Structured prenatal yoga on endothelial function in high-risk preeclampsia of pregnant women focusing on ET-1/NO ratio

Yoga prenatal estructurado sobre la función endotelial en mujeres embarazadas con preeclampsia de alto riesgo, centrándose en la relación ET-1/NO

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Abstract

Introduction: Endothelial dysfunction, marked by a high ET-1/NO ratio, plays a key role in preeclampsia. Prenatal yoga may improve endothelial function by enhancing blood flow and cardiovascular regulation

Objective: This study aimed to evaluate the effect of a structured prenatal yoga program on the ET-1/NO ratio in pregnant women at high risk of developing preeclampsia.

Methodology: An experimental study was carried out involving 46 pregnant women with clinical risk factors for preeclampsia, recruited between 9 and 16 weeks of gestation. Participants were randomly allocated to either a yoga intervention group (n = 23) or a control group (n = 23). All participants received standard care consisting of low-dose aspirin (80 mg/day) and calcium supplementation (1 g/day). The intervention group additionally attended 20 supervised prenatal yoga sessions over a four-week period. Serum concentrations of ET-1 and NO were measured before and after the intervention. The primary outcome was the change in the ET-1/NO ratio.

Results: The yoga intervention group demonstrated a significant reduction in the ET-1/NO ratio, from 1.13 ± 0.42 to 0.94 ± 0.38 ng/mL (p = 0.010), while the control group showed a significant increase from 0.85 ± 0.29 to 1.01 ± 0.38 ng/mL (p = 0.049).

Discussion: Findings suggest that prenatal yoga may enhance endothelial function in high-risk pregnancies by balancing vasoconstrictive and vasodilatory factors through stress reduction and vascular regulation.

Conclusions: Prenatal yoga can be considered a promising complementary approach to improve endothelial function and potentially prevent preeclampsia in high-risk pregnant women.

Keywords

Biomarker modulation; blood pressure; prenatal exercise; relaxation.

Resumen

Introducción: La disfunción endotelial, caracterizada por una alta relación ET-1/NO, desempeña un papel clave en la preeclampsia. El yoga prenatal puede mejorar la función endotelial al mejorar el flujo sanguíneo y la regulación cardiovascular.

Objetivo: Este estudio foi realizado com o objetivo de evaluar el efecto de un programa estructurado de yoga prenatal sobre la relación ET-1/NO en mujeres embarazadas con alto riesgo de desarrollar preeclampsia.

Metodología: Se realizó un estudio experimental con 46 mujeres embarazadas con factores de riesgo clínicos para preeclampsia, reclutadas entre las semanas 9 y 16 de gestación. Las participantes fueron asignadas aleatoriamente a un grupo de intervención de yoga (n = 23) o a un grupo control (n = 23). Todas las participantes recibieron atención estándar consistente en aspirina a dosis baja (80 mg/día) y suplementos de calcio (1 g/día). El grupo de intervención asistió además a 20 sesiones supervisadas de yoga prenatal durante un período de cuatro semanas. Se midieron las concentraciones séricas de ET-1 y NO antes y después de la intervención. El resultado principal fue el cambio en la relación ET-1/NO.

Resultados: El grupo de intervención con yoga demostró una reducción significativa en la relación ET-1/NO, de 1,13 ± 0,42 a 0,94 ± 0,38 ng/mL (p = 0,010), mientras que el grupo control mostró un aumento significativo de 0,85 ± 0,29 a 1,01 ± 0,38 ng/mL (p = 0,049).

Discusión: Los hallazgos sugieren que el yoga prenatal puede mejorar la función endotelial en embarazos de alto riesgo al equilibrar los factores vasoconstrictores y vasodilatadores mediante la reducción del estrés y la regulación vascular.

Conclusiones: El yoga prenatal puede considerarse un enfoque complementario prometedor para mejorar la función endotelial y potencialmente prevenir la preeclampsia en mujeres embarazadas de alto riesgo.

Palabras clave

Modulación de biomarcadores; presión arterial; ejercicio prenatal; relajación.

Introduction

Preeclampsia is a hypertensive disorder of pregnancy that remains a major contributor to maternal and perinatal morbidity and mortality globally (Ives et al., 2020). It is clinically defined by the new onset of hypertension and proteinuria after 20 weeks of gestation (Tranquilli et al., 2014). The etiology of preeclampsia is multifactorial, but endothelial dysfunction is considered one of the core pathophysiological mechanisms (Jung et al., 2022). This dysfunction leads to an imbalance between vasoconstrictors and vasodilators, notably an increase in endothelin-1 (ET-1) and a decrease in nitric oxide (NO), which contributes to impaired placental perfusion and systemic hypertension (Genovesi et al., 2021.

ET-1 is a potent vasoconstrictive peptide secreted by endothelial cells (Jain, 2012). Under normal physiological conditions, ET-1 helps maintain vascular tone (Sandoo et al., 2010). However, in preeclampsia pregnancies, placental hypoxia resulting from poor trophoblast invasion and inadequate spiral artery remodeling stimulates the release of antiangiogenic and proinflammatory mediators, increasing ET-1 expression and contributing to vascular dysfunction (Staff et al., 2022).

In contrast, NO is a key vasodilator synthesized by endothelial cells in response to mechanical and chemical stimuli (Zhao et al., 2015). NO promotes vascular smooth muscle relaxation via the activation of soluble guanylate cyclase (sGC) and the production of cyclic guanosine monophosphate (cGMP), a secondary messenger involved in vasodilation, platelet inhibition, and anti-inflammatory responses (Degjoni et al., 2022). A decreased level of NO during pregnancy may further aggravate the hypertensive state by promoting vasoconstriction and thrombosis (Ives et al., 2020; Zullino et al., 2018).

Delivery of the fetus and placenta is currently the only proven treatment for preeclampsia. Preventive strategies such as low-dose aspirin and calcium supplementation during early gestation have demonstrated partial success in high-risk populations (“ACOG, 2019; Kinshella et al., 2021). For instance, clinical trials have shown that aspirin (150 mg/day) initiated before 16 weeks gestation can reduce early-onset preeclampsia by over 60% (Rolnik et al., 2017). However, these strategies are not sufficient, and additional non-pharmacological interventions are being explored.

Prenatal yoga has emerged as a promising complementary therapy to improve pregnancy outcomes. It combines physical postures, breathing techniques, and relaxation methods that may reduce maternal stress, enhance cardiovascular regulation, and improve utero-placental blood flow (Corrigan et al., 2022; Rakhmawati et al., 2021). Several studies have indicated that prenatal yoga can lower maternal blood pressure and improve psychological well-being (Karthiga et al., 2022). Despite these findings, limited evidence is available on its direct impact on vascular biomarkers such as ET-1 and NO.

This study aimed to assess the impact of prenatal yoga on the ET-1/NO ratio. Gaining knowledge of this association could help us better understand how yoga can be used as a supportive intervention to help reduce vascular problems during pregnancy.

Method

Study Design and Participants

This experimental study employed a randomized pretest-posttest control group design and was conducted in several public health facilities on Madura Island, East Java, Indonesia, between August 2023 and January 2024. 46 pregnant women who were at high risk of preeclampsia were enlisted and divided into two groups at random: a control group (n = 23) and an intervention group (yoga; n = 23).

Inclusion criteria were pregnant women aged 9 to 16 weeks of gestation with one or more clinical risk factors for preeclampsia, including maternal age >35 years, nulliparity, multiparity with a history of preeclampsia, multiparity with a new partner, multiparity with ≥10 years interpregnancy interval, family history of preeclampsia (mother or sister), multiple pregnancies, pregnancies conceived via donor sperm, oocyte, or embryo, pre-pregnancy obesity, or BMI >30 at the first antenatal visit. Exclusion criteria were diagnosis of diabetes mellitus, chronic hypertension, renal disease, antiphospholipid syndrome (APS), and musculoskeletal disorders. Participants were excluded if they attended <80% of yoga sessions, experienced miscarriage, or developed vaginal bleeding during the study period.

The sample size was calculated using Lemeshow's formula with a= 0.05 confidence interval and 95% power. The minimum required sample per group was 23 participants.

The Faculty of Medicine, Universitas Airlangga, Indonesia's Health Research Ethics Committee gave its approval to this study (No. 194/EC/KEPK/FKUA/2023, granted July 24, 2023). The study adhered to the Declaration of Helsinki principles, including informed consent, participant confidentiality, voluntary withdrawal rights, and safety during the intervention. Before being enrolled, each subject gave written informed consent.

Procedure

Participants were randomized into groups and received standard antenatal care, which included low-dose aspirin (80 mg/day) and calcium supplementation (1 g/day). In addition to standard care, the intervention group participated in a 4-week yoga program consisting of 20 sessions (5 sessions per week, 30 minutes each). Pregnant women received sessions that combined physical postures (asana), breathing techniques (pranayama), relaxation, and meditation (dhyana). Sessions were conducted between 08:30 and 09:00 AM under the supervision of a certified prenatal yoga instructor at the designated public health centers. While blinding participants was not feasible, outcome assessors and data analysts were blinded to group allocation.

Demographic data were collected via structured questionnaires. Venous blood samples (5 mL) were drawn from the right arm and processed to measure serum ET-1 and NO levels before and after the intervention. ET-1 was measured using ELISA (catalog no. E-EL-H1555, Elabscience) at the Clinical Pathology Laboratory, Dr. Soetomo Hospital Surabaya. NO was analyzed using a colorimetric assay (catalog no. E-BC-K035-S) at the Physiology Laboratory, Brawijaya University. Blood samples were stored in vacutainer tubes inside cool boxes before delivery to the respective laboratories.

Data analysis

Data were analyzed using SPSS version 29. Descriptive statistics were used to describe participant characteristics. The Shapiro–Wilk test assessed normality. Chi-square tests were used for categorical variables (e.g., history of preeclampsia), while Levene's test was used for continuous variables (e.g., age, BMI, MAP). Wilcoxon signed-rank tests were employed for non-normal data, and paired sample t-tests for regularly distributed data. A p-value of less than 0.05 was deemed statistically significant for a one-tailed test.

Results

The study included 46 pregnant women who were deemed to be at high risk for preeclampsia and who satisfied the inclusion criteria. Random assignment was used to place participants in the control group (n = 23) or the yoga intervention group (n = 23). Every participant fulfilled the study's requirements and was taken into account for the final analysis.

Table 1 displays the participants' baseline clinical and sociodemographic details.

Maternal age, gestational age, parity, body mass index (BMI), and mean arterial pressure (MAP) did not significantly change between the yoga and control groups ($p > 0.05$ for all variables), suggesting that the groups were comparable before the intervention.

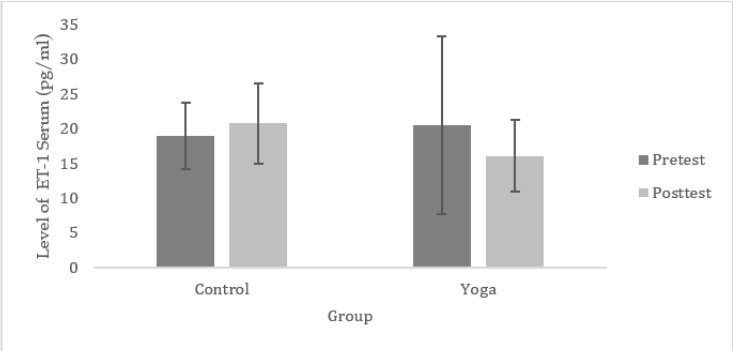
Table 1. Homogeneity of general characteristics and outcome variables between the experimental and comparison groups

Variable	Group		p-Value
	Control (N=23)	Yoga (N=23)	
Mother's age (years)	28 (17-45)	23 (17-43)	0.633
Parity (times)	1 (1-6)	1 (1-7)	0.952
Gestational age (weeks)	15 (13-16)	15 (13-16)	0.945
BMI (kg/m²)	27.67 ± 4.12	28.22 ± 3.68	0.635
History of preeclampsia			
No	18 (78.3%)	15 (65.2%)	0.513
Yes	5 (21.7%)	8 (34.8%)	
History of preeclampsia in mother or sibling	14 (60.9%)	13 (56.5%)	1.000
No	9 (39.1%)	10 (43.5%)	

Yes			
Multipara with a birth interval of more than 10 years			
No	18 (78.3%)	17 (73.9%)	1.000
Yes	5 (21.7%)	6 (26.1%)	
MAP (mmHg)	86.74±6.21	87.14±6.08	0.868

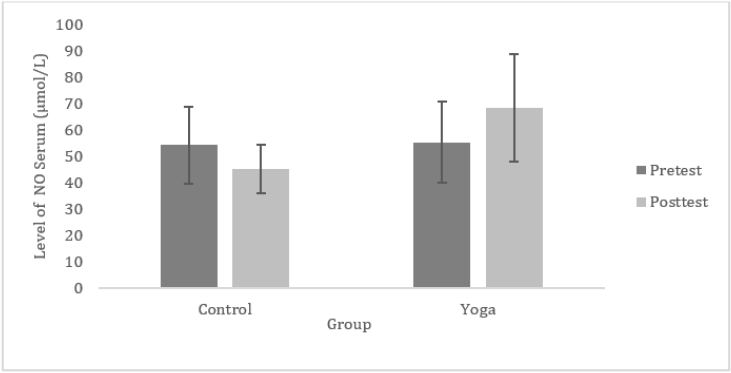
*Significant differences, p<0.05.
Note: general characteristics.

Figure 1. Comparison of mean ± SD serum ET-1 levels in the control group and yoga group in pregnant women at high risk for preeclampsia



Mean serum ET-1 levels in the control and yoga groups before and after the intervention. A significant decrease was observed in the yoga group (p = .039), while the control group showed a significant increase (p = .025).

Figure 2. Comparison of mean ± SD serum NO levels in the control group and yoga group in pregnant women at high risk for preeclampsia



Mean serum NO levels in the control and yoga groups before and after the intervention. The yoga group showed a significant increase (p = .031), while the control group showed a significant decrease (p = .045).

Table 2. Comparison of dependent variables between groups

Variable	Group	Mean ± SD		Delta Post-pre	Between groups test	
		Pretest (n=23)	Posttest (n=23)		p-value 95% (CI)	Effect size 95% (CI)
ET-1/NO Ratio	Control	0.19 ± 0.07	0.24 ± 0.09	0.06 ± 0.09	<.01 .05 to .09	1.12 .49 to 1.74
	Paired sample test	p-value = .016				
	Yoga	0.20 ± 0.12	0.13 ± 0.06	-0,07 ± 0,12		
	Paired sample test	p-value = .008				

Table 2 presents the comparison of dependent variables between the control and prenatal yoga groups. The ET-1/NO ratio significantly decreased in the yoga group (M = −0.07, SD = 0.12, p = .008), while it significantly increased in the control group (M = 0.06, SD = 0.09, p = .016). A considerable effect size was observed (Cohen's d = 1.12, 95% CI [0.49, 1.74]).

Discussion

The ET-1/NO ratio is a critical indicator of endothelial function, reflecting the physiological balance between vasoconstriction (mediated by ET-1) and vasodilation (mediated by NO) (Nishiyama et al., 2017). An elevated ratio is commonly associated with vascular dysfunction and hypertensive complications during pregnancy (Phipps et al., 2019; Ray et al., 2023; Wang et al., 2023; Yang et al., 2025).

Our results demonstrated a statistically significant reduction in the ET-1/NO ratio among participants who completed 20 prenatal yoga sessions over four weeks, with an average decrease of 0.07. While the reduction was statistically significant, it was lower than the ≥0.15 threshold commonly reported in pharmacological interventions, which has been associated with more favorable clinical outcomes (Abdel-Razik et al., 2020). This suggests that prenatal yoga may be best utilized as a complementary strategy rather than a stand-alone intervention in the prevention of preeclampsia.

Although no previous studies have directly examined the impact of yoga on the ET-1/NO ratio in pregnancy, research by Maeda et al., 2003 on aerobic exercise showed improvements in both NO and ET-1 levels, supporting the hypothesis that physical activity can favorably modulate endothelial biomarkers. These findings align with our current results and underscore the potential of prenatal yoga as a non-pharmacological approach to improve vascular function in high-risk pregnancies.

Prenatal yoga may improve endothelial function through several interrelated physiological pathways. The practice has been associated with decreased sympathetic nervous system activity (Gusti et al., 2025) and increased parasympathetic tone, resulting in lower circulating cortisol levels (Hopkins et al., 2016; Satyapriya et al., 2009; Thirthalli et al., 2013). Since cortisol is known to upregulate endothelin-1 (ET-1) synthesis, this reduction may contribute to lower ET-1 concentrations (Vianna et al., 2011). In addition, yoga practices such as pranayama (deep breathing), meditation, and asanas (physical postures) promote endothelial shear stress, which can activate endothelial nitric oxide synthase (eNOS) and enhance nitric oxide (NO) production, supporting vasodilation (Patil et al., 2015). Moreover, prenatal yoga has been shown to mitigate oxidative stress and inflammation both of which are critical modulators of endothelial function (Mishra et al., 2024). By reducing oxidative stress, NO bioavailability is preserved and ET-1 overexpression is prevented, potentially restoring a favorable ET-1/NO balance in pregnant women.

To confirm these results and evaluate their clinical significance, more studies with bigger sample sizes and longer follow-up times are necessary. Additionally, exploring the dose–response relationship between yoga frequency/duration and endothelial biomarkers would enhance our understanding of its preventive potential.

Conclusions

Yoga during pregnancy may be a useful non-pharmacological method for promoting vascular health in expectant mothers who are at risk of developing preeclampsia.

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