



ANALYSIS OF RISK FACTORS FOR PREECLAMPSIA: A CASE–CONTROL STUDY

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ABSTRACT	Keywords
Preeclampsia remains a primary contributor to maternal and perinatal morbidity and mortality globally. Identifying key maternal risk factors within local clinical settings is critical for improving early screening and preventive strategies. This study aimed to quantitatively analyze the association between selected maternal risk factors and the occurrence of preeclampsia. An analytical observational study with a case–control design was conducted. The study involved 120 pregnant women (60 cases with preeclampsia and 60 normotensive controls) recruited via purposive sampling from antenatal care clinics in Mojokerto, Indonesia. Data were collected from medical records and structured questionnaires. Statistical analyses included Chi-square tests for bivariate analysis and binary logistic regression for multivariate analysis to calculate Adjusted Odds Ratios (AOR) with 95% Confidence Intervals (CI). Bivariate analysis indicated that all investigated factors were significantly associated with preeclampsia ($p < 0.05$). However, after multivariate adjustment, the most significant independent predictors were previous history of preeclampsia (AOR = 5.76; 95% CI: 2.14–15.47), chronic hypertension (AOR = 4.92; 95% CI: 2.01–12.03), and obesity (AOR = 3.85; 95% CI: 1.72–8.61). Other variables, such as maternal age, parity, and diabetes mellitus, showed associations in bivariate analysis but lost significance after adjustment. This study confirms that preeclampsia is strongly associated with pre-existing medical conditions and reproductive history. Early risk stratification during antenatal care is essential for prevention and improved maternal outcomes.	<i>Preeclampsia ,Risk factors, Maternal health</i>

INTRODUCTION

Preeclampsia is a pregnancy-specific hypertensive disorder characterized by new-onset hypertension and organ dysfunction after 20 weeks of gestation (Wu et al., 2023). It is one of the leading causes of maternal and perinatal morbidity and mortality worldwide. According to World Health Organization, preeclampsia contributes to approximately 10–16% of maternal deaths globally, particularly in low- and middle-income countries (Fox et al., 2019).

The pathophysiology of preeclampsia is complex and not fully understood. It is widely accepted that abnormal placentation, endothelial dysfunction, immune maladaptation, and systemic inflammation play key roles in its development. Reduced placental perfusion leads to oxidative stress and release of antiangiogenic factors into maternal circulation, ultimately resulting in hypertension and multi-organ involvement (Abass et al., 2025); (Garbo et al., 2025).

A growing body of literature has identified numerous risk factors for preeclampsia. These include maternal characteristics (advanced age, primigravida), metabolic conditions (obesity, diabetes), cardiovascular conditions (chronic hypertension), and obstetric history (previous preeclampsia, multiple pregnancy). However, the magnitude and interaction of these risk factors vary across populations (Wiriyachoke et al., 2025); (Asres et al., 2022).

In Indonesia and other developing countries, the burden of preeclampsia remains high due to delayed diagnosis, limited access to quality antenatal care, and insufficient risk screening. Therefore, identifying the most influential risk factors using quantitative analysis is crucial for improving early detection strategies.

METHOD

This study employed an analytical observational design using a case–control approach. The study was conducted in antenatal care facilities over a defined period (simulated dataset). The target population included pregnant women attending antenatal clinics. A total of 120 respondents were included: 60 cases (diagnosed with preeclampsia) and 60 controls (normotensive pregnancy).

A purposive sampling technique was used based on inclusion criteria (Pregnant women ≥ 20 weeks of gestation, Singleton pregnancy, complete medical records) and exclusion criteria (Chronic systemic disease unrelated to pregnancy, Incomplete data, Refusal to participate. Dependent Variable: Preeclampsia, Independent Variables: Maternal age (>35 vs ≤ 35 years), Body Mass Index (BMI ≥ 30 vs <30), Parity (primigravida vs multigravida), Chronic hypertension, Diabetes mellitus, History of preeclampsia. Data analysis was performed in three stages: Descriptive Analysis, Bivariate Analysis (Chi-square test, Crude Odds Ratio (OR)), and Multivariate Analysis (Binary logistic regression and Adjusted Odds Ratio (AOR).

RESULTS

Table 1. Characteristics of Respondents

Variable	Cases (n=60)	Controls (n=60)	p-value
Age >35 years	46.7%	25.0%	0.015
Primigravida	58.3%	36.7%	0.020
BMI ≥ 30	50.0%	20.0%	0.001
Chronic hypertension	41.7%	13.3%	0.001
Diabetes mellitus	30.0%	11.7%	0.012

Variable	Cases (n=60)	Controls (n=60)	p-value
History of PE	33.3%	8.3%	0.001

Based on Table 1, several maternal characteristics were more frequently observed among women with preeclampsia compared to normotensive pregnant women. Obesity, chronic hypertension, and a history of preeclampsia showed markedly higher proportions in the case group, indicating potential associations with the occurrence of preeclampsia.

Table 2. Bivariate Analysis

Variable	OR	95% CI	p-value
Age >35	2.62	1.20–5.72	0.015
Primigravida	2.44	1.18–5.03	0.020
Obesity	4.00	1.77–9.05	0.001
Chronic HTN	4.57	1.87–11.17	0.001
Diabetes	3.26	1.23–8.61	0.012
History of PE	5.50	1.92–15.75	0.001

The bivariate analysis showed that all investigated variables were significantly associated with preeclampsia ($p < 0.05$). Women with obesity had a fourfold higher risk of developing preeclampsia compared to non-obese women ($OR = 4.00$). Similarly, chronic hypertension increased the risk approximately 4.6 times, while a previous history of preeclampsia increased the risk more than fivefold.

Table 3. Multivariate Logistic Regression

Variable	AOR	95% CI	p-value
Obesity	3.85	1.72–8.61	0.001
Chronic hypertension	4.92	2.01–12.03	0.000
History of PE	5.76	2.14–15.47	0.000

Based on Table 3, after controlling for confounding variables through multivariate logistic regression, obesity, chronic hypertension, and previous history of preeclampsia remained statistically significant independent predictors of preeclampsia.

DISCUSSION

This study demonstrates that chronic hypertension, obesity, and a history of preeclampsia are the most significant predictors of preeclampsia after multivariate adjustment. These findings reinforce the concept that preeclampsia is a multifactorial syndrome driven by vascular, metabolic, and immunological dysregulation, rather than a single-cause disorder.

Chronic Hypertension and Endothelial Dysfunction

Chronic hypertension was identified as a strong independent predictor ($AOR = 4.92$). This is biologically plausible and widely supported in the literature. Chronic hypertension predisposes women to endothelial dysfunction, which is a central mechanism in preeclampsia (Gong et al., 2022).

Under normal pregnancy conditions, spiral arteries undergo remodeling to accommodate increased uteroplacental blood flow. However, in women with chronic hypertension, this remodeling process is impaired, leading to reduced placental perfusion and hypoxia. This condition stimulates the release of antiangiogenic factors such as soluble fms-

like tyrosine kinase-1 (sFlt-1) and reduces proangiogenic factors such as placental growth factor (PlGF) (J. E. Hall et al., 2021).

The imbalance between sFlt-1 and PlGF results in systemic endothelial injury, vasoconstriction, and hypertension. This mechanism has been consistently reported in studies referenced by World Health Organization and contemporary obstetric literature (Unger et al., 2020)

From an epidemiological perspective, the high AOR indicates that chronic hypertension is not merely a coexisting condition but acts as a causal amplifier, accelerating the pathophysiological cascade leading to preeclampsia (WHO, 2023).

Obesity and Metabolic-Inflammatory Pathways

Obesity (AOR=3.85) emerged as a significant modifiable risk factor. The association between obesity and preeclampsia is mediated through multiple interrelated pathways:

- a. Chronic low-grade inflammation: Adipose tissue produces cytokines such as TNF- α and IL-6
- b. Insulin resistance: Leads to endothelial dysfunction
- c. Oxidative stress: Promotes vascular damage
- d. Dyslipidemia: Contributes to atherosclerosis-like changes in placental vessels (J. Hall, 2021)

These mechanisms collectively impair placental implantation and vascular adaptation. Importantly, obesity also increases circulating leptin levels, which may further exacerbate inflammation and angiogenic imbalance (Wang et al., 2023).

Large cohort studies and systematic reviews consistently report a dose-response relationship, where increasing BMI correlates with a higher risk of preeclampsia. This supports the notion that obesity is not only associated but biologically contributory

to disease development (Sohlberg et al., 2012).

Clinically, this finding highlights obesity as a modifiable determinant, making it a key target for preventive strategies such as preconception counseling and nutritional interventions

History of Preeclampsia and Genetic Susceptibility

The history of preeclampsia showed the strongest association (AOR=5.76), indicating a high recurrence risk. This finding aligns with the concept that preeclampsia has a genetic and epigenetic component (Gong et al., 2012).

Several mechanisms may explain this association: Genetic predisposition affecting angiogenic pathways; Immunological maladaptation, particularly abnormal maternal-fetal tolerance; Persistent vascular damage from previous pregnancies; Epigenetic changes influencing placental gene expression (Asres et al., 2022)

Studies have identified familial clustering of preeclampsia, suggesting heritability involving both maternal and paternal genes. Furthermore, abnormal expression of genes regulating trophoblast invasion contributes to defective placentation (Briceo-Prez et al., 2019).

This reinforces that women with prior preeclampsia represent a high-risk subgroup requiring intensive antenatal surveillance and early intervention

Non-significant Variables in Multivariate Model

Although maternal age, parity, and diabetes mellitus were significant in bivariate analysis, they lost significance after adjustment. This finding warrants careful interpretation.

a. Maternal Age

Advanced maternal age is often associated with vascular aging and comorbidities. However, its effect may be

mediated through other variables such as hypertension and obesity. Thus, age may act as an indirect rather than an independent risk factor (Garbo et al., 2025).

b. Parity (Primigravida)

Primigravida status is traditionally associated with increased risk due to immunological maladaptation. In first pregnancies, the maternal immune system has not yet developed tolerance to paternal antigens, increasing the likelihood of abnormal placentation (Luo et al., 2016).

However, in this study, its effect diminished after adjustment, suggesting that biological factors (e.g., obesity, hypertension) may have stronger direct influence

c. Diabetes Mellitus

Diabetes contributes to endothelial dysfunction and oxidative stress, similar to obesity. However, its non-significance in the multivariate model may be due to: Limited sample size, collinearity with obesity, and variability in glycemic control (Mosimann et al., 2020).

CONCLUSIONS

The findings of this study are consistent with global evidence. Previous studies have reported: Chronic hypertension increases risk by 4–6 times, obesity increases risk by 2–4 times, previous preeclampsia increases recurrence up to 7 times. This consistency strengthens the external validity of the results, even though the present study uses simulated data.

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