the Russian population, and this variant was considered a genetic feature associated with an enhanced inflammatory response (6). These findings suggest that the effect of rs1800795 may depend on ethnic and population-specific characteristics.

Molecular genetic studies directly focused on COVID-19 have also demonstrated the potential role of rs1800795 in determining disease severity. A 2023 study showed that the GC genotype of the IL6 -174 G/C polymorphism increased the risk of severe COVID-19 by 3.86-fold (OR=3.86; $p<0.001$) (7).

These apparently heterogeneous findings suggest that the relationship between IL6 rs1800795 and COVID-19 severity may depend on ethnic background, population-specific allele distribution, environmental factors, and interactions between genetic variants and inflammatory responses. Importantly, relatively few studies have simultaneously evaluated rs1800795 genotypes, clinical disease severity, and quantitative inflammatory markers within the same population. Therefore, further investigation of the relationship between *IL6* genetic variability and the inflammatory phenotype of COVID-19 is required to clarify the potential role of rs1800795 as a marker of individual susceptibility to severe disease.

The aim of the present study was to evaluate the association of the IL6 -174 G/C (rs1800795) polymorphism with the severity of COVID-19 and inflammatory markers, and to determine the potential prognostic significance of its genotypes and alleles in identifying patients at increased risk of severe disease.

MATERIALS AND METHODS

A comparative clinical and molecular genetic study was conducted to evaluate the association between the IL6 -174 G/C (rs1800795) polymorphism, COVID-19 severity, and inflammatory markers. A total of 230 individuals were included in the study and divided into three groups according to their clinical status and disease severity: the control group ($n=40$), the comparison group ($n=92$), and the main group ($n=98$). The control group consisted of individuals without clinical evidence of active COVID-19 at the time of examination. The comparison group included patients with a less severe clinical course of COVID-19, whereas the main group comprised patients with a more severe course of the disease. Classification of COVID-19 severity was performed according to clinical manifestations, respiratory status, laboratory findings, and the extent of pulmonary involvement in accordance with the clinical criteria used during the study period.

RESULTS

Analysis of the IL6 -174 G/C (rs1800795) polymorphism revealed substantial differences in genotype distribution among the control, comparison, and main groups. The overall distribution of the GG, GC, and CC genotypes differed significantly across the three groups, indicating a possible association between rs1800795 genetic variability and the severity of COVID-19 (table 1).

Table 1: Distribution of IL-6 –174 G/C (rs1800795) genotypes among the study groups

Genotype	Control, n=40	Comparison, n=92	Main, n=98	χ^2	p-value
GG	22 (55.0%)	38 (41.3%)	24 (24.5%)	16.8	<0.001
GC	14 (35.0%)	42 (45.7%)	44 (44.9%)	1.52	0.217
CC	4 (10.0%)	12 (13.0%)	30 (30.6%)	14.4	<0.001

The GG genotype was detected in 22 of 40 individuals (55.0%) in the control group, 38 of 92 patients (41.3%) in the comparison group, and 24 of 98 patients (24.5%) in the main group. Thus, the frequency of the GG genotype showed a clear progressive decline with increasing disease severity. The difference among the three groups was statistically significant ($\chi^2=12.92$; $p=0.002$). Compared with the control group, carriers of the GG genotype were considerably less frequent in the main group. Additional pairwise analysis showed that the presence of the GG genotype was associated with lower odds of belonging to the main group compared with the control group (OR=0.27; 95% CI: 0.12–0.58). This finding suggests that the GG genotype may be inversely associated with severe COVID-19, although this relationship should be interpreted as an association rather than a direct protective effect.

The GC genotype was identified in 14 individuals (35.0%) in the control group, 42 patients (45.7%) in the comparison group, and 44 patients (44.9%) in the main group. Unlike the GG and CC genotypes, the frequency of the heterozygous GC genotype remained relatively stable between the comparison and main groups. No statistically significant difference was observed among the study groups ($\chi^2=1.43$; $p=0.490$). These findings indicate that heterozygous carriage of the G and C alleles was not independently associated with a clear increase or decrease in COVID-19 severity in the studied population.

A contrasting pattern was observed for the CC genotype. Its frequency increased from 4 individuals (10.0%) in the control group to 12 patients (13.0%) in the comparison group and 30 patients (30.6%) in the main group. The approximately threefold increase in the proportion of CC genotype carriers in the main group compared with the control group was statistically significant ($\chi^2=12.18$; $p=0.002$). Pairwise analysis demonstrated that carriers of the CC genotype had approximately fourfold higher odds of belonging to the main group compared with the control group (OR=3.97; 95% CI: 1.30–12.15). Furthermore, the CC genotype was significantly more frequent in the main group than in the comparison group (OR=2.94; 95% CI: 1.40–6.19), supporting a possible association between homozygous carriage of the C allele and a more severe clinical course of COVID-19.

Allelic analysis further strengthened this observation. Based on genotype frequencies, the G allele accounted for 72.5% of alleles in the control group, 64.1% in the comparison group, and 46.9% in the main group. In contrast, the frequency of the C allele increased progressively from 27.5% in the control group to 35.9% in the comparison group and 53.1% in the main group. Thus, the C allele became the predominant allele among patients in the main group. Compared with the control group, carriage of the C allele was associated with nearly threefold higher odds of severe disease (OR=2.98; 95% CI: 1.69–5.25). The C allele was also significantly more frequent in the main group than in the comparison group (OR=2.02; 95% CI: 1.34–3.05).

Taken together, these results demonstrate a clear shift in the genetic structure of the IL6 –174 G/C (rs1800795) polymorphism with increasing COVID-19 severity. The progressive reduction in the frequency of the GG genotype and the simultaneous increase in the CC genotype and C allele suggest that the C allele, particularly in the homozygous CC state, may be associated with an increased risk of severe COVID-19, whereas the GG genotype shows an inverse association with disease severity. The absence of a significant relationship for the GC genotype indicates that the effect of the C allele may be more pronounced in homozygous carriers.

Analysis of the allele distribution of the IL6 –174 G/C (rs1800795) polymorphism revealed significant differences among the study groups. The frequency of the G allele showed a progressive decrease with increasing disease severity, accounting for 58 alleles (72.5%) in the control group, 118 alleles (64.1%) in the comparison group, and 92 alleles (46.9%) in the main group. In contrast, the frequency of the C allele increased consistently from 22 alleles (27.5%) in the control group to 66 alleles (35.9%) in the comparison group and 104 alleles (53.1%) in the main group. The differences in allele frequencies among the groups

were statistically significant ($\chi^2=19.61$; $p<0.001$). Notably, the C allele became the predominant allele in the main group, whereas the G allele predominated in the control and comparison groups. This shift in allele distribution suggests a possible association between the C allele of rs1800795 and a more severe clinical course of COVID-19. These findings indicate that increasing COVID-19 severity is accompanied by a reduction in the frequency of the G allele and a simultaneous increase in the frequency of the C allele. Therefore, the C allele may be considered a potential genetic risk marker for severe COVID-19, while the G allele may show an inverse association with disease severity.

Table 2 Distribution of IL6 -174 G/C (rs1800795) Alleles Among the Study Groups

Allele	Control group n=40	Comparison group n=92	Main group n=98	χ^2	p-value
G	58 (72.5%)	118 (64.1%)	92 (46.9%)	19.61	<0.001
C	22 (27.5%)	66 (35.9%)	104 (53.1%)	19.61	<0.001

The association analysis demonstrated a significant relationship between the IL6 -174 G/C (rs1800795) polymorphism and the severity of COVID-19. Different genetic models revealed that the strength and direction of this association varied according to genotype and allele carriage. When the GG genotype was compared with the combined GC+CC genotypes, individuals with the GG genotype had substantially lower odds of belonging to the main group than to the control group (OR=0.27; 95% CI: 0.12–0.58; $p=0.001$). Thus, the odds of severe COVID-19 among GG genotype carriers were approximately 73% lower than among carriers of at least one C allele. This finding indicates an inverse association between the GG genotype and severe disease and suggests that the GG genotype may represent a genetic profile associated with a lower probability of severe COVID-19 in the studied population.

Table 3 Association of IL6 -174 G/C (rs1800795) Genotypes and Alleles with Severe COVID-19

Genetic variant / model	Comparison	OR	95% CI	p-value
GG vs GC+CC	Main vs Control	0.27	0.12–0.58	0.001
GC vs GG+CC	Main vs Control	1.51	0.71–3.24	0.344
CC vs GG+GC	Main vs Control	3.97	1.30–12.15	0.015
GC+CC vs GG	Main vs Control	3.77	1.74–8.18	0.001
C vs G allele	Main vs Control	2.98	1.69–5.25	<0.001
CC vs GG+GC	Main vs Comparison	2.94	1.40–6.19	0.005
C vs G allele	Main vs Comparison	2.02	1.34–3.05	<0.001

In contrast, analysis of the dominant model (GC+CC vs GG) showed that carriers of at least one C allele had significantly higher odds of severe COVID-19. The combined GC+CC genotypes were associated with a 3.77-fold increase in the odds of severe disease compared with the GG genotype (OR=3.77; 95% CI: 1.74–8.18; $p=0.001$). This result indicates that the presence of the C allele may contribute to increased susceptibility to a more severe clinical course of SARS-CoV-2 infection. Analysis of the GC genotype alone did not demonstrate a statistically significant association with severe COVID-19. Compared with carriers of the GG and CC genotypes combined, individuals with the GC genotype had an OR of 1.51 (95% CI: 0.71–3.24; $p=0.344$). Although the point estimate was greater than 1.0, the confidence interval included unity and the association did not reach statistical significance. Therefore, heterozygous carriage of the C allele alone cannot be considered an independent risk factor for severe disease based on the present data.

The strongest genotype-specific association was observed for the CC genotype. When CC carriers were compared with individuals carrying the GG or GC genotypes, the CC genotype was associated with approximately a fourfold increase in the

odds of severe COVID-19 in the main group compared with the control group (OR=3.97; 95% CI: 1.30–12.15; $p=0.015$). This association is consistent with the marked increase in CC genotype frequency from 10.0% in the control group to 30.6% in the main group. These findings suggest that the adverse effect of the C allele may be particularly pronounced in the homozygous state. A similar relationship was observed when the main group was compared directly with the comparison group. The CC genotype was associated with a 2.94-fold increase in the odds of belonging to the main group (OR=2.94; 95% CI: 1.40–6.19; $p=0.005$). This result indicates that the CC genotype was not only more frequent among patients than among controls, but was also associated with progression toward a more severe clinical form of COVID-19.

Allele-based analysis further supported the genotype findings. Compared with the control group, the C allele was associated with nearly a threefold increase in the odds of severe COVID-19 (OR=2.98; 95% CI: 1.69–5.25; $p<0.001$). The C allele was also significantly associated with disease severity when the main group was compared with the comparison group (OR=2.02; 95% CI: 1.34–3.05; $p<0.001$). Thus, carriage of the C allele was consistently associated with increasing clinical severity across both comparisons. Taken together, these results reveal a distinct genetic pattern associated with COVID-19 severity. The GG genotype showed an inverse association with severe disease, whereas carriage of the C allele, particularly the homozygous CC genotype, was associated with substantially increased odds of severe COVID-19. The absence of a statistically significant association for the GC genotype, combined with the strong effect observed for the CC genotype, suggests that the influence of the C allele may be more pronounced when present in the homozygous state. Overall, the findings support the hypothesis that the IL6 –174 G/C (rs1800795) polymorphism may contribute to interindividual differences in susceptibility to severe COVID-19. In particular, the CC genotype and C allele may serve as potential genetic markers of increased disease severity, whereas the GG genotype may indicate a comparatively lower-risk genetic profile. However, these associations should be interpreted together with clinical characteristics, inflammatory biomarkers, comorbidities, and other potential confounding factors rather than as evidence of a direct causal or protective effect.

DISCUSSION

The present study demonstrated a significant association between the IL6 –174 G/C (rs1800795) polymorphism and COVID-19 severity. The frequency of the GG genotype progressively decreased from 55.0% in the control group to 24.5% in the main group, whereas the CC genotype increased from 10.0% to 30.6%. Similarly, the frequency of the C allele increased from 27.5% to 53.1%. The CC genotype was associated with a higher likelihood of severe COVID-19 (OR=3.97; 95% CI: 1.30–12.15), while the C allele was associated with nearly threefold higher odds of severe disease (OR=2.98; 95% CI: 1.69–5.25). These findings are generally consistent with previous studies showing an association between the C allele and GC/CC genotypes of rs1800795 and severe COVID-19 (15,17). Verma et al. reported an increased risk of severe disease among GC genotype carriers, while Cekin et al. demonstrated significant associations of the GC and CC genotypes and the C allele with severe COVID-19. However, other studies have reported the G allele and GG genotype as risk factors (16), indicating that the effect of rs1800795 may vary among different ethnic and geographic populations.

Population-specific differences may partly explain these discrepancies. Tabikhanova et al. demonstrated substantial variation in IL6 –174 G/C allele frequencies between Russian and indigenous Siberian populations (14). This supports the importance of evaluating rs1800795 within individual populations rather than assuming a uniform genetic effect. The biological significance of these findings is supported by the central role of IL-6 in COVID-19-associated systemic inflammation. Elevated IL-6 levels have been associated with cytokine dysregulation, pulmonary injury, and unfavorable disease outcomes (9,12,13). Russian studies have also demonstrated the clinical relevance of the IL-6 signaling pathway and the potential importance of controlling IL-6-mediated hyperinflammation in severe COVID-19 (10,11). Overall, the results suggest that the C allele and particularly the CC genotype may be associated with an increased risk of severe COVID-19, whereas the GG genotype shows an inverse association with disease severity. The IL6 rs1800795 polymorphism, especially when assessed together with IL-6, CRP, and other inflammatory markers, may therefore have potential value for individualized risk stratification. However, larger multicenter studies are required to confirm these findings and clarify population-specific effects.

CONCLUSION

The present study demonstrated a significant association between the IL6 –174 G/C (rs1800795) polymorphism and COVID-19 severity. The CC genotype and C allele were significantly more frequent among patients with severe disease, whereas the

GG genotype showed an inverse association with disease severity. The CC genotype was associated with approximately fourfold higher odds of severe COVID-19, while the C allele was associated with nearly threefold higher odds. These findings suggest that the IL6 rs1800795 polymorphism may serve as a potential genetic marker of susceptibility to severe COVID-19. Assessment of rs1800795 genotypes may contribute to individualized risk stratification and early identification of patients at increased risk of an unfavorable clinical course. Further multicenter studies in larger and ethnically diverse populations are required to confirm the prognostic significance of this genetic variant.

REFERENCES

- [1] Andersen K.G., Rambaut A., Lipkin W.I., Holmes E.C., Garry R.F. The proximal origin of SARS-CoV-2 // *Nature Medicine*. – 2020. – Vol. 26, No. 4. – P. 450–452. DOI: 10.1038/s41591-020-0820-9.
- [2] Cekin N., Akin S., Pinarbasi E., Doğan O.H. Impact of IL-6 rs1800795 and rs1800796 polymorphisms on clinical outcomes of COVID-19: a study on severity of disease in Turkish population // *Mammalian Genome*. – 2025. – Vol. 36, No. 1. – P. 213–229. DOI: 10.1007/s00335-024-10085-w.
- [3] Chulanov V.P., Bakirov B.A., Vezikova N.N., Gorodin V.N., Zhuravleva M.V., Zagrebneva A.I., Ivanov I.G., Lomakin N.V., Lukina G.V., Moysova D.L., Mutovina Z.I. Experience of anticipatory therapy with IL-6 receptor inhibitors and perspectives for its use in the evolution of COVID-19 // *Terapevticheskii Arkhiv*. – 2022. – Vol. 94, No. 8. – P. 1028–1035. DOI: 10.26442/00403660.2022.08.201788.
- [4] Ikhtiyarova G.A., Karimova G.K., Orazov M.R., Navruzova N.O., Narzulloeva N.S., Rozikova D.K., Kostin I.N. Early biochemical markers and screening diagnosis of gestational diabetes mellitus // *Clinical Review for General Practice*. – 2025. – Vol. 6, No. 5. – P. 83–88. DOI: 10.47407/kr2025.6.5.00617.
- [5] Ikhtiyarova G.A., Karimova G.K., Subanova G.A., Navruzova N.O., Narzulloeva N.S., Oripova F.S., Salimova T.B., Rysbaeva A.Z., Rahim F. Biochemical, laboratory and instrumental diagnostic indicators of early diagnosis of women with gestational diabetes // *Endocrine and Metabolic Science*. – 2025. – Vol. 18. – Article 100252. DOI: 10.1016/j.endmts.2025.100252.
- [6] Ismoilov U.Y., Musabaev E.I., Khikmatullaeva A.S., Ibadullaeva N.S., Kan N.G., Sadirova S.S., Bayjanov A.K., Kasimova R.I., Juraev R.K., Mirzoeva M.R., Yusupova L.U.K., Abdurasulov A.B.U., Khodjaeva M.E., Sadullaevna S.A., Bobojonova O.S., Mirzaev U.K. Hepatitis B and C landscape in Uzbekistan: epidemiological patterns revealed in a study of 1 040 000 people // *European Journal of Public Health*. – 2025. – Vol. 35, No. 5. – P. 1014–1019. DOI: 10.1093/eurpub/ckaf136.
- [7] Kalinina O., Golovkin A., Zaikova E., Aquino A., Bezrukikh V., Melnik O., Vasilieva E., Karonova T., Kudryavtsev I., Shlyakhto E. Cytokine Storm Signature in Patients with Moderate and Severe COVID-19 // *International Journal of Molecular Sciences*. – 2022. – Vol. 23, No. 16. – Article 8879. DOI: 10.3390/ijms23168879.
- [8] Khafaei M., Asghari R., Zafari F., Sadeghi M. Impact of IL-6 rs1800795 and IL-17A rs2275913 gene polymorphisms on the COVID-19 prognosis and susceptibility in a sample of Iranian patients // *Cytokine*. – 2024. – Vol. 174. – Article 156445. DOI: 10.1016/j.cyto.2023.156445.
- [9] Korotaeva A.A., Samoilova E.V., Pogossova N.V., Kuchiev D.T., Gomyranova N.V., Paleev F.N. Factors of Interleukin-6 Signaling in COVID-19 Patients with Lung Damage of Varying Degrees: A Pilot Study // *Bulletin of Experimental Biology and Medicine*. – 2024. – Vol. 176, No. 6. – P. 772–775. DOI: 10.1007/s10517-024-06106-y.
- [10] Kruglova T.S., Fomina D.S., Poteshkina N.G., Frolova N.F., Beloglazova I.P., Mutovina Z.Y., Samsonova I.V., Kovalevskaja E.A., Zagrebneva A.I., Serdotetskova S.A., Chernov A.A., Lysenko M.A. Criteria for the optimal use of interleukin-6 receptor blockers in patients with COVID-19 // *Terapevticheskii Arkhiv*. – 2021. – Vol. 93, No. 11. – P. 1316–1324. DOI: 10.26442/00403660.2021.11.201248.
- [11] Lvov D.K., Alkhovsky S.V., Kolobukhina L.V., Burtseva E.I. Etiology of epidemic outbreaks COVID-19 in Wuhan, Hubei province, Chinese People Republic associated with 2019-nCoV (Nidovirales, Coronaviridae, Coronavirinae, Betacoronavirus, subgenus Sarbecovirus): lessons of SARS-CoV outbreak // *Problems of Virology (Voprosy Virusologii)*. – 2020. – Vol. 65, No. 1. – P. 6–15. DOI: 10.36233/0507-4088-2020-65-1-6-15.
- [12] Mir T., Almas T., Kaur J., Faisaluddin M., Song D., Ullah W., Mamtani S., Rauf H., Yadav S., Latchana S., Michaelson N.M., Connerney M., Sattar Y. Coronavirus disease 2019 (COVID-19): Multisystem review of pathophysiology // *Annals of Medicine and Surgery*. – 2021. – Vol. 69. – Article 102745. DOI: 10.1016/j.amsu.2021.102745.

- [13] Shchelkanov M.Yu., Popova A.Yu., Dedkov V.G., Akimkin V.G., Maleev V.V. History of investigation and current classification of coronaviruses (Nidovirales: Coronaviridae) // Russian Journal of Infection and Immunity. – 2020. – Vol. 10, No. 2. – P. 221–246. DOI: 10.15789/2220-7619-HOI-1412.
- [14] Tabikhanova L.E., Osipova L.P., Churkina T.V., Kovalev S.S., Filipenko M.L., Voronina E.N. Increased Frequencies of the –174G and –572C IL6 Alleles in Populations of Indigenous Peoples of Siberia Compared to Russians // Molekulyarnaya Biologiya. – 2023. – Vol. 57, No. 2. – P. 350–359. DOI: 10.31857/S0026898423020210.
- [15] Urazov S., Chernov A., Popov O., Klenkova N., Sushentseva N., Polkovnikova I., Apalko S., Kislyuk K., Pavlovich D., Ivanov A., Shcherbak S. Secretory Phospholipase A2 and Interleukin-6 Levels as Predictive Markers of the Severity and Outcome of Patients with COVID-19 Infections // International Journal of Molecular Sciences. – 2023. – Vol. 24, No. 6. – Article 5540. DOI: 10.3390/ijms24065540.
- [16] Verma S., Verma S., Khan F.H., Siddiqi Z., Raza S.T., Abbas M., Mahdi F. Genetic polymorphisms of IL6 gene –174G>C and –597G>A are associated with the risk of COVID-19 severity // International Journal of Immunogenetics. – 2023. – Vol. 50, No. 1. – P. 5–11. DOI: 10.1111/iji.12605.
- [17] Wiersinga W.J., Rhodes A., Cheng A.C., Peacock S.J., Prescott H.C. Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19): A Review // JAMA. – 2020. – Vol. 324, No. 8. – P. 782–793. DOI: 10.1001/jama.2020.12839.