



ENVIRONMENTAL, METABOLIC, AND ENDOTHELIAL DETERMINANTS OF DISEASE ACTIVITY IN POST-COVID INFLAMMATORY AND DEGENERATIVE JOINT DISORDERS

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ABSTRACT

Rheumatic diseases represent a multifactorial group of conditions in which genetic predisposition, immune dysregulation, endothelial dysfunction, and environmental exposures interact to determine disease onset and progression. The COVID-19 pandemic has intensified these interactions by inducing persistent systemic inflammation, vascular injury, and metabolic imbalance. Post-COVID-19 conditions have been associated with worsening clinical outcomes in ankylosing spondylitis, rheumatoid arthritis, reactive arthritis, osteoarthritis, allergic vasculitis, and systemic sclerosis, as well as in patients with comorbid ischemic heart disease.

Introduction. Rheumatic diseases represent a multifactorial group of conditions in which genetic predisposition, immune dysregulation, endothelial dysfunction, and environmental exposures interact to determine disease onset and progression. The COVID-19 pandemic has intensified these interactions by inducing persistent systemic inflammation, vascular injury, and metabolic imbalance. Post-COVID-19 conditions have been associated with worsening clinical outcomes in ankylosing spondylitis, rheumatoid arthritis, reactive arthritis, osteoarthritis, allergic vasculitis, and systemic sclerosis, as well as in patients with comorbid ischemic heart disease.

Environmental factors—such as air pollution, occupational exposure to chemicals, and lifestyle-related metabolic stress—are well-established contributors to immune activation in rheumatic diseases. In the post-COVID context, these factors appear to synergize with viral-induced endothelial dysfunction, leading to amplified cytokine production, impaired tissue perfusion, and accelerated connective tissue remodeling. This is particularly evident in patients with pre-existing inflammatory joint diseases, where post-COVID sequelae may precipitate disease flares and structural joint damage.

Biomarkers including anti-CD74 antibodies, COMP, IL-6, TNF- α , TGF- β , LOX, and CXCL10 have gained prominence in characterizing disease activity and prognosis. Advanced imaging modalities and genetic profiling further enhance understanding of disease heterogeneity, especially in reactive arthritis. This thesis explores how environmental and metabolic determinants interact with endothelial and immune pathways to influence post-COVID rheumatic disease progression.

Methods. A narrative-integrative analysis was conducted using peer-reviewed studies published between 2020 and 2024 in Scopus, PubMed, and Web of Science, alongside regional clinical observations. Data from over 130 studies were synthesized.

The methodological framework included:

- Assessment of environmental exposure (urban air pollution indices, occupational risk factors)
- Measurement of immune biomarkers (IL-6, TNF- α , CXCL10)
- Evaluation of endothelial function (NO levels, VCAM-1, ICAM-1)
- Determination of cartilage metabolism using COMP assays
- Serological detection of anti-CD74 antibodies
- Fibrotic marker profiling (TGF- β , LOX)
- Imaging assessment (MRI, ultrasound)
- Genetic susceptibility analysis in reactive arthritis
- Biochemical evaluation of hepatobiliary function in ischemic heart disease

Comparisons were made between post-COVID and pre-COVID rheumatic disease cohorts.

Results. Environmental exposure was associated with heightened immune activation in rheumatoid arthritis patients, with IL-6 and TNF- α levels elevated by 2.3–2.8 times in individuals residing in high-pollution urban areas. These changes were accompanied by endothelial dysfunction in approximately 63% of post-COVID patients, as evidenced by reduced NO bioavailability and increased VCAM-1 expression.

In ankylosing spondylitis, post-COVID patients exhibited higher disease activity scores and elevated anti-CD74 antibody titers in about 46% of cases, supporting the biomarker's diagnostic relevance in specific populations.

Reactive arthritis patients demonstrated significant variability in joint syndrome severity. Genetic predisposition influenced clinical expression, while MRI identified early inflammatory changes in over 70% of cases, underscoring the importance of imaging in disease assessment.

Osteoarthritis patients undergoing therapeutic interventions aimed at cartilage preservation showed a 27–32% decrease in serum COMP levels, indicating improved cartilage metabolic balance despite ongoing systemic inflammation.

Systemic sclerosis patients revealed markedly elevated TGF- β , LOX, and CXCL10 levels, which correlated strongly with the severity of skin thickening and visceral involvement ($r = 0.68$ – 0.75), reflecting environmentally and metabolically driven fibrotic progression.

In patients with chronic ischemic heart disease, hepatobiliary dysfunction persisted in 44–49% of cases, suggesting that metabolic and endothelial stress remains inadequately addressed by standard therapy alone in the post-COVID setting.

Discussion. The findings demonstrate that environmental and metabolic factors significantly modulate the impact of post-COVID sequelae on rheumatic disease progression. Endothelial dysfunction emerges as a critical mediator linking environmental exposure, immune activation, and tissue remodeling. Persistent cytokine elevation amplifies cartilage degradation, fibrosis, and joint inflammation.

Biomarkers such as anti-CD74 and COMP provide clinically actionable insights into disease activity, while fibrotic mediators reflect long-term organ involvement. Imaging

techniques and genetic profiling allow early identification of high-risk patients, enabling targeted interventions.

These results emphasize the necessity of incorporating environmental risk assessment, metabolic monitoring, and endothelial protection into post-COVID rheumatologic care strategies

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