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# Aggravation of hypertension by gut microbiota dysbiosis; a short-review on new concepts

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**Abstract**
Gut microbiota dysbiosis, characterized by reduced diversity and richness, as well as an imbalance in specific bacterial taxa, is closely associated with hypertension. Therefore, individuals with high blood pressure exhibit distinct microbial signatures, with a greater abundance of pathogenic bacteria like *Prevotella, Klebsiella,* and *Streptococcus*, alongside a reduction in beneficial, SCFA-producing bacteria like *Bacteroidetes*, *Roseburia*, and *Faecalibacterium*. Previous studies showed that animal models of hypertension demonstrated less diverse and rich gut microbiota compared to normotensive controls, suggesting a causal role for gut dysbiosis in blood pressure regulation.
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## Introduction

Hypertensive individuals generally exhibit lower microbial diversity and richness compared to normotensive individuals (1). This condition is indicated by a decrease in the Shannon index and an increase in the Firmicutes/Bacteroidetes ratio, which is a marker of gut microbiota imbalance (2). Hypertensive individuals tend to have a higher abundance of Gram-negative bacteria, particularly from the families Bacteroidetes and Negativicutes (3), and a lower abundance of Gram-positive bacteria, such as those from the families Ruminococcaceae and Lachnospiraceae, which are known for producing short-chain fatty acids (4). The gut microbiota of hypertensive individuals is characterized by a decrease in short-chain fatty acids-producing bacteria, such as Bacteroides and Prevotella, and an increase in inflammation-related bacteria, such as Lactobacillus (5). Meanwhile, hypertensive individuals often show elevated levels of inflammatory cytokines and hyperlipidemia, which are associated with altered gut microbiota (6). The gut microbiota composition is also influenced by dietary patterns. Hypertensive individuals may have different dietary habits that contribute to the observed differences in their gut microbiota (7). These differences suggest that the gut microbiota plays a crucial role in the development and progression of hypertension and that interventions targeting the gut microbiota may be beneficial in managing hypertension (8). In this mini-review, we aimed to discuss the potential impact of gut microbiota dysbiosis on aggravation of hypertension.

## Search strategy

For this review, we searched PubMed, Web of Science, EBSCO, Scopus, Google Scholar, Directory of Open Access Journals (DOAJ), and Embase, using different keywords like; gut microbiota dysbiosis, hypertension, angiotensin II and gut microbiome.

## Association of gut dysbiosis and hypertension

Gut dysbiosis can contribute to hypertension through various pathways, including altered signaling metabolites, activation of the renin-angiotensin system, increased oxidative stress and inflammation, and disruption of the gut-brain axis (9,10). Prior investigations show, specific gut microbial imbalances, such as increased *Firmicutes*/*Bacteroidetes* ratio, can aggravate angiotensin II-induced hypertension (11). Additionally, gut-derived metabolites like trimethylamine N-oxide and hydrogen sulfide can also exacerbate hypertension by promoting vascular dysfunction and inflammation (12). Likewise, patients with obstructive sleep apnea and hypertension exhibit more severe gut dysbiosis compared to hypertensive patients without obstructive sleep apnea that characterized by lower microbial diversity and increased *Firmicutes*/*Bacteroidetes* ratio (13). Besides, the gut microbiome alterations in obstructive sleep apnea-related hypertension are associated with increased inflammation, hyperlipidemia, and metabolic comorbidities, suggesting a critical role for gut dysbiosis in the pathogenesis of this condition (14).

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**Implication for health policy/practice/research/ medical education**

Gut microbiota dysbiosis can significantly aggravate hypertension through various mechanisms, since targeting the gut microbiome may be a promising therapeutic approach for managing hypertension, especially in the context of comorbid conditions like obstructive sleep apnea

## Impact of reversed gut microbiota dysbiosis on hypertension risk

Gut microbiota dysbiosis can potentially be reversed to reduce the risk of hypertension (11). Recent studies indicate that fecal transplantation from hypertensive human donors to germ-free mice was able to transfer elevated blood pressure, demonstrating the direct influence of gut microbiota on blood pressure (15,16). This finding suggests that fecal microbiota transplantation from healthy donors to hypertensive individuals could help restore a healthy gut microbiome and potentially reduce blood pressure (15). Moreover, dietary interventions to correct gut microbiota dysbiosis, such as the administration of probiotics and prebiotics, could be an innovative nutritional therapeutic strategy for hypertension (17), since probiotics containing beneficial bacteria like Lactobacillus and Bifidobacterium species may help rebalance the gut microbiome and mitigate hypertension (16-18). Furthermore, prebiotics that selectively promote the growth of health-associated gut bacteria could also be leveraged to reverse dysbiosis and lower blood pressure (19,20). Recent studies also in animal models detected that, the antibiotic minocycline was able to rebalance the dysbiotic hypertension-associated gut microbiome by reducing the Firmicutes/Bacteroidetes ratio (11). This finding suggests that targeted antimicrobial therapy may be a potential approach to reshape the gut microbiome and attenuate hypertension, though further research is needed on the long-term effects (21,22). Likewise, adopting a healthy diet, reducing salt intake, and maintaining an active lifestyle may help prevent or reverse gut microbiota dysbiosis and lower hypertension risk (23,24).

## Lipid metabolism in gut microbiota dysbiosis

Gut microbiota-derived metabolites play a significant role in lipid metabolism and inflammation, contributing to the development of atherosclerosis (25). For instance, trimethylamine N-oxide is a gut microbiota-derived metabolite which promotes the accumulation of cholesterol in macrophages, leading to the formation of foam cells and atherosclerotic plaques (26). Additionally, some short-chain fatty acids, like butyrate and propionate has anti-inflammatory and protective effects (27). Other substances such as acetate may contribute to atherosclerosis development by impacting lipid metabolism (28). Likewise, gut microbiota can metabolize primary bile acids into secondary bile acids, which have been linked to increased risk of atherosclerosis and cardiovascular disease (29). Furthermore, Phenylacetylglutamine has been associated with an increased risk of coronary artery disease (30).

## Impact of bioactive lipids on atherosclerosis

The gut microbiome produces bioactive lipids that can influence immune responses. Bioactive lipids are crucial modulators of immune responses, influencing immune cell function, inflammation, and homeostasis, as well as the interactions between the immune system and the gut microbiome (31,32). Bioactive lipids can directly regulate immune cell activation, differentiation, and expansion. They can alter immune cell phenotypes, activation, proliferation, migration, and infiltration, as well as cytokine production (33). Additionally, bioactive lipids are involved in the regulation of inflammation and maintenance of homeostasis. They can modulate the inflammatory response, influencing the balance between pro-inflammatory and anti-inflammatory mediators (34). Meanwhile, bioactive lipids can act as signaling molecules, modifying protein function and altering patterns of gene expression. They can covalently modify transcriptional regulatory proteins and enzymes, influencing the activation of various nuclear and membrane receptors (35,36). Finally, certain metabolites like trimethylamine N-oxide can affect the development of atherosclerosis by modulating lipid metabolism and inflammation (37).

## Conclusion

Gut microbiota dysbiosis, characterized by reduced diversity and richness, and also as an imbalance in specific bacterial taxa, is closely associated with elevated blood pressure and hypertension. Besides, a healthy gut microbiome through approaches like fecal transplantation, probiotics/prebiotics, antimicrobials, and lifestyle changes may be effective in reducing the risk and burden of hypertension.

### Conflicts of interest

The author declares that he has no competing interests.

### Ethical issues

The author has adhered to ethical standards in research practices (including the avoidance of plagiarism, data fabrication, and double publication).

### Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the author utilized Perplexity to refine grammar points and language style in writing. Subsequently, the author thoroughly reviewed and edited the content as necessary, assuming full responsibility for the publication's content.

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