

Review Article

The role of gut microbiota in modulating immune responses to neglected tropical diseases: A new frontier in host-pathogen interactions

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Abstract

Neglected tropical diseases (NTDs), such as Leishmaniasis, Chagas' disease, and trypanosomiasis affect billions of people worldwide, particularly in low-income regions, and pose significant public health challenges. Emerging evidence suggests that gut microbiota play a crucial role in modulating immune responses to these infections, influencing disease progression and host defence mechanisms. This review examines the interplay between gut microbiota and the immune system in the context of NTDs, highlighting mechanisms such as microbial-mediated immune priming, modulation of inflammation, and interactions with pathogenic organisms. Dysbiosis—an imbalance in gut microbiota—has been implicated in exacerbating NTDs pathogenesis, while microbiome-targeted interventions offer potential therapeutic strategies. A deeper understanding of host-microbiota interactions may facilitate the development of novel approaches to NTDs management, integrating microbiome modulation into existing treatment and preventive frameworks. Further research is necessary to elucidate specific microbial signatures associated with NTDs and their potential for therapeutic exploitation.

Keywords: Neglected tropical diseases, Microbiota, Immune system, Pathogen, Inflammation

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INTRODUCTION

Neglected Tropical Diseases (NTDs) encompass a wide range of both infectious and non-infectious diseases prevalent in tropical and subtropical areas, impacting around 1.6 billion individuals each year. Most of those affected are marginalized, suffering from poverty, conflict, and stigma, while lacking access to clean drinking water, proper sanitation, and quality healthcare facilities. The World Health Organization currently identifies 20 distinct diseases, caused

by agents such as viruses, bacteria, fungi, helminths, protozoa, and snakebite venom [1].

Neglected Tropical Diseases (NTDs) like Leishmaniasis, Chagas' disease, leprosy, Onchocerciasis, Schistosomiasis, Lymphatic filariasis and trypanosomiasis etc, suffer from insufficient funding and are often overlooked by global funding organizations. Contributing factors include poverty, geographical isolation, stigma, a lack of awareness regarding both local and worldwide prevalence data, and insufficient

political will and financial resources to address these issues. Furthermore, there seems to be limited advocacy for the most vulnerable populations, such as children, the aged, immunocompromised, and endemic dwellers, who are disproportionately affected by these diseases. Beyond causing lifelong disabilities and costing developing nations billions annually for their management, the delay in obtaining healthcare and treatment can be debilitating and stigmatising [2].

Importance of host immune responses in NTD pathogenesis

The pathogenesis of Neglected Tropical Diseases (NTDs) is heavily affected by the host's immune responses, which can either foster or hinder the progression of the disease. Robust immune responses aid in the elimination of pathogens and resolution of the disease, whereas immune evasion or dysregulation can lead to chronic infections, significant inflammation, and ongoing morbidity. Grasping these immunological mechanisms is essential for creating effective treatments and preventive strategies.

The immune system of the host is an intricate protective network that defends against

pathogens while preserving tissue homeostasis. It comprises two main elements: innate immunity, which provides immediate but non-specific defence, and adaptive immunity, which formulates targeted responses to pathogens and develops long-lasting memory. Innate immunity serves as the initial line of defence against infections, with macrophages, dendritic cells (DCs), natural killer (NK) cells, and neutrophils identifying and eliminating pathogens. Pattern recognition receptors (PRRs), such as Toll-like receptors (TLRs), are vital for detecting microbial antigens and initiating inflammatory reactions.

The T and B cells are essential contributors to adaptive immunity. CD4+ T-helper (Th) cells coordinate immune responses, while CD8+ cytotoxic T cells focus on identifying and destroying infected cells. B cells produce antibodies that neutralize pathogens [3].

In the case of schistosomiasis, caused by *Schistosoma japonicum*, the host's immune response performs dual roles. On one hand, the immune system attempts to combat the parasite, while on the other, the eggs of the parasite can provoke considerable inflammatory reactions, leading to tissue damage and fibrosis.

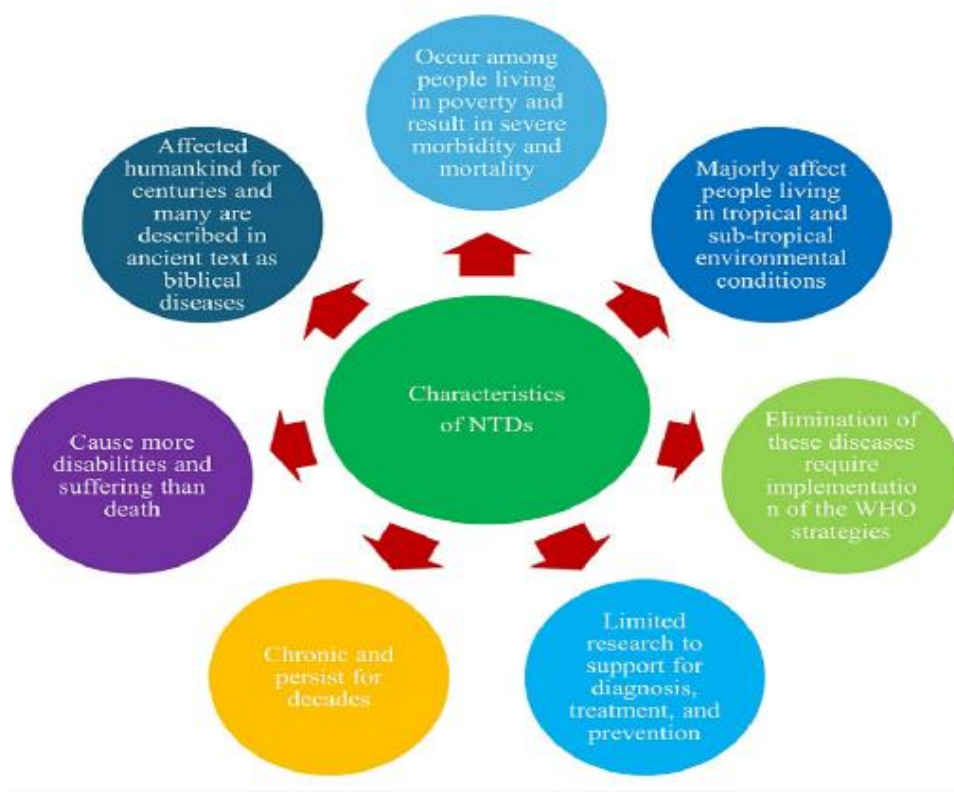


Figure 1: Characteristics of neglected tropical diseases (NTDs) [2]

The immune reaction to schistosome eggs is vital, as genetic therapies like CRISPR/Cas9-mediated gene deletion may enhance the host's immune response toward these eggs [4]. This suggests that strategies aimed at boosting the host's immune response could be beneficial in treating schistosomiasis.

The immune responses to neglected tropical diseases (NTDs) are intricate and significantly influence disease outcomes. The interplay between host immunity and pathogen strategies is essential for comprehending the pathogenesis of these diseases and developing effective therapies.

Emerging role of gut microbiota in immune regulation

The gut microbiota has been identified as a significant player in the regulation of the immune system concerning a range of diseases, including neglected tropical diseases (NTDs). This intricate community of microorganisms affects host immune responses, which can alter the duration and severity of infections caused by pathogens associated with NTDs.

The gut microbiota aids in immune regulation through various mechanisms:

Development of Immune Structures

Commensal bacteria play a crucial role in the formation and function of gut-associated lymphoid tissues (GALTs), which are vital for initiating immune responses [5].

Modulation of Innate Immunity

One of the primary ways the gut microbiota governs immune responses is through the production of metabolites, particularly short-chain fatty acids (SCFAs). These metabolites are generated when gut bacteria ferment dietary fibers and have been shown to enhance the integrity of the intestinal barrier and influence immune responses. Metabolites from the gut microbiota are essential for maintaining intestinal integrity and homeostasis, which is necessary to prevent pathogen invasion and subsequent immune dysregulation. This suggests that a healthy gut microbiota may bolster immune defenses against NTDs by supporting gut barrier function [6].

Influence on Adaptive Immunity

The gut microbiota has also been found to affect the development and functioning of T cells, which

are vital for adaptive immunity. The importance of the relationship between the gut microbiome and the mucosal immune system is significant; a balanced gut microbiota is essential for sustaining mucosal homeostasis and avoiding intestinal diseases [7]. Since many pathogens use mucosal surfaces for entry and persistence, this relationship may be critical in the context of NTDs.

Gut microbiota and immune system crosstalk

Overview of gut microbiota composition

The human gut microbiota is a complex and dynamic ecosystem of microorganisms that plays a vital role in maintaining host health. This varied ecosystem is predominantly composed of bacteria, but it also includes archaea, viruses, and fungi.

The majority of the gut microbiota belongs to a few dominant bacterial phyla:

Firmicutes: This phylum includes genera such as *Clostridium*, *Lactobacillus*, and *Ruminococcus*.

Bacteroidetes: Predominantly represented by the genus *Bacteroides*.

Actinobacteria: Notably includes the genus *Bifidobacterium*.

Proteobacteria: Encompasses a variety of genera, including *Escherichia*.

These groups collectively constitute a significant portion of the bacteria found in the gut. Research indicates that Firmicutes and Bacteroidetes alone account for nearly 90% of the gut microbiota [8]. An intricate interplay of internal and external factors shapes the makeup of the gut microbiota. Recognizing these factors is crucial for understanding the role of gut microbiota in both health and disease, particularly concerning neglected tropical diseases (NTDs). Some of these factors include:

Diet

The composition of gut microbiota is heavily influenced by diet. Eating habits have a profound effect on the diversity and functions of gut microbiota, which subsequently impacts metabolic health and susceptibility to disease. For instance, diets high in fiber promote the proliferation of beneficial bacteria that produce short-chain fatty acids (SCFAs), vital for regulating immune responses and maintaining

gut health. Conversely, a diet rich in fats may lead to an imbalance in the composition of the body's normal microbial community (dysbiosis). This is characterised by reduced microbial diversity and an increase in pro-inflammatory bacteria [9]. This dysbiosis has been associated with various health issues, including metabolic disorders and heightened vulnerability to infections related, in particular, to NTDs.

Age

Studies have shown that the diversity of gut microbiota diminishes as people age, potentially impacting immune function and overall well-being. For example, preterm infants exhibit a gut microbiota that is pro-inflammatory and less diverse compared to that of term infants, possibly making them more susceptible to various health challenges [10]. This highlights the importance of age-related changes in gut microbiota and their potential consequences for immune modulation.

Genetics

Genetic influences also play a crucial role in shaping gut microbiota composition. Variations in host genes may affect the gut microbiome and can contribute to increased susceptibility to diseases [11]. This suggests that the diversity and functionality of gut microbiota can be affected by the interplay between genetic predispositions and environmental influences, such as diet.

Mechanisms of microbiota-immune system interaction

The complex and dynamic relationship between the gut microbiota and the immune system is crucial for maintaining immune balance and influencing disease development. This interaction is facilitated by various mechanisms, including the production of short-chain fatty acids (SCFAs), the modulation of T regulatory cells (Tregs), and the activation of pattern recognition receptors (PRRs) [12].

Short-chain fatty acids (SCFAs)

Gut bacteria ferment dietary fibers to create metabolites known as SCFAs, which encompass butyrate, acetate, and propionate. These metabolites serve as key components in the gut microbiota-immune system relationship [13]. For instance, butyrate inhibits class 1 Histone Deacetylase (HDAC), leading to the hyperacetylation of histones and modulation of gene expression in immune cells. This mechanism enhances T Regulatory cell (Treg)

differentiation and reduces the production of pro-inflammatory cytokines, thereby fostering an anti-inflammatory environment [12].

Modulation of T regulatory cells (Tregs)

Tregs play a vital role in sustaining immunological tolerance and preventing autoimmune reactions. The gut microbiota influences Treg differentiation and function through several mechanisms. For example, butyrate promotes the production of the transcription factor Foxp3, which is crucial for Treg function, by inhibiting histone deacetylases HDACs and activating G protein-coupled receptors GPCRs, thereby enhancing the differentiation of naive T cells into Tregs [12].

Engagement of pattern recognition receptors (PRRs)

The PRRs, such as Toll-like receptors (TLRs), mediate the interface between the immune system and gut microbiota by initiating immune responses to microbial constituents. The interaction between TLRs and microbial elements is essential for sustaining mucosal and systemic immune status [14]. This interaction is crucial for generating appropriate immune responses to pathogens while preventing excessive immunological reactions that could lead to tissue damage.

Moreover, there is ongoing crosstalk between the host's innate and adaptive immune systems and the gut microbiota. The overall immune response may be shaped by the gut microbiota's capacity to influence the activity of various immune cell types, including innate lymphoid cells and T helper cells. Therefore, this interaction is vital for maintaining homeostasis and regulating immune responses to infections.

Microbiota-immune interactions in specific NTDs

Helminth infections (Schistosomiasis, Soil-transmitted helminths)

The relationship between gut microbiota and the immune system during helminth infections, like schistosomiasis and soil-transmitted helminths (STHs), involves intricate and multifaceted dynamics. These relationships can significantly influence gut dysbiosis and immune regulation, ultimately affecting the outcomes of diseases and the health of the host. Research has indicated that helminth infections, such as those from *Schistosoma* species and *Necator americanus*, can alter the gut microbiota's composition. For

instance, helminths may influence the distribution of specific bacterial groups, including *Lactobacillus spp.*, known to play a role in immune regulation [15]. This interaction suggests that helminths might promote a more diverse and stable gut microbiota, potentially countering dysbiosis triggered by other infections or dietary changes. A study showed that human participants experimentally infected with the hookworm *N. americanus* displayed consistent gut microbial diversity [16]. This stability is vital, as a diverse gut microbiota is often linked to enhanced immune function and resistance to infections. Intestinal helminth parasites can reshape the relative abundance of particular microbial populations within the host's gut microbiome by promoting taxonomic reassortment [17].

The microbial modulation of intestinal movement may provide resistance against helminth infections, suggesting that a healthy gut microbiota could enhance the host's defense against these pathogens [18]. This highlights the potential for treatment approaches that focus on restoring the balance of gut microbiota as a strategy for managing helminth infections.

Protozoan infections (Leishmaniasis, Chagas disease, trypanosomiasis)

The pathogenesis and severity of protozoan infections are significantly shaped by interactions between microbiota and the immune system, particularly in neglected tropical diseases (NTDs) like Leishmaniasis, Chagas' disease, and trypanosomiasis. Immune responses to these diseases can be affected by gut microbiota, which may influence disease progression. Leishmaniasis, caused by various species of the *Leishmania* genus, is transmitted by sandflies and presents in cutaneous, mucocutaneous, and visceral forms. Recent studies have shown that the gut microbiota can modulate immune responses to *Leishmania* infections. For instance, infection with *Leishmania major* alters the gut microbiome in both resistant and susceptible mice, suggesting that microbiota may play a role in determining disease susceptibility. Chagas disease, which is caused by *Trypanosoma cruzi* (*T. cruzi*), poses significant public health challenges. Recent research has examined the connection between gut microbiota and immune responses in Chagas disease. Structural changes in the gut microbiota have been linked to chronic Chagas disease, potentially influencing disease progression. The findings suggest that Chagas disease significantly contributes to variations in microbiota composition, indicating that the

infection could lead to dysbiosis [19]. This dysbiosis might compromise the integrity of the intestinal barrier, facilitating systemic spread of the parasite and worsening disease severity. Dysbiosis triggered by *T. cruzi* infection could negatively affect the immune response, as evidenced by changes in cytokine production and reduced activation of immune cells required for parasite elimination [20]. Trypanosomiasis, or sleeping sickness, is caused by the *Trypanosoma brucei* species and transmitted by tsetse flies. Research into the interplay between triatomine bugs, their microbiota, and *T. brucei* was conducted, showcasing the uneven responses of protozoans to an infected blood meal. This study posited that the vector's microbiota may influence both the transmission pattern of the parasite and the immune response of the host. *T. brucei* exploits the antigenic variability of its surface glycoproteins to evade the immune response of the host. The gut microbiota can influence the host's capability to recognize and react to parasites by modifying systemic immune responses. A well-balanced microbiome, for instance, supports the development and function of dendritic cells, which are essential for antigen presentation and the initiation of adaptive immunity [21].

Bacterial NTDs (Buruli ulcer, Leprosy)

Microbiota-immune interactions in bacterial neglected tropical diseases (NTDs), such as Buruli ulcer and leprosy [22], are increasingly recognized as crucial factors that affect disease severity and the host's immune responses. The gut microbiota has the potential to influence the progression of these infections by altering bacterial virulence and the immune system of the host. Buruli ulcer results from *Mycobacterium ulcerans*, which secretes a powerful toxin known as mycolactone, responsible for causing necrotizing skin lesions and significant morbidity. The development of Buruli ulcer is intricate and comprises interactions among the bacterium, the host's immune response, and the gut microbiota [23]. Mycolactone has been shown to inhibit dendritic cell activation, preventing them from effectively priming T cells and establishing adaptive immune responses. This inhibition fosters the bacterial persistence within host tissues [24]. This interaction may influence the inflammatory response and the disease's progression. The local skin microbiome may shift due to the ulcerative lesions typical of Buruli ulcer. The environment of necrotic tissue may become more vulnerable to opportunistic infections, potentially worsening the disease's course [25]. Leprosy, which is caused by *Mycobacterium leprae*, represents another

bacterial NTD [22] with notable microbiota-immune interactions. The immune reaction to *M. leprae* is intricate and varies among individuals, leading to different clinical manifestations of the disease. Recent findings suggest that the gut microbiome can modify the immune response to leprosy, possibly affecting the severity of the disease [26,27]. Research has indicated an increase in Tregs within leprosy lesions, especially in the lepromatous form. These cells produce anti-inflammatory cytokines such as IL-10, which can suppress effective immune responses, allowing the bacteria to thrive and multiply [28].

Potential microbiota-based therapeutic approaches

Probiotics, prebiotics, and faecal microbiota transplantation (FMT)

Modulating the gut microbiota has become increasingly popular as an effective therapeutic approach for a variety of diseases, including neglected tropical diseases (NTDs). Probiotics, prebiotics, and faecal microbiota transplantation (FMT) are approaches targeted at restoring or improving the composition and function of the gut microbiota, ultimately enhancing immune responses and overall health outcomes [29].

Probiotics

Probiotics are live microbes that, when taken in sufficient amounts, provide health benefits to the host. These microorganisms are often present in fermented foods such as yogurt, kimchi, and sauerkraut, as well as in dietary supplements. Research has demonstrated that probiotics can aid in digestion, strengthen the immune system, and reduce gastrointestinal problems [29]. They may alter the gut microbiota composition and enhance immune responses, making them a potential treatment for various diseases, including neglected tropical diseases (NTDs). As studies on probiotics progress, the mechanisms by which they support health are becoming clearer. Recently, a significant discovery has been their ability to prevent pathogens from attaching to the gut lining, maintaining the epithelial barrier, and modifying immune responses. Probiotics also influence the gut micro-ecology, proving advantageous to the human body. As a group of beneficial microbes, probiotics are crucial in regulating gut microbiota, which is increasingly acknowledged as an important factor in immune responses and disease severity in NTDs. Probiotic therapy can help restore microbial balance by increasing beneficial bacteria (such as *Oscillibacter* and

Prevotella) and short-chain fatty acids (SCFAs) that enhance immune response. Probiotics affect the immune system by interacting with intestinal epithelial cells (IECs), dendritic cells (DCs), macrophages, and B cells, all of which are essential for immune defense in neglected tropical diseases (NTDs). Others include: Activation of Innate Immunity, Enhancement of Humoral Immunity, Regulation of Antigen-Presenting Cells, Proinflammatory and Antimicrobial Effects [30].

Prebiotics

Prebiotics are carbohydrates that cannot be digested and specifically promote the growth and activity of beneficial gut bacteria, thereby affecting immune responses and metabolic functions. Some examples of prebiotics are fructooligosaccharides (FOS), galactooligosaccharides (GOS), inulin, and fructans. Their roles include stimulating the growth of beneficial native gut bacteria, producing short-chain fatty acids (SCFA), enhancing the absorption of micronutrients in the colon, modulating enzymes involved in xenobiotic metabolism, influencing immune responses, and altering gene expression in bacterial cells found in the cecum, colon, and feces. These functions are especially important in neglected tropical diseases (NTDs), where gut dysbiosis negatively impacts immunity. The metabolism of GOS leads to an increase in lactate and SCFAs, which improve gut barrier integrity and lower inflammatory markers, potentially helping to mitigate gut inflammation caused by NTDs. While the independent effects of these substances are still being studied, prebiotic compounds that promote growth are frequently combined with probiotic bacteria to achieve a synergistic effect known as "Synbiotics," aiming to enhance therapeutic outcomes. For instance, research has shown that the combination of inulin with *Lactobacillus rhamnosus* and *Bifidobacterium lactis* exhibits anti-inflammatory and antitumorigenic properties, indicating its possible role in the management of NTDs by enhancing host immunity and gut health [31].

Faecal microbiota transplantation (FMT)

The FMT represents a pioneering method used to modify the gut microbiota, characterized by the transfer of gut microbiota from healthy donors into ill patients through either the upper or lower gastrointestinal tract, aiming to restore the diversity of intestinal microbes [31]. It can also be described as a process that involves the transfer of the complete and stable faecal microbial

community from healthy donors to individuals suffering from specific diseases related to altered microbiota, with the main goal of correcting dysbiosis and alleviating disease symptoms. Unlike probiotics, which may only introduce a few microbial species into the gut of the host, FMT offers the significant advantage of delivering the entire gut micro-ecology as a functional "organ" and, in contrast to other organ transplants, it is very safe and does not provoke an immune rejection response [32]. There are established banks of donated faeces for FMT, and these samples are processed following strict standards to mitigate any potential risks (like the presence of viruses or parasites). The FMT has the potential to replenish beneficial bacteria, enhancing immune responses and reducing intestinal inflammation. Studies suggest that FMT can diminish colonization by antibiotic-resistant bacteria (ARB), which could be significant in bacterial NTDs like Buruli ulcer and trachoma, where antibiotic resistance poses a challenge. Although FMT shows promise as a therapeutic option, it remains largely underutilized for the restoration of gut microbiota due to the lack of long-term safety data and risk of transmission of pathogens [31].

Other Microbiota-targeted therapies for NTDs

Antimicrobial Peptides (AMPs)

The AMPs are substances produced by commensal bacteria that can inhibit pathogenic organisms like *Staphylococcus aureus*, *Escherichia coli*, and *Salmonella enterica*. Utilizing AMPs or encouraging their production may provide therapeutic advantages [33]. For instance, AMPs in the treatment of Buruli ulcer (West Africa) are being explored. Buruli ulcer, which is caused by *Mycobacterium ulcerans*, is commonly found in West African nations such as Ghana and Côte d'Ivoire. The bacterium generates mycolactone, which hampers immune responses and delays healing. Researchers are examining naturally occurring AMPs from gut bacteria to counteract the effects of mycolactone and promote wound healing [25].

Diet

Dietary modifications, including the use of natural polysaccharides, can change the composition of gut microbiota. This kind of alteration has been shown to improve metabolic disorders and may hold significance for NTDs by promoting gut health and immune function [33]. An example is dietary fiber and microbiota restoration in soil-transmitted helminth infections (Sub-Saharan Africa & Southeast Asia). Dietary interventions

with fiber-rich foods (like plantain (*Musa paradisiaca*), cassava (*Manihot esculenta*), and baobab fruit (*Adansonia digitata*) have been tried in Nigeria and Kenya to restore gut microbial diversity, enhance intestinal health, and improve the effectiveness of anti-helminthic drugs [34].

Challenges and opportunities

The research on the interactions between gut microbiota and neglected tropical diseases (NTDs) faces several limitations and challenges, but also holds promising prospects for future advancements and microbiome-based interventions in NTD-endemic regions. Addressing the following challenges is essential for exploiting microbiome-based interventions in NTD-endemic regions:

Limitations in current microbiota-NTD research

Geographical Research Shortfalls

A considerable number of microbiome studies are carried out in developed nations, leading to a lack of data from regions where neglected tropical diseases (NTDs) are common. This gap hinders the creation of targeted treatments. A systematic review highlighted significant deficiencies in microbiome research in Africa, emphasizing the need for studies addressing public health issues in these areas [35].

Absence of longitudinal studies

Most investigations into NTDs and gut microbiota have employed a cross-sectional approach, limiting insight into how the microbiome evolves over the course of an infection or as a disease advances [36,37].

Limited mechanistic understanding

Even though relationships between gut microbiota and NTDs have been identified, the fundamental mechanisms that drive these interactions remain unclear [38,39].

Complexity of microbiome structure

The intricate and ever-changing nature of the microbiome complicates the differentiation between causal relationships and simple correlations. To accurately evaluate the roles of microbial communities in NTDs, advanced methodologies are necessary due to their extensive diversity. The complexity of the microbiome often produces datasets that require sophisticated statistical techniques for

interpretation, making it challenging to translate research results into clinical applications [9].

Need for longitudinal studies and mechanistic insights

Longitudinal studies

To better understand the temporal dynamics of gut microbiota changes and their effects on the pathogenesis of NTDs and treatment outcomes, future research should concentrate on conducting longitudinal studies [36,37]. Such studies can define causal links and the long-term impacts of interventions.

Mechanistic investigations

Deeper mechanistic research is required to understand the specific pathways and interactions between gut microbiota, the immune system, and NTD-causing pathogens [38,39]. Understanding these pathways can uncover prospective therapeutic targets and guide the formulation of effective remedies. For example, studies have shown significant changes in gut microbiota composition related to Chagas disease, indicating potential indicators and therapeutic targets.

Integrated approaches

A more thorough understanding of the intricate relationships between the microbiota and NTDs can be obtained by combining multi-omics methods, animal models, and clinical research [40].

Prospects for microbiome-based interventions in NTD-endemic regions

Development of targeted therapies

Insights into microbiota-NTD interactions can result in the development of probiotics, prebiotics, FMT, or synbiotics designed to restore healthy microbial communities and improve host resistance to infections. However, the efficacy of such interventions must be established through rigorous clinical trials.

Integration into the existing health framework

Implementing microbiome-based therapeutics requires their inclusion in existing public health guidelines. This integration entails training healthcare workers, educating communities, and assuring the availability of essential resources. The World Health Organization's NTD roadmap emphasises the necessity of innovative tools and

nuanced interventions in meeting control and elimination targets by 2030.

Addressing socioeconomic and cultural factors

The success of these interventions is dependent on comprehending and negotiating the socioeconomic and cultural environments of affected communities. Engaging local populations in the creation and implementation of therapies guarantees cultural acceptability and adherence, both of which are critical for the long-term success of health interventions.

Multidisciplinary collaborations

Facilitating collaborations among researchers, clinicians, and public health experts will be crucial for converting microbiome insight into feasible strategies for managing NTDs [41].

CONCLUSION

The intricate relationship between gut microbiota and immune responses in neglected tropical diseases underscores the importance of microbiome research in infectious disease management. This review has highlighted key mechanisms through which gut microbes influence immune function, shaping both protective and pathological responses in neglected tropical diseases (NTDs). Although compelling evidence supports the role of gut microbiota in host immunity, significant gaps remain in understanding species-specific interactions and their direct implications for disease progression.

Harnessing microbiome-targeted therapies, such as probiotics, prebiotics, and faecal microbiota transplantation, presents a promising avenue for improving NTD outcomes. Future research should focus on characterizing microbiota profiles in NTD patients, identifying microbial biomarkers for early diagnosis, and integrating microbiome modulation into conventional treatment strategies. A multidisciplinary approach involving microbiologists, immunologists, and infectious disease specialists will be essential for advancing this field and translating findings into effective interventions for NTD-affected populations.

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Conflict of Interest

No conflict of interest is associated with this work

Use of Artificial Intelligence/large language models

We declare that artificial intelligence/large language models were used in this work for editorial purposes (writing, editing and paraphrasing).

Contribution of Authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

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