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Review Article

Gut dysbiosis and multiple sclerosis

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ABSTRACT

Multiple sclerosis (MS) is a chronic, immune-mediated disorder of the central nervous system marked by multifocal demyelination, neuroinflammation, and progressive neurodegeneration. Globally, it affects about 2.9 million people, creating significant personal, social, and economic burdens. In India, approximately 100,000 to 150,000 individuals live with MS, with prevalence estimates ranging from 8-11 per 100,000 population, and an estimated 6,500 new diagnoses annually. MS imposes a heavy healthcare burden: early diagnosis is often delayed due to low awareness, limited access to neurologists, and inconsistent diagnostic protocols leading to prolonged hospital stay, longer duration of clinically undiagnosed disease and worse overall outcomes. In India, clinical management of MS faces a multitude of challenges in the form of inadequacies in diagnostic ability arising due to lack of advanced training, medical supplies, diagnostic tools and lack of trained neurologists per capita. Additionally, drugs used to manage MS are often expensive and require longer durations of therapy and frequent adjustments on follow up, leading to financial exhaustion for the patient, and subsequently adding to their inaccessibility. In recent years, there has been evidence suggesting a correlation of altered composition of gut commensals with CNS autoimmune diseases like MS. This association opens new avenues for understanding, diagnosing and managing such diseases beyond conventional neurotropic therapy. Any deviation from normal in the gut flora can trigger oxidative damage, that promotes mitochondrial dysfunction, and sets in motion cascades of inflammation via the gut brain axis that eventually led to demyelination and degeneration. Also, various humoral, endocrine and immune connections exist between the gut and brain, that influence release of neurotransmitters, peptides and cytokines that further serve to modify CNS function. This review aims to consolidate evidence that corroborates the link between gut dysbiosis and MS.

Keywords: Multiple sclerosis, Gut dysbiosis, Gut–brain axis, Neuroinflammation

INTRODUCTION

Multiple sclerosis (MS) is a chronic autoimmune disorder that targets the central nervous system, causing inflammation, demyelination, and progressive neuronal loss. While MS is widely studied in Western populations, its burden in India is increasingly recognised, with delayed diagnosis and limited access to specialised care worsening patient outcomes. Beyond genetic and environmental factors, emerging research highlights the role of the gut-brain axis in MS. The human gut microbiota regulates immune function and influences inflammatory pathways. Alterations in gut microbial composition, known as gut dysbiosis, may trigger immune dysregulation, oxidative stress, and neuroinflammation-mechanisms central to MS development and progression. Understanding how gut dysbiosis contributes to MS offers new possibilities for diagnosis and therapeutic strategies beyond traditional immunomodulatory treatments.[1]

Objectives

Objectives were to examine the current evidence linking gut microbiota composition to immune dysregulation in MS, to analyse how gut dysbiosis contributes to neuroinflammation, oxidative stress, and demyelination in

MS, to evaluate the diagnostic and therapeutic potential of targeting gut microbiota in MS management and to identify research gaps and future opportunities for integrating gut-brain axis-based strategies into MS clinical care.

Problem statement

MS remains challenging to diagnose and manage in India due to limited awareness, inconsistent diagnostic protocols, and restricted access to specialised neurological care. Conventional treatment focuses mainly on immune suppression and symptom control, often overlooking underlying mechanisms contributing to disease progression. Emerging research suggests a significant link between gut dysbiosis and MS through immune modulation and neuroinflammatory pathways, yet this association remains underexplored. Understanding this relationship is crucial to developing improved diagnostic strategies and alternative therapeutic interventions targeting the gut–brain axis.

REVIEW OF LITERATURE

History and epidemiology of MS

The existence of a neurological disease characterised by the eponymously named Charcot's triad-intention tremor, scanning speech, and nystagmus-was first described by Jean-Martin Charcot in 1868, but reports of patients presenting with acute-onset weakness, unilateral blindness and pain appear in records as early as 1300s.[2] Interferons in 1950s, and high-dose steroids from 1980s onwards, have been some landmark treatment strategies used over years, but none have shown to be particularly promising.[1]

Until the mid-1970s, MS was considered rare in India. The first attempt to study the prevalence of the disease was conducted in the west coast regions from 1975 to 1985 by Singhal et al. According to hospital records, prevalence in the 1970s-80s ranged between 0.17-1.33 per 100,000.[3] In the 1990s, prevalence rose to 1.8-2.5%. Today, statistics show a staggering 11 per 100,000.[3] MS affects women more than men, and the average age of onset is between 25 and 30 years old.[3]

AETIOLOGY

MS is a multifactorial autoimmune disease resulting from a convergence of environmental exposures, genetic susceptibility and immune dysregulation.[3,4]

The strongest genetic link is HLA-DRB1*11 allele, which is a member of class II MHC.[5,6] This allele helps enhance antigen presentation to CD4+ cells, reducing immune tolerance to myelin. More than 200 non-HLA single nucleotide polymorphisms (SNPs) located near innate or adapted immunity genes indicate that MS occurs due to an imbalance in the homeostasis of the immune system. This means that the genes responsible are not necessarily diseased genes, but variations of normal genes.

Low levels of vitamin D plays an essential role in incidence, disease progression and recurrence.[7-9] Vitamin D promotes T_{reg} development and suppresses Th_1 and Th_{17}, while also playing an active role in innate immunity, by having receptors (VDR) on macrophages and dendritic cells, resulting in a decrease in auto reactivity of T cells.[10,11] It also helps reduce expression of IL-2, IFN-γ, IL-17 and enhances IL-10. This leads to the dictum that in MS, it is recommended to maintain serum vitamin D levels above 20-30 ng/ml.[6,9,12,13]

Strongest link of a pathogen with MS is that of Epstein-Barr virus, known to cause infectious mononucleosis. The 99% of adults with MS have a history prior EBV infection and seronegativity is extremely rare.[9] EBNA antigens of EBV are structurally similar to CNS myelin proteins-myelin basic protein and glial cell adhesion molecule (GlialCAM).[14] Cross reactive immune responses activate auto reactive CD4+ and CD8+ T cells targeting myelin. Infected B cells persist in the meningeal ectopic lymphoid follicles near subpial cortical lesions and can also act as antigen presenting cells sustaining chronic CNS infection, while also producing antibodies against myelin components, creating a deadly combination of factors that make EBV unique in causing MS, compared to other viruses.[15,16]

People who smoke are two times more susceptible to MS, compared to people who do not.[17] Smoking elevates IL-6, CRP, and fibrinogen. It impairs T cell and APC activity, leading to alteration of lymphocyte distribution and diminished B and NK cell functions.[18] There is evidence that smoking provokes autoimmunity by altering citrullination, an important step of post-translational modification, which causes formation of modified proteins that are presented by HLA-DRB1*15:01, which triggers T-cell attack on myelin. Smoking related lung inflammation may initiate a systemic immune activation, which penetrates the blood-brain barrier and enables autoimmune cells to interact with the CNS.[18]

In the last decade, novel research into the importance of gut microbiota in CNS Physiology and Pathology has been made. This interdependence is now known as the gut brain axis, linking central and enteric nervous systems. Dysbiosis i.e. abnormal gut microbiota composition have been associated with autism, anxiety depressive behavioral disorders and functional GI disorder.[19] Similarly, there have been new insights into immunomodulatory effects of gut microbiota which shape T cell responses and metabolic pathways crucial to the pathogenesis of MS.

PATHOPHYSIOLOGY

The nervous system of the spinal cord is arranged in the form of tracts, which are streamlined bundles of nerve fibres grouped by their origin, destination and function.

The corticospinal tracts, namely the anterior and lateral corticospinal tracts, are two such groups of nerve fibres, that function to carry impulses from the motor cortex of the brain to peripheral effector sites via the spinal cord. While the anterior corticospinal tract descends through the spinal cord on the same side of the body as the hemisphere of the brain it originated in before crossing over at the spinal level, and controls movements of the axial skeleton, the lateral corticospinal tract decussates at the level of the medulla and is responsible for fine motor control of limbs.

In MS, it is this lateral corticospinal tract that loses its sheath of myelin, leading to slowed/blocked conduction of impulses and disruption of saltatory conduction. There is leakage of ionic currents across demyelinated segments as well as increased capacitance paired with decrease membrane resistance. These molecular aberrations, acting together, hinder the maintenance of resting membrane potentials and the generation of action potentials.[8] Voltage gated Na^+ channels become redistributed/downregulated, leading to conduction block, slowed propagation and ectopic discharges, causing spasms and paresthesias. Over time, remodeling of ionic channels occurs due to abnormal distribution of Na^+ and K^+ channels. Upregulation of Na^+ channels may temporarily restore conduction, but increases Na influx, which can reverse the Na^+/Ca^{2+} exchanger and cause intracellular Ca^{2+} overload resulting in axon injury and degeneration.[5,6]

Activated microglia and macrophages in MS lesions generate reactive oxygen species and NO. This impairs mitochondrial ATP production, affecting Na^+/K^+ ATPase function, Axonal transport and maintenance of RMP. In chronic MS, plaques cause axonal transection, disrupting transport of vesicles containing neurotransmitters and synaptic scaffolding proteins, leading to synaptic disconnection and progressive neurological disability.[9]

GUT DYSBIOSIS IN MS

Intestinal population may be affected by the Th1/Th2 ratio while establishing a balance between pro-inflammatory and anti-inflammatory states in the gut. Naive B cells are also converted into B_{reg} cells, that produce IL10, an anti-inflammatory marker. Production of IgA also helps maintain balance of gut microbes.

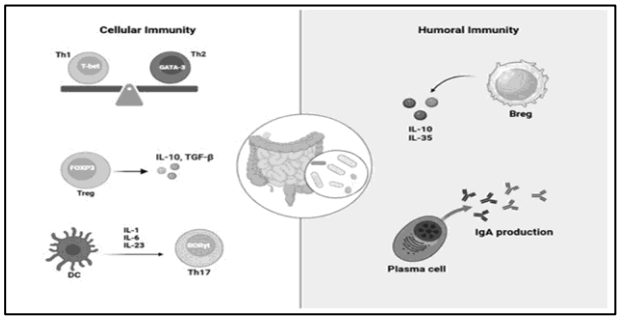

Figure 1: Some bacteria can signal dendritic cells to cause differentiation of Th17.

The gut microbes are capable of consuming neurotransmitters such as dopamine, GABA, glutamate, serotonin and noradrenaline, which reach the CNS via the vagus nerve and alter neuronal and glial functions.[20,21] Studies conducted in germ-free (GF) animals allowed researchers to study immune functions in the absence of gut microbes. Such animals had under-developed lymphoid tissues, imbalance in Th1/Th2 cells with skewing towards Th2 response. There was also a lack of Th17 cells and T_{reg} cells.[22-26] Mice with intact microbiome had a quicker immune response.[27] Via the microbe-associated molecular patterns (MAMPs) and pattern recognition receptors (PRRs), which are expressed on immune cells, the innate immune system is able to recognize the colonization pattern of the gut. This in turn leads to initiation of the adaptive immune response and promotion of immunotolerance and killing of pathogens.[28] Commensals in the gut provide signals stimulating the differentiation of T cells into their various phenotypes-T-bet$^+$ Th1 cells, RORγt$^+$ Th17 cells, GATA3$^+$ Th2 cells and Th17/T_{reg} cell balance.[29]

T_{reg} cells in the small intestine and lamina propria of the colon are inducted by several bacteria such as *Lactobacillus, Streptococcus, Clostridium, Bacterioides, Bifidobacteria, Escherichia.*[30] *Lactobacillus* strains may induce T_{reg} cell production and suppress Th1 and Th17 as well as alter Th1/Th2 ratio, leading to changing the M1/M2 macrophage subset ratio.[31] Colonisation of mice with polysaccharide A (PSA) from *Bacterioides fragilis* provided a preventive and curative protection against development of Experimental autoimmune encephalomyelitis (EAE). The protective effect is conferred by induction of T_{reg} activity and control of Th1 responses. To treat MS, the gut commensal *Prevotella histicola* is found to produce short chain fatty acids (SCFAs) that help suppress inflammation in CNS and slow down demyelination. This therapy is used along with Glatiramer acetate and interferon beta, which help control Th1/Th17 responses, increase VD4+FoxP3+ T_{reg} cells and reduce macrophage activity.

Segmented filamentous bacteria (SFB) induce Th17 in the lamina propria.[28] They adhere to the lamina propria and produce serum amyloid A (SAA), which affects local dendritic cells to start production of IL-1β, IL-6, IL-23 and ROS, which lead to production of Th17 via CD4+ cells. SFBs hence induce growth of pathogenic bacteria in the gut. *Prevotella* is another bacteria that causes inflammatory disorders by mediating Th17 production via TLR-2 dependence. Other Th17 inducing bacteria are *Staphylococcus aureus, Candida albicans, Bifidobacterium adolescents and Escherichia coli*. Recently, reduction of population of many bacteria have been shown to develop MS-*Prevotella, Lactobacillus, Bacterioides, Parabacterioides, Aldercreutzia, F. Praunsnitzii*, and abundance of *Acinetobacter, Akkermansia, Pseudomonas, Mycoplana, Haemophilus, Blautia genera*.

In animal models, gut dysbiosis has been shown to have strong associations with autoimmune CNS disease severity. Sahani et al showed that mice put on a high-fat diet with subsequently induced obesity had increased gut permeability and systemic inflammation. These obese mice had more severe autoimmune encephalitis as compared to control mice on normal diets. However, amelioration of disease severity was noted in mice depleted of their gut microbiota.

Corroboration of such findings with human studies is tantamount to establishing their role in disease diagnosis and treatment. Multiple landmark studies exist which have attempted to fill this void.

Studies have also shown that MS therapies can alter the gut microbiome. Patients receiving interferon-β or glatiramer acetate had higher levels of *Prevotella* and *Sutterella* and lower levels of *Sarcina* than untreated patients, indicating that immunomodulatory drugs may influence gut microbial composition. A study showed that vitamin D supplementation in RRMS patients led to a decreased *Bacterioidaceae* and *Faecalibacterium* and increased *Ruminococcus*.

Table 1: Summary of key studies linking gut dysbiosis, immune dysfunction, and multiple sclerosis.

Authors	Study focus/ sample	Key finding (microbiota/ immune link)	Treatment/ intervention
Zhang et al[1]	Review on gut flora in MS	Dysbiosis linked to MS progression (*Akkermansia*, *Faecalibacterium*)	-
Alves et al[3]	Genetic patterns (HLA-DRB1)	Genetic allele increases MS susceptibility	-
Zhou et al[4]	SNP association study	SNP variants affect immune dysfunction	-
Morali et al[10]	Dendritic cell immune role	IL-10 producing dendritic cells regulate autoimmune signaling	Immunotherapy
Cosorich et al[30]	Gut microbiota analysis	TH17 elevation linked to dysbiosis	-
Laeeq et al[31]	Fecal microbiota transplant (FMT)	Clinical improvement in MS after FMT	FMT
Liu et al[21]	Gut-brain axis therapy	Microbiota modulation reduces neuroinflammation	Microbiota targeted therapy
Zhao et al[22]	Immune disorders and dysbiosis	Dysbiosis activates pro-inflammatory cytokines	-
Ding et al[31]	Probiotic regulation on immune cells	Probiotics reduce immune inflammation	Probiotic therapy
Ivanov et al[28]	SFB and Th17 autoimmune mechanism	SFB activates Th17-autoimmune response	-

Early human studies primarily focused on comparing gut microbiota profiles between individuals with MS and healthy controls, but they offered little insight into the underlying mechanisms.[32] Most of these investigations involved relatively small and heterogeneous study groups, with cases and controls matched only approximately for age and sex (Table 1). Findings from this initial research indicated alterations in certain bacterial genera among MS patients, including *Akkermansia, Faecalibacterium, Prevotella, and Methanobrevibacter.*

A subsequent wave of research shifted toward larger, more rigorously defined cohorts of patients with MS and healthy controls, while also beginning to address mechanistic aspects. Two complementary studies illustrate this approach, in which germ-free mice were colonized with fecal microbiota obtained from MS patients and controls.

In one study, 34 monozygotic twin pairs discordant for MS were examined, effectively controlling for genetic influences on the microbiome.[1] Although the overall gut microbial composition was broadly similar between twins, certain genera, such as *Akkermansia*, were found in greater abundance in untreated individuals with MS. When fecal samples from these participants were transplanted into germ-free transgenic mice predisposed to spontaneous EAE, the mice that received microbiota from MS patients developed spontaneous EAE at a significantly higher rate than those colonized with bacteria from the healthy twins.[2]

The second study assessed 71 untreated MS patients alongside 71 healthy controls.[1] While overall microbial diversity showed no major shifts, specific bacterial taxa were linked to MS. For example, *Akkermansia muciniphila* and *Acinetobacter calcoaceticus* promoted pro-inflammatory responses in human peripheral blood mononuclear cells and in mice colonized with these bacteria. In contrast, *Parabacteroides distasonis*, which was found to be reduced in MS patients, enhanced anti-inflammatory T cell activity. Moreover, fecal transplants from MS patients into germ-free mice worsened actively induced EAE and lowered IL-10+ T_{reg} cell levels, whereas transplants from healthy individuals had no such effect.

Tremlett and colleagues examined the relationship between gut microbial diversity and relapse risk in

children with MS. They observed that lower levels of Fusobacteria were associated with a higher likelihood of relapse, implying that certain microbial groups may contribute to disease activity and vulnerability to recurrence.

Analysis of small-intestinal samples from patients with active MS showed a higher *Firmicutes*-to-*Bacteroidetes* ratio, increased abundance of *Streptococcus*, and reduced levels of *Prevotella* compared with both healthy controls and patients in remission. Cosorich et al similarly observed elevated *Firmicutes/Bacteroidetes* proportions and greater *Streptococcus* representation, alongside decreased *Prevotella*, in active MS cases.[33] These findings highlight the influence of gut microbial alterations on disease activity and support the potential of microbiota-targeted strategies as therapeutic approaches in MS management.

Collectively, these studies offered the first functional evidence implicating the human gut microbiota in driving CNS-specific autoimmunity.

A newer case control study done in 2025 by Lan et al enrolled 84 individuals with relapsing-remitting MS (RRMS), along with 106 healthy controls (HC).[33] Gut microbial composition was analyzed with genomic sequencing. In addition, clinical, demographic, anthropometric, and dietary data were collected. Serum zonulin and fecal calprotectin concentrations were measured. They found that patients with MS exhibited reduced microbial diversity. Evidence of gut dysbiosis in MS was reflected by marked reductions in commensal species such as *Monoglobus pectinilyticus*, and *Bacillus* spp. Biosynthetic routes for long-chain fatty acids (LCFAs) enriched in MS, whereas short-chain fatty acid (SCFA) production was more prominent in healthy controls. Additionally, MS patients demonstrated elevated levels of zonulin, suggesting impaired intestinal barrier function, but without concurrent rise in calprotectin levels.

DIAGNOSIS

To rule in MS, there must be evidence of white matter damage over time and possible diagnostic alternatives must be ruled out.[13] In the late 1950s, for the first time in India, Schumacher clinical criteria were used to diagnose MS. The Schumacher clinical criteria were heavily clinical examination based; hence it had many drawbacks owing to differences in clinical assessment from physician to physician. To get to a diagnosis of clinically definite MS (CDMS), a patient must show the following:[13] Clinical signs of a defect in the CNS, dissemination in space (evidence of damage in two or more areas of the CNS), Evidence of white matter involvement, dissemination in time (two ore more relapses, each lasting ≥ 24 hours and separated by at least one month), patient age between 10-50 years and no better explanation for symptoms and signs. Since the 1980s, the McDonald's standards have been followed including Gadolinium enhanced MRI, which detects active inflammation, aids early diagnosis.

CSF analysis additionally aids in confirmation of MS. Presence of oligoclonal bands (OCB), which are abnormal antibodies, secreted in response to inflammation are hallmark of MS. OCBs made of IgG indicate presence of MS, but lipid specific IgM indicates a more severe course.[14] When MS is superseded by optic neuritis, the visual evoked potentials (VEP) test may be conducted. Serum and CSF levels of NO are higher than in non-inflammatory neurological diseases.[25] Raised NO levels mean that BBB is breached and that there is demyelination, axon degeneration, damage to mitochondrial DNA and respiratory chain complexes.[26] sGFAP levels help indicate severity of MS. Raised levels indicate astrocyte death and severe disability. Predictive Biomarkers are decreased levels of salivary MBP, presence of HHV-6. Prognostic biomarkers are Chitin's-3-Like-1, Neurofilaments, miRNA, CXCL13, CSCL12, SIRT1, PI3K/AKT/mTOR, JAK/STAT, PPAR-γ, EBNA IgG.

Table 2: Diagnostic criteria for MS based on clinical attacks and lesions (McDonald criteria).

Clinical attacks	Lesions	Additional criteria
2 or more	2 or more	Clinical evidence alone
2 or more	1 lesion	Dissemination in space on MR (attack affecting different area of CNS/Lesions in different areas shown on MRI)
1 attack	2 lesions	Dissemination in time on MR (Additional clinical attacks/lesions detected on MR/presence of OCB in CSF)
1 attack	1 lesion	Dissemination in space and time on MR

Table 3: Biomarkers associated with MS and their clinical significance.

Test	Description
OCB (IgG and IgM)	Elevated in CSF, not serum.[37] IgG OCB is generated by B cells, help detect CDMS Helps predict which patients of radiologically isolated syndrome will develop. Clinically isolated syndrome, and which will develop MS.[38] Prognostic indicator-more tissue damage, brain atrophy, more optic nerve atrophy.[39,40]
NO	Found in macrophages and astrocytes. Primarily responsible for demyelination and cell death.[33]
sGFAP	Also found in enteral glial cells. Higher in PPMS and RRMS.[41]
Salivary MBP	Second most prevalent protein. Levels are lower than threshold in MS.[42]

MANAGEMENT

Management of MS is limited to symptomatic relief and therapies to slow the progression of disease, there is still no cure to reverse neuronal damage.[3,43] As a result of these limitations, the course of MS in India does not change. However, exploration and expanding studies considering newer mechanisms of disease development and course have broadened horizons in hopes of developing more reliable and perhaps curable outcomes of MS.

FECAL MICROBIOTA TRANSPLANTATION IN MS

Fecal microbiota transplantation (FMT) is a therapeutic approach that replaces a patient's gut microbiome with that of a healthy donor to correct structural and functional imbalances. By eliminating abnormal microbial communities and restoring a healthy microbiota, FMT aims to reverse disease-related dysbiosis. This strategy has shown potential benefits across a range of conditions, including neurological disorders and autoimmune diseases such as inflammatory bowel disease (IBD), where disrupted gut microbial composition plays a key role.

In individuals with MS, the gut microbiome is deficient in microbial species that support regulatory T cell (Treg) development, resulting in an increased proportion of peripheral Th1 and Th17 cells. This immune imbalance promotes central nervous system (CNS) inflammation and enhances blood-brain barrier (BBB) permeability, thereby worsening neuroinflammation.[13] Therapeutic modulation of the gut microbiota to favor Treg induction could potentially limit the expansion of pathogenic T cell populations.

In experimental MS models, FMT from healthy donors to immunized mice reshaped gut microbial communities, leading to reduced severity of EAE symptoms, decreased expression of neurodegenerative markers, and attenuation of pathological changes.[44]

Clinical evidence is also emerging. A single-patient study tracked over one year following double FMT reported clinical benefits, including improved gait, which correlated with microbial shifts and increased levels of brain-derived neurotrophic factor (BDNF).

In a randomized controlled trial involving individuals with relapsing-remitting MS (RRMS), FMT produced donor-specific alterations in gut microbiome composition. However, significant interindividual variability limited detectable changes in microbial diversity. Although the trial was terminated early, it still suggested FMT's capacity to modulate gut microbiota.

Additional studies have reported encouraging results. Laeeq et al observed symptomatic relief in 15 MS patients receiving FMT, with sustained improvements and no adverse effects, supporting its potential as a therapeutic option.[49]

Altogether, while current findings highlight FMT as a promising intervention for MS, large-scale and well-controlled studies are necessary to confirm its efficacy and safety.

FUTURE OF GUT MICROBIOTA RESEARCH AND APPLICATIONS IN MS

Exploration of the gut microbiota in MS represents a promising interdisciplinary field with potential to generate novel therapeutic strategies.[31] Despite substantial advances, much remains unexplored, and translating theoretical insights into clinical applications requires extensive research. One of the most promising directions is personalized medicine, as inter-individual differences in microbiota composition suggest the need for tailored interventions. High-throughput sequencing technologies now allow the identification of specific microbial profiles that may support accurate diagnosis and precision-targeted therapies. The discovery of reliable microbiota-derived biomarkers could further aid prognosis, predict relapse risk, and guide therapeutic response.[32] Studies investigating specific bacterial strains with beneficial (*Prevotella histicola*) or detrimental (*Akkermansia muciniphila*) effects provide the foundation for probiotic or prebiotic formulations directed at MS management.

Targeting the microbiota offers an innovative extension of MS therapies. Engineered probiotics expressing anti-inflammatory molecules such as IL-10 or short-chain fatty acids (SCFAs) may shape adaptive immune responses, while customized prebiotics enriched with beneficial taxa like *Lactobacillus* and *Bifidobacterium* could restore microbial balance and strengthen the gut-brain axis. Although early studies on FMT suggest therapeutic potential, standardized protocols and well-designed double-blind trials are essential for validation.

Dietary modification provides another accessible route to influence microbiota composition. Interventions such as ketogenic or anti-inflammatory diets have been linked to reduced abundance of pro-inflammatory bacteria and an enrichment of beneficial strains.[31] Nutritional supplementation with vitamin D, omega-3 fatty acids, and polyphenols may further modulate microbial communities, contributing to symptom reduction. Aligning local dietary practices with evidence-based nutritional recommendations may optimize patient outcomes.

Emerging multi-omics technologies-including metagenomics, transcriptomics, and metabolomics-hold promise for unraveling host-microbiota interactions. Future studies should assess how CNS inflammation and neurodegeneration affect microbial metabolites, while integrating omics data to build predictive models of therapeutic responses.[13] Understanding how established

MS drugs (e.g., interferon-β) reshape gut microbiota will also be critical.

Despite encouraging progress, fundamental questions remain. It is still unclear whether gut dysbiosis contributes causally to MS pathogenesis or arises as a secondary effect.[17] Addressing this requires well-designed longitudinal studies. Standardized protocols for sampling, data analysis, and microbiota-based therapies must be established.[44] Ultimately, large randomized controlled trials (RCTs) are necessary to confirm the long-term efficacy and safety of microbiota-targeted interventions. Bridging the gap from research to practice will depend on multicenter RCTs, patient and clinician education, and collaboration with regulatory agencies to streamline approval processes for microbiota-derived therapies.

The complex interplay between the gut microbiota and MS provides unprecedented opportunities for patient-centered treatment approaches. By overcoming current limitations and advancing clinical translation, future research may fundamentally transform MS management and improve patient outcomes.

CONCLUSION

This review highlights the emerging link between gut dysbiosis and MS, demonstrating that alterations in gut microbial composition influence immune regulation, oxidative stress, and neuroinflammation, all contributing to demyelination. Unlike traditional MS management, which focuses on symptomatic relief and immunomodulation, the gut-brain axis introduces a novel biological pathway that may support early diagnosis, personalised treatment strategies, and improved patient outcomes. By consolidating current evidence, this study advances understanding by positioning gut microbiota as a potential therapeutic and diagnostic target in MS. Future research exploring microbiome-based interventions, such as probiotics, diet modulation, and FMT, could transform MS management beyond conventional neurocentric approaches.

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