CLINICAL HETEROGENEITY AND PROGNOSTIC STRATIFICATION OF POST-COVID RHEUMATIC DISEASES: FROM MOLECULAR BIOMARKERS TO JOINT SYNDROME PHENOTYPES

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ABSTRACT

Rheumatic diseases are clinically heterogeneous conditions in which disease activity, progression rate, and organ involvement vary widely among patients. This heterogeneity has become even more pronounced in the post-COVID-19 era. SARS-CoV-2 infection acts as a systemic stressor capable of reprogramming immune responses, disrupting endothelial homeostasis, and accelerating fibrotic and degenerative processes. Consequently, patients with ankylosing spondylitis, rheumatoid arthritis, reactive arthritis, osteoarthritis, allergic vasculitis, and systemic sclerosis frequently experience altered disease trajectories following COVID-19

Introduction. Rheumatic diseases are clinically heterogeneous conditions in which disease activity, progression rate, and organ involvement vary widely among patients. This heterogeneity has become even more pronounced in the post-COVID-19 era. SARS-CoV-2 infection acts as a systemic stressor capable of reprogramming immune responses, disrupting endothelial homeostasis, and accelerating fibrotic and degenerative processes. Consequently, patients with ankylosing spondylitis, rheumatoid arthritis, reactive arthritis, osteoarthritis, allergic vasculitis, and systemic sclerosis frequently experience altered disease trajectories following COVID-19.

Post-COVID conditions are associated with persistent immune activation, microvascular injury, and metabolic dysregulation. These mechanisms overlap with established pathways in rheumatic diseases and contribute to worsening joint syndrome, increased structural damage, and greater extra-articular involvement. Importantly, traditional clinical assessment tools alone are often insufficient to capture these complex changes.

Recent research highlights the prognostic value of molecular biomarkers such as anti-CD74 antibodies, cartilage oligomeric matrix protein (COMP), TGF-β, LOX, and CXCL10, alongside inflammatory cytokines (IL-6, TNF-α). Genetic susceptibility and environmental exposure further modify disease expression, particularly in reactive arthritis and rheumatoid arthritis. Advanced imaging techniques allow early detection of joint pathology, enabling more accurate phenotyping and prognostic stratification.

The aim of this thesis is to characterize clinical heterogeneity and identify prognostic markers that define joint syndrome phenotypes and systemic involvement in post-COVID rheumatic diseases.

Methods. An integrative analysis was conducted using observational and cohort studies published between 2020 and 2024, retrieved from Scopus, PubMed, and Web of Science. Additional clinical data from post-COVID rheumatology cohorts in Central Asia were included.

The evaluation framework comprised:

- Clinical disease activity indices (BASDAI, DAS28, joint count scores)
- Endothelial markers (NO, VCAM-1, endothelin-1)
- Inflammatory cytokines (IL-6, TNF-α, CXCL10)
- Fibrotic mediators (TGF-β, LOX)
- Autoimmune biomarkers (anti-CD74 antibodies)
- Cartilage metabolism marker (COMP)
- Imaging modalities (MRI, ultrasound, radiography)
- Genetic polymorphism analysis in reactive arthritis
- Hepatobiliary biochemical assessment in ischemic heart disease

Patients were stratified based on post-COVID status, disease phenotype, and biomarker profiles.

Results. Post-COVID ankylosing spondylitis patients demonstrated significantly higher disease activity, with BASDAI scores increased by 1.6–1.9 points compared to non-COVID cohorts. Elevated anti-CD74 antibody levels were detected in 43–49% of patients and were associated with more pronounced axial stiffness and reduced spinal mobility.

In rheumatoid arthritis, environmental exposure and post-COVID immune dysregulation resulted in elevated IL-6 and TNF-α levels (2.4–2.9-fold increase), correlating with higher DAS28 scores and increased endothelial dysfunction observed in over 60% of patients.

Reactive arthritis exhibited marked phenotypic variability. Genetic susceptibility significantly influenced disease severity, with MRI revealing early synovitis, enthesitis, and bone marrow edema in approximately 75% of post-COVID cases. These imaging findings preceded clinical deterioration and radiographic changes.

Osteoarthritis patients showed elevated COMP levels during active disease phases. Targeted therapeutic strategies reduced COMP concentrations by 28–35%, reflecting improved cartilage metabolic balance and reduced progression of structural damage.

Systemic sclerosis patients displayed persistently high TGF-β, LOX, and CXCL10 levels, which correlated with both cutaneous thickening and visceral fibrosis ($r = 0.71–0.77$). These biomarkers effectively differentiated patients with rapidly progressive disease from those with stable courses.

Among patients with chronic ischemic heart disease, hepatobiliary dysfunction persisted in 45–50% of cases, indicating ongoing metabolic and endothelial stress in the post-COVID period.

Discussion. This analysis demonstrates that post-COVID rheumatic diseases cannot be adequately managed using uniform clinical approaches. Instead, clinical heterogeneity reflects distinct pathophysiological phenotypes driven by immune, endothelial, fibrotic, genetic, and metabolic factors. Biomarker-based stratification allows early identification of high-risk patients and supports personalized therapeutic decision-making.

Anti-CD74 and COMP serve as valuable disease-specific markers, while fibrotic mediators provide insight into systemic progression. Imaging findings refine phenotypic

classification, particularly in reactive arthritis, and genetic profiling explains inter-individual variability.

These findings underscore the importance of integrated prognostic models combining clinical, laboratory, imaging, and genetic data in the management of post-COVID rheumatic diseases

Literature:

1.Buranova S. N., Khalmetova F. I. STUDY OF THE ROLE OF TGF-B, LOX, AND CXCL10 IN THE PROGRESSION OF SKIN AND VISCERAL LESIONS IN PATIENTS WITH SYSTEMIC SCLERODERMA //JOURNAL OF MULTIDISCIPLINARY BULLETIN. – 2025. – Т. 8. – №. 9. – С. 43-46.

2.Buranova S., Ahmedov X., Rahimova M. Osteoartritli bemorlarda tog ‘ay oligomer matriks oqsili ko’rsatkichlarini yaxshilashga qaratilgan terapevtik tadbirlarning ahamiyati. – 2024.

3.Khalmetova F. et al. GENETIC ASPECTS OF REACTIVE ARTHRITIS //Farg'ona davlat universiteti. – 2023. – №. 1. – С. 133-133