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Determinants of Suboptimal Hemoglobin Response to Oral Iron Supplementation among Pregnant Women with Anemia in Primary Midwifery Care

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Abstract

Background: Iron deficiency anemia remains a major public health problem during pregnancy, particularly in low- and middle-income countries. Although oral iron supplementation is the standard treatment in Indonesian primary midwifery care, many women fail to achieve an adequate hemoglobin response. **Objective:** This study aimed to identify determinants of suboptimal hemoglobin response, defined as a hemoglobin increase of less than 1 g/dL after 90 days of oral iron supplementation, among pregnant women with anemia in primary midwifery care in Medan. **Methods:** An analytical cross-sectional study with prospective hemoglobin follow-up was conducted in seven primary midwifery care units involving 286 pregnant women with mild-to-moderate anemia. Data were collected using structured questionnaires, dietary assessments, compliance records, and maternal health records. Hemoglobin levels were measured at baseline and after 90 days. Multiple logistic regression was performed to identify independent determinants. **Results:** Suboptimal hemoglobin response occurred in 42.3% of participants. Independent determinants included poor adherence to iron supplementation (AOR = 5.34), low dietary iron intake (AOR = 4.52), tea or coffee consumption after meals (AOR = 3.71), moderate baseline anemia (AOR = 3.29), fewer than four antenatal care visits (AOR = 2.84), and inadequate nutritional counseling (AOR = 2.56). **Conclusion:** Behavioral, nutritional, biological, and service-related factors jointly influence hemoglobin response. Strengthening adherence monitoring, nutritional counseling, and risk-based screening within primary midwifery care may improve treatment outcomes among pregnant women with anemia.

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Introduction

Anemia during pregnancy remains one of the most persistent and consequential public health problems of the twenty-first century, disproportionately affecting women in low- and middle-income countries. The World Health Organization estimates that approximately 36.5% of pregnant women worldwide are anemic, with the highest burden concentrated in South Asia, sub-Saharan Africa, and parts of Southeast Asia (World Health Organization, 2023). Despite decades of intervention through universal iron and folic acid supplementation programs, global progress toward the World Health Assembly target of a 50% reduction in anemia among women of reproductive age by 2030 has stalled substantially (Stevens et al., 2022). Maternal anemia contributes to an estimated one-fifth of maternal deaths, and to a substantial share of preterm births, low birth weight infants, and impaired neurodevelopmental outcomes in offspring (Young et al., 2022; Georgieff, 2023).

In Indonesia, the burden of anemia in pregnancy has remained stubbornly high. National Basic Health Research (Riskesdas) reported that the prevalence of anemia among pregnant women rose from 37.1% in 2013 to 48.9% in 2018, and more recent facility-based data from the Ministry of Health suggest that between 40% and 55% of pregnant women continue to be anemic despite active supplementation programs (Ministry of Health of the Republic of Indonesia, 2022; Sungkar et al., 2022). In North Sumatra Province, cross-sectional surveys in primary care settings have documented prevalence figures between 42% and 51%, with the highest burden reported in urban peri-poor neighborhoods where nutritional transitions coexist with limited dietary diversity (Sinaga et al., 2023).

The cornerstone of the Indonesian national anemia control strategy is the provision of at least 90 iron and folic acid tablets during pregnancy, each containing 60 mg of elemental iron and 400 µg of folic acid, distributed principally through primary midwifery care (Puskesmas and Praktik Mandiri Bidan). Under conditions of adequate compliance and absorption, oral supplementation should raise hemoglobin concentration by approximately 1 to 2 g/dL within four to eight weeks (Pavord et al., 2020; Auerbach & Adamson, 2022). Yet in real-world clinical practice, a considerable fraction of women fail to reach this therapeutic benchmark, a phenomenon increasingly labeled as suboptimal or refractory hemoglobin response.

Suboptimal hemoglobin response is not a trivial concern. It signals a persisting iron-deficient erythropoiesis, delays recovery from anemia, and prolongs exposure of the mother and fetus to the well-documented consequences of hypoxia and impaired oxygen delivery (Api et al., 2022; Muñoz et al., 2023). More importantly, it undermines the biological rationale of the entire supplementation program and, if unrecognized by primary care providers, may lead to fatalistic acceptance of anemia as an inevitable feature of pregnancy in low-resource settings.

Existing literature has identified multiple potential contributors to poor hemoglobin response, but they have most often been examined in isolation. Behavioral factors such as nonadherence to the daily regimen, discontinuation because of gastrointestinal side effects, and morning sickness have been described in several cohorts (Georgieff et al., 2022; Tayo et al., 2023). Nutritional determinants, including low dietary iron intake, insufficient vitamin C, and the consumption of tea or coffee within one hour of iron intake, have long been recognized to reduce non-heme iron bioavailability by 40–60% (Piskin et al., 2022; Moretti et al., 2023). Biological determinants such as baseline severity of anemia, chronic energy deficiency reflected in a mid-upper arm circumference (MUAC) below 23.5 cm, subclinical inflammation, and helminth infection also modulate the response to oral iron (Pasricha et al., 2021; Cerami, 2022).

Beyond the woman herself, the quality of primary midwifery care is a key structural determinant that has received far less analytic attention. Antenatal care attendance below the WHO-recommended minimum, absence of individualized nutritional counseling, and inconsistent midwife monitoring of tablet consumption have all been linked to poorer hematological outcomes, yet Indonesian data integrating these service-level factors within a single explanatory model remain scarce (Titaley et al., 2022; Nisa et al., 2024).

Most Indonesian studies to date have either focused narrowly on adherence, or on the prevalence and severity of anemia, without simultaneously examining the determinants of the biological response to supplementation. This constitutes an important knowledge gap. Anemia recovery, rather than anemia occurrence, is the operationally meaningful outcome for the primary midwifery care system, because it is the metric that determines whether the substantial national investment in iron tablets translates into improved maternal and perinatal outcomes.

The present study addresses this gap by identifying and quantifying the determinants of suboptimal hemoglobin response among pregnant women with anemia attending primary midwifery care in Medan, North Sumatra. It contributes to the literature in three specific ways. First, it defines and models suboptimal response as the primary outcome, using a physiologically justified cut-off of a hemoglobin increment below 1 g/dL after 90 days of supervised oral supplementation. Second, it integrates biological, behavioral, nutritional, and service-quality variables within a single multivariable framework, allowing the relative contribution of each domain to be estimated after mutual adjustment. Third, it situates the analysis within primary midwifery care, the specific service context in which the majority of Indonesian pregnant women actually receive supplementation, thereby yielding findings that are immediately relevant to program improvement.

The specific objective of this study was to determine the prevalence and independent determinants of suboptimal hemoglobin response after 90 days of oral iron supplementation among pregnant women with anemia attending seven primary midwifery care units in Medan City in 2026. We hypothesized that behavioral factors (compliance and consumption of iron-inhibitors), nutritional factors (dietary iron intake, vitamin C intake, and baseline nutritional status), biological factors (baseline hemoglobin), and service-quality factors (ANC frequency and quality of nutritional counseling) would each contribute independently to the risk of a suboptimal response.

Materials and Methods

Study Design and Setting

An analytical cross-sectional study with prospective hemoglobin follow-up was conducted between March and October 2026 in seven primary midwifery care units in Medan City, North Sumatra Province, Indonesia. These units were purposively selected to represent the sub-districts of Medan Denai, Medan Amplas, Medan Tembung, Medan Marelan, Medan Belawan, Medan Sunggal, and Medan Helvetia, reflecting the socioeconomic and geographic diversity of the city. Each unit routinely delivers antenatal care and distributes iron and folic acid tablets under the national maternal health program.

Population and Sample

The source population comprised all pregnant women with a laboratory diagnosis of anemia (hemoglobin < 11 g/dL) attending the seven primary midwifery care units during the study period. The sample size was calculated using the single-proportion formula $n = Z^2 \cdot p(1-p)/d^2$, assuming a prevalence of suboptimal hemoglobin response of 40% based on prior regional data (Sinaga et al., 2023), a 95% confidence level (Z = 1.96), and an absolute precision of 5.8%. This yielded a minimum sample of 274; an additional 10% was added to accommodate loss to follow-up, giving a target of 301. A total of 305 women were recruited by consecutive sampling; 19 (6.2%) were subsequently excluded due to loss to follow-up (n=11), miscarriage (n=4), or hospitalization for non-anemia causes (n=4), leaving 286 women in the final analysis.

Eligibility Criteria

Inclusion criteria were: pregnant women aged 17 to 45 years; gestational age between 13 and 32 weeks at enrolment; hemoglobin between 7.0 and 10.9 g/dL at baseline; singleton pregnancy; residing in the Medan metropolitan area for at least six months; and providing written informed consent. Exclusion criteria were: multiple pregnancy; known hemoglobinopathy or hematological malignancy; chronic kidney disease; prior intravenous iron therapy or blood transfusion within three months; hemoglobin below 7.0 g/dL requiring referral for parenteral therapy; and inability to comprehend Bahasa Indonesia.

Variables and Operational Definitions

The dependent variable was suboptimal hemoglobin response, defined as a hemoglobin increment of less than 1 g/dL between baseline and 90 days of oral iron supplementation with a standardized regimen of one tablet daily containing 60 mg elemental iron and 400 µg folic acid. Independent variables included maternal age (<20, 20–35, >35 years), parity (primipara, multipara, grand multipara), gestational age at enrolment, body mass index, mid-upper arm circumference (chronic energy deficiency defined as MUAC <23.5 cm), dietary iron intake from 24-hour recall categorized against the Indonesian recommended dietary allowance for pregnancy (27 mg/day), vitamin C intake, tea or coffee consumption within one hour after meals, compliance with iron tablets (adequate defined as ≥80% of prescribed tablets consumed as documented on the compliance card), self-reported gastrointestinal side effects, morning sickness, self-reported symptoms consistent with intestinal helminth infection confirmed by stool examination in a subsample, birth spacing, socioeconomic status (below/above the Medan minimum wage), education, occupation, family support (adapted from the Multidimensional Scale of Perceived Social Support), ANC visit frequency (<4 versus ≥4 as of the 90-day assessment window), knowledge regarding anemia (validated 15-item scale), nutritional counseling quality (adequate defined as ≥3 structured sessions covering diet, iron intake timing, and inhibitors), midwife monitoring of tablet consumption, history of anemia in previous pregnancies, inflammatory disease during pregnancy, chronic energy deficiency, and baseline hemoglobin category (mild 10.0–10.9 g/dL; moderate 7.0–9.9 g/dL). Malaria was not considered a relevant variable given the non-endemic status of Medan.

Instruments, Validity, and Reliability

Data were collected using a structured questionnaire, a 24-hour dietary recall, a semi-quantitative food frequency questionnaire (FFQ) covering 78 locally consumed food items, a compliance card, an observation checklist for midwife counseling quality, and maternal health records (buku KIA). Hemoglobin was measured using the HemoCue Hb 301 point-of-care system, previously validated in Indonesian antenatal settings with an intra-class correlation of 0.96 against automated cyanmethemoglobin methodology. The knowledge questionnaire and family support scale were pretested on 30 pregnant women not included in the main study; the resulting Cronbach's alpha values were 0.83 and 0.87 respectively, and content validity indices exceeded 0.90. All measurements were performed by trained midwives who completed a two-day standardization workshop.

Data Collection Procedure

At enrolment, baseline hemoglobin was measured, and structured interviews were conducted to obtain sociodemographic, obstetric, nutritional, and behavioral information. Each participant received 90 iron and folic acid tablets and standardized counseling. Compliance cards were distributed for daily self-recording of tablet intake and were verified by weekly phone reminders and reviewed at each ANC visit. After 90 days of supplementation, follow-up hemoglobin was measured, and the compliance card, side-effect log, and dietary recall were re-administered.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics version 27. Categorical variables were summarized as frequencies and percentages, and continuous variables as means with standard deviations or medians with interquartile ranges depending on distribution assessed by Shapiro-Wilk test. Bivariate associations between each independent variable and suboptimal hemoglobin response were tested using Pearson chi-square (or Fisher's exact test where cell counts were <5) for categorical variables and independent t-test for continuous variables. Variables with $p<0.25$ in bivariate analysis were entered into a multiple logistic regression model using the enter method, following the Hosmer-Lemeshow recommendation. Adjusted odds ratios (AOR) with 95% confidence intervals were reported. Multicollinearity was examined using tolerance and variance inflation factors, with tolerance <0.4 or VIF >2.5 considered problematic. Model fitness was assessed using the Hosmer-Lemeshow goodness-of-fit test, Nagelkerke R^2, and classification accuracy. A two-sided p-value of <0.05 was considered statistically significant.

Ethical Approval

Ethical approval for this study was obtained from the Health Research Ethics Committee of Universitas Bunda Thamrin, Medan, Indonesia (Approval Number: 017/KEPK-UBT/EC/VII/2025). Written informed consent was obtained from all participants before enrolment and prior to data collection. Participation was voluntary, and the confidentiality of participants was ensured through the use of anonymized identification codes. Women who were found to have severe anemia (hemoglobin <7.0 g/dL) at any stage of the study were promptly referred to a secondary healthcare facility for appropriate clinical management

Results and Discussions

Participant Characteristics

Of the 286 pregnant women included in the final analysis, 121 (42.3%) exhibited a suboptimal hemoglobin response after 90 days of supplementation, while 165 (57.7%) achieved an increment of ≥1 g/dL. The mean baseline hemoglobin was 9.68 ± 0.82 g/dL, rising to 10.71 ± 1.14 g/dL at follow-up, with a mean increment of 1.03 ± 0.91 g/dL. The mean maternal age was 27.4 ± 5.6 years, and 62.6% were multiparous. Sociodemographic and clinical characteristics are presented in Table 1.

Table 1. *Sociodemographic and clinical characteristics of pregnant women with anemia (n = 286)*

Characteristic	Frequency (n)	Percentage (%)
Maternal age (years)		
<20	24	8.4
20–35	218	76.2
>35	44	15.4
Parity		
Primipara	89	31.1
Multipara (2–4)	179	62.6
Grand multipara (≥5)	18	6.3
Gestational age at enrolment		
Second trimester	162	56.6
Third trimester	124	43.4
Education		
≤ Junior high school	97	33.9
Senior high school	138	48.3
Higher education	51	17.8
Occupation		
Housewife	196	68.5
Employed	90	31.5
Socioeconomic status		
Below minimum wage	163	57.0
Above minimum wage	123	43.0
MUAC < 23.5 cm (CED)	78	27.3
Baseline anemia severity		
Mild (10.0–10.9 g/dL)	151	52.8
Moderate (7.0–9.9 g/dL)	135	47.2
Suboptimal Hb response	121	42.3

Independent Variable Distribution

Behavioral, nutritional, and service-quality distributions are summarized in Table 2. Poor compliance with iron tablets was observed in 39.2% of women, and 44.4% reported drinking tea or coffee within one hour after meals. Low dietary iron intake was documented in 51.7%, and only 62.6% had attended at least four ANC visits by the 90-day assessment.

Table 2. *Distribution of behavioral, nutritional, biological and service-quality variables*

Variable	**n**	**%**
Compliance with iron tablets		
Adequate (≥80%)	174	60.8
Poor (<80%)	112	39.2
Dietary iron intake		
Adequate (≥27 mg/day)	138	48.3
Low (<27 mg/day)	148	51.7
Vitamin C intake		
Adequate	156	54.5
Low	130	45.5
Tea/coffee ≤1h after meals		
No	159	55.6
Yes	127	44.4
Morning sickness	84	29.4
GI side effects reported	108	37.8
Suspected helminth infection	31	10.8
Short birth spacing (<24 mo)	62	21.7
ANC frequency		
≥4 visits	179	62.6
<4 visits	107	37.4
Adequate nutritional counseling	153	53.5
Regular midwife monitoring	168	58.7
Adequate knowledge on anemia	142	49.7
Adequate family support	185	64.7
History of anemia in prior pregnancy	104	36.4
Inflammatory disease	22	7.7

Bivariate Analysis

Bivariate analysis identified thirteen variables significantly associated with suboptimal hemoglobin response at $p<0.25$ (Table 3). The strongest bivariate associations were observed for poor compliance, low dietary iron intake, tea or coffee consumption after meals, baseline moderate anemia, low ANC attendance, and inadequate nutritional counseling. Maternal age, parity, occupation, and family support did not reach statistical significance.

Table 3. *Bivariate analysis of factors associated with suboptimal hemoglobin response (n = 286)*

Variable	Suboptimal n (%)	Optimal n (%)	OR (95% CI)	p-value
Poor compliance (<80%)	78 (69.6)	34 (30.4)	6.32 (3.72–10.75)	<0.001
Low dietary iron intake	89 (60.1)	59 (39.9)	5.06 (3.02–8.47)	<0.001
Tea/coffee after meals	77 (60.6)	50 (39.4)	4.02 (2.44–6.63)	<0.001
Low vitamin C intake	70 (53.8)	60 (46.2)	2.40 (1.48–3.90)	<0.001
<4 ANC visits	62 (57.9)	45 (42.1)	2.80 (1.71–4.60)	<0.001
Inadequate counseling	72 (54.1)	61 (45.9)	2.51 (1.55–4.07)	<0.001
Irregular midwife monitoring	60 (50.8)	58 (49.2)	1.82 (1.13–2.94)	0.014
Baseline moderate anemia	78 (57.8)	57 (42.2)	3.44 (2.10–5.62)	<0.001
MUAC < 23.5 cm	44 (56.4)	34 (43.6)	2.20 (1.30–3.72)	0.003
GI side effects	58 (53.7)	50 (46.3)	2.12 (1.30–3.44)	0.002
Morning sickness	43 (51.2)	41 (48.8)	1.67 (1.00–2.80)	0.049
Low anemia knowledge	68 (47.2)	76 (52.8)	1.50 (0.93–2.41)	0.094
History of prior anemia	52 (50.0)	52 (50.0)	1.64 (1.01–2.66)	0.045
Maternal age >35	20 (45.5)	24 (54.5)	1.16 (0.61–2.21)	0.646
Grand multipara	9 (50.0)	9 (50.0)	1.36 (0.52–3.55)	0.531

Multivariable Logistic Regression

After adjustment for potential confounders, six variables retained independent statistical significance as determinants of suboptimal hemoglobin response (Table 4). Poor compliance with iron tablets emerged as the strongest determinant, followed by low dietary iron intake, tea or coffee consumption after meals, baseline moderate-severity anemia, low ANC attendance, and inadequate nutritional counseling. The final model exhibited good calibration (Hosmer-Lemeshow χ^2 = 6.42, df = 8, p = 0.601), acceptable discrimination (Nagelkerke R^2 = 0.487; overall classification accuracy 82.5%; sensitivity 76.9%; specificity 86.7%), and no problematic multicollinearity (all VIF ≤ 2.13; tolerance ≥ 0.47). Model diagnostics are summarized in Table 5.

Table 4. *Multiple logistic regression of determinants of suboptimal hemoglobin response (n = 286)*

Determinant	β	SE	AOR (95% CI)	p-value
Poor compliance (<80%)	1.675	0.309	5.34 (2.91–9.78)	<0.001
Low dietary iron intake	1.509	0.307	4.52 (2.48–8.23)	<0.001
Tea/coffee after meals	1.311	0.302	3.71 (2.05–6.71)	<0.001
Baseline moderate anemia	1.191	0.311	3.29 (1.78–6.08)	<0.001
<4 ANC visits	1.044	0.306	2.84 (1.56–5.17)	0.001
Inadequate counseling	0.940	0.301	2.56 (1.42–4.62)	0.002
Constant	−3.921	0.512	—	<0.001

Table 5. *Model diagnostics of the final logistic regression model*

Indicator	Value
Hosmer-Lemeshow χ^2 (df = 8)	6.42 (p = 0.601)
Nagelkerke R^2	0.487
Cox & Snell R^2	0.362
−2 Log Likelihood	265.14
Overall classification accuracy	82.5%
Sensitivity (suboptimal detected)	76.9%
Specificity (optimal detected)	86.7%
Area under ROC curve	0.884 (95% CI 0.845–0.923)
Highest VIF among predictors	2.13
Lowest tolerance among predictors	0.47

Discussion

This study documents that 42.3% of pregnant women with anemia attending primary midwifery care in Medan failed to achieve the physiologically expected hemoglobin increment after 90 days of daily oral iron supplementation. Six independent determinants of this suboptimal response were identified, distributed across behavioral, nutritional, biological, and service-quality domains. The magnitude of the observed prevalence closely mirrors the 38–46% range reported in recent multi-country analyses of iron supplementation programs conducted by the WHO and BMC Pregnancy and Childbirth authors (World Health Organization, 2023; Owais et al., 2023), suggesting that the phenomenon of pharmacological non-response is a systemic feature of program-based supplementation rather than an isolated local artefact.

Poor compliance emerged as the single strongest determinant, with women adhering to less than 80% of prescribed tablets exhibiting more than a fivefold increase in the odds of suboptimal response after adjustment for all other factors (AOR 5.34; 95% CI 2.91–9.78). This finding is consistent with pooled evidence from The Lancet series on maternal anemia, which identified adherence as the principal modifiable driver of program effectiveness (Pasricha et al., 2021). Recent cohort work in Ethiopia and Bangladesh reported adjusted odds ratios of 4.6 and 5.1 respectively for the same association, supporting external validity (Gebreamlak et al., 2022; Kabir et al., 2023). The mechanisms are well understood: intermittent intake blunts the gradual replenishment of iron stores and, importantly, prevents the sustained downregulation of hepcidin that is required for efficient enterocyte iron absorption (Moretti et al., 2023). What the present data add is a demonstration that in primary midwifery settings, where supervision is limited and side effects are frequent, compliance below 80% is neither rare nor evenly distributed but is concentrated among women receiving inadequate counseling and less frequent monitoring, suggesting that adherence is not merely a patient attribute but a co-produced outcome of the mother–midwife interaction.

Low dietary iron intake was the second strongest determinant (AOR 4.52; 95% CI 2.48–8.23). Although oral supplementation is designed to be therapeutically sufficient on its own, its efficiency is nonetheless modulated by concurrent dietary intake. Recent PLOS ONE and Frontiers in Nutrition analyses have demonstrated that mothers whose habitual diets fall below 50% of the recommended daily allowance for iron display attenuated hemoglobin responses despite comparable pill counts (Piskin et al., 2022; Al-Naseem et al., 2023). Our finding aligns with this pattern and reinforces the argument that supplementation should not be positioned as a substitute for dietary improvement, but as a complementary strategy embedded within nutritional counseling. In Medan, as in many rapidly urbanizing Indonesian cities, the diet of pregnant women is dominated by refined carbohydrates and low-cost protein sources, with limited intake of red meat, dark green leafy vegetables, and legumes. This nutritional transition, which coexists with rising overweight prevalence, produces a paradoxical population in which mothers are simultaneously overweight and iron-deficient, a pattern also observed in urban India and Vietnam (Nguyen et al., 2022).

The consumption of tea or coffee within one hour after meals emerged as a robust independent determinant (AOR 3.71; 95% CI 2.05–6.71). This is biologically expected: polyphenols and tannins bind non-heme iron in the intestinal lumen and can reduce absorption by 40–70% (Moretti et al., 2023). Yet many Indonesian women view tea as a benign beverage and are unaware that its timing critically influences supplementation efficacy. Similar findings have been reported in the Journal of Obstetrics and Gynaecology Research and in Midwifery (Api et al., 2022; Tayo et al., 2023), and the consistency across settings suggests that a simple counseling intervention targeting the temporal separation of beverages from iron tablets and iron-rich meals may offer disproportionately large returns for maternal hematological outcomes.

Baseline moderate anemia was independently associated with a threefold increase in the odds of suboptimal response (AOR 3.29; 95% CI 1.78–6.08). Two mechanisms plausibly contribute. First, the deeper the iron deficit at the start of therapy, the longer the time required to replete tissue stores before hemoglobin normalizes; a 90-day window may be insufficient to detect a full 1 g/dL response in the most depleted women. Second, women with lower baseline hemoglobin have often experienced longer-standing deficiency, with associated inflammatory activation and elevated hepcidin, which further restricts iron absorption (Cerami, 2022; Pasricha et al., 2021). The International Journal of Gynecology & Obstetrics has recently called for the routine incorporation of baseline severity into risk stratification protocols in antenatal care (Api et al., 2022), and our findings support this recommendation.

Antenatal care attendance below four visits during the 90-day supplementation window was associated with an adjusted 2.84-fold increase in the odds of suboptimal response. ANC visits are not merely occasions for iron tablet delivery; they are the principal opportunity for reinforcement of adherence, resolution of side effects, and adjustment of dietary practice. UNICEF has emphasized that quality-oriented rather than quantity-oriented ANC is central to reducing maternal anemia (UNICEF, 2023). Our finding echoes recent BMC Public Health analyses which showed that each additional ANC contact reduces the odds of persistent anemia by approximately 18–22% (Tesfaye et al., 2022). In the Indonesian context, where the standard is at least six ANC visits with two by a physician, our data suggest that the timing and content of these visits deserve as much programmatic attention as their sheer number.

Inadequate nutritional counseling was independently associated with 2.56-fold higher odds of suboptimal response. This is arguably the most actionable finding of the present study, because the quality of counseling is entirely under the control of the primary midwifery care system. Structured nutritional counseling covering iron-rich food sources, timing of tablet intake in relation to meals and beverages, and management of gastrointestinal side effects has been shown in Midwifery and Frontiers in Public Health to increase hemoglobin response rates by 15–25 percentage points at negligible additional cost (Nisa et al., 2024; Owais et al., 2023). Our results reinforce the case for integrating a standardized, competency-based nutritional counseling module into midwifery pre-service and in-service training.

Several factors that reached bivariate significance did not retain independence in the adjusted model, including gastrointestinal side effects, morning sickness, MUAC below 23.5 cm, and history of anemia. Their effects appear to be transmitted through, rather than independent of, the six retained determinants. For instance, women with more severe side effects were also less compliant, and women with a prior history of anemia frequently exhibited moderate baseline anemia. This pattern is consistent with a cascading rather than additive causal structure, and highlights the importance of intervening at the level of the proximal, modifiable determinants that dominate the final model.

Considered together, our findings support a syndemic interpretation of suboptimal hemoglobin response, in which nutritional, behavioral, biological, and service-quality vulnerabilities converge in the same subset of women. The syndemic framing has important programmatic implications: single-issue interventions (for example, a tablet-only or a counseling-only strategy) are unlikely to produce large improvements, whereas a bundled midwifery care package that simultaneously enhances counseling quality, tracks adherence, and stratifies risk by baseline severity is likely to yield synergistic benefit. This aligns with the maternal anemia framework recently proposed in The Lancet Global Health (Owais et al., 2023) and reinforces WHO recommendations for integrated antenatal care (World Health Organization, 2023).

The novelty of this study lies in three points. First, it explicitly models suboptimal hemoglobin response rather than anemia prevalence as the primary outcome, aligning research metrics with program-relevant biological endpoints. Second, it integrates biological, behavioral, nutritional, and midwifery service-quality domains within a single multivariable model, producing mutually adjusted effect estimates that can inform intervention design. Third, it grounds these estimates in the specific context of primary midwifery care in an Indonesian urban setting, generating findings that are directly applicable to Puskesmas and Praktik Mandiri Bidan networks that deliver the bulk of national antenatal services.

Strengths

This study has several strengths. It employed prospective hemoglobin measurement using a validated point-of-care device with independent operator standardization, minimizing measurement error. Compliance was assessed through triangulated methods combining a compliance card, weekly phone verification, and midwife-recorded ANC observations. The multivariable model integrated biological, behavioral, nutritional, and service-quality variables, providing an unusually comprehensive picture of the determinants of hemoglobin response. Sample size and diagnostic performance of the final model support the robustness of the inferences.

Limitations

Several limitations must be acknowledged. The study was conducted in seven primary midwifery care units in a single urban setting; extrapolation to rural or highly remote populations should be undertaken cautiously. Dietary intake was assessed by 24-hour recall supplemented by FFQ, which is subject to recall bias; nevertheless, both instruments have been widely validated for antenatal populations. Serum ferritin, hepcidin, and inflammatory biomarkers were not measured, limiting insight into the specific mechanisms of pharmacological non-response. Finally, although compliance was verified by multiple methods, self-reported measures may still overestimate true adherence

Conclusion

Suboptimal hemoglobin response after oral iron supplementation is common among pregnant women with anemia attending primary midwifery care in Medan, affecting more than four in every ten women. Six independent determinants, namely poor compliance, low dietary iron intake, tea or coffee consumption after meals, baseline moderate anemia, fewer than four antenatal care visits, and inadequate nutritional counseling, explained a substantial proportion of the variation in treatment response. These findings indicate that anemia control programs should move beyond tablet distribution by integrating structured adherence monitoring, standardized nutritional counseling, and risk-based screening into routine antenatal care within primary midwifery services. Future research should employ prospective multicenter cohort studies or randomized controlled trials involving more diverse populations to evaluate the effectiveness of integrated adherence-support and nutrition counseling interventions. In addition, the inclusion of biological markers such as serum ferritin, transferrin saturation, C-reactive protein, and hepcidin would provide a more comprehensive understanding of the mechanisms underlying suboptimal hemoglobin response and help optimize individualized anemia management during pregnancy.

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Conflict of Interest

The authors declare no conflict of interest, financial or otherwise, related to the design, conduct, analysis, or reporting of this study.

Ethical Approval

This study received ethical approval from the Health Research Ethics Committee of Universitas Bunda Thamrin, Medan, Indonesia (Approval Number: 017/KEPK-UBT/EC/VII/2025). Written informed consent was obtained from all participants before enrolment. Participation was voluntary, and all participant information was kept confidential through the use of anonymized identification codes. Participants were informed of their right to withdraw from the study at any time without any consequences.

Authors' Contribution

AB conceptualized the study, led the design, coordinated data collection, and drafted the manuscript. AZS contributed to the study design, supervised the statistical analysis, and revised the manuscript for intellectual content. ERT contributed to the design of the nutritional assessment instruments and led the dietary data analysis. AFT participated in participant recruitment, hemoglobin measurement standardization, and data curation. PYS coordinated field logistics and midwife training. MLG participated in questionnaire validation and manuscript revision. All authors read and approved the final manuscript.

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