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THE EFFECTIVENESS OF PROBIOTIC ADMINISTRATION AS A NOVEL THERAPEUTIC TARGET FOR HYPERTENSION DURING PREGNANCY INDUCED BY PRIMARY AND SECONDARY FACTORS: A SYSTEMATIC LITERATURE REVIEW OF PRECLINICAL STUDIES

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ABSTRACT
Hypertension during pregnancy, including preeclampsia, remains one of the leading causes of maternal and perinatal morbidity and mortality worldwide. The complex pathogenesis of pregnancy-related hypertension involves endothelial dysfunction, impaired angiogenesis, oxidative stress, and immune dysregulation. Conventional pharmacological therapies continue to face limitations in terms of efficacy and safety for pregnant women. Therefore, there is an urgent need for safer and more effective molecular-based therapeutic alternatives, one of which is the use of probiotics. The aim of this systematic review is to analyse the potential effectiveness of probiotic administration as a novel therapeutic target for pregnancy-induced hypertension driven by primary and secondary factors. This systematic review was conducted following the PRISMA guidelines. A comprehensive literature search was performed across databases including Google Scholar, PubMed, Taylor & Francis, and ScienceDirect, covering publications from 2015 to 2025. Inclusion criteria were applied based on the PICOS framework. A total of 14 preclinical in vivo studies met the inclusion criteria. Probiotics such as Akkermansia muciniphila, Bifidobacterium bifidum, Lactobacillus spp., Limosilactobacillus spp., and Lactiplantibacillus plantarum demonstrated significant effectiveness in reducing systolic and diastolic blood pressure, improving endothelial function, suppressing inflammation, and mitigating oxidative stress. These effects were mediated through mechanisms involving gut microbiota modulation and regulation of the renin-angiotensin system. Probiotics hold promise as a safe and effective alternative therapy for reducing hypertension during pregnancy and may support the development of future non-pharmacological, microbiota-based therapeutic strategies.

Keywords: hyperten

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INTRODUCTION

Hypertension is a pathological condition characterised by a chronic increase in blood pressure, with systolic pressure ≥140 mmHg and/or diastolic pressure ≥90 mmHg (Mancia et al, 2023). Hypertension is a major global health issue, significantly contributing to morbidity and mortality by regulating pathological conditions within the cardiovascular system (Mills et al, 2020; Zhou et al, 2021). It can lead to target organ damage, including heart failure, stroke, renal failure, and hypertensive retinopathy, among others (Masenga et al, 2023). In the context of pregnancy, hypertension represents a significant and serious obstetric complication, which can be classified into chronic hypertension, gestational hypertension, preeclampsia, and superimposed preeclampsia (Garovic et al, 2021). Hypertension during pregnancy increases the risk not only for the mother manifesting as eclamptic seizures, placental abruption, and HELLP syndrome (Hemolysis, Elevated Liver enzymes, and Low Platelet count) but also for the fetus, including intrauterine growth restriction, prematurity, and even perinatal death (Braunthal et al, 2019; Rocha et al, 2021).

The causes of hypertension during pregnancy are multifactorial and can be classified into two main categories: primary factors and secondary (supporting) factors. The most common primary factor is preeclampsia, a condition characterised by hypertension accompanied by proteinuria or other organ dysfunction after 20 weeks of gestation (Karrar et al, 2025). In addition to preeclampsia, chronic hypertension and gestational hypertension are also considered primary factors contributing to the aetiology of pregnancy-related hypertension (Magee et al, 2022; di Pasquo et al, 2024). On the other hand, secondary factors further increase the risk of hypertension during pregnancy, including medical conditions such as diabetes mellitus, systemic lupus erythematosus, chronic kidney disease, obesity, and a family history of hypertension with hereditary patterns (Aziz et al, 2024; Simard et al, 2021; Ernawati et al, 2023). The interaction between genetic predisposition, endothelial dysfunction, oxidative stress, and immune dysregulation exacerbates vascular conditions during pregnancy, making the diagnosis and management of pregnancy-induced hypertension require a holistic and evidence-based clinical approach (Steinthorsdottir et al, 2020).

The potential use of probiotics as an alternative therapy in the management of hypertension has become an increasingly applied strategy in recent years (Zarezadeh et al, 2023; Chen et al, 2023). Probiotics, which are live microorganisms, can confer health benefits to humans, particularly in the treatment of cardiovascular diseases, including the regulation of blood pressure, while minimally inducing pathological conditions in the body (Romero et al, 2023). The mechanisms by which probiotics lower blood pressure in hypertension include the increased production of short-chain fatty acids (SCFAs), modulation of gut microbiota to support systemic homeostasis, reduction of oxidative stress, suppression of systemic inflammation, and regulation of the renin–angiotensin–aldosterone system (RAAS), which serves as a key regulator of blood pressure (Zarezadeh et al, 2023; Mahmoudi et al, 2021; Yang et al, 2020).

Preclinical studies and several clinical trials have demonstrated that regular consumption of probiotics can reduce both systolic and diastolic blood pressure, improve endothelial function, and enhance lipid profiles (Mahdavi et al, 2022). Currently, the potential use of probiotics is being increasingly investigated in the context of pregnancy-related pathological conditions, including hypertension during pregnancy. Reported studies have indicated that probiotics can help suppress excessive inflammatory processes and enhance the immunological balance of pregnant women, thereby potentially preventing or reducing the severity of preeclampsia. Probiotic supplementation during pregnancy has also been reported to improve metabolic conditions, such as insulin resistance and lipid profiles, which are often exacerbated in high-risk pregnancies. With their ability to maintain gut integrity and reduce endotoxemia, probiotics emerge as promising therapeutic candidates for supporting healthier pregnancies, particularly among individuals at risk of developing hypertension.

Therefore, based on the aforementioned issues, a systematic review is needed to comprehensively and critically examine the potential of probiotics as a novel therapeutic target for managing hypertension during pregnancy, particularly hypertension induced by primary factors such as preeclampsia and supporting factors such as diabetes and kidney disease. This review is essential to integrate various preclinical findings scattered across the scientific literature and to provide a comprehensive understanding of the effectiveness and underlying mechanisms of probiotics in this context. The aim of this systematic review it is expected that a robust scientific foundation can be established for the development of safer and more applicable non-pharmacological therapeutic strategies for pregnant women in the future. Accordingly, the researchers propose the title for this systematic review: "The Effectiveness of Probiotic Administration as a Novel Therapeutic Target for Hypertension During Pregnancy Induced by Primary and Supporting Factors: A Systematic Literature Review of Preclinical Studies."

METHOD

To ensure transparent reporting of the analysed journal articles, this systematic review employed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram (Page et al, 2021). The assessment and analysis were conducted independently by the authors.

Search Strategy

The article search was conducted using the following keywords: (Probiotics and Pregnancy and Maternal and Hypertension and Rat or Mice or Probiotic on Hypertension Pregnancy), across four health-related databases: Google Scholar, PubMed, Taylor & Francis, and ScienceDirect. Only journal articles published within the last ten years (2015–2025) were included.

Inclusion and Exclusion Criteria

The inclusion criteria were established based on the PICOS framework (Population, Intervention, Comparison, Outcomes, and Study Design), as shown in Table 1 (Methley et al, 2014; Amir et al, 2020). Additional inclusion criteria included: articles written in English, available in full text, and conforming to the predetermined study design.
The exclusion criteria were as follows: (i) articles outside the *in vivo* study design; (ii) meta-analyses, systematic reviews, and literature reviews; (iii) articles not available in full text; and (iv) studies focusing on topics unrelated to probiotics, hypertension, or pregnancy.

Table 1.
Table of PICOS Criteria

Criteria	Inklusi
Problems	The increasing and severe development of hypertension during pregnancy, exacerbated by supporting or primary factors, which current therapies may not adequately address.
Intervation	The role of probiotics in reducing hypertension during pregnancy.
Comparasion	The potential of probiotic use, particularly in reducing hypertension during pregnancy in pathological conditions, compared to control groups.
Outcome	Probiotics as a novel therapy for hypertension during pregnancy, whether induced by primary or supporting factors.
Study Design	Preclinical studies, including *in vivo* studies, with publication dates within the last ten years (2015–2025).

Data Extraction

Data extraction was performed independently by the authors. The following data were extracted from the included studies: (1) authors and year of study; (2) study sample type; (3) hypertension induction; (4) type of probiotics administered; (5) type of hypertension measurement; and (6) study outcomes.

RESULT

The designed systematic review successfully identified 14 studies from a total of 7,475 articles. Articles that met the inclusion criteria were subsequently extracted according to the chosen data extraction form. The article search process was valid based on the inclusion criteria, leading to the identification of 14 studies, as shown in Figure 1.

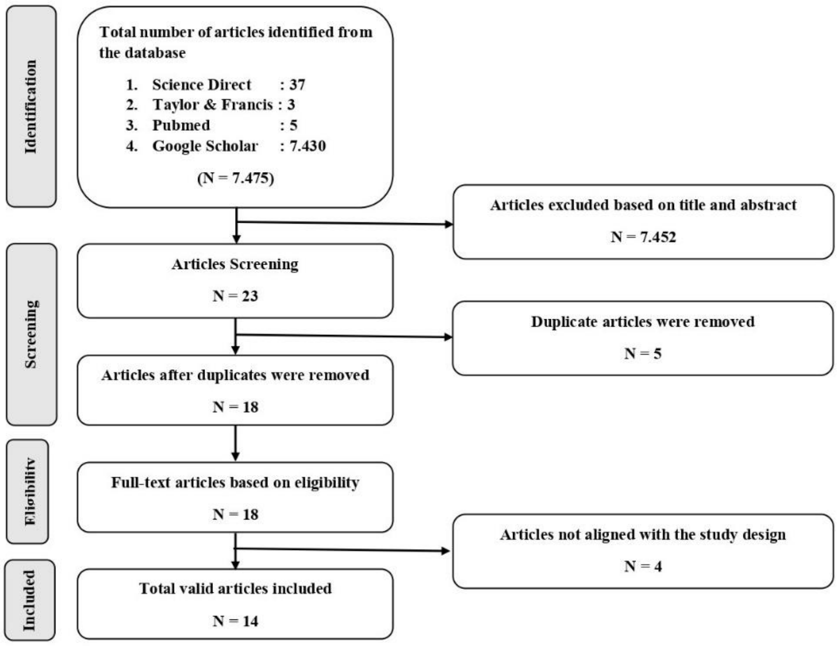

Figure 1. PRISMA Diagram

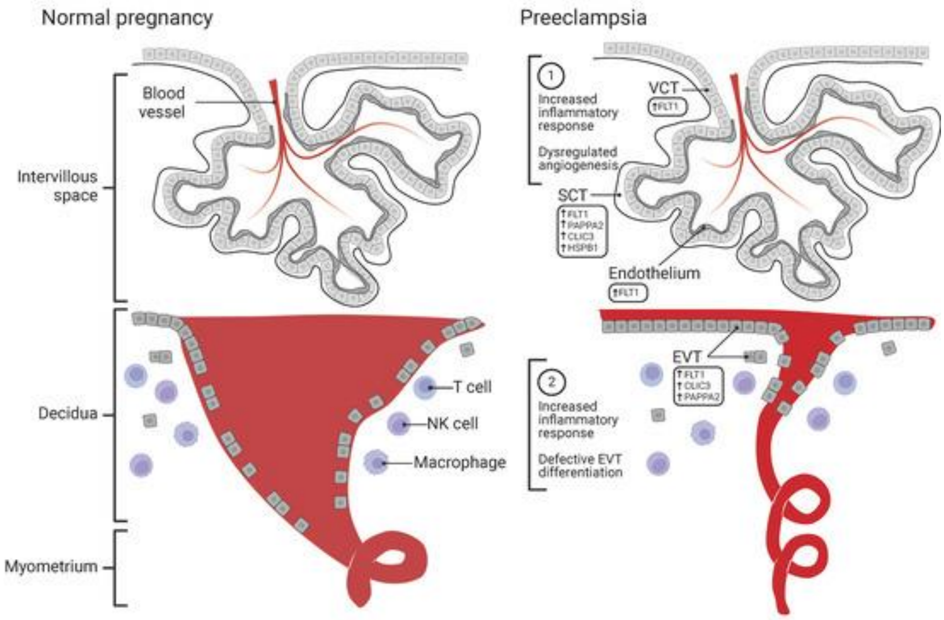

Figure 2. Comparison of Placental Development in A) Normal Pregnancy and B) Preeclamptic Pregnancy (Cao et al, 2024).

Probiotics in the Management of Hypertension During Pregnancy: Types of Probiotics and Their Role in Blood Pressure Regulation

The use of probiotics as part of emerging therapeutic strategies has become a growing focus, particularly within the field of basic medical science. Probiotics are known to play diverse roles in health, including enhancing immune function, regulating physiological and homeostatic processes, and offering therapeutic benefits in various diseases, particularly those related to the cardiovascular system (Bodke et al, 2022; Pavlidou et al, 2022). Recent advancements have reported the potential of probiotics to reduce blood pressure in hypertensive conditions, suggesting their value as a novel therapeutic modality for hypertension-related diseases, such as pregnancy-induced hypertension, also known as preeclampsia (McDougall et al, 2024).

Recent studies investigating probiotic-based therapies for hypertension during pregnancy have increasingly been reported, especially in *in vivo* models. Several investigations have demonstrated the beneficial effects of specific probiotic strains in managing pregnancy-associated hypertension, as summarised in Table 2 below.

Table 2.
The Role of Probiotics in the Treatment of Hypertension During Pregnancy

Genus	Species	Authors (Year)
Akkermansia sp.	*Akkermansia muciniphila*	Liu *et al.*, 2023[46] Peng *et al.*, 2024[47] Chen *et al.*, 2023[48]
Bifidobacterium sp.	*Bifidobacterium bifidum*	He *et al.*, 2020[49]
	Bifidobacterium sp.	Sun *et al.*, 2020[50]
Lactobacillus sp.	*Lactobacillus sp.*	Sun *et al.*, 2020[50]
	Lactobacillus gasseri A, Lactobacillus plantarum B, Lactobacillus plantarum R5, Lactobacillus plantarum R7	Yi *et al.*, 2024[51]
	Lactobacillus casei	Hsu *et al.*, 2018[52] Hsu *et al.*, 2019[53]
	Lactobacillus gasseri	Chao *et al.*, 2022[54]
	Lactobacillus fermentum 139, Lactobacillus fermentum 263, Lactobacillus fermentum 296	Oliveira *et al.*, 2020[55]
	Lactobacillus fermentum CECT5716	Toral *et al.*, 2019[56]
Limosilactobacillus sp.	*Limosilactobacillus reuteri CALM 603*	Li *et al.*, 2023[57]
	Limosilactobacillus fermentum 139, Limosilactobacillus fermentum 263, Limosilactobacillus fermentum 296	Nascimento *et al.*, 2022[58]
Lactiplantibacillus sp.	*Lactiplantibacillus plantarum WJL*	Guimares *et al.*, 2020[59]

Table 3.
Blood Pressure Levels in Control and Treatment Groups Following Probiotic Administration

Authors (Year)	Probiotic	Blood Pressure (mm Hg) Control Group		Blood Pressure (mm Hg) Treatment Group	
		Systolic	Diastolic	Systolic	Diastolic
Liu *et al.*, 2023	*Akkermansia muciniphila*	>140	NR	<125	NR
Peng *et al.*, 2024	*Akkermansia muciniphila*	>140	NR	<120	NR
Chen *et al.*, 2023	*Akkermansia muciniphila*	>130	NR	<120	NR
He *et al.*, 2020	*Bifidobacterium bifidum*	>130	NR	<120	NR
Sun *et al.*, 2020	*Bifidobacterium sp.* Dan *Lactobacillus sp.*	155,80	98,80	134,50	80,60
Yi *et al.*, 2024	*Lactobacillus gasseri A, Lactobacillus plantarum B, Lactobacillus plantarum R5, Lactobacillus plantarum R7*	133,94	108,17	107,33	86,39
Hsu *et al.*, 2018	*Lactobacillus casei*	154	NR	145	NR
Hsu *et al.*, 2019	*Lactobacillus casei*	150	78	144	68
Chao *et al.*, 2022	*Lactobacillus gasseri*	>130	NR	<120	NR
Oliveira *et al.*, 2020	*Lactobacillus fermentum 139, Lactobacillus fermentum 263, Lactobacillus fermentum 296*	>150	>100	<150	<100
Toral *et al.*, 2019	*Lactobacillus fermentum CECT5716*	>160	NR	<120	NR
Li *et al.*, 2023	*Limosilactobacillus reuteri CALM 603*	>140	NR	<120	NR
Nascimento *et al.*, 2022	*Limosilactobacillus fermentum 139, Limosilactobacillus fermentum 263, Limosilactobacillus fermentum 296*	>120	>80	<110	<80
Guimares *et al.*, 2020	*Lactiplantibacillus plantarum WJL*	>160	>120	<150	<110

DISCUSSION

Pathophysiology and Pathogenesis of Hypertension During Pregnancy

Hypertension during pregnancy, commonly referred to as preeclampsia, is a complex condition involving intricate interactions between the placenta, the maternal vascular system, and the immune system (Ives et al, 2020). The pathogenesis originates from impaired trophoblast implantation during early pregnancy, leading to inadequate remodelling of the spiral arteries. In normal pregnancy, trophoblasts invade the decidual and myometrial layers, replacing the endothelial lining of the spiral arteries with trophoblastic cells, thereby forming low-resistance vessels that ensure high blood flow to the placenta (Staff et al, 2022; Lyall et al, 2013). However, in pathological pregnancies characterised by hypertension, trophoblast invasion is disrupted, resulting in placental hypoperfusion. This condition subsequently triggers the release of inflammatory and anti-angiogenic mediators into the maternal circulation (Cao et al, 2024).

An imbalance between pro-angiogenic and anti-angiogenic factors is a key contributor to endothelial dysfunction in pathological pregnancy-related hypertension. Specifically, there is an upregulation of Chloride Intracellular Channel 3 (CLIC3), Pappalysin 2 (PAPPA2), and Heat Shock Protein Family B (Small) Member 1 (HSPB1), which are involved in the induction of oxidative stress, regulation of inflammation, and the migration and invasion of trophoblasts. This is followed by an increase in soluble fms-like tyrosine kinase-1 (sFlt-1), a circulating receptor for vascular endothelial growth factor (VEGF) and placental growth factor (PlGF), which binds to VEGF and PlGF and inhibits their normal interaction with endothelial receptors (Cao et al, 2024; Hesson et al, 2023; Cerdeira et al, 2020). As a result, VEGF and PlGF activity is suppressed, leading to endothelial dysfunction, reduced vasodilation, and systemic vascular damage. In addition, elevated levels of soluble endoglin (sEng), a co-receptor of transforming growth factor-β (TGF-β), further impair TGF-β signalling, which is essential for vascular integrity. The combined increase of sFlt-1 and sEng creates a profoundly anti-angiogenic environment in the maternal circulation (Torres et al, 2021).

Endothelial dysfunction subsequently leads to an imbalance in the production of vasodilators and vasoconstrictors, particularly characterised by a reduction in nitric oxide (NO) levels and an increase in endothelin-1 (ET-1) expression (Titus et al, 2023; Li et al, 2013). NO, synthesised by endothelial nitric oxide synthase (eNOS), serves as a principal vasodilator during normal pregnancy. Studies have demonstrated that in preeclampsia, eNOS expression is downregulated, thereby reducing NO production and contributing to increased vascular resistance (Ssengonzi et al, 2024; Kaihara et al, 2023). Conversely, endothelin-1, a potent vasoconstrictive peptide, is upregulated under the influence of placental hypoxia and oxidative stress. Activation of the ET_A receptor by ET-1 triggers systemic vasoconstriction, culminating in hypertension (Saleh et al, 2016). Moreover, dysregulated activation of the renin–angiotensin–aldosterone system (RAAS) further exacerbates the elevation of blood pressure (Tsikouras et al, 2025).

Abnormal immune responses also play a crucial role in the pathogenesis of pregnancy-induced hypertension (LaMarca et al, 2013). There is an increase in pro-inflammatory T cells (Th1 and Th17) and a decrease in regulatory T cells (Treg), which leads to an elevated production of pro-inflammatory cytokines such as TNF-α, IL-6, and IL-17 (Salazar et al, 2018; Zhou et al, 2023). These cytokines exacerbate endothelial dysfunction and activate the NF-κB pathway, which upregulates pro-inflammatory gene expression and enhances oxidative stress (Aouache et al, 2018). Excessive production of reactive oxygen species (ROS) in the endothelium and placenta due to oxidative stress mechanisms then inhibits nitric oxide (NO) bioavailability, reinforcing vasoconstriction and worsening vascular damage (Page et al, 2021; Phoswa et al, 2021). Furthermore, elevated autoantibodies against the angiotensin II receptor (AT1-AA) have been found in preeclamptic patients, which pathologically activate the AT1 receptor and aggravate hypertension (Deer et al, 2021). Overall, hypertension during pregnancy results from an interconnected molecular process involving placental hypoperfusion, endothelial dysfunction, disrupted angiogenesis, systemic inflammation, oxidative stress, and abnormal immune activation. Key genes and proteins involved include sFlt-1, PlGF, VEGF, sEng, eNOS, ET-1, TNF-α, IL-6, IL-17, NF-κB, AT1-AA, as well as factors in the renin-angiotensin-aldosterone system (RAAS) such as angiotensinogen, renin, ACE, and AT1R.

Probiotics in the Management of Hypertension During Pregnancy: Types of Probiotics and Their Role in Blood Pressure Regulation
Akkermansia spp., particularly *Akkermansia muciniphila*, are Gram-negative *coccobacilli* that naturally inhabit the mucus layer of the human gut (Iwaza et al, 2022). This species, classified within the phylum *Verrucomicrobia*, exhibits a unique ability to metabolise mucin, the primary glycoprotein constituent of the gastrointestinal mucus layer (Panzetta et al, 2024). Its physiological traits anaerobic growth, non-motility, and strong adaptability to mucosal environments position *A. muciniphila* as a promising probiotic candidate. Multiple studies have shown that the presence of *A. muciniphila* is positively correlated with improved gut barrier integrity, reduced systemic inflammation, and better metabolic profiles in conditions such as obesity, type 2 diabetes, inflammatory bowel disease, and cardiovascular disorders (Xu et al, 2023; Pena et al, 2024; Liu et al, 2024).

Recent research by Liu *et al.* (2023), Peng *et al.* (2024), and Chen *et al.* (2023) has demonstrated the role of *A. muciniphila* in lowering blood pressure in pregnancy-induced hypertension (preeclampsia). Liu *et al.* (2023) reported a significant reduction in systolic blood pressure in preeclamptic models ($p < 0.01$) following administration of *A. muciniphila* (Liu et al, 2023). Similarly, Peng *et al.* (2024) observed a marked decrease in systolic blood pressure ($p < 0.001$) after probiotic treatment with *A. muciniphila* (Pang et al, 2024). Notably, their study also found that pasteurised *A. muciniphila* produced an even greater antihypertensive response, likely due to reduced endotoxin-related adverse effects (Druart et al, 2021). Furthermore, the extracellular fractions of *A. muciniphila* demonstrated significant blood pressure-lowering effects ($p < 0.001$), comparable to those of the intact bacterium, suggesting potential for combination therapies involving drug delivery systems such as encapsulation technologies (Chen et al, 2023; Liu et al, 2022; Qioan et al, 2025).

Bifidobacterium sp., commonly represented by the species *Bifidobacterium bifidum*, is a Gram-positive, branched rod-shaped bacterium belonging to the phylum *Actinobacteria* and is predominantly found in the human gastrointestinal tract, particularly in breastfed infants, as a probiotic (Sadeghpour et al, 2023; Ma et al, 2024). This bacterium is a facultative anaerobe, non-spore-forming, and possesses fermentative abilities toward oligosaccharides and complex polysaccharides, yielding lactic acid and acetic acid as primary metabolic products. These physiological and metabolic properties enable *B. bifidum* to act as a beneficial probiotic by maintaining gut microbiota balance, enhancing mucosal immune responses, and inhibiting pathogenic growth through nutrient competition and antimicrobial compound production (Yakoob et al 2019; Sibanda et al, 2024).

The therapeutic role of *B. bifidum* has been widely studied for its potential in alleviating gastrointestinal disturbances such as diarrhoea, irritable bowel syndrome (IBS), and intestinal inflammation. Additionally, it has been evaluated as an adjuvant in therapy to support immune modulation, inflammatory response control, and metabolic homeostasis in various pathological conditions (Henrick et al, 2021; Gavzy et al, 2023; Aghamohammad, 2023; Choi et al, 2022). A study conducted by He *et al.* [49] in 2020 reported a significant reduction in blood pressure during pregnancy ($p<0.001$) following administration of *B. bifidum*. Further, Sun *et al.* [50] in 2020 also demonstrated a significant antihypertensive effect ($p=0.000$) of a probiotic combination of *Bifidobacterium sp*. and *Lactobacillus sp*. These findings support the efficacy of Bifidobacterium sp. as a promising agent in future therapeutic strategies for the management of hypertension during pregnancy, especially in cases of preeclampsia.

Probiotic gut microbiota of the genus *Lactobacillus* including species such as *Lactobacillus plantarum*, *Lactobacillus casei*, *Lactobacillus gasseri*, and *Lactobacillus fermentum* comprise Gram-positive, rod-shaped, non-motile, and non-spore-forming bacteria (Kullar et al, 2023).. These bacteria belong to the phylum Firmicutes and are facultative anaerobes known for their ability to survive acidic environments through the production of lactic acid as the main metabolic product of carbohydrate fermentation (Dempsey et al, 2022). The characteristics of *Lactobacillus* spp. as natural probiotics contribute significantly to gut microbiota balance, strengthening epithelial barrier function, and suppressing pathogen colonization through adhesion competition and the production of antimicrobial compounds such as bacteriocins (Wiktorczyl et al, 2024).

Clinically, various *Lactobacillus* species have been widely used as probiotics in therapeutic applications, including the treatment of infectious diarrhoea, improvement of irritable bowel syndrome symptoms, reduction of urinary tract infection risk, and support for metabolic therapy in obesity and diabetes. Their effectiveness in modulating immune responses and reducing inflammation makes *Lactobacillus* spp. central to microbiome-based therapeutic strategies (Daisley et al, 2020; Aghamohammad, 2022).

Hsu *et al.* [52,53] in 2018 and 2019 demonstrated the antihypertensive effect of *L. casei* in maternal rats fed with a high-sucrose and high-fat diet ($p<0.05$). The study also reported improvements in renal condition and reductions in the levels of Trimethylamine N-oxide (TMAO), Trimethylamine (TMA), and Dimethylamine (DMA)—markers of dyslipidaemia—thus contributing to blood pressure reduction and improvement of pregnancy-related hypertension)Wang et al, 2022; Tain et al, 2024; Koirala et al, 2024; Li et al, 2022). Chao *et al.* [54] in 2022 also reported the significant ($p<0.05$) blood pressure-lowering effect of *L. gasseri* in maternal rats induced with a high-sucrose diet. *L. gasseri* administration, which led to the production of Short-Chain Fatty Acids (SCFAs), improved the expression of GPR41 and OLFR78, both of which are Free Fatty Acid Receptors (FFARs) that influence vasoconstriction and vasodilation processes relevant in hypertensive pregnancy (Li et al, 2022; Xu et al, 2022).

Yi *et al.* [51] in 2024 showed that probiotic strains *L. plantarum B*, *L. plantarum R5*, and *L. plantarum R7*—present in buffalo milk yogurt—significantly reduced blood pressure ($p<0.05$) in pregnancy-induced hypertensive rats. Their study also indicated that the yogurt-based probiotic formulation was more effective than the generic antihypertensive drug, Labetalol (Miller et al, 2025). Oliveira *et al.* [55] in 2020 reported that *L. fermentum* strains (*L. fermentum* 139, 263, and 296) had significant antihypertensive effects ($p<0.05$) in dyslipidaemic pregnant rats. The study further highlighted that dyslipidaemia plays a key role in the pathogenesis of hypertension through mechanisms such as vasoconstriction and vascular stenosis caused by elevated VLDL, cholesterol, and triglyceride levels. Accordingly, administration of *L. fermentum* exerted anti-inflammatory, immunomodulatory, antidyslipidaemic, and antihypertensive effects (Lin et al, 2022; Hosier et al, 2023; Zhao et al, 2019).

Further research by Toral *et al.* [56] in 2019 demonstrated the significant antihypertensive effect ($p<0.01$) of *Limosilactobacillus fermentum* strain CECT5716 in pregnant hypertensive rats induced by systemic lupus erythematosus (SLE). This study revealed that administration of *L. fermentum* CECT5716 improved both hypertension and SLE via immune modulation, as evidenced by alterations in immune factor activity (Zhao et al, 2019). Specifically, the probiotic reduced the number of T helper 17 (Th17), regulatory T cells (Treg), and Th1 cells, along with decreased levels of proinflammatory cytokines including TNF-α, IL-18, IL-1β, and IL-17a, as well as the anti-inflammatory cytokine IL-10 (Cristofori et al, 2021). Transcription factors FOXP3 and RORγ, which regulate T cell differentiation, were also downregulated, indicating reduced inflammatory activity previously contributing to hypertension (Lee et al, 2018; Dinakis et al, 2024). Interestingly, the expression of endothelial nitric oxide synthase (eNOS) was elevated, suggesting improved endothelial function via increased nitric oxide production, which enhanced vasodilation and reduced blood pressure (Kursun et al, 2025; Zhao et al, 2021).

Limosilactobacillus spp. are Gram-positive, rod-shaped lactic acid bacteria closely related to *Lactobacillus* spp. Among them, *L. fermentum* is morphologically curved and facultative anaerobic (Wei et al, 2025). It is notable for its ability to ferment a wide range of carbohydrates, producing lactic acid as the main by-product. *L. fermentum* also shows resistance to acidic and bile environments and exhibits adaptability within the gastrointestinal tract (Hossain et al, 2022). As a probiotic, it supports gut microbiota balance, enhances immune responses, and produces antimicrobial compounds such as bacteriocins (Pruthviraj et al, 2023). Its therapeutic potential extends to inflammatory disorders, gastrointestinal infections, and supportive therapy for metabolic diseases via immunomodulatory mechanisms and reinforcement of epithelial barrier function, particularly in the placenta (Tarannum et al, 2024; Hao et al, 2024; Liu et al, 2024).

Li *et al.* [57] in 2023 confirmed the significant blood pressure-lowering effects ($p<0.001$) of *L. reuteri* strain CALM 603 in hypertensive pregnant rats. Likewise, Nascimento *et al.* [58] in 2022 supported the effectiveness of *L. fermentum* strains 139, 263, and 296 in reducing blood pressure ($p<0.05$) in hypertensive rats with dyslipidaemia as a comorbidity. Their findings also addressed the role of oxidative stress by observing elevated malondialdehyde (MDA) levels—indicative of increased lipid peroxidation—and changes in antioxidant enzyme activities. These included increased superoxide dismutase (SOD) activity and decreased catalase (CAT) and glutathione S-transferase (GST) activities. The rise in SOD is interpreted as an initial compensatory response to free radical accumulation, while the reduced CAT and GST activities suggest enzymatic fatigue or regulatory dysfunction due to chronic oxidative stress (de Luna Freire et al, 2021).

L. fermentum probiotics may alter antioxidant metabolic pathways through the production of bioactive metabolites. These metabolites reinforce primary defense mechanisms (e.g., SOD) while potentially reducing the expression or requirement of secondary antioxidant enzymes (e.g., CAT and GST) (Zhang et al, 2024). This highlights the nuanced role of probiotics in modulating oxidative homeostasis, which is context-dependent and shaped by the cell's adaptive capacity in pathological conditions. Another probiotic genus identified as a gut microbiota-based therapy is *Lactiplantibacillus* spp., a group of Gram-positive, rod-shaped lactic acid bacteria with important roles in the human gastrointestinal tract.

Among the most well-known species in this genus is *Lactiplantibacillus plantarum*, which exhibits a straight to slightly curved rod morphology and facultative anaerobic properties (Heo et al, 2024). *L. plantarum* is highly adaptable, capable of surviving in extreme pH conditions and high salt concentrations, and proficient in fermenting a wide variety of sugars (Popova-Krumova, 2024; Zhang et al, 2025). As a probiotic, it offers therapeutic potential through several mechanisms, including enhancement of intestinal barrier function, modulation of immune responses, and production of bioactive metabolites such as lactic acid and bacteriocins that inhibit pathogenic bacteria (Ma et al, 2025; Tobias et al, 2025). A study by Guimarães *et al.* [59] in 2020 demonstrated the significant antihypertensive effect ($p<0.05$) of *L. plantarum* strain WJL in hypertensive rats with dyslipidaemia as a comorbid condition.

CONCLUSION
Administration of probiotics particularly from the genera *Akkermansia*, *Bifidobacterium*, *Lactobacillus*, *Limosilactobacillus*, and *Lactiplantibacillus* has demonstrated efficacy in reducing blood pressure in animal models of preeclampsia and pregnancy-induced hypertension, both in primary and comorbidity-induced contexts. The antihypertensive effects of these probiotics are mediated through multiple mechanisms, including restoration of endothelial function, modulation of immune responses, attenuation of oxidative stress, and regulation of the renin–angiotensin system.

These findings support the potential of probiotics as a safe, non-pharmacological therapeutic strategy for managing hypertensive disorders during pregnancy.

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