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First-trimester Ferritin as a Predictor of Postpartum Transfusion: A Retrospective Cohort Study

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ABSTRACT

Objective: Iron deficiency is the most common nutritional deficiency in pregnancy and a key contributor to maternal anemia and postpartum transfusion. However, no consensus exists regarding optimal screening strategies or ferritin thresholds for early detection in non-anemic women. To evaluate whether first-trimester maternal ferritin levels predict postpartum blood transfusion in non-anemic pregnant women and to establish population-specific ferritin cut-off values for transfusion risk.

Materials and Methods: This retrospective study included 386 singleton pregnancies followed and delivered at a tertiary university hospital between September 2022 and February 2024. Women with first-trimester hemoglobin (Hb) ≥11 g/dL were eligible. Patients with hemorrhage-related complications, hemoglobinopathies, or early iron therapy were excluded. Maternal demographic and laboratory parameters and neonatal outcomes were retrieved from electronic records. Receiver operating characteristic analyses were performed to determine optimal first-trimester thresholds for predicting postpartum transfusion.

Results: According to World Health Organization criteria (ferritin <15 µg/L), 29% of women were iron-deficient; using the 30 µg/L criterion, 66.6% showed depleted iron stores. Postpartum anemia occurred in 43%, and 8% required transfusion. Patients who required transfusion were significantly older and had higher parity (p=0.019 and <0.001, respectively). Median first-trimester ferritin was 22.65 µg/L. Optimal predictive threshold was 19.6 µg/L for ferritin (Area under the curve =0.634; p=0.012). In multivariable analysis, parity independently predicted transfusion (Odds ratio [OR]=1.85, p=0.001), while ferritin showed a borderline inverse association (OR=0.98, p=0.056). No significant association was observed between first-trimester ferritin and composite neonatal outcomes.

Conclusion: First-trimester ferritin <19 µg/L identifies women at increased risk of postpartum transfusion, even when Hb is normal. Routine ferritin screening in early pregnancy could enhance patient blood-management strategies by enabling timely detection and treatment of subclinical iron deficiency.

Keywords: Anemia, Blood transfusion, Ferritins, First trimester, Iron deficiency, Pregnancy trimester

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INTRODUCTION

Iron deficiency is the most common nutritional disorder worldwide and remains the leading cause of anemia in both high-income and resource-limited settings.[1] Its prevalence among pregnant women varies substantially, ranging from 20% to 90%, depending on geographic, socioeconomic, and healthcare access-related factors.[2,3] Women of reproductive age are particularly vulnerable due to menstrual blood loss and the markedly increased iron requirements of pregnancy. Because childbirth inherently carries the risk of significant blood loss, optimizing maternal iron status during gestation is essential to improve maternal outcomes and reduce the need for peripartum transfusion.

Iron deficiency and iron deficiency anemia (IDA) in pregnancy have well-documented adverse effects on both mother and fetus. In mothers, IDA has been associated with fatigue, impaired cognitive and physical performance, increased susceptibility to infections, heightened risk of peripartum hemorrhage, cardiovascular strain, greater transfusion requirements, and prolonged hospital stays. For the fetus, maternal iron deficiency has been linked to preterm birth, intrauterine growth restriction, impaired placental development, and reduced neonatal iron stores.[4-6]

Despite the recognized burden of iron deficiency, no universal consensus exists regarding optimal screening, diagnostic thresholds, or management strategies during pregnancy. While hemoglobin (Hb)-based anemia screening is widely implemented, standardized guidance for detecting non-anemic iron deficiency remains absent. Routine ferritin testing in the first trimester is not currently recommended in clinical practice, and treatment algorithms for patients with low ferritin are lacking. Furthermore, discrepancies in defining iron deficiency particularly ferritin cut-off values ranging from <10 µg/L to <30 µg/L, with the World Health Organization (WHO) recommending <15 µg/L – combined with the absence of pregnancy-specific reference ranges, complicate clinical decision-making.[7-10]

The present study aimed to determine whether first-trimester maternal ferritin levels can predict the need for postpartum blood transfusion, a major contributor to maternal morbidity and prolonged hospitalization. And also, we evaluated the association between early pregnancy iron status and neonatal outcomes. In the second part, we aimed to determine population-specific cut-off values for ferritin, Hb, and hematocrit (Hct) were established to predict transfusion requirements.

MATERIALS AND METHODS

This study includes pregnant women who were followed during pregnancy and delivered at University Hospital setting between September 01, 2022, and February 01, 2024. This is a tertiary referral center with approximately 1,000 births/year. Ethical approval for this study was obtained from the Lokman Hekim University Scientific Research Ethics Committee (Date: 28.03.2024, Approval No: 2024/89). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Pregnancies in which a positive fetal heartbeat was detected by sonography during the first trimester whose ferritin and Hb levels were measured at their first visit, and who completed antenatal follow-up and delivery at our clinic were enrolled in the study. First-trimester ferritin levels were below 15 µg/L were classified as the iron-deficiency group as defined by a threshold of 15 µg/L ferritin by WHO. In addition, regarding the WHO guideline criterion for anemia (Hb levels <11 g/dL in the first TRIMESTER), only patients with Hb levels ≥11 g/dL at the first trimester were included in the study. In addition, guidelines such as those issued by the American College of Obstetricians and Gynecologists and the National Institute for Health and Care Excellence consider a ferritin level of 30 µg/L as the diagnostic cut-off for iron deficiency.

Patients with conditions that could lead to excessive bleeding during delivery – such as placenta previa, postpartum atony, multiple pregnancy, placental abruption, or placenta percreta – were excluded from the study. In addition, patients with known thalassemia or other hemoglobinopathies, as well as those who delivered at another facility, were also excluded. Individuals who had received any form of iron supplementation, including oral preparations or intravenous replacement, during the first trimester were excluded from the analysis.

Each pregnant participant underwent complete blood count (hemogram) testing at both the beginning of the second and third trimesters. Patients with Hb levels <10.5 g/dL in the second trimester or <11 g/dL in the third trimester were started on oral ferrous sulfate therapy, which was continued throughout the remainder of pregnancy. Hemogram assessments were repeated 4 weeks after initiation of treatment. Pregnant women who were unable to tolerate oral iron, whose anemia did not improve with oral therapy, or who remained anemic within 4 weeks of the expected delivery were administered ferric carboxymaltose.

In the postpartum period, blood transfusion was administered to patients with Hb levels <7 g/dL or to those exhibiting clinical symptoms (such as tachypnea, tachycardia, or hypotension) in conjunction with a decline in hemogram values. Intravenous ferric carboxymaltose was given to asymptomatic patients with Hb levels <10 g/dL in the postpartum period.

Clinical and laboratory data of the patients retrospectively reviewed using the hospital's electronic medical record system. Information regarding maternal age, body mass index (BMI), obstetric history, and first-trimester Hb, Hct, and ferritin levels was collected. Mode of delivery, peripartum complications, postpartum Hb and Hct levels, and the need for blood transfusion were assessed. Neonatal birth weight, appearance, pulse, grimace, activity, respiration (APGAR) scores, Hb, and Hct levels were recorded. Apgar score <7, intrauterine growth restriction, preterm labor, and fetal distress were classified under the composite adverse neonatal outcome.

The primary goal of this study is to analyze the relationship between first-trimester ferritin levels and the need for postpartum blood transfusion, as well as the association between ferritin levels and neonatal outcomes. The secondary outcome was to determine the population-specific cut-off values for ferritin, Hb, and Hct to predict the likelihood of transfusion requirements.

RESULTS

A total of 386 patients were included in the study. According to the first-trimester ferritin cut-off values of WHO, 112 patients (29%) were identified as having iron deficiency. If the ferritin cut-off value of 30 µg/L is applied, 257 women (66.6%) in the first trimester can be identified as having depleted iron stores.

The median age of the participants was 28 years (min-max: 19–42), the median BMI was 24 kg/m^2 (min-max: 17–42), and the median parity was 1 (min-max: 0–5). The first-trimester laboratory results revealed the median Hb and Hct levels as 12.6 g/dL (min-max: 11–15.3) and 37.5% (min-max: 30.6–44.5), respectively. For ferritin, the median value was calculated as 22.65 µg/L (min-max: 2.4–155).

During pregnancy, 18 patients (4.5%) were administered ferric carboxymaltose in the third trimester, and 243 patients (63%) received oral iron supplementation during the second or third trimester. Postpartum anemia was observed in 166 patients (43%). A total of 32 patients (8%) required postpartum transfusion, while 7 patients (1.8%) received ferric carboxymaltose in the postpartum period.

When comparing demographic parameters (age, BMI, and parity) between patients with and without a history of postpartum transfusion, statistically significant differences were observed in age and parity (p=0.019 and p<0.001, respectively) (Table 1).

The median gestational age at delivery was 38 weeks (min-max: 30–40), and the median neonatal birth weight was 3160 g (min-max: 1300–4424). The median Apgar scores were 8 (min-max: 2–10) at 1 min and 9 (min-max: 7–10) at 5 min. Vaginal delivery occurred in 314 patients (78.5%). No significant differences were observed in first-trimester Hb, Hct, or ferritin levels with respect to combined neonatal outcomes (p=0.281, 0.369, and 0.905, respectively).

The correlation between first-trimester ferritin levels and maternal characteristics was evaluated. A significant positive correlation was observed between first-trimester ferritin and BMI, postpartum Hb and Hct, and 1 and 5 min APGAR scores. A significant negative correlation was observed between first-trimester ferritin and parity (Table 2).

Comparison of first-trimester Hb, Hct, and ferritin levels according to postpartum transfusion status revealed significant differences for all three parameters (p<0.001, <0.001, and 0.012, respectively) (Table 3). The optimal first-trimester cut-off values for predicting postpartum transfusion

Table 1. Comparison of demographic characteristics according to postpartum transfusion status

Variable	No transfusion median (Min-Max)	Transfusion median (Min-Max)	*p*
Age (years)	28 (19–42)	32 (22–40)	**0.019**
Body mass index (kg/m^2)	25 (17–47)	25 (21–35)	0.968
Parity	1 (0–4)	2 (0–5)	**<0.001**

Table 2. Correlation between first-trimester ferritin levels and maternal-neonatal parameters

	Spearman's r	*p*
Maternal outcomes		
Maternal age	–0.049	0.333
BMI (kg/m^2)	+0.159	**0.001**
Parity	–0.102	**0.041**
Gestational age at delivery	—	0.510
Postpartum hemoglobin	+0.126	**0.011**
Postpartum hematocrit	+0.115	**0.022**
Fetal/Neonatal outcomes		
1st-min APGAR score	+0.143	**0.004**
5th-min APGAR score	+0.103	**0.039**
Neonatal birth weight	—	0.956
Neonatal hemoglobin	—	0.069
Neonatal hematocrit	—	0.070

BMI: Body mass index, Hb: Hemoglobin, Hct: Hematocrit, APGAR: Appearance, Pulse, Grimace, Activity, Respiration

Table 3. Predictive performance of first-trimester parameters for postpartum transfusion

Variable	Cut-off	Sensitivity (%)	Specificity (%)	AUC	95% CI	*p*
Hemoglobin (g/dL)	12.05	70	69	0.750	0.65–0.84	<0.001
Hematocrit (%)	36.05	70	66	0.745	0.64–0.84	<0.001
Ferritin (µg/L)	19.60	60	63	0.634	0.54–0.71	0.012

*Cut-off values were determined according to the Youden index. AUC: Area under the curve, CI: Confidence interval.

Table 4. Logistic regression analysis of factors associated with postpartum transfusion

Variable	B	S.E.	Wald	*p*	OR	95% CI
First-trimester ferritin	−0.025	0.013	3.654	0.056	0.975	0.950–1.001
Parity	+0.615	0.181	11.575	**0.001**	1.849	1.298–2.635
Age	—	—	—	—	—	—

OR: Odds ratio, CI: Confidence interval, S.E.: Standard error, B: Regression coefficient.

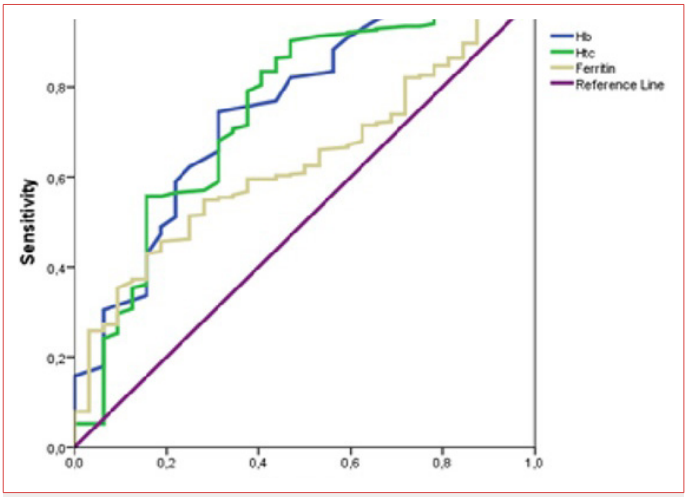

Figure 1. Receiver operating characteristic (ROC) curves of first-trimester hemoglobin (Hb), hematocrit (Hct), and ferritin levels for predicting postpartum transfusion.

were 12.05 g/dL for Hb (70% sensitivity, 69% specificity), 36.05% for Hct (70% sensitivity, 66% specificity), and 19.6 µg/L for ferritin (60% sensitivity, 63% specificity) (Fig. 1).

In the multivariable logistic regression model including parity, age, and first-trimester ferritin; parity remained an independent predictor of postpartum transfusion (Odds ratio [OR]=1.85, *p*=0.001). First-trimester ferritin level demonstrated a borderline inverse association with transfusion risk (OR=0.98, p=0.056) in the model, suggesting that lower iron stores may predispose to transfusion when unadjusted for Hb. Maternal age was not a significant factor (Table 4).

DISCUSSION

The most important finding of our study is the identification of a first-trimester ferritin cut-off of 19.6 µg/L that predicts the need for postpartum transfusion in non-anemic patients. To the best of our knowledge, no prior study has established a ferritin threshold specifically for this outcome, making our results a novel contribution to maternal hematology and patient blood management (PBM).

International literature strongly supports the role of ferritin as the most robust early pregnancy biomarker for later hematologic outcomes.[11] Judistiani *et al.*[12] demonstrated that first-trimester ferritin ≤27.3 µg/L was the best predictor of third-trimester anemia. In this study, a cut-off value for ferritin was determined; however, only Hb levels in the last trimester were assessed, and postpartum follow-up was not conducted. Similarly, Resseguier *et al.*,[13] in a French cohort, found that first-trimester Hb and ferritin were reliable predictors of third-trimester anemia, though their study did not extend the outcome to transfusion. It can be anticipated that iron stores will predict subsequent anemia; however, it should be noted that the early postpartum period, referred to as the fourth stage of labor, is also part of pregnancy follow-up. The fact that this period constitutes the endpoint of our study distinguishes it from others.

Similar to our study, Crispin *et al.*[11] showed that ferritin measured in the first trimester, but not later in pregnancy, was predictive of anemia at delivery and suggested ferritin screening as part of patient PBM programs. These findings align with ours, but our study extends the predictive value of ferritin from anemia to the more clinically tangible outcome of transfusion, thereby filling a critical gap.

Another key consideration is the threshold used to define iron deficiency. WHO recommends <15 µg/L, while most guidelines adopt <30 µg/L, based on bone marrow iron depletion.[7,8] Recently, Mei *et al*.[14] analyzed 1040 pregnant women's NHANES data and proposed physiologically based trimester-specific thresholds: ~25 µg/L for the first trimester. Moreover, it was reported that the value identified in this study was not influenced by ethnic differences. These thresholds, which better align with iron physiology, indicate that the prevalence of iron deficiency in pregnancy has likely been underestimated when the traditional 15 µg/L cut-off is applied. In our study, however, the median value was found to be 22.65 µg/L. The clinical relevance of these findings is substantial. Anemia is a well-documented risk factor for adverse peripartum outcomes, including postpartum hemorrhage, transfusion, and maternal morbidity.

Our study demonstrated that when a ferritin cut-off value of 30 µg/L was applied, two-thirds (66.6%) of women in the first trimester were identified as having depleted iron stores, whereas using a threshold of 15 µg/L classified 116 patients (29%) as such. In contrast, applying our ferritin and Hb thresholds clearly identifies a much sensible proportion in non-anemic patients. This finding highlights the insufficiency of screening approaches based solely on hemogram parameters. By integrating ferritin into routine first-trimester antenatal screening, as already suggested by national guidelines in some countries, earlier detection and intervention could significantly reduce both third-trimester anemia and postpartum transfusion rates.[10,15]

From a health policy perspective, these results also contribute to patient blood management strategies. Early treatment of iron deficiency is cost-effective, reduces transfusion demand, and improves maternal outcomes. Systematic ferritin screening in the first trimester, combined with individualized treatment thresholds, may be a more efficient strategy than universal supplementation or reliance on Hb alone.

This study has several limitations. First, its retrospective and single-center design may limit the generalizability of the findings. Second, factors such as dietary intake, inflammatory status, or chronic subclinical infections that could influence ferritin levels were not systematically evaluated. Third, although postpartum transfusion was selected as a clinically objective endpoint, longer-term follow-up – including postpartum iron status and recovery – was not available. Finally, despite these limitations, the large sample size and uniform data collection strengthen the reliability of our results. As a conclusion, our study demonstrates that first-trimester ferritin serves as a novel predictor of postpartum transfusion.

CONCLUSION

The cut-off of 19 µg/L we identified provides a population-specific threshold with immediate clinical and public health relevance. These findings emphasize the importance of including ferritin in routine first-trimester screening, refining PBM protocols, and guiding early iron supplementation strategies. Future multicenter validation studies are warranted to confirm these results and assess their generalizability across diverse populations.

DECLARATIONS

Ethics Committee Approval: Ethical approval for this study was obtained from the Lokman Hekim University Scientific Research Ethics Committee (Date: 28.03.2024, Approval No: 2024/89).

Informed Consent: Written informed consent was obtained.

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