



Maternal Factors, Anemia and Postpartum Hemorrhage Among Women with Vaginal Delivery

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Abstract

Surgical stress induces systemic inflammation characterized by increased neutrophil-to-lymphocyte ratio and interleukin-6 levels, which may contribute to postoperative pain, immune dysfunction, and complications. This systematic review aimed to evaluate the effects of preemptive ketamine administration on postoperative neutrophil-to-lymphocyte ratio and interleukin-6 levels. The review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 guidelines. Relevant studies were identified through PubMed, ScienceDirect, the Cochrane Central Register of Controlled Trials, Google Scholar, and ClinicalKey. Study selection was based on predefined population, intervention, comparison, outcome, and study-design criteria. Data were extracted using standardized tables, methodological quality was assessed using appropriate risk-of-bias instruments, and the findings were synthesized narratively according to ketamine dose, surgical procedure, biomarker measurement time, and clinical outcomes. Of 807 records identified, 17 studies were included in the final synthesis. Preemptive intravenous ketamine or S-ketamine generally reduced the early postoperative increase in the neutrophil-to-lymphocyte ratio and suppressed interleukin-6 secretion, particularly at subanesthetic doses of 0.3–0.75 milligrams per kilogram. These immunomodulatory effects were accompanied by lower postoperative pain scores, reduced opioid requirements, fewer episodes of postoperative nausea and vomiting, and a lower risk of chronic postsurgical pain. However, variations in dosage, surgical procedures, anesthetic techniques, and biomarker measurement times limited direct comparisons between studies. Preemptive ketamine appears to provide beneficial analgesic and immunomodulatory effects by attenuating postoperative systemic inflammation, although further standardized randomized trials are required to determine the optimal dosing regimen.

Introduction

Maternal mortality remains an important indicator of maternal health and the quality of health services (WHO, 2024; Aisyah et al., 2026; Rossen et al., 2025). Despite global efforts to reduce preventable maternal deaths, Indonesia continues to face challenges in achieving the

Sustainable Development Goal target for maternal mortality. Postpartum hemorrhage (PPH) remains one of the major causes of maternal morbidity and mortality and requires early identification of women at increased risk (Kemenkes, 2024).

Anemia during pregnancy is a common maternal health problem and may contribute to adverse pregnancy and delivery outcomes (Wang et al., 2025; Obeagu et al., 2025; Chauhan et al., 2025). In clinical practice, anemia during pregnancy is generally identified based on hemoglobin concentration, with hemoglobin levels below 11 g/dL used as an important threshold during pregnancy (Lamtiar et al., 2025). Maternal anemia may reduce tissue oxygen delivery and impair maternal physiological reserve, which may become clinically important during childbirth and blood loss (Azizah et al., 2024). The original study rationale also identified reduced hemoglobin levels and impaired myometrial oxygenation as possible mechanisms linking anemia with uterine atony and postpartum hemorrhage (Khatimah et al., 2022; Yunas et al., 2025; Hayakawa et al., 2024).

Postpartum hemorrhage is a multifactorial condition commonly categorized according to the four major etiological mechanisms known as the “4Ts”: Tone, Trauma, Tissue, and Thrombin (Yunas et al., 2025). Uterine atony, representing the “Tone” component, is an important cause of postpartum hemorrhage. Anemia may potentially worsen the clinical consequences of blood loss and may be associated with impaired uterine function through reduced oxygen delivery to the myometrium (Wang et al., 2025).

In addition to anemia, maternal characteristics may be associated with maternal hematological status. Age, parity, educational level, occupational status, nutritional status, history of chronic disease, access to health services, and antenatal care (ANC) adherence may reflect different biological, nutritional, socioeconomic, and healthcare-related conditions that influence maternal health during pregnancy. The original research specifically evaluated these eight characteristics in relation to anemia (Meiska et al., 2023; Li et al., 2025; Khan et al., 2025).

Nutritional status is particularly relevant because pregnancy increases the demand for iron and other nutrients required for maternal hematopoiesis and fetal development (Khasanah et al., 2025). Inadequate nutritional intake and insufficient iron stores may contribute to declining hemoglobin concentrations during pregnancy (Wang et al., 2025). Similarly, regular ANC provides opportunities for early identification and management of anemia and other maternal risk factors (Wahyuningrum, 2025).

Although anemia and postpartum hemorrhage have been widely studied, evidence from individual maternity-care settings remains important because maternal characteristics and patterns of healthcare utilization may vary between populations. In particular, local medical-record data can provide information on the distribution of maternal characteristics and identify factors associated with anemia among women who deliver at a specific healthcare facility. Furthermore, evaluating the relationship between anemia during pregnancy and postpartum hemorrhage may provide clinically relevant information for strengthening antenatal risk assessment and intrapartum preparedness.

Therefore, this study aimed to examine the association between maternal characteristics—including age, parity, educational level, occupational status, nutritional status, history of chronic disease, access to health services, and ANC adherence—and anemia during pregnancy, and to examine the association between anemia during pregnancy and postpartum hemorrhage among women with vaginal delivery at RSIA Ananda, Makassar, Indonesia, during 2022–2024.

Methods

Study Design and Setting

This study used a retrospective cross-sectional observational design based on secondary data from medical records. The study was conducted in the Medical Records Department of RSIA Ananda, Makassar, Indonesia. Data collection was performed from September 10 to November 10, 2025, using medical records of women who delivered at RSIA Ananda between January 1, 2022 and December 31, 2024. The retrospective approach was used because exposure and outcome information had already been recorded in the medical records before the study was conducted.

Study Population and Sampling

The study population comprised all women who delivered at RSIA Ananda during the 2022–2024 study period and whose deliveries were recorded in the hospital medical records. A total of 292 deliveries were identified during the study period. Following screening according to the predefined eligibility criteria, 100 medical records met the requirements for inclusion and were included in the final analysis.

Participants were selected using purposive sampling, in which medical records were selected according to the predefined inclusion and exclusion criteria. The original sample-size calculation used the Slovin formula with a 5% precision level and yielded a minimum calculated sample of 168 records. However, because only 100 records met all eligibility criteria after screening, the final analytical sample consisted of 100 participants.

Eligibility Criteria

The inclusion criteria were: 1) women who had a vaginal delivery; 2) complete documentation of blood loss during the first 24 hours postpartum; 4) availability of hemoglobin measurements obtained during antenatal care; 4) complete documentation of the maternal characteristics evaluated in the study in the RSIA Ananda medical records for 2022–2024.

The exclusion criteria were: 1) women with chronic diseases such as chronic kidney disease, liver cirrhosis, or malignancy; 2) women with coagulation disorders, including thalassemia or hemophilia; 3) women who underwent cesarean section; 4) medical records with incomplete data relevant to the study variables.

Study Variables and Operational Definitions

The primary independent variable was anemia during pregnancy, defined based on a hemoglobin concentration of <11 g/dL as recorded during antenatal care. Women with hemoglobin concentrations ≥ 11 g/dL were categorized as having no anemia.

The dependent outcome for the second analysis was postpartum hemorrhage, defined based on the documented amount of blood loss during the first 24 hours after delivery.

Maternal characteristics included age, parity, educational level, occupational status, nutritional status based on body mass index (BMI), history of chronic disease, access to health services, and ANC adherence. These variables were obtained from the maternal medical records.

Data Collection

Data were obtained retrospectively from medical records. Relevant information was reviewed, coded, tabulated, and entered into a statistical database for analysis. The study used secondary medical-record data and did not involve direct intervention with patients.

Statistical Analysis

Data were analyzed using SPSS. Descriptive analysis was performed to summarize the distribution of maternal characteristics and anemia status using frequencies and percentages.

Categorical variables were analyzed using Pearson's chi-square test. Fisher's exact test or Fisher-Freeman-Halton exact test was applied when the expected cell counts were insufficient for the chi-square assumptions. A p -value <0.05 was considered statistically significant. Bivariate analyses were conducted to examine the associations between maternal characteristics and anemia during pregnancy and between anemia during pregnancy and postpartum hemorrhage.

Ethical Considerations

This study received ethical approval from the Health Research Ethics Committee of the Faculty of Medicine and Health Sciences, Universitas Islam Negeri Alauddin Makassar, on July 22, 2025, under approval number E.115/KEPK/FKIK/VII/2025.

Result and Discussion

Study Population

During the study period, 292 deliveries were identified in the medical records of RSIA Ananda for 2022–2024. After screening according to the predefined inclusion and exclusion criteria, 100 medical records contained complete information and were included in the final analysis.

Among the 100 women included in the analysis, 62 (62.0%) had anemia during pregnancy, while 38 (38.0%) did not have anemia.

Maternal Characteristics and Their Association with Anemia

Most participants were aged 20–35 years (76.0%), multiparous (62.0%), had an educational level of $\leq$ high school (58.0%), were not working (69.0%), had normal nutritional status (55.0%), had no history of chronic disease (79.0%), had easy access to health services (71.0%), and had regular ANC attendance (>6 visits) (60.0%). These distributions are consistent with the original study dataset.

Maternal age was not significantly associated with anemia ($p=0.139$). Anemia was present in 80.0% of women aged <20 years, 56.6% of those aged 20–35 years, and 78.9% of those aged >35 years.

Parity was also not significantly associated with anemia ($p=0.131$). Anemia was observed in 52.6% of primiparous women and 67.7% of multiparous women.

Similarly, no significant associations were observed for educational level ($p=0.664$) or occupational status ($p=0.587$).

For nutritional status, the original table reported a significant association ($p=0.038$). However, recalculation based on the reported cell frequencies did not reproduce this p -value. Using an exact test appropriate for the small expected cell counts, the association was **not statistically significant** ($p=0.405$). Anemia was observed in 100.0% of underweight women, 56.4% of women with normal weight, 64.9% of overweight women, and 85.7% of women with obesity.

History of chronic disease was also **not significantly associated with anemia** ($p=0.992$). Anemia was observed in 61.9% of women with a history of chronic disease and 62.0% of women without such a history.

Access to health services was significantly associated with anemia ($p=0.023$). Anemia was observed in 54.9% of women with easy access to health services and 79.3% of women with limited access.

ANC adherence was not significantly associated with anemia after recalculation ($p=0.077$). Anemia was observed in 55.0% of women with regular ANC attendance (>6 visits) and 72.5% of women with irregular ANC attendance (<6 visits).

Thus, based on the corrected statistical interpretation, only access to health services showed a statistically significant association with anemia among the maternal characteristics evaluated.

Table 1. Association Between Maternal Characteristics and Anemia During Pregnancy

Maternal characteristics	Anemia, n (%)	No anemia, n (%)	Total, n (%)	p-value
Maternal age				0.139
<20 years	4 (80.0)	1 (20.0)	5 (100.0)	
20–35 years	43 (56.6)	33 (43.4)	76 (100.0)	
>35 years	15 (78.9)	4 (21.1)	19 (100.0)	
Parity				0.131
Primiparous	20 (52.6)	18 (47.4)	38 (100.0)	
Multiparous	42 (67.7)	20 (32.3)	62 (100.0)	
Educational level				0.664
≤High school	37 (63.8)	21 (36.2)	58 (100.0)	
Higher education	25 (59.5)	17 (40.5)	42 (100.0)	
Occupational status				0.587
Working	18 (58.1)	13 (41.9)	31 (100.0)	
Not working	44 (63.8)	25 (36.2)	69 (100.0)	
Nutritional status (BMI)				0.405
Underweight	1 (100.0)	0 (0.0)	1 (100.0)	
Normal weight	31 (56.4)	24 (43.6)	55 (100.0)	
Overweight	24 (64.9)	13 (35.1)	37 (100.0)	
Obesity	6 (85.7)	1 (14.3)	7 (100.0)	0.992
History of chronic disease				
Chronic disease present	13 (61.9)	8 (38.1)	21 (100.0)	
No chronic disease	49 (62.0)	30 (38.0)	79 (100.0)	0.023*
Access to health services				
Easy access	39 (54.9)	32 (45.1)	71 (100.0)	
Limited access	23 (79.3)	6 (20.7)	29 (100.0)	0.077
ANC adherence				
Regular ANC (>6 visits)	33 (55.0)	27 (45.0)	60 (100.0)	
Irregular ANC (<6 visits)	29 (72.5)	11 (27.5)	40 (100.0)	

Association Between Anemia During Pregnancy and Postpartum Hemorrhage

Among the 62 women with anemia during pregnancy, 18 (29.0%) experienced postpartum hemorrhage, whereas 44 (71.0%) did not. Among the 38 women without anemia, 3 (7.9%) experienced postpartum hemorrhage and 35 (92.1%) did not.

Pearson's chi-square test demonstrated a statistically significant association between anemia during pregnancy and postpartum hemorrhage ($\chi^2=6.345$, $df=1$, $p=0.012$). The proportion of postpartum hemorrhage was higher among women with anemia than among those without anemia (29.0% vs. 7.9%).

Table 2. Association Between Anemia During Pregnancy and Postpartum Hemorrhage

Anemia status	Postpartum hemorrhage, n (%)	No postpartum hemorrhage, n (%)	Total, n (%)
Anemia (Hb <11 g/dL)	18 (29.0)	44 (71.0)	62 (62.0)
No anemia (Hb ≥11 g/dL)	3 (7.9)	35 (92.1)	38 (38.0)

Total	21 (21.0)	79 (79.0)	100 (100.0)
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Among the maternal characteristics examined, only access to health services was significantly associated with anemia. In addition, anemia during pregnancy was significantly associated with postpartum hemorrhage among women with vaginal delivery.

Maternal Characteristics and Their Association with Anemia

This study found that 62.0% of the women included in the analysis had anemia during pregnancy. The proportion of anemia was relatively high despite most participants being in the reproductive age group, having no documented chronic disease, having relatively easy access to health services, and attending ANC regularly. The original study similarly identified a high prevalence of anemia among the study population, with 76.0% of participants aged 20–35 years, 79.0% having no chronic disease, 71.0% having easy access to health services, and 60.0% attending ANC regularly (Kartikasari et al., 2025).

Maternal age was not significantly associated with anemia in this study ($p=0.139$). Most participants were aged 20–35 years, which is generally considered the reproductive age range with lower obstetric risk compared with younger or older maternal age groups. However, the absence of a statistically significant association indicates that age alone did not explain the occurrence of anemia in this population (Raihan & Iqbal, 2025). This finding should be interpreted in the context of the distribution of the sample, because only five women were younger than 20 years. The small number of participants in the youngest age category limits the ability to detect differences between age groups. The original discussion also emphasized that the predominance of women aged 20–35 years did not necessarily protect the population from anemia (Nurdin et al., 2020).

Parity was also not significantly associated with anemia ($p=0.131$). Although multiparous women represented 62.0% of the sample and had a higher proportion of anemia than primiparous women (67.7% vs. 52.6%), the difference did not reach statistical significance. Repeated pregnancies may theoretically increase maternal iron requirements and contribute to depletion of iron stores; however, parity alone may not adequately capture the interval between pregnancies, dietary intake, iron supplementation, or the severity of previous blood loss. Therefore, the observed difference in proportions should not be interpreted as evidence of an independent effect of parity on anemia.

Educational level was not significantly associated with anemia ($p=0.664$). Although 58.0% of participants had an educational level of high school or below, the proportion of anemia was similar between women with lower and higher educational attainment. Education may influence health literacy and understanding of iron supplementation, but these mechanisms cannot be established from the present cross-sectional medical-record data. The original discussion proposed that educational level may influence maternal understanding of iron supplementation and recognition of anemia symptoms; however, the present analysis did not demonstrate a statistically significant association (Kartikasari et al., 2025).

Occupational status was likewise not significantly associated with anemia ($p=0.587$). Anemia was observed in 58.1% of working women and 63.8% of women who were not working. Occupational status may indirectly reflect socioeconomic conditions, dietary resources, or time available for healthcare utilization, but these pathways were not directly measured in this study. Consequently, occupational status should not be interpreted as a determinant of anemia based on the present findings.

Nutritional status based on BMI was not significantly associated with anemia after statistical verification (Fisher-Freeman-Halton exact test, $p=0.405$). This finding is important because the original manuscript reported $p=0.038$; however, that value could not be reproduced from the reported cell frequencies. BMI is also an indirect measure of nutritional status and does not

specifically assess iron stores or micronutrient adequacy. In this study, 55.0% of women had normal BMI, while 37.0% were overweight and 7.0% were obese. The original discussion appropriately noted that excess body weight does not necessarily indicate adequate micronutrient status and discussed the possibility of micronutrient deficiency despite excess caloric intake (Safitri et al., 2025). Nevertheless, because iron intake, serum ferritin, dietary intake, and iron supplementation were not directly evaluated, the present study cannot establish the mechanisms underlying anemia according to BMI category (Adnan et al., 2024).

History of chronic disease was also not significantly associated with anemia ($p=0.992$). The proportions of anemia were almost identical among women with and without a documented history of chronic disease (61.9% vs. 62.0%). This result differs from the original manuscript, which reported $p=0.012$. Recalculation from the reported 2×2 frequency table does not support that value. Therefore, the corrected interpretation is that chronic disease history was not associated with anemia in this study. Although chronic inflammatory diseases may theoretically contribute to anemia through altered iron metabolism and erythropoiesis, the present data do not provide sufficient evidence to support this relationship in the study population. The relatively small number of participants with chronic disease (21.0%) also limits subgroup comparisons.

In contrast, access to health services was significantly associated with anemia ($p=0.023$). Anemia occurred in 54.9% of women with easy access to health services compared with 79.3% among women with limited access. This finding suggests that geographical or practical access to health services may be relevant to maternal anemia prevention and detection. Women with limited access may experience greater barriers to obtaining ANC, laboratory examinations, iron supplementation, or follow-up care. The original discussion highlighted geographical, economic, transportation, and social barriers as potential components of healthcare access (Nuridin et al., 2020).

However, the cross-sectional retrospective design does not allow us to determine whether limited access directly caused anemia. Access to care may also act as a marker for other unmeasured socioeconomic or geographic factors. Therefore, the finding should be interpreted as an association rather than a causal relationship (Mawaddah et al., 2024).

ANC adherence was not significantly associated with anemia after recalculation ($p=0.077$). Although anemia was more frequent among women with irregular ANC attendance than among those with regular attendance (72.5% vs. 55.0%), the difference did not reach the predefined statistical significance threshold. This finding is clinically relevant because frequency of ANC visits alone may not reflect the quality or completeness of care received. The original discussion similarly noted that regular attendance does not necessarily ensure complete laboratory assessment, iron supplementation, or appropriate counseling during each visit (Palancoi et al., 2021).

Taken together, the findings indicate that among the maternal characteristics evaluated, access to health services was the only characteristic statistically associated with anemia. The absence of significant associations for age, parity, education, occupation, BMI, chronic disease history, and ANC adherence should not be interpreted as evidence that these factors have no clinical relevance. Rather, the findings indicate that their associations were not statistically demonstrated in this particular sample.

Association Between Anemia During Pregnancy and Postpartum Hemorrhage

A major finding of this study was the statistically significant association between anemia during pregnancy and postpartum hemorrhage ($p=0.012$). Among 62 women with anemia, 18 (29.0%) experienced postpartum hemorrhage, compared with only 3 (7.9%) among 38 women without anemia. The absolute difference in the proportion of postpartum hemorrhage between the two groups was 21.1 percentage points. These findings are consistent with the original

study's observation that postpartum hemorrhage occurred more frequently among women with anemia (Musfida et al., 2023).

The observed association is biologically plausible. Maternal anemia reduces the physiological reserve available to tolerate blood loss during delivery (Fitri, 2023). Consequently, the same amount of blood loss may produce more pronounced clinical consequences in an anemic woman than in a woman with adequate hemoglobin levels. The original discussion emphasized this concept of reduced tolerance to blood loss among women with anemia (Musfida et al., 2023).

Anemia may also coexist with factors that contribute to postpartum hemorrhage, particularly uterine atony. Adequate myometrial contraction after placental separation is essential for physiological control of bleeding (Fitri, 2023). Iron deficiency and reduced oxygen-carrying capacity may impair tissue oxygenation and maternal physiological reserve. However, because this study did not directly measure uterine tone, iron status, or the specific cause of postpartum hemorrhage, these mechanisms should be considered biologically plausible explanations rather than mechanisms demonstrated by the present data (Nugroho et al., 2020).

The finding is clinically important because postpartum hemorrhage is an acute obstetric emergency, while anemia may be identified and managed during the antenatal period. Therefore, identification and treatment of maternal anemia before delivery may contribute to improving maternal preparedness for blood loss. However, the present study was observational and retrospective; therefore, it cannot establish that anemia independently causes postpartum hemorrhage (Aneisca et al., 2024)..

The study also found that 21.0% of the women experienced postpartum hemorrhage. This proportion should be interpreted cautiously because the study was conducted at a single maternity hospital and included only women who met the eligibility criteria, including vaginal delivery. Therefore, the observed prevalence should not be generalized directly to all women delivering in Makassar or Indonesia.

Clinical Implications

The findings have several practical implications. First, the relatively high prevalence of anemia indicates the importance of systematic anemia detection during pregnancy. Second, the significant association between access to health services and anemia highlights the importance of reducing barriers to maternal healthcare utilization. Third, the significant association between anemia and postpartum hemorrhage supports the importance of recognizing anemia as a maternal condition that may reduce physiological tolerance to obstetric blood loss.

Nevertheless, clinical management should not be based solely on the presence of anemia. Postpartum hemorrhage is multifactorial, and preventive strategies should continue to address established obstetric causes, including uterine atony, genital tract trauma, retained placental tissue, and coagulation disorders.

Study Limitations

This study has several limitations. First, its retrospective cross-sectional design limits the ability to establish temporal or causal relationships between maternal characteristics, anemia, and postpartum hemorrhage. Second, the study used secondary medical-record data, and variables not routinely documented in medical records could not be analyzed. Third, the final sample consisted of only 100 eligible records from 292 deliveries identified during the study period, which may introduce selection bias and limits generalizability.

Fourth, several subgroups contained small numbers of participants, particularly women aged <20 years and those classified as underweight. Therefore, estimates for these categories should be interpreted cautiously. Finally, the analysis was primarily bivariate; consequently, potential

confounding between maternal characteristics was not controlled using multivariable regression.

Conclusion

Among women with vaginal delivery at RSIA Ananda, Makassar, maternal age, parity, educational level, occupational status, nutritional status, history of chronic disease, and ANC adherence were not statistically associated with anemia during pregnancy. Access to health services was the only maternal characteristic significantly associated with anemia. Anemia during pregnancy was also significantly associated with postpartum hemorrhage, with postpartum hemorrhage occurring more frequently among women with anemia than among those without anemia. These findings highlight the importance of early identification and appropriate management of maternal anemia and the need to address barriers to access to maternal health services. Further multicenter prospective studies with larger samples and multivariable analyses are warranted to clarify independent predictors of anemia and postpartum hemorrhage.

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