

# Malaria and Gastrointestinal System

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## Abstract

The formation of a healthy immune response is dependent on the human gut microbiome, as is the case with most disorders. An advanced state of the illness might result from clinical malnutrition and the pathophysiologically detrimental impact of the disease on the gut microbiota. We have attempted to provide clear information on the relationship between a healthy gut microbiota and malaria, the potential impact of malaria on the gut microbiome, and the application of oral synbiotics as a therapy.

## Introduction

The parasite illness malaria is spread by female Anopheles mosquitoes that bite people. It is a public health problem despite the fact that there were 241 million new cases and over 627,000 fatalities recorded in 2020. More than 90% of severe and deadly cases are caused by *P. falciparum*. The severity of this illness, which results in broad organ damage in addition to infected red blood cells (iRBC), is determined by several variables. Recent research has demonstrated that some aspects of the gut microbiota increase the likelihood of developing severe malaria [1]. In Sub-Saharan Africa, malaria is the primary cause of parasite-related mortality, accounting for the daily deaths of about 1200 children. Since many people in endemic locations are probably asymptomatic, transmission can continue [2].

Malaria is a systemic illness that can cause severe anemia, multiple organ failure, fever, encephalopathy, headache, myalgia, nausea, weakness, respiratory distress and even death. The immune response's devastation of the adherent iRBCs due to their adherence to the endothelium layer of tiny arteries causes physiopathology. Other enteropathogens, including non-typhoidal Salmonella (NTS), can cause invasive bacterial diseases as a result of this condition. 6.5% of cases of severe malaria result in bacteremia. Gastrointestinal symp-

toms, such as nausea, vomiting, and diarrhea, may appear in less severe instances.

The World Health Organization states that diarrhea is a symptom of malaria; however, since other gastroenteritis-causing factors are also common in endemic countries, and because some antimalarial drugs (like doxycycline, mefloquine, and chloroquine) can also cause diarrhea, it is unclear whether diarrhea is solely related to malaria. However, increased intestinal permeability, cecal inflammation, mononuclear infiltration, and mastocytosis were found in the malaria mouse model. This study found that malaria also induced neutrophil dysfunction, disruption of intestinal homeostasis, intestinal dysbiosis, and IL-10-mediated inhibition of antibacterial immunity [3].

After being bitten by a mosquito several times as an adult, the parasite's normal cycle-which includes three stages: liver, blood, and sexual-continues to produce antibodies and, in reality, a natural immunity. This immunity may block the parasite's ability to enter the liver and invade erythrocytes, even though it has no direct effect on the parasite. By eradicating the parasite in the early stages of infection, cytokines generated by the immune system also play a crucial role. Given the rise in medication resistance and vaccine deficiencies, maintaining a healthy immune system and a balanced microbiome are cru-



cial [4]. It is generally recognized that the generation of antibodies is required for partial protection, even if the adaptive immune response to *Plasmodium* appears to be highly complicated. The development of memory cells may be lost upon leaving the endemic region and is probably connected to years of exposure. Uncertainties persist regarding the protective antibody threshold and the pace at which asymptomatic malaria develops [5].

A population of bacteria, viruses, and fungus coexisting peacefully in an area is referred to as a microbiome, together with the genetic material that makes up the microbiota. Culture-independent research into a range of disorders has been sparked by developments in genome sequencing and biocomputational study of the human microbiome, and these efforts have produced fresh discoveries [6]. The immune system and its functioning depend heavily on a healthy diet, and malnutrition increases a person's susceptibility to infectious illnesses, including malaria [7]. Our gut microbiota, which is actually a predictor of our future health, is formed by the food we eat. The intestinal microbiome trains 70–80% of immune cells, which are found in the gut. The importance of both acquired and natural immunity in the battle against malaria highlights the role the gut microbiota plays in this regard [1].

From the perspective of the mosquito, the cycle is finished when the male and female gametocytes are ingested by *Plasmodium*, pass through the midgut epithelium following fusion and zygote formation, and transform into ookinetes, which produce sporozoites that eventually become oocysts and are transferred to the salivary glands and circulatory fluid. At this point, it is indisputable that the mosquito's midgut microbiota influences the parasites' ability to adapt and spread. With appropriate vector control techniques, perhaps this impact can be altered [2, 8]. The connection between *Plasmodium* and the human microbiota has not received as much research. The kind of disease and the likelihood of infection and alteration of the gut microbiota may be correlated in both directions, according to preliminary research [9].

Intestinal injury and leakage may result from iRBCs attaching to vascular endothelial cells, obstructing the microcirculatory system. Considering that there has been evidence in certain studies that patients with severe malaria had increased risks of concomitant bacteremia. A complicated interplay between the host, parasite, and intestinal microorganisms is actually indicated by changes in the composition and diversity of the intestinal microbiota in severe instances of malaria, albeit it is yet unknown if these changes contribute to the pathogenesis. Additionally, research on mice have demonstrated that the nature of the gut microbiota may influence an individual's vulnerability to malaria. Furthermore, in the serum of individuals with severe malaria, microbial metabolites that are involved in metabolic and other clinical observations have been found [10].

It is less expensive to make changes to the gut microbiota while treating infectious disorders like malaria. Probiotic intervention is predicted to reduce severe malaria cases by 2–14 times by mathematical modeling, leading to the conclusion that this treatment will be economically viable in sub-Saharan Africa [11]. Probiotic supplements are inexpensive and can prevent the loss of efficacy caused by *Plasmodium* resistance by enhancing the host immune system's ability to combat the parasite. It has been noted that oral synbiotic treatment lowers the number of mortality attributable to sepsis and lower respiratory tract infections in newborns born in rural India [12]. After receiving Lactobacillus and Bifidobacterium therapy, mice's susceptibility to malaria decreased, however it was noted that this happened after using broad-spectrum antibiotics for several weeks. Indeed, it has been determined that the optimal timing for using intestinal microbiota should be selected [13].

Uncertainties about gut microbiota and infectious illnesses are starting to become more clear in light of the COVID-19 pandemic. Antimicrobial medication resistance, particularly in relation to malaria, is linked to the growing interest in probiotics. The sustainable development goals of the United Nations include the supply of food that is safe, nourishing, functional, and adequate; this will help prevent infectious illnesses and fight hunger at the same time. In particular, foods undergoing fermentation include bacteria that may aid in the prevention or treatment of malarial illnesses [4].

## Conclusion

There is still much to learn about the relationships between infectious agents and the gut microbiome, which is regarded as the human body's second genome. The associations found between alterations in the intestinal microbiota of people and mice and the severity of *Plasmodium* infections provide insight for future research. Probiotics have the potential to alter the gut microbiota, which might lead to the development of novel malaria therapies, particularly for younger patients who are more susceptible to the disease's consequences and potential mortality.

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