

Research Article

Correlation Between First-Trimester Anemia in Pregnancy and the Incidence of Preeclampsia: A Retrospective Cohort Study

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Received: May 12, 2026 | Accepted: July 6, 2026 | Published: July 10, 2026

Abstract

Introduction: Preeclampsia affects 2 – 4% of pregnancies worldwide and is a leading cause of maternal and perinatal morbidity and mortality. Anemia in pregnancy—defined as hemoglobin <11 g/dL in the first or third trimester—remains prevalent, affecting 48.9% of Indonesian pregnant women (Riskesmas 2018). First-trimester anemia may contribute to preeclampsia through oxidative stress, endothelial dysfunction, and impaired placentation.

Objective: To analyze the association between first-trimester anemia and preeclampsia at Prof. Dr. Margono Soekarjo Regional General Hospital (January – December 2023).

Methods: This retrospective cohort study used total sampling of pregnant women treated at the hospital from January to December 2023. Variables included first-trimester hemoglobin and preeclampsia status. Logistic regression analysis was performed using SPSS 27.0.

Results: The model showed good fit (Hosmer–Lemeshow = 2.491, $p=0.778$; Nagelkerke $R^2=0.367$). First-trimester hemoglobin was significantly associated with preeclampsia ($p<0.001$; OR=0.884, 95% CI: 0.849–0.921). Each 1 g/dL increase in hemoglobin was associated with an 11.6% reduction in the odds of preeclampsia.

Conclusion: First-trimester anemia was significantly associated with preeclampsia. Adequate early hemoglobin levels were associated with lower odds of preeclampsia, underscoring the importance of early hematologic monitoring and iron–folate supplementation in antenatal care.

Keywords: Anemia; first trimester; hemoglobin; preeclampsia; pregnancy

Korelasi antara Anemia Trimester-Pertama pada Kehamilan dan Kejadian Preeklampsia: Studi Kohort Retrospektif

Abstrak

Pendahuluan: Preeklampsia memengaruhi 2 – 4% kehamilan di seluruh dunia dan merupakan penyebab utama morbiditas serta mortalitas maternal dan perinatal. Anemia pada kehamilan—didefinisikan sebagai hemoglobin <11 g/dL pada trimester pertama atau ketiga—masih banyak terjadi, memengaruhi 48,9% ibu hamil Indonesia (Riskesmas 2018). Anemia trimester pertama dapat berkontribusi terhadap preeklampsia melalui oxidative stress, disfungsi endotel, dan gangguan plasentasi.

Tujuan: Penelitian ini bertujuan menganalisis korelasi antara anemia trimester pertama dan preeklampsia di Rumah Sakit Umum Daerah Prof. Dr. Margono Soekarjo (Januari – Desember 2023).

Metode: Penelitian ini merupakan studi retrospektif bersifat kohort dengan teknik total sampling terhadap ibu hamil yang dirawat di rumah sakit dari Januari hingga Desember 2023. Variabel yang diteliti meliputi hemoglobin trimester pertama dan status preeklampsia. Analisis *logistic regression* dilakukan menggunakan SPSS 27.0.

Hasil: Model menunjukkan kecocokan yang baik (Hosmer–Lemeshow = 2.491, $p=0.778$; Nagelkerke $R^2=0.367$). Hemoglobin trimester pertama berhubungan signifikan dengan preeklampsia ($p<0.001$; OR=0.884, 95% CI: 0.849–0.921). Kenaikan hemoglobin sebesar 1 g/dL berhubungan dengan penurunan peluang preeklampsia sebanyak 11,6%.

Kesimpulan: Anemia trimester pertama berhubungan secara signifikan dengan preeklampsia. Kadar hemoglobin awal yang memadai berhubungan dengan penurunan peluang terjadinya preeklampsia, sehingga menekankan pentingnya pemantauan hematologi dini dan suplementasi zat besi–folat dalam pelayanan antenatal.

Kata Kunci: Anemia; hemoglobin; kehamilan; preeklampsia; trimester pertama

Introduction

Preeclampsia is a progressive, unpredictable, and serious pregnancy complication that affects approximately 2–4% of pregnancies worldwide and is associated with an estimated 46,000 maternal deaths and 500,000 fetal and neonatal deaths annually, with a disproportionate burden among women in low- and middle-income countries and those who are socioeconomically disadvantaged.¹ Preeclampsia has a complex, multifactorial etiology and develops in two main stages: abnormal placentation in the first trimester followed by a maternal syndrome in the second and third trimesters characterized by increased antiangiogenic factors.^{1–2} Major risk factors include a history of preeclampsia, chronic hypertension, pregestational diabetes mellitus, multiple pregnancy, obesity with BMI >30, antiphospholipid syndrome, systemic lupus erythematosus, prior stillbirth, nulliparity, history of placental abruption, assisted reproductive technologies, chronic kidney disease, and advanced maternal age (older than 35 years).^{1–2}

Anemia in pregnancy is among the most prevalent obstetric complications and is characterized by reduced oxygen-carrying capacity of the blood, reflected by decreased hemoglobin concentration. It is generally defined as a hemoglobin level below 11 g/dL in the first and third trimesters or below 10.5 g/dL in the second trimester, and may be absolute or relative, the latter arising from physiological hemodilution attributable to a greater increase in plasma volume compared with red cell mass, known as physiological anemia of pregnancy.^{3–4} The global prevalence of anemia in pregnancy remains high, affecting 37% of pregnant women worldwide, with a prevalence of 41.6% in Asia; in Indonesia, the proportion of anemia in pregnant women increased from 37.1% in 2013 to 48.9% in 2018, indicating that anemia in pregnancy remains a major public

health problem.⁵

The etiology of anemia in pregnancy is diverse, but iron deficiency accounts for approximately 75% of cases, driven by increased iron requirements that cannot be met by diet alone, while folate deficiency commonly causes megaloblastic anemia and less frequent causes include vitamin B12 deficiency, chronic disease, infections, and genetic disorders such as thalassemia. Anemia in pregnancy is intricately linked to preeclampsia through several potential mechanisms, including increased oxidative stress due to tissue hypoxia, endothelial dysfunction from impaired nitric oxide synthesis, and systemic inflammation characterized by elevated proinflammatory cytokines such as TNF- α and IL-6, all of which can damage placental vasculature and disrupt normal trophoblast invasion and spiral artery remodeling.^{6–7} The first trimester is a critical window for placentation, and hemoglobin levels below 11 g/dL may interfere with vascular remodeling through placental hypoxia, increased reactive oxygen species, and reduced endothelial nitric oxide synthase activity, making early pregnancy the optimal period for evaluating and addressing anemia to prevent subsequent preeclampsia.^{8–10}

Despite the high prevalence of anemia among pregnant women in Indonesia and the well-established association between anemia and adverse pregnancy outcomes, evidence on the specific contribution of first-trimester anemia to the risk of preeclampsia remains limited in the Indonesian context. Given that both conditions impose a substantial burden on maternal and neonatal health—contributing to increased rates of preterm birth, low birth weight, intensive care admission, and maternal mortality—early identification of anemia as a modifiable risk factor for preeclampsia represents a clinically meaningful opportunity for targeted intervention. Early antenatal screening and correction of anemia through iron–folate

supplementation may therefore serve not only to optimize hematologic status but also to mitigate the downstream risk of preeclampsia, with potential impact at the population level in settings where both conditions are highly prevalent.

This study aimed to analyze the association between first-trimester anemia and the occurrence of preeclampsia at Prof. Dr. Margono Soekarjo Regional General Hospital, Purwokerto, Indonesia, from January to December 2023, with the expectation that its findings may contribute to evidence-based antenatal care practices in similar clinical settings.

Methods

This retrospective cohort study was conducted to examine the association between first-trimester anemia in pregnancy and the occurrence of preeclampsia at Prof. Dr. Margono Soekarjo Regional General Hospital, Purwokerto, Indonesia, from January to December 2023. Secondary data were obtained from hospital medical records of pregnant women managed in the outpatient and inpatient obstetric units during this period.

The study population comprised all pregnant women who received care in these units during the study period. Eligible subjects were pregnant women who delivered at the hospital between January and December 2023 and had complete medical records, including first-trimester hemoglobin measurements and documented pregnancy outcomes. Women with incomplete or missing key medical record data were excluded. Women with a history of chronic hypertension, pregestational diabetes mellitus, prior preeclampsia, multiple pregnancy, or other significant comorbidities known to independently increase preeclampsia risk were also excluded to minimize confounding. A total sampling technique was applied,

whereby all subjects meeting the inclusion and exclusion criteria were included as the study sample.

Patient identification numbers were obtained from the hospital register of pregnant women for the period January to December 2023, after which relevant data were extracted from medical records. Collected variables included sociodemographic characteristics (age, education, occupation), obstetric history (gestational age, parity, previous pregnancy history), first-trimester hemoglobin levels, and preeclampsia status based on blood pressure and proteinuria documentation. Preeclampsia was defined according to the American College of Obstetricians and Gynecologists (ACOG) criteria as new-onset hypertension (systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg on two occasions at least four hours apart after 20 weeks of gestation) accompanied by proteinuria (≥ 300 mg in 24-hour urine or protein/creatinine ratio ≥ 0.3) or, in the absence of proteinuria, by severe features including thrombocytopenia, renal insufficiency, impaired liver function, pulmonary edema, or new-onset headache. First-trimester anemia was defined as hemoglobin < 11 g/dL, and patients were classified accordingly. The independent variable was first-trimester anemia status, and the dependent variable was the occurrence of preeclampsia. All data were tabulated in a spreadsheet and analyzed using SPSS software version 27.0. Univariable logistic regression was first performed to assess the crude association between first-trimester hemoglobin and preeclampsia. A multivariable logistic regression model was subsequently constructed incorporating first-trimester hemoglobin together with BMI, parity, and maternal age as covariates, to evaluate the independent association of hemoglobin after adjustment for these potential confounders.

This study adhered to established research ethics principles. All data were

anonymized before analysis to prevent patient identification, and access to identifiable data was restricted to the investigators and designated hospital staff. Physical documents are stored securely and will be destroyed, and electronic data will be deleted from the investigators' repository, within five years after completion of the study. This retrospective study using anonymized secondary data from hospital medical records received ethical approval and institutional permission from the Ethics Committee of Prof. Dr. Margono Soekarjo Regional General Hospital and the Faculty of Medicine, Universitas Jenderal Soedirman (Approval No. 420/09105/2025). In accordance with institutional guidelines for retrospective studies, individual written informed consent was waived because the data were fully anonymized, no additional interventions were performed, and patient privacy was protected. All procedures adhered to the principles of the Declaration of Helsinki.

Results

Table 1 presents the clinical and obstetric characteristics of the study subjects according to preeclampsia status. Women with preeclampsia were older (mean age 33.3 ± 7.3 years) than those without preeclampsia (30.4 ± 6.6 years). The proportion of obesity class II was higher in the preeclampsia group (30.0%) compared with the non-preeclampsia group (9.7%), whereas normal BMI was more frequent among women without preeclampsia. Multigravidity (≥ 3 pregnancies) was more common in the preeclampsia group (56.6% versus 36.9%), while nulliparity was slightly more frequent in the non-preeclampsia group. The distribution of term and preterm deliveries was similar between groups. Statistical comparison revealed that maternal age ($p=0.049$) and BMI distribution ($p=0.009$) differed significantly between the preeclampsia and non-preeclampsia groups, whereas gravida, parity, and delivery timing were not statistically significant.

Table 1 Baseline Characteristics of Study Subjects

Variable	Preeclampsia (n=30)	Non-preeclampsia (n=103)	p-value
Age, years (mean $\pm$ SD)	33.3 ± 7.3	30.4 ± 6.6	0.049*
BMI normal	8 (26.7%)	49 (47.6%)	0.009†
BMI overweight	7 (23.3%)	23 (22.3%)	
BMI obese I	5 (16.7%)	12 (11.7%)	
BMI obese II	9 (30.0%)	10 (9.7%)	
Gravida = 1	7 (23.3%)	33 (32.0%)	0.286†
Gravida = 2	6 (20.0%)	32 (31.0%)	
Gravida ≥ 3	17 (56.6%)	38 (36.9%)	
Parity = 0	8 (26.7%)	38 (36.9%)	0.579†
Parity = 1	7 (23.3%)	32 (31.1%)	
Parity = 2	8 (26.7%)	18 (17.5%)	
Parity ≥ 3	7 (23.3%)	15 (14.6%)	
Term delivery	16 (53.3%)	55 (53.4%)	0.993*
Preterm delivery	14 (46.7%)	48 (46.6%)	

*Independent samples t-test; †Chi-square test. Values are expressed as n (%) unless otherwise stated.

Table 2 Univariable Logistic Regression of first-trimester Hemoglobin and Preeclampsia

Variable	B	SE	Wald	p-value	OR [Exp(B)]	95% CI lower	95% CI upper
Hemoglobin	-0.123	0.021	35.52	<0.001	0.884	0.849	0.921

B = regression coefficient; SE = standard error; OR = odds ratio; CI = confidence interval.

Table 3 Multivariable Logistic Regression for Risk Factors of Preeclampsia

Variable	B	SE	Wald	p-value	OR [Exp(B)]	95% CI lower	95% CI upper
Hemoglobin	-0.123	0.021	35.52	<0.001	0.884	0.849	0.921
BMI	0.116	0.046	6.47	0.011	1.123	1.027	1.229
Parity	0.085	0.229	0.14	0.709	1.089	0.696	1.705
Age	0.036	0.044	0.68	0.410	1.037	0.951	1.131

B = regression coefficient; SE = standard error; OR = odds ratio; CI = confidence interval.

Univariable logistic regression analysis demonstrated that first-trimester hemoglobin level was significantly associated with the occurrence of preeclampsia. The model showed good calibration (Hosmer–Lemeshow $\chi^2=2.491$, $p=0.778$) and explained 36.7% of the variance in preeclampsia (Nagelkerke $R^2=0.367$). Each 1 g/dL increase in hemoglobin was associated with an 11.6% reduction in the odds of preeclampsia (OR 0.884; 95% CI 0.849–0.921; $p<0.001$), indicating an inverse association between first-trimester hemoglobin and preeclampsia risk. The regression coefficient (B) for hemoglobin was -0.123, which corresponds to an Exp(B) of 0.884, confirming internal consistency between the reported B and OR values.

In the multivariable model incorporating first-trimester hemoglobin together with BMI, parity, and maternal age, first-trimester hemoglobin remained significantly associated with preeclampsia (OR 0.884; 95% CI 0.849–0.921; $p<0.001$; $B = -0.123$), indicating that the association persisted after adjustment for the included covariates. BMI remained significantly associated with preeclampsia risk (OR 1.123; 95% CI 1.027–1.229; $p=0.011$), corresponding to a 12.3% increase in risk for each unit increase in BMI. Parity and maternal age were not

significantly associated with preeclampsia in the multivariable model ($p=0.709$ and $p=0.410$, respectively).

Discussion

This study demonstrated meaningful differences in maternal characteristics between the preeclampsia and non-preeclampsia groups, with higher mean maternal age and a greater proportion of obesity among women with preeclampsia. These findings are consistent with previous studies from Finland, Pakistan, Sudan, and Indonesia, which have identified advanced maternal age (>35 years) as an independent risk factor for preeclampsia and severe maternal complications.¹¹ Similarly, the higher proportion of obese women in the preeclampsia group aligns with evidence that elevated BMI (particularly ≥ 30 –35 kg/m²) is a major risk factor for preeclampsia through mechanisms involving insulin resistance, endothelial dysfunction, and chronic systemic inflammation.¹²

The principal finding of this study is the statistically significant inverse association between first-trimester hemoglobin concentration and the occurrence of preeclampsia, with an odds ratio of 0.884, indicating an 11.6% reduction in the odds

of preeclampsia for each 1 g/dL increase in hemoglobin. This result is consistent with the study hypothesis that inadequate hematologic status in early pregnancy—reflecting impaired iron stores, suboptimal oxygen delivery, and heightened oxidative stress—disrupts normal trophoblast invasion and spiral artery remodeling, thereby predisposing to the placental dysfunction that underlies the preeclampsia cascade. These findings support earlier work showing that severe anemia is associated with a higher risk of preeclampsia and adverse perinatal outcomes, while mild-to-moderate anemia or adequately maintained hemoglobin may have a more complex relationship with hypertensive disorders of pregnancy.¹³ Large systematic reviews and cohort studies have reported U-shaped associations in which both low (<110 g/L) and high (≥ 130 g/L) maternal hemoglobin levels are linked to increased maternal complications, including preeclampsia.¹⁴

From a pathophysiological perspective, adequate hemoglobin in early pregnancy likely reflects sufficient iron stores, optimal oxygen-carrying capacity, and better uteroplacental perfusion, thereby reducing placental hypoxia and oxidative stress that may trigger the preeclampsia cascade.¹⁵ Effective iron therapy and careful monitoring of hematologic status have been shown to be associated with lower risks of hypertensive and other obstetric complications, underscoring the importance of early detection and management of anemia as part of preeclampsia prevention strategies.¹⁶ In parallel, the independent association of BMI observed in this study reinforces the need for preconception counseling, weight optimization, and close surveillance of obese pregnant women, given the consistently reported two- to threefold increase in preeclampsia risk among women with elevated pre-pregnancy BMI.¹⁷

From a clinical standpoint, the findings

of this study underscore the practical value of routine first-trimester hemoglobin screening as part of standard antenatal care. Identifying women with hemoglobin below 11 g/dL in the first trimester may allow clinicians to initiate timely iron–folate supplementation, provide targeted nutritional counseling, and implement closer obstetric surveillance for signs of preeclampsia throughout pregnancy. In resource-limited settings such as district-level hospitals in Indonesia, integration of hematologic monitoring into existing antenatal care protocols represents a feasible, low-cost strategy that may contribute to a reduction in preeclampsia-associated maternal and perinatal morbidity.

Strengths and Limitations.

This study has several strengths. The use of a retrospective cohort design with total sampling ensured complete enumeration of eligible cases within the study period, minimizing selection bias. The application of standardized ACOG diagnostic criteria for preeclampsia and WHO-based hemoglobin thresholds for anemia enhanced the validity of case classification. Furthermore, the multivariable logistic regression approach allowed adjustment for key potential confounders including BMI, parity, and maternal age, thereby strengthening the internal validity of the observed association.

However, this study has several limitations that warrant acknowledgment. First, the retrospective design and reliance on medical record data precluded prospective ascertainment of exposures and outcomes, and important confounders such as chronic hypertension, pregestational diabetes mellitus, prior preeclampsia, and multiple gestation could not be fully accounted for due to the limitations of the available medical record data. Second, the relatively small number of preeclampsia cases ($n=30$) may have reduced statistical power to detect associations with

less prevalent confounders and contributed to the low sensitivity of the multivariable model (10.0%), which limits its clinical utility for preeclampsia prediction. Third, the study was conducted at a single tertiary referral center, which may limit generalizability to other settings with different case-mix profiles. Fourth, the observational design precludes causal inference, and all associations should be interpreted accordingly. Future prospective multicenter studies incorporating a broader set of confounders and larger sample sizes are warranted to confirm these findings.

Conclusion

This study demonstrated a statistically significant inverse association between first-trimester hemoglobin concentration and the occurrence of preeclampsia (OR 0.884; 95% CI 0.849–0.921; $p < 0.001$), whereby each 1 g/dL increase in hemoglobin was associated with an 11.6% reduction in the odds of preeclampsia. These findings highlight the importance of early hematologic monitoring and routine iron–folate supplementation in antenatal care as a potential strategy to reduce preeclampsia risk in pregnant women.

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