

## Molecular and Physiological Mechanisms of Antenatal Exercise for Preventing Hypertensive Disorders in Pregnancy: A Systematic Review

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### ABSTRACT

Hypertensive Disorders in Pregnancy (HDP) is a complex vascular complication associated with impaired placental angiogenesis and endothelial dysfunction. Globally, HDP represents a significant cause of adverse outcomes for both mothers and newborns. This systematic review aims to explore the molecular and physiological mechanisms contributing to the prevention of HDP through antenatal exercise. Research articles published between 2015 and 2025 were systematically identified from PubMed, ScienceDirect, and Google Scholar databases, resulting in 10 studies meeting the inclusion criteria. Findings indicate that regular exercise during pregnancy improves endothelial function, balances angiogenic activity, and reduces oxidative stress and inflammation. Molecular mechanisms include increases in vascular endothelial growth factor (VEGF) and nitric oxide (NO), as well as decreases in inflammatory markers. This supports improved placental perfusion and decreased vascular resistance, leading to lower systolic and diastolic blood pressure. This review concludes that antenatal exercise provides multifactorial protection through physiological and molecular pathways, potentially becoming a safe, accessible, and affordable non-pharmacological strategy to mitigate HDP risk and promote maternal health.

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## 1. INTRODUCTION

Hypertensive disorders in pregnancy (HDP) represent one of the most significant and life-threatening complications affecting pregnancies worldwide. The International Society for the Study of Hypertension in Pregnancy (ISSHP) defines HDP as the presence of systolic and/or diastolic blood pressure equal to or exceeding 140/90 mmHg (Magee et al., 2022). HDP encompass chronic hypertension, gestational hypertension, chronic hypertension complicated by superimposed preeclampsia, preeclampsia, and eclampsia (Luger & Kight, 2022). HDP remains a leading cause of maternal and perinatal morbidity globally in the past five years. Several studies have linked maternal obesity, metabolic syndrome, and advanced maternal age to an increased risk of preeclampsia (Mathew et al., 2023; Sun et al., 2025). The global prevalence of HDP is estimated to affect approximately 5–10% of all pregnancies and shows an increasing trend with changes in maternal demographic characteristics, such as older maternal age and increased pre-pregnancy weight (Khedagi & Bello, 2021; Luger & Kight, 2022). The global prevalence of HDP is also reported to reach 116

cases per 100,000 women of childbearing age (Jiang et al., 2022). In Indonesia, the 2023 Survei Kesehatan Indonesia (SKI) reported that approximately 3.2% of pregnant women experienced hypertension, out of a total of 18.9% of woman who reported pregnancy-related health complaints.

HDP is complex and multifactorial. Several etiologies can contribute to HDP, such as maternal age over 40, pre-pregnancy obesity, excessive gestational weight gain, and gestational diabetes mellitus (Singh et al., 2018). The pathogenesis of HDP is influenced by a combination of genetic factors, an inadequate immunological response, and abnormal placental function. Although the pathophysiological mechanisms are not fully understood, some evidence suggests that imbalanced placental perfusion, endothelial dysfunction, and genetic predisposition play a role in triggering this pathological process (Hailu et al., 2025). Endothelial dysfunction is associated with increased release of antiangiogenic factors from placental tissue, which plays a role in the pathogenesis of systemic hypertension (Luger & Kight, 2022). Beyond angiogenic imbalance and endothelial dysfunction, recent evidence highlights maternal metabolic dysregulation notably insulin resistance and abnormal lipid profiles as well as pregnancy-specific immune maladaptation, including shifts in Th1/Th2 cytokine balance and altered decidual NK cell function, in the pathogenesis of hypertensive disorders of pregnancy (Phoswa et al., 2023; Preda et al., 2024; Qin et al., 2025; Wei & Yang, 2023). Furthermore, impaired trophoblast differentiation and failure of endothelial invasion caused by imbalances in the regulation of cytokines, adhesion molecules, major histocompatibility complexes, and metalloproteinase activity contribute to the pathogenesis of gestational hypertension (Luger & Kight, 2022).

The occurrence of hypertension during pregnancy not only elevates the risk of maternal and perinatal morbidity and mortality, but also contributes to long-term complications. Studies have shown that HDP is associated with various serious complications, such as maternal and fetal death, stillbirth, placental abruption, disseminated intravascular coagulation, cerebral hemorrhage, liver failure, and acute renal failure (Poon et al., 2019; von Dadelszen & Magee, 2016). Mothers with HDP are also recognized as having an elevated risk of developing cardiovascular disease later in life (Garovic et al., 2022).

Consequently, HDP prevention has become an important focus in obstetric and public health practice. Effective preventive strategies are urgently needed, and currently, lifestyle modifications have shifted. Lifestyle modifications before and during pregnancy have been shown to reduce the risk of obstetric complications. Exercise has emerged as a promising non-pharmacological strategy capable of modulating these pathways. Recent mechanistic studies show that antenatal exercise improves endothelial function, enhances nitric oxide bioavailability, reduces oxidative stress, and positively influences metabolic and inflammatory profiles. These physiological effects support its potential role in preventing HDP (Bhattacharjee et al., 2021; Karthiga et al., 2022; Ramírez-Vélez et al., 2013). Antenatal exercise represents a potentially effective non-pharmacological intervention for mitigating the risk of HDP. Physical exercise is defined as any type of bodily movement generated by skeletal muscle activity that necessitates energy expenditure (Hailu et al., 2025). Scientific evidence suggests that regular physical exercise can reduce the risk of gestational hypertension by approximately 30% and preeclampsia by approximately 40% (Davenport et al., 2018). The American College of Obstetricians and Gynecologists (ACOG) and the World Health Organization (WHO) advises that pregnant women engage in moderate-intensity physical activity considered safe, such as walking, swimming, and aerobics (Hailu et al., 2025). However, a thorough understanding of the molecular and physiological mechanisms underlying the protective effects against HDP remains elusive. Several studies suggest that exercise is thought to mediate its effects through reduce oxidative stress and inflammation, enhanced placental function, and modulate the production of angiogenic factors (such as placental growth factor) (Korsager Larsen & Matchkov, 2016; Pahlavani et al., 2023). Moreover, exercise contributes to optimal weight management, improved insulin sensitivity, and blood pressure regulation through a decrease in systolic and diastolic (Cox, 2017; Korsager Larsen & Matchkov, 2016).

However, despite increasing evidence linking exercise to improved maternal vascular and metabolic health, few reviews synthesize both the physiological and molecular mechanisms through which antenatal physical activity may influence HDP risk. Most previous reviews focus on clinical outcomes alone, without integrating biomarker-level findings. Therefore, a systematic review that consolidates recent mechanistic evidence is needed to clarify how exercise may contribute to HDP prevention. Therefore, this study aims to synthesize clinical evidence on the molecular and physiological mechanisms underlying the protective effect of antenatal exercise against HDP. A clearer understanding of these mechanisms may support the development of targeted preventive interventions based on individual HDP risk profiles in maternal healthcare.

## **2. METHOD**

The type of research method is a systematic review. The source of data is derived from the results of previous research studies obtained online (secondary data). The literature sources were retrieved from three electronic databases, namely Google Scholar, PubMed, and ScienceDirect. The search term employed are related to the variables and connected by using Boolean “OR” or “AND”. The following is a search strategy that used in this article, including “antenatal exercise” OR “prenatal exercise” OR “physical activity” AND “hypertensive disorders” AND “pregnancy” AND “mechanism” AND “molecular” AND “physiological”.

The inclusion criteria used in this systematic review include, (a) Journals published in the range of 2015-2025; (b) The language of the article used is English; (c) Articles must be available in full text and open access; (d) The type of scientific article is an original article. While the exclusion criteria were, (a) The research method of the article uses review; (b) The article does not provide full text; (c) The content of the article is not relevant to the topic area discussed.

The data extraction process was conducted after articles met the inclusion and exclusion criteria. Extraction was performed manually in tabular form to ensure consistency and reduce the risk of bias. Data extracted from each article included: (1) Bibliographic information (author, year); (2) Study characteristics using the PICO method (population, intervention, comparison, and outcome); (3) Key findings related to molecular and physiological mechanisms (e.g., effects on oxidative stress, endothelial regulation, vascular function, inflammatory response, etc).

To ensure accuracy and transparency, the literature selection and assessment process for this article was guided by the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) protocol. The systematic steps involved included topic determination, research question formulation, literature search using keywords, inclusion and exclusion criteria determination, step-by-step screening (title, abstract, keywords), full-text collection, and finally, data synthesis of relevant articles.

Furthermore, an abstraction process was performed, summarizing all key findings from each article to facilitate comparison between studies. Data synthesis was conducted using a narrative synthesis approach. The synthesis also considered the methodological quality of each study to determine the strength of the evidence generated.

## **3. RESULTS AND DISCUSSION**

The search results from 3 databases yielded 237 articles, all of which were screened using PRISMA. The PRISMA flowchart of the article search process can be seen in Figure 1. After applying the eligibility parameters, ten studies fulfilled the criteria for inclusion in this systematic review.

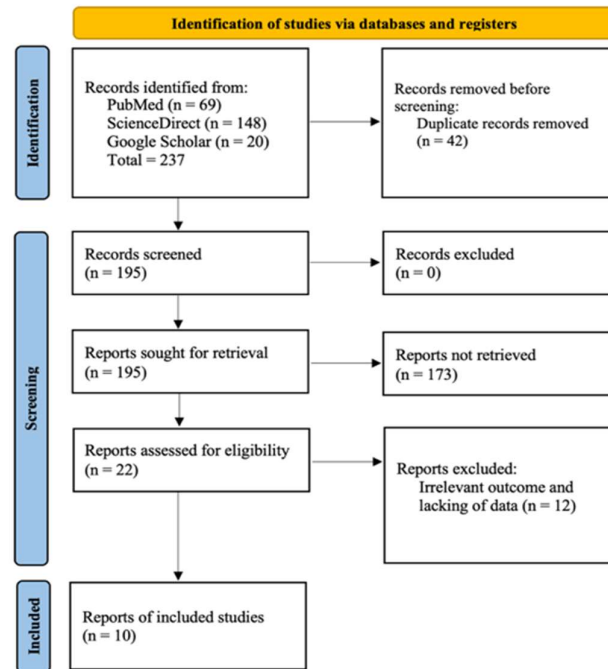


Figure 1. PRISMA Diagram of Article Search Process



### 3.1. Data Synthesis Based on Characteristics Study

Table 1. Result of Data Synthesis

| No. | (Author, Year)          | Study Design                      | Population (P)  | Intervention (I)  | Comparison (C)   | Outcomes (O)   | Key Molecular / Physiological Findings  |
|-----|-------------------------|-----------------------------------|---|---|--|--|---|
| 1.  | (Barakat et al., 2016)  | Randomized Controlled Trial (RCT) | 765 normal pregnant women (382 intervention, 382 control) with an average age of 31–32 years from primary care centers in Madrid, Spain                             | Each training session included:<br>- 10–20 minutes period for warming up and cooling down<br>- Main exercise session (25-30 minutes)                              | The control group received standard prenatal care from a healthcare provider but was also not restricted from exercising. They still can do regular structured exercise ( $\geq 3$ days/week for $\geq 20$ minutes/day). | The incidence of hypertension was significantly higher in non-exercising women, being approximately threefold greater than in the exercise group (5.7% vs. 2.1%, $P = 0.009$ ).      | - $\uparrow$ aerobic capacity and improves cardiovascular function, potentially lowering blood pressure.<br>- $\downarrow$ maternal oxidative stress byproducts and prevent endothelial dysfunction, potentially preventing preeclampsia. |
| 2.  | (Haakstad et al., 2016) | RCT                               | 61 healthy nulliparous pregnant women with normal pregnancy conditions and having a normal BMI.   | A structured aerobic program conducted twice weekly for 12 weeks, with each session lasting 60 minutes.   | The control group performed their usual daily physical activities without any additional exercise intervention.  | A significant drop in resting systolic pressure (7.5 mmHg) and a marginal reduction in diastolic pressure were recorded in the exercise group when contrasted with the control group | Consistent exercise enhanced vascular endothelial performance, reduced oxidative burden, modulated immune and inflammatory responses, and elevated cardiac output.  |
| 3.  | (Awad et al., 2019)     | RCT with a parallel-group design  | 40 primigravida with mild preeclampsia (BMI $\geq 35$ ) aged 25–35 years without other complications were divided into two non-pharmacological intervention groups. | Stretching (Group A) vs autogenic training (Group B), with 30 seconds of exercise and 30–40 seconds of focus, 3 $\times$ /week for six weeks.                     | Parallel-group randomized study comparing two non-pharmacological intervention groups for preeclampsia. Both groups also received individual doses of methyldopa as antihypertensive therapy                             | Significant declines in systolic and diastolic pressures, along with reduced proteinuria, were observed in both groups ( $P < 0.05$ )  | Both non-pharmacological interventions have been shown to be effective in alleviating preeclampsia symptoms, including hypertension and proteinuria, by regulating autonomous vascular endothelial function.                              |
| 4.  | (Catov et al., 2018)    | Prospective Cohort Study          | Nulliparous pregnant women enrolled at 8 US clinical centers with the criteria of singleton pregnancy, gestational age 6-14 weeks (n= 10,038), no history of        | Observations of the self-reported physical activity patterns of nulliparous pregnant women during their free time, by linking the participants' physical activity | There's no comparison but using high leisure-time physical activity pattern (referent) vs lower/other patterns.  | - Sedentary behavior increased PE risk<br><br>- According to medical records, limited engagement in physical activity was  | Physical activity $\uparrow$ vascular endothelial function and nitric oxide bioavailability, $\uparrow$ insulin sensitivity via skeletal muscle glucose uptake, and $\downarrow$ systemic   |

|    |                              |   |  |   |   |   |   |
|----|------------------------------|---|--|---|---|---|---|
|    |                              |   | pregnancy $\geq 20$ weeks, major fetal anomalies, or planned termination   | patterns with various pregnancy outcomes.   |   | linked to an elevated risk of preterm delivery and GDM  | inflammation and sympathetic hyperactivity.   |
| 5. | (Do et al., 2020)            | Prospective Observational Cohort Study                  | A total of 189 pregnant participants with prior type 1 or type 2 diabetes and single-fetus pregnancies, and gestational age below 20 weeks were recruited from two gestational diabetes centers in Denmark between 2015 and 2018.                                      | Self-reported physical activity patterns at median gestational ages of 10, 21, and 36 weeks using <i>Pregnancy Physical Activity Questionnaire</i> (PPAQ).  | Comparing women with preeclampsia (PE) with non-PE women adjusted for nulliparity, diastolic blood pressure, smoking status, education level, HbA1c, renal impairment, movement and sedentary habits in the first trimester of pregnancy. | Sedentary behavior was consistently higher in the PE group across all trimesters. Sedentary activity in early pregnancy was positively correlated with the risk of preeclampsia (OR 1.04; 95% CI 1.00–1.08; $p = 0.03$ ). | High sedentary behavior increases PE risk via endothelial dysfunction and vascular stress.  |
| 6. | (Bhattacharjee et al., 2021) | Prospective Observational Cohort Study Design           | Forty-five healthy pregnant women from Ottawa (BMI 18.5–29.9 kg/m <sup>2</sup> ) were classified by their second-trimester activity level into an active group meeting $\geq 150$ minutes of moderate exercise weekly ( $n = 23$ ) and an inactive group ( $n = 22$ ). | Moderate to vigorous activity in the second trimester ( $\geq 150$ minutes weekly according to Canadian guidelines) was quantified using Actical® accelerometers. The devices were worn for seven consecutive days at two gestational assessments: 24–28 weeks and 34–38 weeks. | The comparison group consisted of women whose activity levels fell below the guideline benchmark of roughly 150 minutes of moderate exercise per week during the second trimester.  | Placental findings showed increased VEGF and VEGFR-1 expression with stronger endothelial and trophoblast markers in the active group, while VEGFR-2 and PlGF showed no notable differences                               | Physical activity increases VEGF and VEGFR-1 expression in placental tissue, and has been shown to increase angiogenesis and endothelial function.  |
| 7. | (Reynolds et al., 2022)      | Observational Cross-Sectional Study                     | 257 pregnant women from the 2003–2006 National Health and Nutrition Examination Survey (NHANES) aged approximately 28 years old, BMI 27.8–29.5 kg/m <sup>2</sup> .   | Objective assessment of physical activity was obtained using a hip-worn accelerometer (Actigraph AM-7164) for seven consecutive days. The device recorded two primary indicators: time spent in moderate-to-vigorous activity and the total number of steps per day             | Participants classified as highly active versus those categorized as less active (based on MVPA and steps/day); secondary comparison between upper vs. lower quartiles and $>7500$ vs. $<5000$ steps/day groups.                          | Significant difference in plasma homocysteine levels between the $<5,000$ steps/day group and the $>7,500$ steps/day group, with the sedentary group having the highest homocysteine levels ( $p = 0.003$ ).              | High homocysteine levels are associated with preeclampsia. Higher activity can reduce homocysteine, improving vascular function.  |
| 8. | (Karthiga et al., 2022)      | Parallel-design Single-blinded Randomized Control Trial | 234 pregnant women at 16 weeks' gestation with high risk for gestational hypertension (GH), history of preeclampsia, and BMI $>35$ . 121 participants in the intervention group and 113 in   | Standard antenatal care and a structured yoga program from week 16 – 36 of pregnancy. Yoga was practiced twice daily for 30 minutes per session (morning and evening).  | Control group received standard antenatal care and not allowed to practice yoga. Participants with hypertension in both groups received labetalol or nifedipine.  | Incidence of GH/PE was significantly reduced among women in the yoga program (6.6%) relative to the control participants (38.1%) ( $p < 0.001$ ) and improved endothelial and   | Yoga can increase nitric oxide (NO) levels, which are associated with lower blood pressure, reduces inflammatory markers (IL-6, hsCRP) and oxidative stress (MDA), improve endothelial function |



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|     |                              |  | control group (22 participants excluded due to COVID-19)   |  |   | inflammatory markers (↑ NO, HRV; ↓ BP, IL-6, hsCRP, MDA).  | through increased NO bioavailability.  |
|-----|------------------------------|--|--|--|---|--|--|
| 9.  | (Jaatinen et al., 2024)      | cross-sectional case-control multicenter study | 1.432 pregnant women (708 for PE group, 724 for control group) from the Finnish FINNPEC cohort. Inclusion: age > 18 years, singleton pregnancy, can provide informed consent.                                    | Self-reported physical activity before and during pregnancy from participants that were categorized into two groups: divided into individuals maintaining regular activity (≥2–3 sessions each week) and those with lower exercise frequency | PE vs non-PE groups stratified by physical activity level (case-control comparison) and angiogenic marker concentrations  | Physical activity measures and angiogenic biomarker concentrations (including sFlt-1, PlGF, sEng, and the sFlt-1/PlGF ratio) did not differ significantly either between participants with and without PE, or between women with higher (≥2–3 sessions/week) and lower exercise frequency. | A pro-angiogenic serum profile (higher PlGF, lower sFlt-1 and sEng) is thought to reduce the risk of PE in physically active women, suggesting improved angiogenic balance |
| 10. | (Kılıçlı & Zeyneloğlu, 2025) | RCT  | 66 pregnant women (33 for intervention group, 33 for control group) diagnosed with preeclampsia in Perinatology Service of Şanlıurfa Training and Research Hospital, Türkiye, between October 2023 - March 2024. | Mindfulness-based Breathing Exercise (MBBE) for 20 min every 8h for a total 72h. The exercises included body alignment, counting exhales, counting inhales, and free attention, or "Zazen," with each session lasting 5 minutes.             | Participants in the control condition spent 20 minutes sitting at eight-hour intervals throughout the 72 hours. Both groups received standard pharmacological treatment for preeclampsia. | The MBBE group showed a 59.2% improvement in health profile, significant improvements in vital signs, and an increase in mean basal fetal heart rate.  | MBBE increases parasympathetic tone, oxygenation, VEGF expression, and decreases the sFlt-1/PlGF ratio, which supports angiogenesis and placental health.                  |



### 3.2 Summary of Findings

Across all included studies, a consistent physiological pattern emerges. Nearly all exercise interventions whether stretching-based aerobics, yoga, or breathing-centered training demonstrate improvements in maternal blood pressure, autonomic cardiovascular regulation, and uteroplacental circulation. These convergent findings reinforce the physiological benefits of antenatal exercise in supporting vascular stability and reducing early indicators of hypertensive disorders. At the molecular level, several studies report increased nitric oxide availability, reductions in pro-inflammatory markers such as IL-6 and hsCRP, and enhanced endothelial responsiveness following exercise. Collectively, these effects support a mechanistic link between physical activity and improved vascular homeostasis during pregnancy, suggesting that molecular pathways may mediate the protective impacts of exercise. However, consistency in molecular responses varies across studies. Some studies indeed observe enhanced regulation of angiogenic markers such as VEGF and VEGFR-1, yet others such as Jaatinen et al. (2024) find no significant relationship between physical activity and angiogenic biomarker profiles. This variability reflects heterogeneity in participant characteristics, exercise intensity, adherence, timing of assessments, and biomarker measurement methods, underscoring the need for more standardized mechanistic research.

### 3.3 Molecular Mechanisms Underlying the Protective Effects of Antenatal Exercise

Several studies in this systematic review suggest that the physiological effects of antenatal exercise are mediated by molecular mechanisms that regulate vascular homeostasis and placental function. Key pathways underlying the protective effects against gestational hypertensive disorders include angiogenic regulation, nitric oxide signaling, and modulation of oxidative and inflammatory responses (Bhattacharjee et al., 2021; Jaatinen et al., 2024; Karthiga et al., 2022; Kılıçlı & Zeyneloğlu, 2025). Engaging in physical activity during pregnancy may upregulating Vascular Endothelial Growth Factor (VEGF) and its receptor VEGFR-1 at both protein and mRNA levels in the placenta of active mothers. This molecular response enhances placental performance by promoting the growth and branching of terminal villi, thereby improving maternal and fetal nutrient and oxygen exchange and reducing the likelihood of preeclampsia, gestational hypertension, and gestational diabetes (Bhattacharjee et al., 2021).

Similarly, yoga practice has been reported to elevate serum nitric oxide (NO) concentrations, contributing to lowered arterial pressure and a reduced likelihood of cardiovascular complications. Yoga also reduced inflammation marker, such as interleukin-6 (IL-6), which supports an independent association with increased NO levels, further supporting its role for improving endothelial function and better pregnancy outcomes (Karthiga et al., 2022). Complementary to these findings, Mindfulness-Based Breathing Exercise (MBBE) has been found to improve maternal health parameters, including overall well-being, physiological indicators, resting fetal heart rate, and fetal movement patterns. These benefits are primarily mediated through activation of the parasympathetic pathway via deliberate, slow, and deep breathing, which suppresses sympathetic responses such as elevated heart rate and blood pressure. This intervention can improve uteroplacental oxygenation and circulation while reducing stress hormones (Kılıçlı & Zeyneloğlu, 2025). In contrast to the other three studies, (Jaatinen et al., 2024) found no statistically meaningful link between physical activity and angiogenic biomarkers (sFlt-1, PlGF, sEng). These contrasting findings suggest that the molecular response to maternal exercise may vary depending on maternal characteristics, exercise intensity, type of exercise, and timing of assessment.

Across the studies identified in this systematic review, two primary mechanisms emerge through which antenatal exercise may prevent HDP: increased bioavailability of nitric oxide (NO) and improved angiogenic balance, particularly involving VEGF signaling. Enhanced NO production promotes vasodilation, augments endothelial responsiveness, and reduces systemic vascular resistance, three changes that directly counteract the endothelial dysfunction characteristic of HDP. Similarly, increased regulation of VEGF and VEGFR-1 during exercise may support placental vascular development, facilitate more efficient maternal-fetal exchange, reduce placental hypoxia, and modulate the release of sFlt-1. Taken together, these molecular pathways suggest that structured, moderate-intensity exercise can be integrated into antenatal care as a strategy to maintain vascular health. Such interventions offer a lower-cost, scalable approach to reducing HDP risk, particularly in settings where access to advanced angiogenic biomarker screening is limited.



### 3.4 Physiological Responses and Clinical Implications

Antenatal exercise has been shown to confer substantial physiological and psychological advantages for pregnant women through various mechanisms. Several clinical studies have reported a lowering of blood pressure after participating in antenatal exercise program (Awad et al., 2019; Haakstad et al., 2016; Kılıçlı & Zeyneloğlu, 2025). Antenatal exercise helps minimize the need for antihypertensive medications such as methyldopa, maintain blood pressure, and reduce obstetric complications (Awad et al., 2019; Barakat et al., 2016). Mechanistically, regular exercise is thought to reduce blood pressure through two main pathways: (1) increased parasympathetic activity and decreased sympathetic dominance, such as increased HRV and BRS, thereby improving blood pressure regulation and reducing cardiovascular stress; and (2) improved endothelial function in the form of increased nitric oxide (NO) production and decreased peripheral vascular resistance, which lowers systemic vascular pressure (Karthiga et al., 2022). Experimental and clinical reviews support the role of autonomic modulation and endothelial repair as mediators of the antihypertensive effects of exercise in pregnancy (Awad et al., 2019; Karthiga et al., 2022; Skow et al., 2017).

Studies have shown a reduced the probability of GH or PE in participants who actively exercised during pregnancy (Barakat et al., 2016; Karthiga et al., 2022). Prevention of HDP is likely mediated by a combination of: (1) decreased systemic inflammation (such as decreased IL-6, TNF- $\alpha$ ) which reduces pathological vascular activation; (2) increased NO bioavailability and improved endothelial function which prevents pathological vasoconstriction; and (3) modulation of placental angiogenic factors (improving the pro- vs. anti-angiogenic ratio) thereby suppressing placental pathways that contribute to HDP (Jaatinen et al., 2024; Karthiga et al., 2022). Furthermore, physical activity during pregnancy has the potential to improve maternal vascular health through homocysteine regulation mechanisms. Homocysteine is a sulfur-containing amino acid generated as an intermediate product in the metabolic pathway of methionine and is a biomarker associated with cardiovascular disease (Kumar et al., 2017; Reynolds et al., 2022). Physical activity contributes to reducing homocysteine levels, which in turn reduces the risk of endothelial disorders, GH, and other cardiovascular complications (Reynolds et al., 2022).

Antenatal exercise also enhances maternal physiological by improving ventilatory efficiency, pulmonary and tissue perfusion through endothelial vasodilation, and reducing cardiac afterload due to decreased vascular resistance (Haakstad et al., 2016; Karthiga et al., 2022; Kılıçlı & Zeyneloğlu, 2025). These adaptations improve maternal-fetal oxygenation, suggesting enhanced cardiorespiratory capacity and uteroplacental perfusion that support overall maternal-fetal homeostasis (Nagpal & Mottola, 2020). Empirical evidence also highlights psychological benefits, including reduced stress and anxiety, greater self-confidence and self-control during pregnancy, and improved sleep and energy levels, reinforcing the importance of integrating exercise into antenatal care (Awad et al., 2019; Barakat et al., 2016; Karthiga et al., 2022; Kılıçlı & Zeyneloğlu, 2025; Reynolds et al., 2022). Exercise contributes to emotional stability by promoting the release of endorphins and serotonin, key neurotransmitters involved in mood regulation (Bhattacharjee et al., 2021). From both mechanistic and public health perspectives, antenatal exercise fulfills the characteristics of an effective primary intervention, it is non-invasive, safe, low-cost, and adaptable across clinical contexts, making it a valuable preventive strategy for hypertensive disorders of pregnancy (Danielli et al., 2022). Furthermore, exercise supports cardiovascular and metabolic health while ensuring maternal psychological balance and favorable pregnancy outcomes (Bhattacharjee et al., 2021; Catov et al., 2018; Haakstad et al., 2016). Its effectiveness in preventing HDP is influenced by exercise type, intensity, duration, and initiation timing (Danielli et al., 2022), underscoring the need for structured, supervised antenatal exercise programs within clinical care frameworks (Genest et al., 2012; Karthiga et al., 2022).

Overall, most studies indicate that antenatal exercise exerts a protective effect on blood pressure and the risk of hypertensive disorders of pregnancy (HDP); however, considerable variability exists across studies, warranting critical evaluation. These inconsistencies are largely influenced by heterogeneity in exercise protocols, including differences in intervention intensity, frequency, and duration. Some studies have reported reductions in blood pressure even with light to moderate intensity aerobic exercise (Haakstad et al., 2016), whereas others have shown significant benefits only with structured and supervised moderate-intensity programs (Barakat et al., 2016). Variations in outcomes may also be shaped by participant characteristics, particularly the gestational age at which exercise is initiated. Interventions commenced early in pregnancy appear more consistently effective in preventing HDP (Barakat et al., 2016; Do et al., 2020) compared with those initiated later, likely due to enhanced cardiovascular conditioning, improved endothelial function, and a

longer physiological for maternal adaptation. In addition, the mode of implementation, such as unsupervised home-based exercise versus structured training, contributes to inconsistencies in findings, leading several authors to recommend structured and supervised exercise programs (Barakat et al., 2016; Bhattacharjee et al., 2021; Do et al., 2020; Haakstad et al., 2016; Jaatinen et al., 2024; Karthiga et al., 2022; Kılıçlı & Zeyneloğlu, 2025).

### 3.5 Limitations and Strengths

Across the reviewed articles, there is consistent scientific evidence indicating that antenatal exercise confers significant physiological, psychological, and clinical benefits for pregnant women, especially decreased incidence of gestational hypertension and preeclampsia. The primary strength of this work lies in the diversity of interventions (from aerobic exercise, yoga, stretching, and autogenic training to mindfulness-based breathing), which collectively demonstrate that various forms of exercise can be adapted to the individual needs of pregnant women while still yielding positive outcomes. These studies also employed comprehensive clinical and psychological indicators, including blood pressure, autonomic parameters, oxygen saturation, health profile scores, as well as obstetric and neonatal outcomes, thereby enhancing the clinical validity of the intervention recommendations. Furthermore, the use of RCT designs in several studies adds methodological robustness and strengthens the causal inference of the findings.

Despite the overall positive trend of evidence, several limitations must be critically acknowledged. This review is constrained by considerable heterogeneity among existing studies in terms of exercise modality, intensity, frequency, and gestational timing. Such variability limits the ability to generalize findings or conduct direct inter-study comparisons, making it challenging to establish an optimal standardized exercise protocol. Moreover, some studies relied heavily on self-reported outcomes, particularly regarding psychological responses and physical activity levels, which may introduce recall bias and subjective interpretation. In addition, although there is consistent evidence supporting reductions in the incidence of HDP, few studies have explored the underlying molecular mechanisms and biomarkers that mediate the relationship between exercise, vascular function, and placental adaptation.

### 3.6 Recommendation

Future research should be directed toward the standardization of antenatal exercise protocols, encompassing the optimal duration, intensity, frequency, and modality of exercise that yield the most effective outcomes, particularly for populations at specific risk, such as HDP. Multicenter investigations employing larger sample sizes and longitudinal designs are warranted to enhance the generalizability of findings and to assess the long-term postpartum effects of antenatal exercise on maternal cardiovascular health. Furthermore, the integration of antenatal exercise into routine antenatal care standards should be accompanied by structured training for healthcare providers to ensure evidence-based, safe, accessible, and cost-effective implementation in clinical and community settings.

In addition, future work should more clearly delineate how specific molecular mechanisms into practical antenatal exercise, such as increased nitric oxide (NO) bioavailability, enhanced VEGF-mediated angiogenic signaling, improved endothelial repair pathways, and reductions in oxidative stress. These mechanistic links will help refine exercise prescriptions that optimize vascular protection and reduce HDP risk while enhancing their applicability in midwifery and public health practice. Moreover, research should prioritize the development of context-appropriate implementation strategies for low-resource settings, including simplified antenatal exercise protocols and task-shifting models for community health workers. Such recommendations will broaden relevance of antenatal exercise interventions and support access across diverse healthcare environments.

## 4. CONCLUSION

This systematic review demonstrates that antenatal exercise offers molecular and physiological benefits as an alternative for the prevention of gestational hypertension. Molecularly, exercise enhances vascular stability via nitric oxide signaling and angiogenesis, and supports endothelial health by lowering oxidative and inflammatory activity. Physiologically, these mechanisms can lower and control blood pressure, improve uteroplacental perfusion, and result in better maternal-fetal outcomes. Therefore, incorporating structured

maternal exercise into prenatal care may be a more effective, safe, and low-cost strategy for the prevention of gestational hypertension and preeclampsia.

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