

Autoimmune Neuromuscular Disorders: A Mini-Review Of Immunopathogenesis And Emerging Therapeutic Perspectives

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Abstract:

Autoimmune neuromuscular disorders (aNMDs) comprise a heterogeneous group of immune-mediated conditions affecting the neuromuscular junction, peripheral nerves, and skeletal muscle. Despite differing clinical phenotypes, these disorders share overlapping immunopathogenic mechanisms involving autoantibodies, innate and adaptive immune dysregulation, and variable responsiveness to immunomodulatory therapies. This mini-review summarizes recent PubMed-indexed literature on autoimmune neuromuscular disorders, integrating findings from reviews, clinical studies, editorials, and case reports. A focused bibliometric overview highlights publication trends, disease representation, and thematic emphasis. Myasthenia gravis emerges as the most frequently studied entity, followed by inflammatory myopathies and immune-mediated neuropathies. The review illustrates immunopathogenic convergence, diagnostic challenges, and evolving therapeutic strategies, while also identifying important research gaps. The review is limited to PubMed-indexed literature, and future studies incorporating multiple databases and longitudinal designs are needed to further clarify immunological processes and optimize therapeutic strategies.

Keywords: Autoimmune neuromuscular disorders; Immunopathogenesis; Immunotherapy; Myasthenia gravis.

Date of Submission: 12-01-2026

Date of Acceptance: 22-01-2026

I. Introduction

Autoimmune neuromuscular disorders represent a broad spectrum of diseases in which immune-mediated mechanisms target structures essential for neuromuscular function, including the neuromuscular junction, peripheral nerves, and skeletal muscle. Clinically, these disorders manifest as fluctuating weakness, easy fatigability (rapid exhaustion with repeated muscle use), sensory deficits, myalgia, or acute neuromuscular emergencies, depending on the site and severity of immune involvement[1], [2]. Well-recognized conditions include myasthenia gravis (MG), chronic inflammatory demyelinating polyneuropathy (CIDP), Guillain–Barré syndrome (GBS), and idiopathic inflammatory myopathies, alongside rarer entities such as Isaacs syndrome and conditions with coexisting features of more than one autoimmune neuromuscular disorder.

Over recent years, advances in immunology and neuroimmunology have shifted the understanding of autoimmune neuromuscular disorders from isolated disease entities toward a continuum of immune-mediated neuromuscular pathology. Editorial perspectives and narrative reviews increasingly emphasize shared immune mechanisms, including pathogenic autoantibodies, complement activation, innate immune signaling, and impaired immune tolerance [3]. This evolving conceptual framework has important implications for diagnosis, classification, and therapy. At the same time, clinical practice continues to face challenges due to heterogeneous presentations, atypical cases, and variability in treatment response. Diagnostic uncertainty is particularly evident in rare autoimmune neuromuscular disorders, where classical disease boundaries may not apply [4], [5]. Viral infections have also been implicated as triggers or modulators of autoimmune neuromuscular disorders, with SARS-CoV-2 associated neuromuscular complications highlighting immune-mediated mechanisms beyond direct viral injury[6]. Against this background, concise narrative syntheses remain valuable to integrate mechanistic insights with clinical observations. The present mini-review aims to provide an overview of recent PubMed-indexed literature on autoimmune neuromuscular disorders, identify common trends, and highlight areas requiring further investigation.

II. Material And Methods

A focused literature search was conducted in PubMed using the term “Autoimmune Neuromuscular Disorders” applied to the Title/Abstract field. Fifteen English-language, peer-reviewed articles published between 2016 and 2025 were identified. Included publications comprised narrative reviews, editorials, observational studies, retrospective cohort studies, and case reports. Data extracted included year of publication, journal, study type, disease focus, and thematic emphasis. The review is limited to PubMed-indexed literature, and findings should be interpreted within this scope. Future reviews incorporating additional databases may provide a broader perspective.

III. Results

Overview of the Included Studies

The increasing publication trend reflects growing interest in autoimmune neuromuscular disorders, driven by advances in immunological understanding and targeted therapeutic strategies [3]. Narrative reviews constituted the largest proportion of publications, followed by clinical studies and case reports, indicating an active phase of conceptual consolidation rather than large-scale interventional research. Myasthenia gravis was the most frequently addressed condition, either as a primary focus or as part of broader discussions on autoimmune neuromuscular disorders [2], [7], [8]. Inflammatory myopathies and immune-mediated neuropathies were also commonly represented, while rare disorders and overlap syndromes appeared predominantly in case-based reports [9].

Immunopathogenic Convergence in Autoimmune Neuromuscular Disorders

Despite clinical heterogeneity, accumulating evidence supports immunopathogenic convergence across autoimmune neuromuscular disorders. Shared mechanisms include autoantibody-mediated tissue injury, complement activation, dysregulated T-cell responses, and impaired immune tolerance [10]. Myasthenia gravis has served as a prototype for understanding these processes, but similar immune pathways are increasingly recognized in inflammatory neuropathies and myopathies.

Innate immune activation, particularly through toll-like receptor signaling, has emerged as an important modulator of adaptive immunity in autoimmune neuromuscular disorders. Innate immune cells, including natural killer cells, may contribute to immune dysregulation and represent potential biomarkers or therapeutic targets across autoimmune neuromuscular and systemic autoimmune diseases [11]. Abnormal activation of toll-like receptors (TLRs), which play a key role in innate immune signaling, has been associated with persistent inflammatory responses and continued autoantibody production, particularly in myasthenia gravis [7]. Clinical observations of overlap syndromes further reinforce the concept of shared immune drivers across traditionally distinct disorders [4], [5].

IV. Discussion

Diagnosis of autoimmune neuromuscular disorders remains challenging due to phenotypic overlap, atypical presentations, and variable serological findings. Case reports illustrate diagnostic complexity when classical features are absent or when multiple autoimmune conditions coexist [4], [9]. Imaging modalities such as whole-body MRI have been explored to improve detection of inflammatory involvement, particularly in myopathies [12].

Acute neuromuscular emergencies, including respiratory failure, emphasizes the clinical importance of timely diagnosis and intervention [1]. Consensus guidelines aim to standardize diagnostic approaches, yet their practical applicability remains debated [2].

Immunomodulatory therapy remains the cornerstone of management for autoimmune neuromuscular disorders. Immunoglobulin-based therapies are widely used for both acute exacerbations and chronic disease control, particularly in myasthenia gravis [8]. Recent developments in targeted immunotherapies, such as complement inhibitors and neonatal Fc receptor (FcRn) antagonists, demonstrate how improved understanding of immune-mediated disease processes is being translated into more precise clinical treatment strategies [3], [10]. Long-term immunomodulatory treatment is associated with infection risk across autoimmune neuromuscular disorders, highlighting the need for balanced therapeutic strategies and infection surveillance [13].

The COVID-19 pandemic highlighted additional management challenges, including altered vaccine responses and infection risk in patients receiving immunosuppressive therapy [14], [15]. These findings emphasize the need for individualized therapeutic decision-making and ongoing risk assessment.

Current literature is disproportionately focused on myasthenia gravis, with comparatively limited data on rare autoimmune neuromuscular disorders and overlap syndromes. Case reports and small observational studies dominate these areas, demonstrating the need for larger, multicenter investigations [4], [9].

Further gaps include limited integration of molecular biomarkers into routine clinical practice, variability in guideline adoption, and insufficient longitudinal outcome data. Future research should prioritize mechanism-

driven classification, standardized outcome measures, and multi-database evidence synthesis. The authors acknowledge that the this mini-review is limited by its reliance on a single database (PubMed) and a modest number of included studies. Heterogeneity in study design and disease focus limits direct comparison across publications.

V. Conclusion

Autoimmune neuromuscular disorders encompass a diverse yet immunologically interconnected group of conditions. Recent literature highlights shared immunopathogenic pathways, evolving diagnostic strategies, and expanding therapeutic options. Viewing these disorders through a unified immunological framework may facilitate earlier diagnosis, rational therapeutic selection, and future development of precision immunotherapies.

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