Gut Microbiome Dysbiosis as a Novel Modifier of Relapse Risk in MOG-Associated ADEM Phenotypes

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Date of Submission: 25th May 2026 Date of Acceptance:5th June 2026 Date of Publication: 15th June 2026

To the Editor,

The brain-gut axis controls the immune response in neuroinflammatory diseases by using microbial products and immune system communication. Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) presents high relapse danger through its acute disseminated encephalomyelitis (ADEM) symptoms, which affect over half of all patients and especially young patients who show a statistically significant increase in relapses ($p<0.001$) that lead to more severe Expanded Disability Status Scale results (rho=0.442, $p<0.001$) 1. The evidence about this axis has developed new scientific insights about its importance, which Devolder et al. proved through their research that specific gut microbiome patterns create a direct link to increased disability, which indicates that microbial dysbiosis controls the development of neuroinflammatory diseases instead of only showing their current state. Particular changes in essential gut bacteria, together with decreased total gut bacteria count, led to ongoing disease progression while showing how gut bacteria produce substances that activate the immune system and cause central nervous system demyelination. The research indicates that gut microbial imbalances drive relapse rates and impact long-term outcomes in MOGAD, which particularly affects young patients who show high immune response in their ADEM symptoms[1].

The gut microbiome dysbiosis, which occurs after infections, leads to more severe ADEM development in MOGAD through immune system interactions because changes in microbial composition cause Th17 immune responses together with blood-brain barrier breaches, resembling experimental autoimmune encephalomyelitis models. The recent research proves that the gut microbiota establishes a connection with neuroinflammation, which occurs when microbial metabolites, including short-chain fatty acids and tryptophan derivatives, change because these metabolites activate microglial cells and shift peripheral immune systems, which leads to increased autoimmune attacks on the central nervous system. The research by Liu et al. demonstrated that dysbiosis leads to increased IL-6, IL-17, and TNF-α signaling, enabling the maintenance of chronic neuroinflammatory circuits through vagal and systemic immune pathways, thus establishing a link between peripheral microbial imbalance and central demyelinating pathology. The research indicates that microbiome disturbances in post-infectious MOGAD-related ADEM begin the immune response but continue to cause demyelination through ongoing microglial activation and blood-brain barrier damage[2].

The connection between gut pathogens and MOG-associated ADEM occurs through molecular mimicry, which allows Mycoplasma pneumoniae pathogens to produce anti-MOG antibodies that increase multiphasic relapse risk for seropositive individuals. The research results show that immune system disturbances create changes in how gut microbiomes interact with their human hosts, which leads to increased inflammatory response activities and breakdown of immune defense systems. The research shows that changes in gut bacteria composition following immune system activation lead to abnormal T-cell behavior and increased central nervous system autoimmunity, proving that microbiome instability can drive or worsen anti-MOG antibody production in vulnerable people. The results support the idea that post-infectious dysbiosis functions as both a trigger and an ongoing element that leads to repeated demyelination episodes in people with MOG-associated disorders[3].

Fecal microbiota profiling provides a non-invasive prognostic marker that predicts neuroinflammatory outcomes in demyelinating diseases through post-treatment taxonomic changes that include Akkermansella muciniphila, which demonstrates greater predictive power than clinical factors used in relapse models. Emerging case-based evidence further underscores that immune-triggered demyelinating syndromes, which include seropositive anti-myelin oligodendrocyte glycoprotein (MOG) antibody-associated acute disseminated encephalomyelitis (ADEM) that follows Mycoplasma pneumoniae infection, may reflect a microbiota-immune axis interplay because infectious priming changes systemic immune tolerance leading to CNS-directed autoimmunity. This observation strengthens the rationale for integrating gut microbial signatures with serological biomarkers, particularly anti-MOG antibodies, to refine prognostic stratification and anticipate monophasic versus relapsing disease trajectories in post-infectious demyelinating disorders[4].

Access this article online

Website: https://www.nepjol.info/index.php/NJN

DOI: https://doi.org/10.3126/njn.v23i2.91205

HOW TO CITE
Talha, M., Shah, S. A., Rehman, U. U., Ali, U., & Antar, A. Gut Microbiome Dysbiosis as a Novel Modifier of Relapse Risk in MOG-Associated ADEM Phenotypes. NJNS. 2026;23(2):69-70

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ISSN: 1813-1948 (Print), 1813-1956 (Online)

The study results demonstrate that microbiome analysis should become an essential component of MOGAD protocols, which doctors need to use for their patients' care of determining relapse probabilities and choose microbiota treatment solutions. Fecal microbiota composition may outperform traditional clinical predictors in forecasting disease recurrence, which demonstrates that microbial signatures have a better ability to differentiate between risks than standard risk factors do. ADEM management will transform prospective trials, which will validate fecal profiling as a biomarker because standardized microbial diversity indices and taxonomic profiling will enable early identification of high-risk inflammatory phenotypes, which will inform personalized preventive strategies that include targeted microbiota restoration approaches [5].

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