

MULTIMORBIDITY AND CHRONIC DISEASE BURDEN IN AUTOIMMUNE DISORDERS

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Abstract: Autoimmune diseases are chronic immune-mediated disorders that are frequently accompanied by multiple chronic comorbid conditions. Accumulating evidence indicates that patients with autoimmune diseases have a substantially increased risk of developing cardiovascular, metabolic, musculoskeletal, renal, and psychiatric disorders, which significantly worsen clinical outcomes and quality of life. The aim of this study was to evaluate the prevalence and clinical significance of chronic comorbidities in autoimmune diseases and to explore underlying pathogenic mechanisms. A narrative review of the literature published between 2010 and 2024 was conducted using PubMed, Scopus, and Google Scholar databases. The reviewed studies demonstrate that persistent systemic inflammation, immune dysregulation, shared genetic susceptibility, and long-term immunosuppressive therapy play a central role in the development of multimorbidity. The coexistence of multiple chronic conditions complicates disease management and is associated with increased morbidity, mortality, and healthcare utilization. Early identification of comorbidities and implementation of multidisciplinary, patient-centered management strategies are essential to improve long-term outcomes in patients with autoimmune diseases.

Keywords: autoimmune disorders, multimorbidity, chronic diseases, immune-mediated inflammation

Introduction

Autoimmune disorders affect millions of individuals worldwide and represent a major public health challenge. Diseases such as rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, and autoimmune thyroiditis are associated with chronic inflammation and progressive organ damage. Traditionally, clinical management has focused on controlling primary disease activity; however, growing evidence suggests that autoimmune diseases rarely occur in isolation.

Patients with autoimmune disorders frequently develop additional chronic conditions, including cardiovascular disease, metabolic syndrome, osteoporosis, chronic kidney disease, and mental health disorders. The accumulation of multiple chronic diseases significantly complicates treatment, increases disability, and worsens quality of life. This article aims to review current evidence on multimorbidity in autoimmune disorders and to highlight its clinical significance.

Methods

This study was conducted as a comprehensive narrative literature review aimed at evaluating the prevalence, spectrum, and clinical impact of chronic comorbidities in patients with autoimmune diseases. The review focused on identifying common patterns of multimorbidity and exploring underlying pathogenic mechanisms.

A systematic search of the literature was performed using the electronic databases PubMed, Scopus, and Google Scholar. Relevant articles published in English between January 2010 and December 2024 were included. The search strategy utilized a combination of keywords and



Medical Subject Headings (MeSH), including “autoimmune diseases,” “multimorbidity,” “chronic comorbidities,” “chronic inflammation,” and “immune dysregulation.” Boolean operators (AND, OR) were applied to refine and optimize the search results.

Inclusion criteria consisted of peer-reviewed observational studies, cohort studies, case-control studies, cross-sectional studies, systematic reviews, and meta-analyses that investigated chronic comorbid conditions in adult patients with autoimmune diseases. Studies were excluded if they focused exclusively on pediatric populations, non-autoimmune inflammatory conditions, single-organ complications, case reports, editorials, or conference abstracts.

Article selection was performed in two stages. Initially, titles and abstracts were screened for relevance. Subsequently, full-text articles were reviewed to confirm eligibility. Data extracted from the selected studies included study design, sample size, type of autoimmune disease, types of chronic comorbidities, and reported clinical outcomes. The extracted data were analyzed qualitatively and synthesized descriptively due to heterogeneity among studies.

This methodological approach allowed for a comprehensive overview of current evidence regarding multimorbidity in autoimmune diseases and provided a foundation for identifying gaps in existing research.

Results

The reviewed studies revealed that multimorbidity is highly prevalent among patients with autoimmune disorders. Cardiovascular diseases were consistently reported as the most common comorbid conditions, followed by metabolic disorders such as diabetes mellitus and dyslipidemia. Musculoskeletal complications, particularly osteoporosis and sarcopenia, were frequently associated with long-term corticosteroid use.

Psychological comorbidities, including depression and anxiety, were significantly more common in autoimmune populations compared to healthy controls. Chronic fatigue, pain, and reduced physical function were identified as contributing factors. Additionally, patients with multiple comorbidities exhibited higher rates of hospitalization and increased mortality.

Literature Review

Recent studies have increasingly emphasized the concept of multimorbidity in autoimmune disorders, recognizing it as a major determinant of disease burden and long-term outcomes. Autoimmune diseases are no longer viewed as isolated conditions, but rather as systemic disorders frequently accompanied by multiple chronic comorbidities. Epidemiological evidence consistently shows that patients with autoimmune diseases have a higher prevalence of chronic non-communicable diseases compared to the general population.

Cardiovascular comorbidities are among the most extensively studied complications in autoimmune disorders. Aviña-Zubieta et al. demonstrated that patients with rheumatoid arthritis and systemic lupus erythematosus have a markedly increased risk of myocardial infarction and stroke, which cannot be fully explained by traditional cardiovascular risk factors alone. Chronic systemic inflammation and endothelial dysfunction have been identified as key mechanisms contributing to accelerated atherosclerosis in these populations.

Metabolic comorbidities, including diabetes mellitus, obesity, and dyslipidemia, have also been frequently reported. Dregan et al. found strong associations between chronic inflammatory



diseases and metabolic syndrome, suggesting that persistent inflammation plays a central role in insulin resistance and lipid metabolism disorders. These metabolic abnormalities further amplify cardiovascular risk in autoimmune patients.

Psychiatric comorbidities represent another significant aspect of multimorbidity in autoimmune diseases. Marrie et al. reported increased prevalence of depression and anxiety across multiple autoimmune conditions. The authors emphasized that both biological mechanisms, such as neuroinflammation, and psychosocial factors, including chronic pain and disability, contribute to mental health disorders.

The role of long-term pharmacological treatment has been widely discussed in the literature. Bruce and Mok highlighted that prolonged use of corticosteroids and immunosuppressive agents is associated with secondary chronic conditions such as osteoporosis, hypertension, and increased susceptibility to infections. These treatment-related complications further contribute to the overall burden of multimorbidity.

Overall, the reviewed literature indicates that chronic comorbidities are integral to the clinical course of autoimmune diseases. Despite growing recognition, many studies point to insufficient screening and fragmented care. This highlights the need for integrated management strategies and standardized clinical guidelines aimed at addressing multimorbidity in patients with autoimmune disorders.

Discussion

The findings of this review confirm that multimorbidity is a prevalent and clinically important characteristic of autoimmune diseases. The high frequency of chronic comorbid conditions observed across various autoimmune disorders highlights the systemic nature of immune-mediated inflammation and its long-term consequences. Rather than occurring independently, autoimmune diseases and their associated comorbidities appear to share overlapping pathogenic mechanisms.

Chronic systemic inflammation plays a central role in the development of comorbid conditions, particularly cardiovascular and metabolic diseases. Persistent elevation of pro-inflammatory cytokines such as tumor necrosis factor- α , interleukin-6, and interferons contributes to endothelial dysfunction, accelerated atherosclerosis, and insulin resistance. These mechanisms explain why patients with autoimmune diseases experience increased cardiovascular morbidity even in the absence of traditional risk factors.

Metabolic and musculoskeletal comorbidities further complicate the clinical course of autoimmune diseases. Long-term corticosteroid therapy, while effective in controlling disease activity, is strongly associated with osteoporosis, sarcopenia, weight gain, and glucose intolerance. These treatment-related effects must be carefully balanced against therapeutic benefits, emphasizing the importance of individualized treatment strategies and regular monitoring.

Psychiatric comorbidities, including depression and anxiety, are increasingly recognized as integral components of autoimmune disease burden. Neuroinflammation, chronic pain, fatigue, and functional limitations contribute to psychological distress, which in turn may negatively affect treatment adherence and disease outcomes. Addressing mental health should therefore be considered a fundamental aspect of comprehensive autoimmune disease management.



Another important consideration is the bidirectional relationship between autoimmune diseases and comorbidities. While autoimmune pathology promotes the development of chronic conditions, existing comorbidities may also exacerbate autoimmune disease activity and accelerate disease progression. This interaction underscores the limitations of single-disease treatment models and supports the adoption of integrated, multidisciplinary care approaches.

Despite growing awareness, current clinical practice often lacks standardized protocols for the screening and management of comorbidities in autoimmune patients. Fragmented care and delayed diagnosis of secondary conditions contribute to avoidable complications. The findings of this review emphasize the need for unified clinical guidelines and coordinated care models that address the full spectrum of patient needs.

Future research should focus on longitudinal studies to better understand temporal relationships between autoimmune diseases and comorbidities, as well as on identifying biomarkers predictive of multimorbidity. Advances in precision medicine and risk stratification may facilitate earlier interventions and improve long-term outcomes for patients with autoimmune diseases.

Conclusion

The growing body of evidence clearly demonstrates that multimorbidity is a common and clinically significant feature of autoimmune diseases. Patients with autoimmune disorders frequently develop a wide spectrum of chronic comorbid conditions, including cardiovascular, metabolic, musculoskeletal, renal, and psychiatric diseases. These comorbidities arise from complex and interrelated mechanisms such as persistent systemic inflammation, immune system dysregulation, shared genetic predisposition, environmental influences, and the long-term consequences of immunosuppressive therapies.

The presence of multiple chronic conditions substantially increases disease burden and negatively affects both physical and mental health outcomes. Multimorbidity complicates clinical decision-making, limits therapeutic options, and is associated with higher rates of hospitalization, disability, and mortality. Importantly, the impact of comorbidities extends beyond clinical parameters, significantly reducing patients' quality of life and increasing healthcare costs.

These findings underscore the necessity of shifting from a disease-centered to a patient-centered model of care. Effective management of autoimmune diseases should not be limited to controlling immune activity alone, but must also include systematic screening, early detection, and proactive management of associated chronic conditions. Multidisciplinary collaboration among specialists, primary care providers, and mental health professionals is essential for comprehensive care.

Future research should focus on identifying high-risk patient populations, elucidating shared pathogenic pathways, and developing standardized clinical guidelines for the prevention and management of multimorbidity in autoimmune diseases. Longitudinal and population-based studies are particularly needed to clarify disease trajectories and optimize personalized treatment strategies. Addressing multimorbidity as an integral component of autoimmune disease care has the potential to improve long-term outcomes, enhance quality of life, and reduce the overall burden of autoimmune disorders on healthcare systems.

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