Dysbiosis Malaria and Hypertension: The Mechanistic Links

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ABSTRACT

According to new research, dysbiosis is a crucial link between chronic non-communicable diseases and infectious diseases. This review examines how malaria-induced dysbiosis and hypertension may exacerbate gut dysbiosis and summarizes the current understanding of the mechanisms underlying this relationship. Reduced microbial diversity, fewer bacteria that produce short-chain fatty acids (SCFAs), and elevated levels of pro-hypertensive metabolites such as trimethylamine-N-oxide (TMAO) and lipopolysaccharides (LPS) are the hallmarks of dysbiosis in hypertension. These changes result in increased gut permeability, endothelial dysfunction, and systemic inflammation, all of which raise blood pressure. At the same time, parasite toxins from Plasmodium infection cause severe gut dysbiosis (e.g., hemozoin), systemic inflammation (TNF-α, IFN-γ), and related malnutrition. This dysbiosis linked to Malaria weakens the integrity of the gut barrier and impairs immune regulation, resulting in a leaky gut and a pro-inflammatory phenotype. We proposed that the dysbiotic state brought on by acute or recurrent Malaria may act as a latent risk factor, setting up the host environment for the emergence of hypertension via persistent barrier dysfunction, impaired SCFA signaling, and prolonged inflammation. This intersection implies that novel approaches to reducing the risk of hypertension in malaria-endemic populations may involve microbiome-targeted interventions.

Keywords: Dysbiosis, Hypertension, Malaria, Gut Microbiome, Short-Chain Fatty Acids, Gut Permeability, Inflammation

INTRODUCTION

Dysbiosis and Hypertension

Dysbiosis, an imbalance in the gut microbiota, has been strongly linked to the onset and maintenance of hypertension. The bacterial community living in the gut maintains a symbiotic relationship with the host, and its

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imbalance has been associated with the progression of a wide range of intestinal and extraintestinal conditions. Increasing evidence supports the involvement of the gut microbiome in blood pressure regulation and the impairment of CKD prognosis (Felizardo et al., 2019). The imbalance is characterized by decreased microbial diversity and an altered *Firmicutes-to-Bacteroidetes* (F/B) ratio, both of which are linked to an increased risk of hypertension. Leading to metabolic disturbances that affect blood pressure regulation (Ge et al., 2024). Altered gut microbial composition, reduced diversity, and changes in microbial metabolites can causally increase blood pressure through multiple biological pathways.

Hypertension is a major global health challenge, as it represents the main risk factor for stroke and cardiovascular disease. It is a multifactorial clinical condition characterized by elevated and sustained blood pressure, likely resulting from a complex interplay of endogenous and environmental factors (Silveira-Nunes et al., 2020). The gut microbiota has been strongly implicated, but its role in hypertension remains poorly understood (Silveira-Nunes et al., 2020). Recent studies have identified dysbiosis of the intestinal microbiota in hypertensive subjects, characterized by reduced biodiversity and distinct bacterial signatures compared with normotensive subjects (Silveira-Nunes et al., 2020). Along with a reduction in *Bacteroidetes* members, hypertensive individuals showed increased proportions of *Lactobacillus* and *Akkermansia*. They decreased relative abundances of well-known butyrate-producing commensals, including *Roseburia* and *Faecalibacterium* within the *Lachnospiraceae* and *Ruminococcaceae* families (Silveira-Nunes et al., 2020).

In hypertension, the reduced number of short-chain fatty acids (SCFAs)- producing bacteria is associated with modifications in the gut environment, including a reduction in the hypoxic gut profile and worsening of the microbial balance, leading to a loss of epithelial barrier integrity, development of gut inflammation, and reduced SCFAs plasma levels. These modifications compromise blood pressure regulation and, as a consequence, favour end-organ damage, including the kidneys (Felizardo et al., 2019).

Mechanisms Linking Dysbiosis to Hypertension

The gut microbiome can regulate blood pressure through several mechanisms, including dysbiosis-induced changes in host microbiome-associated gene pathways. Microbiota-derived metabolites are either beneficial (for example, short-chain fatty acids and indole-3-lactic acid) or detrimental (for example, trimethylamine *N*-oxide). They can activate several downstream signalling pathways via G protein-coupled receptors or by directly activating immune cells (O'Donnell et al., 2023). These metabolite imbalances lead to decreased SCFAs (which help lower blood pressure) and increased pro-hypertensive metabolites, such as trimethylamine N-oxide (TMAO) and lipopolysaccharides (LPS), promoting inflammation and vascular dysfunction (Verhaar et al., 2020; O'Donnell et al., 2023; Luqman et al., 2024).

Hypertension is associated with pathological changes in the gut, including alterations in gut permeability and i nflammation. These changes can disrupt the gut barrier
functions, leading to systemic inflammation and contributing to the development of hypertension (Deng et al., 2025). Gut barrier dysfunction impairs the gut epithelial barrier, increasing intestinal permeability. Thus, allowing bacterial products (e.g., LPS) to enter circulation, triggering systemic inflammation and immune activation, which contribute to elevated blood pressure (Silveira-Nunes et al., 2020; O'Donnell et al., 2023). Moreover, dysbiosis-associated breakdown of the gut epithelial barrier can elicit systemic inflammation and disrupt intestinal mechano-transduction. These alterations activate mechanisms that are traditionally associated with blood pressure regulation, such as the renin–angiotensin–aldosterone system, the autonomic nervous system, and the immune system (Kim et al., 2018; O'Donnell et al., 2023). Fecal microbiota transplantation from hypertensive humans or animals to germ-free mice raises blood pressure in recipients, demonstrating a direct, causal role for dysbiotic microbiota in hypertension (Yan et al., 2022; Lin et al., 2024).

Specific mechanisms, such as the intestinal microbiota-mediated metabolism of dietary L-carnitine, a nutrient in red meat, have been demonstrated to promote atherosclerosis and increase cardiovascular disease risk by producing trimethylamine and trimethylamine-N-oxide (Li et al., 2017). Targeting gut microbial production of trimethylamine specifically and non-lethal microbial inhibitors were confirmed to relieve diet-induced atherosclerotic lesion development. Thus, the gut microbiome may also serve as a therapeutic target for cardiovascular and metabolic diseases (Li et al., 2017).

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Reduced microbial diversity in hypertensive individuals consistently shows lower gut microbial richness and diversity, with a shift toward harmful bacteria (e.g., *Prevotella, Klebsiella*) and a reduction in beneficial, short-chain fatty acid (SCFA)-producing bacteria (e.g., *Roseburia, Faecalibacterium*) (Silveira-Nunes et al., 2020; Tsiavos et al., 2024; Mardanparvar, 2025).

Several methodological and technological challenges remain in gut microbiome research, and solutions involve minimizing confounding factors, establishing causality, and increasing global sample diversity. New clinical trials, precision microbiome medicine, and computational methods such as Mendelian randomization have the potential to enable leveraging of the microbiome for translational applications to lower blood pressure (O'Donnell et al., 2023).

KEY PATHWAYS BY WHICH DYSBIOSIS AFFECTS HYPERTENSION

SCFA Production by Gut Bacteria and Its Impact on Blood Pressure

The fermentation of dietary fiber by gut bacteria produces short-chain fatty acids (SCFAs), primarily acetate, propionate, and butyrate. These SCFA-producing bacteria and their metabolites play a protective role in blood pressure regulation, mainly by promoting vasodilation, reducing inflammation, and supporting vascular and kidney health. SCFA-producing gut bacteria and their metabolites are essential for healthy blood pressure regulation.

SCFAs Mechanisms

SCFAs activate G protein-coupled receptors (GPR41 and GPR43) on blood vessels and the kidneys, leading to vasodilation and lower blood pressure. Butyrate, in particular, lowers arterial pressure via colon-vagus nerve signaling and GPR41/43 activation (Verhaar et al., 2020; Fusco et al., 2023). SCFAs also possess anti-inflammatory effects, thus reducing systemic inflammation and oxidative stress, both of which are linked to hypertension (Yang et al., 2020; Wu et al., 2021). Furthermore, SCFAs have been reported to strengthen gut barrier integrity and modulate immune responses, preventing the leakage of pro-hypertensive substances into circulation (Yang et al., 2020; Nogal et al., 2021). Efficient absorption of SCFAs into the bloodstream is crucial; lower plasma SCFA levels and higher fecal SCFA levels are observed in hypertensive individuals, suggesting that impaired absorption may contribute to high blood pressure (Calderón-Pérez et al., 2020; Verhaar et al., 2020).

Table 1: Summary of Key Findings SCFA production, gut bacteria, and blood pressure regulation

Factor	Effect on Blood Pressure	Citations
Increased SCFA-producing bacteria	Lower blood pressure	(Yang et al., 2020; Wu et al., 2021).
Decreased SCFA-producing bacteria	Higher blood pressure	(Yang et al., 2020; Verhaar et al., 2021).
SCFA supplementation (animal/human studies)	Reduces blood pressure	(Wu et al., 2021; Yan et al., 2025).
High-fiber/probiotic diet	Increases SCFA, lowers BP	(Wu et al., 2021; Yan et al., 2025).

Strategies that boost SCFA production, such as high-fiber diets and probiotics, may help prevent or manage hypertension by enhancing vasodilation, reducing inflammation, and supporting gut and vascular health.

Blood Pressure Elevation and Gut Bacterial Metabolites LPS and TMAO

Lipopolysaccharides (LPS) and trimethylamine-N-oxide (TMAO) are key metabolites produced or influenced by gut bacteria. Both have been implicated in the development and progression of hypertension through mechanisms involving inflammation, vascular dysfunction, and altered neuro-hormonal signalling.

LPS Mechanistic Role in Inflammation and Vascular Effects

LPS are components of the outer membrane of Gram-negative gut bacteria. Increased gut permeability (often due to dysbiosis) allows LPS to enter the bloodstream, where they trigger systemic inflammation by activating

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immune receptors (e.g., TLR4), leading to the release of pro-inflammatory cytokines (TNF-α, IL-1, IL-6) (Verhaar et al., 2020; Samarraie et al., 2023). LPS-induced inflammation promotes endothelial dysfunction, increases sympathetic nervous system activity, and can directly affect blood pressure regulation. Animal and limited human studies have shown that elevated LPS levels are associated with higher blood pressure and neuroinflammation relevant to hypertension (Verhaar et al., 2020; Samarraie et al., 2023).

TMAO Mechanistic Role in Vascular Dysfunction and Hormonal Effects

Gut bacteria metabolize dietary choline, carnitine, and phosphatidylcholine into trimethylamine (TMA), which is converted in the liver to TMAO (Canyelles et al., 2023; Zhen et al., 2023). High TMAO levels are linked to increased risk of hypertension. TMAO prolongs the hypertensive effect of angiotensin II, enhances vasoconstriction, increases water reabsorption via the TMAO-AVP-AQP2 axis, and promotes vascular inflammation and endothelial dysfunction (Canyelles et al., 2023; Samarraie et al., 2023; Zhen et al., 2023). Clinical evidence has shown that elevated TMAO is consistently associated with higher blood pressure in both animal models and human studies, and interventions that reduce TMAO (e.g., antibiotics, dietary changes) can lower blood pressure (Jiang et al., 2021; Samarraie et al., 2023; Zhen et al., 2023).

Table 2: Summary of LPS and TMAO Mechanisms and Effects on Blood Pressure

Metabolite	Mechanism	Effect on BP	Citations
LPS	Inflammation, endothelial dysfunction	Raises BP	(Moludi et al., 2020; Samarraie et al., 2023; Zhen et al., 2023).
TMAO	Vasoconstriction, hormonal effects, vascular inflammation	Raises BP	(Jiang et al., 2021; Samarraie et al., 2023; Zhen et al., 2023).

Additionally, both LPS and TMAO, produced or modulated by gut bacteria, contribute to hypertension by promoting inflammation, vascular dysfunction, and neuro-hormonal changes. Targeting of gut microbiota to reduce LPS and TMAO may offer new strategies for blood pressure control.

Mechanisms Linking Gut Permeability and Blood Pressure

Increased gut permeability, often called "leaky gut," is strongly associated with higher blood pressure and hypertension. Raised gut permeability is both a marker and a potential driver of high blood pressure. It promotes systemic inflammation and allows harmful bacterial products into circulation, contributing to hypertension. This relationship is mediated by the translocation of bacterial products (such as LPS) and by increased inflammation, which contribute to vascular dysfunction and elevated blood pressure. Hypertensive patients exhibit elevated levels of gut permeability markers (zonulin, DAO, LPS, D-lactate), suggesting impaired intestinal barrier function. This dysfunction allows bacterial products to enter the bloodstream, triggering systemic inflammation and immune activation, which are known contributors to hypertension (Kim et al., 2018; Li et al., 2021; Yang et al., 2023). Hypertension is usually associated with reduced diversity of beneficial gut bacteria and decreased production of short-chain fatty acids (SCFAs), both of which help maintain barrier integrity. Dysbiosis further weakens the barrier and promotes inflammation (Kim et al., 2018; Li et al., 2021; Yang et al., 2023). The increased sympathetic drive in hypertension can also reduce gut blood flow, damaging the intestinal lining and increasing permeability. This creates a feedback loop where hypertension worsens gut barrier function, and barrier dysfunction exacerbates hypertension (Ntlahla et al., 2021; Vemuri et al., 2022; Yang et al., 2023). Strategies that restore gut barrier integrity, such as dietary changes, probiotics, and antihypertensive medications, may help manage or prevent hypertension.

Table 3. Key Evidence from Human and Animal Studies linking gut permeability and blood pressure

Finding	Evidence Type	Citations
Hypertensive patients have higher gut permeability markers (zonulin, LPS, DAO)	Human studies	(Kim et al., 2018; Li et al., 2021; Ntlahla et al., 2021)
Gut permeability correlates with systolic BP	Human studies	(Kim et al., 2018; Ntlahla et al., 2021).

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XIII Issue IV April 2026

Increased permeability precedes hypertension	Animal studies	(Verhaar et al., 2020; Yang et al., 2023).
Restoring barrier function lowers BP	Animal/intervention	(Yang et al., 2019; Del bo et al., 2020).

Fecal Microbiota Transplantation (FMT) and Blood Pressure Regulation

Transferring gut microbiota via fecal microbiota transplantation (FMT) can causally alter blood pressure in both animal models and humans. The effect depends on the donor's microbiota: hypertensive donor microbiota raises recipients' blood pressure, while normotensive donor microbiota can lower it. Multiple animal studies have shown that FMT from hypertensive animals or humans to normotensive or germ-free recipients increases blood pressure, transferring the hypertensive phenotype. Conversely, FMT from normotensive donors to hypertensive animals lowers blood pressure (Zhong et al., 2021; Lin et al., 2024; Xu et al., 2024). Washed microbiota transplantation (WMT) from normotensive donors to hypertensive patients significantly reduced both systolic and diastolic blood pressure, especially in those not on antihypertensive drugs or receiving lower GI tract delivery (Zhong et al., 2021; Fan et al., 2025). However, some clinical trials found the BP-lowering effect to be modest and not always sustained (Fan et al., 2025). The transfer of gut microbiota alters the composition of gut microbes, increases beneficial bacteria (e.g., butyrate producers), improves gut barrier integrity, reduces inflammation, and modulates neuro-hormonal signalling, all contributing to blood pressure regulation (Zhong et al., 2021; Yan et al., 2022; Xu et al., 2024).

Table 4. Effects of Microbiota Transfer on Blood Pressure

Donor Microbiota Type	Recipient Effect on BP	Key Mechanisms	Citations
Hypertensive	Increase the BP	Inflammation, dysbiosis, neuroinflammation	(Yan et al., 2022; Lin et al., 2024; Xu et al., 2024).
Normotensive	Decreases the BP	SCFA production, improved barrier, reduced inflammation	(Yan et al., 2022; Xu et al., 2024; Fan et al., 2025).

Microbiome transfer can directly raise or lower blood pressure, depending on the donor’s microbiota composition. Highlighting the gut microbiome as a promising target for hypertension therapy, though its effects in humans are variable and require further research for clinical application.

ROLE OF DYSBIOSIS IN MALARIA PATHOGENESIS AND PROGRESSION

Dysbiosis plays a significant role in malaria pathogenesis and progression by modulating immune responses, increasing disease severity via several pathways, disrupting host-microbiota balance, and amplifying the parasite's immunopathology. Gut dysbiosis refers to an imbalance in the composition and function of the intestinal microbiome, characterized by reduced microbial diversity, overgrowth of pathogenic bacteria, and depletion of beneficial taxa (e.g., *Bifidobacterium* and *Lactobacillus* species). Malaria, caused by *Plasmodium* parasites (primarily *P. falciparum* and *P. vivax*), progresses through liver invasion, erythrocytic cycles, and systemic inflammation, leading to symptoms such as fever, anemia, and organ dysfunction. Gut dysbiosis has been reported to play a significant role in the progression and pathogenesis of Malaria, influencing disease severity through immune modulation, barrier dysfunction, and persistent microbiome alterations. Emerging research highlights a bidirectional relationship between Malaria and gut dysbiosis: Malarial infection disrupts the microbiome, and dysbiosis exacerbates disease severity.

Differences between *Plasmodium* species significantly influence the degree, composition, and functional impact of gut dysbiosis (Yañez et al., 2021). Stemming from variations in parasite virulence, tissue tropism, inflammatory profiles, and host immune responses. *P. falciparum* (most virulent) induces more profound dysbiosis than milder species like *P. vivax* (Bangs et al., 2022; Costa et al., 2021).

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XIII Issue IV April 2026

Evidence Linking Malaria to Gut Dysbiosis

In murine models of *Plasmodium* infection (e.g., *P. berghei* or *P. chabaudi*), Malaria induces rapid dysbiosis within days. Studies have shown decreased α-diversity (e.g., loss of Firmicutes and Bacteroidetes). Expansion of Proteobacteria (e.g., *Enterobacteriaceae*) and pathobionts like *Akkermansia muciniphila* (in protective contexts) or *Clostridium* species (Yañez et al., 2021). Studies in humans have reported that children in malaria-endemic areas (e.g., Mali, Uganda) with acute *P. falciparum* infection exhibit dysbiosis, with reduced *levels of Faecalibacterium prausnitzii* (an anti-inflammatory) and increased *levels of Bacteroides* species. Severe Malaria was found to correlate with lower microbial diversity and higher fecal calprotectin levels (an inflammation marker). Longitudinal data indicate that dysbiosis persists even after treatment, potentially increasing the risk of reinfection (Yegorov et al., 2020).

Mechanisms Linking Gut Dysbiosis and Malaria Pathogenesis

Dysbiosis, an imbalance in the gut or lung microbiota, has been identified as a risk factor for severe Malaria. Altered microbiota composition can impair immune regulation, increase systemic inflammation, and disrupt barrier functions, all of which contribute to worsened malaria outcomes (Waide & Schmidt, 2020; Mandal & Schmidt, 2023; David, 2025). In both human and animal models, a diverse and balanced gut microbiome enhances immune competence. It reduces malaria severity, while dysbiosis is associated with higher parasite burden, increased inflammation, and complications such as cerebral Malaria and acute respiratory distress syndrome (MA-ARDS) (Waide & Schmidt, 2020; Mukherjee et al., 2022; David, 2025).

There exists a bidirectional relationship between Malaria and dysbiosis. Malaria infection induces gut dysbiosis, characterized by reduced microbial diversity and shifts in bacterial populations, which, in turn, exacerbates disease severity by impairing immune responses and gut barrier function (Mandal & Schmidt, 2023; Sriboonvorakul et al., 2023; He et al., 2025). Dysbiosis worsens malnutrition (e.g., via reduced vitamin absorption), further promoting pathobiont growth and parasite replication. Another mechanism is through immune modulation; the gut microbiota shapes both innate and adaptive immunity. Dysbiosis can weaken antimalarial immune responses, while certain beneficial bacteria (e.g., Bifidobacterium, Lactobacillus) are associated with resistance to severe Malaria (Villarino et al., 2016; Mandal & Schmidt, 2023; Sriboonvorakul et al., 2023).

Immune Modulation and Disease Progression

Dysbiosis affects both innate and adaptive immunity. It can impair the development of effective humoral (antibody-mediated) responses and regulatory T cell function, leading to inadequate parasite clearance and increased risk of severe disease (Waide & Schmidt, 2020; Mandal & Schmidt, 2023; Fusco et al., 2025). Plasmodium infection itself can induce dysbiosis, creating a feedback loop that exacerbates immunopathology and disease progression (Mukherjee et al., 2022; He & Qi, 2025). In the lungs, dysbiosis driven by malaria infection can promote respiratory complications and mortality (Mukherjee et al., 2022; He & Qi, 2025). Dysbiosis impairs Treg cell function and SCFA production (e.g., butyrate), reducing anti-parasitic Th1/IFN-γ responses while exacerbating Th17-driven pathology. Pathobiont blooms (e.g., *Enterobacteriaceae*) produce pro-inflammatory metabolites, correlating with higher parasitemia and hypoglycaemia (Kers & Saccenti, 2022).

Barrier Dysfunction and inflammation are other mechanisms by which severe Malaria leads to intestinal injury and increased permeability, allowing the translocation of bacteria and metabolites into the bloodstream, which can result in secondary infections and systemic inflammation (Sriboonvorakul et al., 2023; He et al., 2025). Furthermore, malaria infection can induce persistent microbiome alterations; this dysbiosis persists beyond the acute infection phase, resulting in long-term changes in microbiota composition linked to ongoing immune and metabolic imbalances (Van Den Ham et al., 2024; He et al., 2025).

Mechanism of Hemozoin as a Driver of Dysbiosis

Several factors contribute to dysbiosis during malaria infection. These factors include Parasite toxins/hemozoin, Systemic inflammation (cytokines such as IFN-γ and TNF-α), Anemia/malnutrition, etc. Hemozoin and parasite toxins drive dysbiosis in Malaria via immune and inflammatory pathways. During the blood stage of Malaria, Plasmodium parasites digest hemoglobin, producing hemozoin, an insoluble crystalline pigment, which is

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XIII Issue IV April 2026

released into circulation upon red blood cell rupture (De Villiers & Egan, 2021; Garnie et al., 2025). Hemozoin is rapidly phagocytosed by immune cells, triggering strong pro-inflammatory responses. It activates the NLRP3 inflammasome and Toll-like receptor 9 (TLR9), leading to the production of cytokines such as IL-1β and other inflammatory mediators (Kalantari et al., 2014; Denny et al., 2019). This systemic inflammation can disrupt gut barrier integrity and alter the gut environment, promoting dysbiosis (Kalantari et al., 2014; Denny et al., 2019). Dysfunction of dendritic cells results from hemozoin impairment, reducing their ability to prime T cells and skewing immune responses. This immune modulation can further compromise gut immune homeostasis, contributing to dysbiosis (Pack et al., 2021; Lasaviciute et al., 2025). Exposure to hemozoin induces oxidative stress and DNA damage in various tissues, including the gut and placenta, exacerbating inflammation and potentially altering the gut microbiota (Pranty et al., 2024; Sarr et al., 2025). Hemozoin can also carry parasite DNA, which, together, activate both the NLRP3 and AIM2 inflammasomes, amplifying systemic inflammation and immune dysregulation (Kalantari et al., 2014).

Table 5: summarizing mechanisms by which hemozoin induces dysbiosis.

Mechanism	**Evidence Type**	**Citations**
Inflammasome activation	Animal, in vitro	(Kalantari et al., 2014).
Dendritic cell dysfunction	Animal, in vitro	(Pack et al., 2021; Lasaviciute et al., 2025).
Oxidative stress/tissue damage	Human, in vitro	(Pranty et al., 2024; Sarr et al., 2025).
Gut barrier disruption	Animal, human	(Denny et al., 2019).
Immune modulation	Animal, in vitro	(Pack et al., 2021; Lasaviciute et al., 2025).

In summary, hemozoin, a key malaria parasite toxin, induces gut dysbiosis primarily by activating inflammatory pathways (NLRP3 inflammasome, TLR9), impairing immune cell function, and inducing oxidative stress. These processes disrupt gut homeostasis, promoting dysbiosis and potentially worsening malaria outcomes.

Mechanism of Dysbiosis Induction by Systemic Inflammation via IFN-γ and TNF-α

Systemic inflammation, as indicated by elevated levels of cytokines such as interferon gamma (IFN-γ) and tumor necrosis factor alpha (TNF-α), is a defining characteristic of Malaria. Although these cytokines play a crucial role in controlling the parasite, their excessive or prolonged presence can result in immune dysregulation, tissue damage, and disturbances in gut homeostasis, which are critical to the development of gut dysbiosis during Malaria. This occurs due to immune hyperactivation, barrier damage, and ongoing inflammatory signaling, underscoring the importance of cytokine balance in maintaining gut health during infection.

In cases of severe Malaria, the cytokine profile is marked by a shift towards Th1 responses (high levels of IFN-γ and TNF-α) and a decrease in regulatory cytokines (such as IL-10), leading to unregulated inflammation and immune-related tissue damage that can compromise the gut microbiome (Loevenich et al., 2017; Popa & Popa, 2021; Obeagu, 2024). Continuously elevated or chronic expression of IFN-γ, even at lower concentrations, can disrupt gut homeostasis and lead to dysbiosis, as demonstrated in animal studies (Bae et al., 2020). Through mechanisms of immune hyperactivation, IFN-γ and TNF-α play crucial roles in activating macrophages and other immune cells to eliminate Plasmodium parasites. However, when produced in excess, they can cause systemic inflammation that injures tissues, including the gut lining, and disrupt the gut microbiota's equilibrium (Loevenich et al., 2017; Popa & Popa, 2021; Obeagu, 2024). These surges of pro-inflammatory cytokines impair the integrity of the gut barrier, leading to increased permeability and the potential for microbial translocation. This alteration in the gut environment promotes dysbiosis and further intensifies inflammation (Popa & Popa, 2021; Obeagu, 2024).

Table 6: Summary of evidence for cytokine-driven dysbiosis in Malaria.

Mechanism	**Evidence Type**	**Citations**
IFN-γ/TNF-α drive inflammation	Human, animal	(Loevenich et al., 2017; Popa & Popa 2021; Obeagu 2024).
Barrier dysfunction	Animal, review	(Bae et al., 2020; Popa & Popa, 2021; Obeagu, 2024).
Chronic IFN-γ induces dysbiosis.	Animal, multi-omics	(Bae et al., 2020).
Cytokine imbalance in severity	Human, review	(Popa & Popa, 2021; Obeagu, 2024).

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XIII Issue IV April 2026

Mechanisms Connecting Malnutrition, Anemia, and Dysbiosis in Malaria

Another element that exacerbates disease outcomes while also acting as a catalyst for dysbiosis is malnutrition and anemia, which are common in regions where Malaria is endemic and are increasingly identified as significant contributors to gut dysbiosis, potentially affecting the severity of Malaria and leading to poorer health outcomes.

Deficiencies in protein and micronutrients can alter gut structure, diminish immune cell populations, and increase intestinal permeability, resulting in dysbiosis (imbalance of microbes) (Murr et al., 2021; Verma et al., 2025). Dysbiosis resulting from malnutrition can shift immune cells toward a pro-inflammatory phenotype, thereby enhancing gut and systemic inflammation during Malaria. The occurrence of Malaria can also disrupt the gut microbiome, and when this is coupled with malnutrition, the effects are intensified, leading to worse gut barrier dysfunction and immune dysregulation (Murr et al., 2021; Verma et al., 2025). Additionally, chronic malnutrition is typically linked to more severe cases of Malaria (for instance, elevated parasitemia and anemia), with both conditions associated with alterations in gut microbiota and compromised immune responses (Das et al., 2018; Verma et al., 2025).

Table 7: Summarizing how malnutrition and anemia drive dysbiosis and worsen malaria outcomes.

Factor	Effect on Gut/Malaria Outcomes	Citations
Malnutrition	Increases gut permeability, reduces immune cells, and worsens dysbiosis	(Murr et al., 2021; Verma et al., 2025).
Anemia	Associated with severe Malaria and altered gut microbiota	(Das et al., 2018; Verma et al., 2025)
Combined with Malaria	Exacerbates gut inflammation, dysbiosis, and disease severity	(Murr et al., 2021; Verma et al., 2025).
Nutritional Interventions	May improve immune function and reduce malaria severity	(M, 2025)

While animal studies demonstrate clear connections among malnutrition, dysbiosis, and aggravated Malaria, human research presents a more varied picture, with some studies indicating strong correlations and others revealing no direct relationship between infection status and gut microbiota (Das et al., 2018; Mutoni et al., 2025). These interactions are complex and shaped by factors such as age, geographical location, co-infections, and environmental influences (Das et al., 2018; Mutoni et al., 2025).

Current findings support that malnutrition and anemia contribute to gut dysbiosis in Malaria, heightening immune dysfunction and the severity of the disease. It is essential to implement integrated interventions that address nutrition, Malaria, and gut health, particularly among vulnerable groups. Nonetheless, further longitudinal and mechanistic research in humans is necessary to elucidate these relationships and enhance interventions.

Antimalarials/Artemisinin-Based Antimalarials as Drivers of Gut Dysbiosis

In human studies involving malaria patients, artemether-lumefantrine treatment was associated with modest yet notable alterations in gut bacterial populations over a week, with certain bacteria (e.g., E. coli, Klebsiella, Pseudomonas) showing increased abundance. A study conducted in Kenya found that infants treated for Malaria with artemether-lumefantrine displayed no significant variations in gut bacterial diversity or composition pre- and post-treatment. Only one of the top 100 bacterial sequence variants showed a significant change, indicating a minimal effect on the gut microbiota (Mandal et al., 2018). However, these alterations were more significant when ACTs were administered alongside probiotics, although the clinical relevance of these changes remains uncertain (Awah-Nanzdum et al., 2023).

Several murine studies utilizing clinically relevant artemisinin-based combination therapies (ACTs), such as artesunate with amodiaquine and artemether with lumefantrine, found no notable changes in gut microbiota composition, diversity, or abundance following treatment. Any small shifts in microbial populations were temporary and returned to baseline swiftly, suggesting that these antimalarials do not cause gut dysbiosis in mice

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XIII Issue IV April 2026

(Denny & Schmidt, 2019). Species abundance and diversity stayed stable, and any minor fluctuations were transient, reaffirming that ACTs do not disrupt gut microbial equilibrium in this model (Denny & Schmidt, 2019). Furthermore, when artemether-lumefantrine was combined with the probiotic Arthrospira platensis, more pronounced alterations in gut bacterial communities were observed, whereas these effects were absent when only antimalarial drugs were given (Awah-Nanzdum et al., 2023).

Mechanistic Insights and Research Gaps

Numerous studies have provided evidence suggesting that artemisinin derivatives may help preserve gut homeostasis by modulating inflammatory responses rather than causing dysbiosis (Denny & Schmidt, 2019). Some ex vivo studies have shown that gut bacteria can metabolize artemisinin, potentially influencing its effectiveness, but these results do not directly imply dysbiosis or harmful effects on the microbiota (Gomes et al., 2025). While the strongest evidence comes from animal models, more extensive human studies are necessary to validate these findings and clarify any long-term effects (Denny & Schmidt, 2019; Awah-Nanzdum et al., 2023; Gomes et al., 2025). Data regarding non-artemisinin antimalarials (e.g., doxycycline, hydroxychloroquine) is limited, though existing research suggests little or no significant dysbiosis when administered at standard dosages (Pan et al., 2020; Javelle et al., 2021). Current studies indicate that antimalarial medications, particularly ACTs, do not significantly provoke gut dysbiosis during malaria infections. The effects are minimal in comparison to antibiotics, and any changes tend to be temporary. Additional human research is necessary to gain a comprehensive understanding of these interactions. Further investigation is required for other drug categories and among diverse human populations.

Table 8: Summary of antimalarial drug effects on gut microbiota in Malaria.

Study Type	Antimalarial(s) Used	Effect on Gut Microbiota	Citations
Mouse	Artesunate+amodiaquine, artemether+lumefantrine	No significant change; transient minor shifts	(Denny & Schmidt, 2019).
Human (infants)	Artemether-lumefantrine	No significant change	(Mandal et al., 2018).
Human	Artemether-lumefantrine + probiotic	Significant change (with probiotic)	(Awah-Nanzdum et al., 2023)

Increased Gut Permeability and Bacterial Translocation

Malaria elevates zonulin and reduces occludin/claudin expression, allowing gram-negative bacteria/LPS (lipopolysaccharide endotoxin) to translocate into the bloodstream. Circulating LPS triggers TLR4-mediated inflammation, promoting cytoadherence of infected RBCs to the endothelium (via ICAM-1 upregulation). LPS synergizes with hemozoin to drive neuroinflammation (Morffy et al., 2019; Veres-Székely et al., 2023). Mouse models show that germ-free or antibiotic-pretreated mice have milder cerebral Malaria, which is rescued by fecal microbiota transplant (FMT) from infected donors (Douglas et al., 2022).

THERAPEUTIC IMPLICATIONS

Microbiome Modulation

Probiotics, such as Lactobacillus reuteri, have been shown to decrease parasitemia and inflammation in animal models (Radaelli et al., 2021). Fecal microbiota transplantation (FMT) helps restore microbial diversity and offers protection against experimental cerebral Malaria. Prebiotics, such as inulin, enhance the production of short-chain fatty acids (SCFAs) and help alleviate symptoms of leaky gut. Clinical trials are currently underway in endemic regions (e.g., NCT04557865 on ClinicalTrials.gov) to assess the effectiveness of synbiotics in conjunction with artemisinin-based treatments. Co-infections, such as those caused by helminths, as well as dietary factors, present challenges that can alter microbiota and complicate therapeutic strategies.

Differences in Plasmodium Species and Gut Dysbiosis in Malaria

Variations among Plasmodium species significantly affect the levels, composition, and functional consequences of gut dysbiosis. This is due to differences in parasite virulence, tissue tropism, host inflammatory responses,

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and host immune responses. P. falciparum, being the most virulent, causes greater dysbiosis compared to less severe species like P. vivax.

Table 9: Key Evidence linking severity of dysbiosis to Malaria infections from Human Studies

***Plasmodium* Species**	**Dysbiosis Severity**	**Key Findings**
P. falciparum (severe Malaria)	High	Marked loss of diversity (↓α-diversity by 30-50%); ↑Proteobacteria (e.g., *Escherichia, Klebsiella*); ↑fecal LPS; correlates with cerebral malaria and mortality (Bangs et al., 2022; Yegorov et al., 2020).
P. vivax (milder, relapsing)	Moderate	Reduced diversity but less pathobiont bloom; milder barrier disruption; persists longer due to hypnozoites (Costa et al., 2021).
P. ovale/P. malariae	Low	Minimal data; subtle shifts, no strong association with severe gut permeability (Mutapi et al., 2023).

A meta-analysis conducted in co-endemic areas (e.g., Papua New Guinea) found that *P. falciparum* mono-infections show 2-3x greater dysbiosis severity than *P. vivax* (Mutapi et al., 2023).

Table 10: highlighting effects of malarial species in animal models

Model Species	**Dysbiosis Severity**	**Notes**
P. berghei (rodent, cerebral malaria mimic)	Very High	There is a rapid *Proteobacteria* expansion; 80% mortality linked to translocation (Douglas et al., 2022).
P. chabaudi (rodent, non-cerebral)	Moderate	Usually self-resolving; a shift in the protective microbiota that occurs, caused by an increase in *Akkermansia* (Reinhardt et al., 2022).
P. yoelii (rodent, chronic)	Low-Moderate	Less inflammation-driven dysbiosis (Reinhardt et al., 2022).

Mixed infections between species, such as *P. falciparum* + *P. vivax*, have been observed to amplify dysbiosis beyond infections by a single malarial species, most likely due to synergistic inflammation (Ataide et al., 2020).

Mechanisms Driving Species-Specific Dysbiosis

Several mechanisms exist that drive the species-specific gut dysbiosis in malarial infections, including the virulence factors (cytoadherence, inflammation profile, etc.), host microbiota interactions, and dietary/geographic confounders.

Table 11: Showing Virulence Factors between Specie types

Factor	***P. falciparum* (High Dysbiosis)**	***P. vivax* (Moderate Dysbiosis)**
Cytoadherence/Sequestration	Strong (PfEMP1 var genes) → endothelial damage, systemic cytokines → severe leaky gut (Haldar et al., 2018)	Weak → less gut ischemia (Costa et al., 2021)
Inflammatory Profile	High TNF-α/IL-6/IFN-γ → tight junction breakdown (Bangs et al., 2022)	Lower cytokines → milder permeability
Hemozoin/LPS Synergy	Potent TLR activation → pathobiont blooms (Douglas et al., 2022)	Less hemozoin → subdued response
Liver Stage Duration	Short, explosive blood stage → acute dysbiosis (Yañez et al., 2021)	Dormant hypnozoites → chronic low-grade shifts

In the interactions between host and microbiota, infection with P. falciparum disrupts the population of SCFA-producing bacteria more significantly, leading to impaired Treg cells and worsening Th1 pathology (Yegorov et al., 2020). Factors such as geographic and dietary variations in endemic microbiomes (e.g., African versus

Amazonian) influence outcomes, but the parasite's species remains a major factor (Mutapi et al., 2023). Research indicates that humans with a higher level of Bacteroidetes in their microbiota tend to recover more robustly from post-P. falciparum infections, while mice with a Firmicutes-dominant microbiota experience a prolonged state of dysbiosis (Douglas et al., 2022). Studies with germ-free humanized mice validate that the effects of parasite species are consistent across different hosts (Douglas et al., 2023). In non-human primates, for instance, P. cynomolgi in macaques mimics a P. vivax-like state of moderate dysbiosis (Yañez et al., 2021).

Moreover, a higher dysbiosis index is indicative of severe outcomes, with an odds ratio of 2.5 for cerebral Malaria in cases of P. falciparum (Bangs et al., 2022). Customized microbiome-based therapeutic strategies, such as aggressive probiotics, show support for P. falciparum infections in conjunction with P. vivax. Although there are few direct comparative studies in humans, much of the evidence comes from endemic cohorts (Mutapi et al., 2023). Essentially, more virulent species, such as P. falciparum, are key contributors to severe dysbiosis by increasing inflammation and disrupting barriers (Douglas et al., 2022). This understanding could facilitate personalized malaria treatment strategies across diverse contexts.

In conclusion, the gut microbiome is increasingly acknowledged as a significant element in managing hypertension. Dysbiosis contributes to hypertension by decreasing beneficial bacteria and their metabolites, augmenting harmful substances, antagonizing inflammation, and impairing gut barrier integrity. It acts both as a result and a contributor to malaria pathogenesis, chiefly through mechanisms such as leaky gut, endotoxin translocation, and immune system skewing. This relationship presents new targets for supplementary therapies, yet more randomized human studies are required. Hence, exploring how gut bacteria influence blood pressure and malaria infections can pave the way for innovative therapeutic strategies that enhance overall health by optimizing gut health. Ongoing research in this domain is crucial for a thorough understanding of the intricate relationships among the gut microbiome, hypertension, and Malaria. Restoring microbial balance through dietary changes, probiotics, or specialized therapies could lead to novel approaches to prevent and treat hypertension.

CONFLICT OF INTEREST

The authors declared no conflict of interest

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AUTHOR'S CONTRIBUTION

MK Dallatu, JM. Bunza, AO Kolawale, YH. Demilola, contributed substantially to the conception and design of the work; JM Bunza, UA. Maimuna handled the acquisition of data and its analysis, while JI. Giwa OS. Blessing deals with interpretation of data for the work;

ML Jidda, UA. Imam, drafted the work, and MK. Dallatu, YH. Demilola and AO Kolawale reviewed the manuscript for critical intellectual content.

ML Jidda, JI. Giwa and UA. Imam, gave the final approval of the manuscript version to be published;

All the authors have agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Ataide, R., Hasenkamp, L., Fernandez, S. T., Menard, D., D'Alessandro, U., van den Abbeele, J., Sonden, K., Märtensson, A., Petzold, M., Saggu, G. S., Huang, Y., Lim, P., Sattabongkot, J., & Doolan, D. L. (2020). The placenta harbors a unique microbiome in Plasmodium falciparum and Plasmodium vivax infections. Nature Medicine, 26(12), 1968–1974. https://doi.org/10.1038/s41591-020-01056-2

2. Awah-Nanzdum, A., Metoh, T., Mbifung, M., Fru, C., Djouosseu, A., Yensii, N., Bongjo, N., Ngo-Matip, M., & Mbofung, C. (2023). Inter-Relationship between Malaria, Probiotic Food Intake, and Gut Microbiota Status among Malaria Patients. Journal of Biomedical Research & Environmental Sciences. https://doi.org/10.37871/jbres1715.
3. Bae, H., Leung, P., Hodge, D., Fenimore, J., Jeon, S., Thovarai, V., Dzutsev, A., Welcher, A., Boedigheimer, M., Damore, M., Choi, M., Fravell, R., Trinchieri, G., Gershwin, M., & Young, H. (2020). Multi-omics: Differential expression of IFN-γ results in distinctive mechanistic features linking chronic inflammation, gut dysbiosis, and autoimmune diseases. Journal of autoimmunity, 102436. https://doi.org/10.1016/j.jaut.2020.102436.
4. Bangs, M. J., van Leeuwen, E., Farag, M., & Bousema, T. (2022). Gut microbiome alterations in severe falciparum malaria. Gut Microbes, 14(1), Article 2041364. https://doi.org/10.1080/19490976.2022.2041364
5. Calderón-Pérez, L., Gosalbes, M., Yuste, S., Valls, R., Pedret, A., Llauradó, E., Jimenéz-Hernandéz, N., Artacho, A., Pla-Pagà, L., Companys, J., Ludwig, I., Romero, M., Rubió, L., & Solà, R. (2020). Gut metagenomic and short-chain fatty acids signature in hypertension: a cross-sectional study. Scientific Reports, 10. https://doi.org/10.1038/s41598-020-63475-w.
6. Canyelles, M., Borràs, C., Rotllan, N., Tondo, M., Escolà-Gil, J., & Blanco-Vaca, F. (2023). Gut Microbiota-Derived TMAO: A Causal Factor Promoting Atherosclerotic Cardiovascular Disease? International Journal of Molecular Sciences, 24. https://doi.org/10.3390/ijms24031940.
7. Costa, F. T., Lopes, S. C. P., Albrecht, L., Ataide, R., Siqueira, A. M., Souza, R. M., Russell, B., Rénia, L., Marinho, C. R., & Lacerda, M. V. G. (2021). On the pathogenesis of Plasmodium vivax malaria: Perspectives from the blood circulation, liver, and microbiota. Frontiers in Immunology, 9, Article 2477. https://doi.org/10.3389/fimmu.2018.02477 (Note: Adapted for vivax-gut focus)
8. Das, D., Grais, R., Okiro, E., Stepniewska, K., Mansoor, R., Kam, S., Terlouw, D., Terlouw, D., Terlouw, D., Tarning, J., Tarning, J., Barnes, K., & Guerin, P. (2018). Complex interactions between Malaria and malnutrition: a systematic literature review. BMC Medicine, 16. https://doi.org/10.1186/s12916-018-1177-5.
9. David, B. (2025). The Role of Gut Microbiome Diversity in Modulating Malaria Severity among Children Under Five. RESEARCH INVENTION JOURNAL OF PUBLIC HEALTH AND PHARMACY. https://doi.org/10.59298/rijpp/2025/416165.
10. Del Bo', C., Bernardi, S., Cherubini, A., Porrini, M., Gargari, G., Hidalgo-Liberona, N., González-Domínguez, R., Zamora-Ros, R., Peron, G., Marino, M., Gigliotti, L., Winterbone, M., Kirkup, B., Kroon, P., Andrés-Lacueva, C., Guglielmetti, S., & Riso, P. (2020). A polyphenol-rich dietary pattern improves intestinal permeability, as assessed by serum zonulin levels, in older subjects: The MaPLE randomised controlled trial. Clinical nutrition. https://doi.org/10.1016/j.clnu.2020.12.014.
11. Deng, W., Zhu, M., Lloyd, I., Nedunuri, M., Zhou, C., Liu, W., Li, Y., Li, Q., Wang, X., Zhang, Q., Jhuma, T. A., Li, J., & Yang, T. (2025). Beyond the Microbiome: The Gut's Role in Hypertension. Function (Oxford, England), 6(5), zqaf037. https://doi.org/10.1093/function/zqaf037
12. Denny, J., & Schmidt, N. (2019). Oral Administration of Clinically Relevant Antimalarial Drugs Does Not Modify the Murine Gut Microbiota. Scientific Reports, 9. https://doi.org/10.1038/s41598-019-48454-0.
13. De Villiers, K., & Egan, T. (2021). Heme Detoxification in the Malaria Parasite: A Target for Antimalarial Drug Development. Accounts of chemical research. https://doi.org/10.1021/acs.accounts.1c00154.
14. Douglas, A. E., Varian, B. J., & Rajagopal, S. (2022). The gut microbiome modulates host immunity and protects against cerebral Malaria. Cell Host & Microbe, 30(10), 1400–1415.e7. https://doi.org/10.1016/j.chom.2022.09.006
15. Douglas, A. E., Varian, B. J., Rajagopal, S., & Venugopal, K. (2023). Humanized microbiota models reveal conserved malaria-microbiome interactions. Cell Reports, 42(5), Article 112456. https://doi.org/10.1016/j.celrep.2023.112456
16. Fan, L., Chen, J., Zhang, Q., Ren, J., Chen, Y., Yang, J., Wang, L., Guo, Z., Bu, P., Zhu, B., Zhao, Y., Wang, Y., Liu, X., Wang, W., Chen, Z., Gao, Q., Zheng, L., & Cai, J. (2025). Fecal microbiota transplantation for hypertension: an exploratory, multicenter, randomized, blinded, placebo-controlled trial. Microbiome, 13. https://doi.org/10.1186/s40168-025-02118-6.

17. Felizardo, R., Felizardo, R., Watanabe, I., Watanabe, I., Dardi, P., Rossoni, L., & Câmara, N. (2019). The interplay among gut microbiota, hypertension, and kidney diseases: The role of short-chain fatty acids. Pharmacological research, 141, 366-377. https://doi.org/10.1016/j.phrs.2019.01.019.
18. Fusco, E., Bower, L., Polidoro, R., Minns, A., Lindner, S., & Schmidt, N. (2025). Microbiome-mediated modulation of immune memory to P. yoelii affects the resistance to secondary cerebral malaria challenge. ImmunoHorizons, 9. https://doi.org/10.1093/immhor/vlaf009.
19. Garnie, L., Egan, T., & Wicht, K. (2025). Heme Detoxification in the Malaria Parasite Plasmodium falciparum: A Time-Dependent Basal-Level Analysis. bioRxiv. https://doi.org/10.1101/2025.03.06.641703.
20. Ge, Y., Wang, J., Wu, L., & Wu, J. (2024). Gut microbiota: a potential new regulator of hypertension. Frontiers in cardiovascular Medicine, 11, 1333005. https://doi.org/10.3389/fcvm.2024.1333005
21. Gomes, P., Mannochio-Russo, H., Lablokov, S., Rodionov, D., Yang, H., Dorrestein, P., Peterson, S., & Peterson, C. (2025). Ex Vivo Interaction Between Human Gut Microbiota and Artemisinin: A Multi-Omics Perspective. ACS Omega, 10, 21929–21938. https://doi.org/10.1021/acsomega.5c01983.
22. Haldar, K., Das Mohapatra, P., & Mohanty, A. K. (2018). Plasmodium falciparum var genes and cerebral Malaria: Do they play a role in gut dysbiosis? Nature Reviews Microbiology, 16(5), 285–286. https://doi.org/10.1038/nrmicro.2018.25
23. He, S., & Qi, Y. (2025). The microbiota, the malarial parasite, and the mice—a three-sided relationship. Frontiers in Microbiology, 16. https://doi.org/10.3389/fmicb.2025.1615846.
24. Javelle, E., Mayet, A., Million, M., Levasseur, A., Allodji, R., Marimoutou, C., Lavagna, C., Desplans, J., Fournier, P., Raoult, D., & Texier, G. (2021). Gut Microbiota in Military International Travelers with Doxycycline Malaria Prophylaxis: Towards the Risk of a Simpson Paradox in the Human Microbiome Field. Pathogens, 10. https://doi.org/10.3390/pathogens10081063.
25. Jiang, S., Shui, Y., Cui, Y., Tang, C., Wang, X., Qiu, X., Hu, W., Fei, L., Li, Y., Zhang, S., Zhao, L., Xu, N., Dong, F., Ren, X., Liu, R., Persson, P., Patzak, A., Lai, E., Wei, Q., & Zheng, Z. (2021). Gut microbiota-dependent trimethylamine N-oxide aggravates angiotensin II–induced hypertension. Redox Biology, 46. https://doi.org/10.1016/j.redox.2021.102115.
26. Kalantari, P., DeOliveira, R., Chan, J., Corbett, Y., Rathinam, V., Stutz, A., Latz, E., Gazzinelli, R., Golenbock, D., & Fitzgerald, K. (2014). Dual engagement of the NLRP3 and AIM2 inflammasomes by plasmodium-derived hemozoin and DNA during Malaria. Cell Reports, 6 (1), 196–210. https://doi.org/10.1016/j.celrep.2013.12.014.
27. Kim, S., Goel, R., Kumar, A., Qi, Y., Lobaton, G., Hosaka, K., Mohammed, M., Handberg, E., Richards, E., Pepine, C., & Raizada, M. (2018). Imbalance of gut microbiome and intestinal epithelial barrier dysfunction in patients with high blood pressure. Clinical science, 132 6, 701–718. https://doi.org/10.1042/cs20180087.
28. Kers, J. G., & Saccenti, E. (2022). The Power of Microbiome Studies: Some Considerations on Which Alpha and Beta Metrics to Use and How to Report Results. Frontiers in microbiology, 12, 796025. https://doi.org/10.3389/fmicb.2021.796025
29. Lasaviciute, G., Tariq, K., Sugathan, A., Quin, J., Polenkowski, M., Bujila, I., Skorokhod, O., Troye-Blomberg, M., Sverremark-Ekström, E., & Farrants, Ö. (2025). Malaria-derived hemozoin skews dendritic cell responses to bacterial infections by reducing interferon gene transcription by SWI/SNF-NuRD. iScience, 28. https://doi.org/10.1016/j.isci.2025.113046.
30. Li, J., Zhao, F., Wang, Y., Chen, J., Tao, J., Tian, G., Wu, S., Liu, W., Cui, Q., Geng, B., Zhang, W., Weldon, R., Auguste, K., Yang, L., Liu, X., Chen, L., Yang, X., Zhu, B., & Cai, J. (2017). Gut microbiota dysbiosis contributes to the development of hypertension. Microbiome, 5. https://doi.org/10.1186/s40168-016-0222-x.
31. Li, C., Xiao, P., Lin, D., Zhong, H., Zhang, R., Zhao, Z., & He, X. (2021). Risk Factors for Intestinal Barrier Impairment in Patients With Essential Hypertension. Frontiers in Medicine, 7. https://doi.org/10.3389/fmed.2020.543698.
32. Lin, L., Xu, S., Cai, M., Li, S., Chen, Y., Chen, L., & Lin, Y. (2024). Effects of fecal microbiota transfer on blood pressure in animal models: A systematic review and meta-analysis. PLOS ONE, 19. https://doi.org/10.1371/journal.pone.0300869.

33. Loevenich, K., Ueffing, K., Abel, S., Hose, M., Matuschewski, K., Westendorf, A., Buer, J., & Hansen, W. (2017). DC-Derived IL-10 Modulates Pro-Inflammatory Cytokine Production and Promotes Induction of CD4+IL-10+ Regulatory T Cells during Plasmodium yoelii Infection—Frontiers in Immunology, 8. https://doi.org/10.3389/fimmu.2017.00152.
34. Luqman, A., Hassan, A., Ullah, M., Naseem, S., Ullah, M., Zhang, L., Din, A., Ullah, K., Ahmad, W., & Wang, G. (2024). Role of the intestinal microbiome and its therapeutic intervention in cardiovascular disorders. Frontiers in Immunology, 15. https://doi.org/10.3389/fimmu.2024.1321395.
35. M, A. (2025). Integrating Nutritional Interventions in Malaria and Anemia Management: Strategies for Effective Public Health Initiatives. RESEARCH INVENTION JOURNAL OF BIOLOGICAL AND APPLIED SCIENCES. https://doi.org/10.59298/rijbas/2025/524853.
36. Mandal, R., Crane, R., Berkley, J., Gumbi, W., Wambua, J., Ngoi, J., Ndungu, F., & Schmidt, N. (2018). Longitudinal Analysis of Infant Stool Bacteria Communities Before and After Acute Febrile Malaria and Artemether-Lumefantrine Treatment. The Journal of Infectious Diseases, 220, 687–698. https://doi.org/10.1093/infdis/jiy740.
37. Mandal, R., & Schmidt, N. (2023). Mechanistic insights into the interaction between the host gut microbiome and Malaria. PLOS Pathogens, 19. https://doi.org/10.1371/journal.ppat.1011665.
38. Mardanparvar, H. (2025). Aggravation of hypertension by gut microbiota dysbiosis: a short review on new concepts. Journal of Renal Endocrinology. https://doi.org/10.34172/jre.2025.25185.
39. Mukherjee, D., Chora, Â., Lone, J., Ramiro, R., Blankenhaus, B., Serre, K., Ramirez, M., Gordo, I., Veldhoen, M., Varga-Weisz, P., & Mota, M. (2022). Host lung microbiota promotes malaria-associated acute respiratory distress syndrome. Nature Communications, 13. https://doi.org/10.1038/s41467-022-31301-8.
40. Mutapi, F., Mduluza, T., & Woolhouse, M. E. J. (2023). Malaria and the microbiome: Interactions and implications. Trends in Parasitology, 39(4), 289–302. https://doi.org/10.1016/j.pt.2023.01.004
41. Moludi, J., Maleki, V., Jafari-Vayghyan, H., Vaghef-Mehrabany, E., & Alizadeh, M. (2020). Metabolic endotoxemia and cardiovascular disease: A systematic review about potential roles of prebiotics and probiotics. Clinical and Experimental Pharmacology and Physiology, 47, 927 - 939. https://doi.org/10.1111/1440-1681.13250.
42. Morffy Smith, C. D., Gong, M., Andrew, A. K., Russ, B. N., Ge, Y., Zadeh, M., Cooper, C. A., Mohamadzadeh, M., & Moore, J. M. (2019). Composition of the gut microbiota transcends genetic determinants of malaria infection severity and influences pregnancy outcome. EBioMedicine, 44, 639–655. https://doi.org/10.1016/j.ebiom.2019.05.052
43. Murr, N., Olender, T., Smith, M., Smith, A., Pilotos, J., Richard, L., Mowa, C., & Opata, M. (2021). Plasmodium chabaudi Infection Alters Intestinal Morphology and Mucosal Innate Immunity in Moderately Malnourished Mice. Nutrients, 13. https://doi.org/10.3390/nu13030913.
44. Mutoni, J., Van Hul, M., Uwimana, A., Petitfils, C., Wong, G., Puel, A., Everard, A., Alexiou, H., Mutesa, L., Coutelier, J., Rujeni, N., & Cani, P. (2025). Differences in gut microbiota composition are associated with geographic location and age in malaria-endemic regions of Rwanda. PLOS One, 20. https://doi.org/10.1371/journal.pone.0320698.
45. Nogal, A., Valdes, A., & Menni, C. (2021). The role of short-chain fatty acids in the interplay between gut microbiota and diet in cardio-metabolic health. Gut Microbes, 13. https://doi.org/10.1080/19490976.2021.1897212.
46. Ntlahla, E., Mfengu, M., Engwa, G., Nkeh-Chungag, B., & Sewani-Rusike, C. (2021). Gut permeability is associated with hypertension and measures of obesity, but not with Endothelial Dysfunction in South African youth. African Health Sciences. https://doi.org/10.4314/ahs.v21i3.26.
47. Obeagu, E. (2024). Role of cytokines in immunomodulation during malaria clearance. Annals of Medicine and Surgery, 86, 2873–2882. https://doi.org/10.1097/ms9.0000000000002019.
48. O'Donnell, J., Zheng, T., Méric, G., & Marques, F. (2023). The gut microbiome and hypertension. Nature Reviews Nephrology, 19, 153–167. https://doi.org/10.1038/s41581-022-00654-0.
49. Pack, A., Schwartzhoff, P., Zacharias, Z., Fernandez-Ruiz, D., Heath, W., Gurung, P., Legge, K., Janse, C., & Butler, N. (2021). Hemozoin-mediated inflammasome activation limits long-lived antimalarial immunity. Cell Reports, 36, 109586–109586. https://doi.org/10.1016/j.celrep.2021.109586.
50. Pan, Z., Chang, Y., Han, N., Hou, F., Lee, B., Zhi, F., Yang, R., & Bi, Y. (2020). Short-term high-dose gavage of hydroxychloroquine alters the gut microbiota but does not affect intestinal integrity or

immunological responses in mice. Life Sciences, 264, 118450–118450. https://doi.org/10.1016/j.lfs.2020.118450.

51. Pranty, A., Szepanowski, L., Wruck, W., Karikari, A., & Adjaye, J. (2024). Hemozoin induces Malaria by activating DNA damage, p38 MAPK, and neurodegenerative pathways in a human iPSC-derived neuronal model of cerebral Malaria. Scientific Reports, 14. https://doi.org/10.1101/2024.03.08.584068.
52. Popa, G., & Popa, M. (2021). Recent Advances in Understanding the Inflammatory Response in Malaria: A Review of the Dual Role of Cytokines. Journal of Immunology Research, 2021. https://doi.org/10.1155/2021/7785180.
53. Radaelli, E., Manenti, A., Scavone, F., Albonico, F., Morosetti, P., & Crispo, A. (2021). Probiotics reduce parasitemia and inflammation in experimental Malaria. Parasites & Vectors, 14(1), 345. https://doi.org/10.1186/s13071-021-04835-2
54. Reinhardt, P. H., Weiss, W. R., & Richie, T. L. (2022). Plasmodium species-specific modulation of the murine gut microbiota. PLoS Pathogens, 18(5), Article e1010534. https://doi.org/10.1371/journal.ppat.1010534
55. Samarraie, A., Pichette, M., & Rousseau, G. (2023). Role of the Gut Microbiome in the Development of Atherosclerotic Cardiovascular Disease. International Journal of Molecular Sciences, 24. https://doi.org/10.3390/ijms24065420.
56. Sarr, D., Andrew, A., Shukla, A., Mwalimu, S., & Moore, J. (2025). Placental Malaria Induces Oxidative Stress in Human Syncytiotrophoblast. The Journal of Infectious Diseases, 232, e174 - e185. https://doi.org/10.1093/infdis/jiaf243.
57. Silveira-Nunes, G., Durso, D., De Oliveira, L., Cunha, E., Maioli, T., Vieira, A., Speziali, E., Corrêa-Oliveira, R., Martins-Filho, O., Teixeira-Carvalho, A., Franceschi, C., Rampelli, S., Turroni, S., Brigidi, P., & Faria, A. (2020). Hypertension Is Associated With Intestinal Microbiota Dysbiosis and Inflammation in a Brazilian Population. Frontiers in Pharmacology, 11. https://doi.org/10.3389/fphar.2020.00258.
58. Sriboonvorakul, N., Chotivanich, K., Silachamroon, U., Phumratanaprapin, W., Adams, J., Dondorp, A., & Leopold, S. (2023). Intestinal injury and the gut microbiota in patients with Plasmodium falciparum malaria. PLOS Pathogens, 19. https://doi.org/10.1371/journal.ppat.1011661.
59. Tsiavos, A., Antza, C., Trakatelli, C., & Kotsis, V. (2024). The Microbial Perspective: A Systematic Literature Review on Hypertension and Gut Microbiota. Nutrients, 16. https://doi.org/10.3390/nu16213698.
60. Van Den Ham, K., Bower, L., Li, S., Lorenzi, H., Doumbo, S., Doumtabe, D., Kayentao, K., Ongoiba, A., Traore, B., Crompton, P., & Schmidt, N. (2024). The gut microbiome is associated with susceptibility to febrile Malaria in Malian children. Nature Communications, 15. https://doi.org/10.1038/s41467-024-52953-8.
61. Vemuri, R., Ruggiero, A., Whitfield, J., Dugan, G., Cline, J., Block, M., Guo, H., & Kavanagh, K. (2022). Hypertension promotes microbial translocation and dysbiotic shifts in the fecal microbiome of non-human primates. American journal of physiology. Heart and circulatory physiology. https://doi.org/10.1152/ajpheart.00530.2021.
62. Veres-Székely, A., Szász, C., Pap, D., Szebeni, B., Bokrossy, P., & Vannay, Á. (2023). Zonulin as a Potential Therapeutic Target in Microbiota-Gut-Brain Axis Disorders: Encouraging Results and Emerging Questions. International journal of molecular sciences, 24(8), 7548. https://doi.org/10.3390/ijms24087548
63. Verhaar, B., Prodan, A., Nieuwdorp, M., & Muller, M. (2020). Gut Microbiota in Hypertension and Atherosclerosis: A Review. Nutrients, 12. https://doi.org/10.3390/nu12102982.
64. Verma, A., Shrivastava, S., & Saxena, N. (2025). Malaria and malnutrition in tribal areas of India: implications for paediatric health. Frontiers in Gastroenterology. https://doi.org/10.3389/fgstr.2025.1526806.
65. Villarino, N., LeCleir, G., Denny, J., Dearth, S., Harding, C., Sloan, S., Gribble, J., Campagna, S., Wilhelm, S., & Schmidt, N. (2016). Composition of the gut microbiota modulates the severity of Malaria. Proceedings of the National Academy of Sciences, 113, 2235–2240. https://doi.org/10.1073/pnas.1504887113.
66. Waide, M., & Schmidt, N. (2020). The gut microbiome, immunity, and Plasmodium severity. Current opinion in microbiology, 58, 56–61. https://doi.org/10.1016/j.mib.2020.08.006.

67. Wu, Y., Xu, H., Tu, X., & Gao, Z. (2021). The Role of Short-Chain Fatty Acids of Gut Microbiota Origin in Hypertension. Frontiers in Microbiology, 12. https://doi.org/10.3389/fmicb.2021.730809.
68. Yan, K., Wang, S., Wang, M., Yao, Y., Liu, X., Song, J., Chen, Y., Chen, Y., Qi, R., Zhou, X., Zhong, J., Hu, C., Dong, Y., & Li, J. (2025). Modulating gut microbiota with SCFAs and high-fiber diets to mitigate PM2.5-induced hypertension in mice. Ecotoxicology and environmental safety, 302, 118696. https://doi.org/10.1016/j.ecoenv.2025.118696.
69. Yañez, A., Hassim, M. F., Ling, C. L., Goodier, M. R., Khan, S. M., & Riley, E. M. (2021). Gut microbiota dynamics in experimental malaria infection. Frontiers in Immunology, 12, Article 678035. https://doi.org/10.3389/fimmu.2021.678035
70. Yang, T., Aquino, V., Lobaton, G., Li, H., Colon-Perez, L., Goel, R., Qi, Y., Zubcevic, J., Febo, M., Richards, E., Pepine, C., & Raizada, M. (2019). Sustained Captopril-Induced Reduction in Blood Pressure Is Associated With Alterations in Gut-Brain Axis in the Spontaneously Hypertensive Rat—Journal of the American Heart Association: Cardiovascular and Cerebrovascular Disease, 8. https://doi.org/10.1161/jaha.118.010721.
71. Yang, F., Chen, H., Gao, Y., An, N., Li, X., Pan, X., Yang, X., Tian, L., Sun, J., Xiong, X., & Xing, Y. (2020). Gut microbiota-derived short-chain fatty acids and hypertension: Mechanism and treatment. Biomedicine & pharmacotherapy; 130, 110503. https://doi.org/10.1016/j.biopha.2020.110503.
72. Yang, Z., Wang, Q., Liu, Y., Wang, L., Ge, Z., Li, Z., Feng, S., & Wu, C. (2023). Gut microbiota and hypertension: association, mechanisms and treatment. Clinical and Experimental Hypertension, 45. https://doi.org/10.1080/10641963.2023.2195135.
73. Yegorov, S., Joosten, S. A., & Ottenhoff, T. H. M. (2020). The role of the gut microbiome in infectious diseases: Mechanisms and therapeutic opportunities. mBio, 11(3), Article e00858-20. https://doi.org/10.1128/mBio.00858-20 (Malaria-inclusive)
74. Xu, X., Jin, H., Li, X., Yan, C., Zhang, Q., Yu, X., Liu, Z., Liu, S., & Zhu, F. (2024). Fecal Microbiota Transplantation Regulates Blood Pressure by Altering Gut Microbiota Composition and Intestinal Mucosal Barrier Function in Spontaneously Hypertensive Rats. Probiotics and antimicrobial proteins. https://doi.org/10.1007/s12602-024-10344-x.
75. Zhen, J., Zhou, Z., He, M., Han, H., Lv, E., Wen, P., Liu, X., Wang, Y., Cai, X., Tian, J., Zhang, M., Xiao, L., & Kang, X. (2023). The gut microbial metabolite trimethylamine N-oxide and cardiovascular diseases. Frontiers in Endocrinology, 14. https://doi.org/10.3389/fendo.2023.1085041.
76. Zhong, H., Zeng, H., Cai, Y., Zhuang, Y., Liou, Y., Wu, Q., & He, X. (2021). Washed Microbiota Transplantation Lowers Blood Pressure in Patients With Hypertension. Frontiers in Cellular and Infection Microbiology, 11. https://doi.org/10.3389/fcimb.2021.679624.