IMMUNOGENETIC ASPECTS OF COVID-19 IN THE REPUBLIC OF KARAKALPAKSTAN

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Relevance of the topic. The global pandemic caused by SARS-CoV-2 highlighted significant inter-individual variation in disease severity, ranging from asymptomatic infection to fatal acute respiratory distress syndrome (ARDS) and systemic hyperinflammation. Beyond classical risk factors like age and cardiovascular comorbidities, host immunogenetic architecture specifically human leukocyte antigen (HLA) gene polymorphisms and cytokine single nucleotide polymorphisms (SNPs) critically dictates susceptibility and clinical progression. Major histocompatibility complex (MHC/HLA) class I (HLA-A, HLA-B) and class II (HLA-DRB1) allele binding affinities govern early T-cell activation and viral clearance, directly influencing whether an infection remains mild or advances to pulmonary damage.

Concurrently, functional polymorphisms within promoter regions of key inflammatory genes (such as IL-6 -174 G/C, TNF-α -308 G/A, and IL-10 -1082 A/G) modulate baseline transcript levels and systemic secretion rates. Genetically driven hyper-activation of these pro-inflammatory pathways triggers a "cytokine storm," exacerbating microvascular endothelial disruption, excessive neutrophil recruitment, and systemic oxidative stress. Despite extensive global research, the immunogenetic landscape of COVID-19 in Central Asia, particularly within the Republic of Karakalpakstan, remains understudied.

Material and methods

This clinical investigation was conducted at the Bukhara Regional Infectious Diseases Hospital (2020–2023) to evaluate the immunogenetic and clinical characteristics of COVID-19. The study cohort comprised 450 participants: 450 hospitalized patients with confirmed SARS-CoV-2 infection and 20 age- and sex-matched healthy controls. Inclusion criteria for patients required age under 65 years, admission within 10 days of symptom onset, and absence of major severe chronic comorbidities.

Patients were categorized into two distinct clinical presentation variants based on primary evaluation parameters, including general intoxication, respiratory symptoms, altered consciousness, and initial laboratory derangements.

Statistical processing was performed using variation statistics. Continuous variables were expressed as mean and standard error (M±m), and categorical data as percentages (%). Group comparisons were evaluated using Student's t-test, applying four standard significance thresholds ($p < 0.001$, $p < 0.010$, $p < 0.050$ and $p > 0.050$).

Results

Statistically significant differences in COVID-19 manifestation were observed between patients from Karakalpakstan districts and Nukus city. Patients from the districts more frequently presented with severe or extremely severe disease, wave-like clinical courses, "CT-3" lung involvement (50–75%), grade 3 respiratory failure, and requirement for mechanical ventilation. While common symptoms like fatigue, headache, dry cough, dyspnea, sore throat, and anosmia were present in both cohorts, district patients reported higher frequencies of air-hunger dyspnea, wet cough, rhinorrhea, sore throat, and diarrhea. Conversely, reported severe fatigue was less frequent in district patients, likely reflecting reduced cytokine storm severity. Regarding complications, district patients showed higher rates of thrombosis but lower incidences of liver failure and hyperglycemia. Concomitant pathology was

generally comparable, though stage 3 hypertension and chronic cholecystitis were significantly less prevalent in district patients. Recovery rates were significantly higher among residents of Nukus city.

Immunogenetic evaluation of the MTHFR C677T polymorphism revealed notable allelic and genotypic variations. Compared to controls, the main COVID-19 group exhibited a significantly lower frequency of the wild-type C allele (OR 0.6) and a higher frequency of the mutant T allele (OR 1.7, 2 = 4.5, p = 0.05), identifying the T allele as a susceptibility marker. In patients with moderate disease severity, the protective role of the C allele (OR 0.5) and risk association of the T allele (OR 2.0, 2 = 5.6, p = 0.03) were further pronounced, with the C/C genotype demonstrating a significant protective effect (OR 0.4, 2 = 5.4, p = 0.03). In contrast, no statistically significant differences in allelic or genotypic distributions of the MTHFR C677T variant were observed when comparing severe COVID-19 patients directly to the control group.

Conclusion

By 2023, the epidemiological trajectory of COVID-19 in the Republic of Karakalpakstan demonstrated stabilization and a progressive decline in overall morbidity rates. However, the disease disproportionately affected working-age individuals (31–54 years), accompanied by a gradual shift toward older demographics. Nukus city remained the primary focal point for SARS-CoV-2 transmission, underscoring the need for targeted preventative measures, enhanced vaccination coverage, and sustained population-level immunity.

Immunogenetic profiling revealed distinct territory-specific genetic susceptibility patterns across the region. Among rural populations, the G/A genotype of the TNF G4682A polymorphism served as a significant negative prognostic marker for severe disease compared to urban Nukus residents. These results confirm that regional immunogenetic profiling provides a

precise framework for personalized risk stratification and targeted public health interventions across urban and rural populations.

References

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