Obstetrics; *Maternal Fetal Medicine and Perinatology*

Anemia and Postpartum Depression: The Role of Anemia Phenotype

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ABSTRACT

OBJECTIVES: To evaluate the relationship between anemia and postpartum depressive symptoms in term pregnant women and to examine whether different anemia phenotypes and hematological parameters are associated with postpartum depressive symptoms.

STUDY DESIGN: This retrospective observational cohort study included 326 term pregnant women who delivered at Torbalı State Hospital between January and December 2025. Hematological parameters were obtained from the complete blood count performed at hospital admission before labor or cesarean section. Postpartum depressive symptoms were assessed using the Edinburgh Postnatal Depression Scale (EPDS) at the routine postpartum follow-up visit at 4-6 weeks postpartum. Participants were grouped according to EPDS score as <10 and ≥10. Univariate and multivariable logistic regression analyses were performed to identify factors associated with EPDS ≥10.

RESULTS: Anemia was present in 112 women (34.4%). The median EPDS score was 1.0 (IQR: 0.0-4.0), and 32 women (9.8%) had EPDS scores ≥10. Women with EPDS scores ≥10 had significantly lower hemoglobin levels and higher RDW values than those with EPDS scores <10. Anemia was significantly more frequent among women with EPDS ≥10 (84.4% vs. 28.9%, p<0.001). The EPDS score showed a significant negative correlation with hemoglobin level (ρ = -0.221, p < 0.001). After adjustment for potential confounders, anemia remained an independent predictor of EPDS ≥10 (adjusted OR 13.95, 95% CI 5.06-38.44, p<0.001).

CONCLUSION: Anemia was strongly and independently associated with postpartum depressive symptoms in term pregnant women. Evaluation of anemia phenotypes suggests that this relationship may extend beyond simple iron deficiency and may reflect more complex underlying biological mechanisms.

Keywords: Anemia; Hematological parameters; Maternal mental health; Postpartum depression; Pregnancy

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Introduction

Postpartum depression (PPD) is an important problem that occurs in the postpartum period and negatively affects the mother's mood, functionality, and mother-infant interaction. Its prevalence in the general population has been reported to be between 10% and 15% (1,2). PPD not only affects the mother's quality of life, but may also cause long-term negative effects on the cognitive and emotional development of the newborn (3).

In recent years, the number of studies examining the relationship between postpartum depression and biological markers has increased in the literature. Among these markers, anemia, which is a common clinical condition during pregnancy, is also included, and it has been suggested that anemia may be associated with postpartum depressive symptoms (4,5). Anemia may contribute to the development of depression through mechanisms such as reduced tissue oxygenation, changes in neurotransmitter synthesis, and increased physical fatigue (6). However, the results of current studies are heterogeneous, and it has not been clearly shown whether this relationship depends only on hemoglobin level or whether underlying hematological features and inflammatory processes play a role (5).

In this study, we aimed to evaluate the relationship between the presence of anemia and postpartum depressive

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symptoms in term pregnant women. Our secondary aim was to examine the relationship between different anemia types and hematological parameters and postpartum depressive symptoms.

Material and Method

Study Design: A retrospective observational cohort study was performed at Torbali State Hospital between January 2025 and December 2025. Women who gave birth at our center during this period constituted the study population.

Ethical Approval: The study protocol was approved by the Ethics Committee of Ege University Medical Research (approval number: 26-4T/71, date: 02.04.2026). All participants were informed about the study, and written informed consent was obtained from all individuals included in the study. All procedures were carried out in line with the principles of the Declaration of Helsinki.

Study Population: A total of 326 women were included in the study. Women who delivered at 37 weeks of gestation or later during the study period, had a complete blood count test obtained during hospital admission before delivery, had accessible medical records, and had Edinburgh Postnatal Depression Scale (EPDS) data available at 4-6 weeks postpartum were included.

Women with systemic diseases, known psychiatric disorders, antidepressant use, known hematological diseases including thalassemia, missing clinical data, or no EPDS assessment were excluded. In addition, pregnancies complicated by gestational diabetes mellitus, preeclampsia, placenta previa, or other obstetric complications were excluded. Women whose newborns required neonatal intensive care after delivery and those who developed maternal or fetal complications during delivery were also excluded. To minimize the potential confounding effect of infection-related inflammatory changes, women with culture-confirmed urinary tract infection, chorioamnionitis, or postpartum endometritis were also excluded.

Data Collection: Maternal demographic, obstetric, hematologic, and neonatal data were retrospectively extracted from hospital records. Recorded variables included maternal age, gravida, parity, smoking status, weight, height, hemoglobin level, mean corpuscular volume (MCV), red cell distribution width (RDW), platelet count, neutrophil count, lymphocyte count, gestational age at birth, mode of delivery, birth weight, and neonatal sex. BMI was calculated as weight in kilograms divided by height in meters squared (kg/m²). NLR (neutrophil-to-lymphocyte ratio) was calculated as the absolute neutrophil count divided by the absolute lymphocyte count. Maternal hematological parameters were obtained from the complete blood count performed at hospital admission for delivery, before labor or cesarean section.

Definition of Anemia and Anemia Subtypes: Maternal anemia was defined as a hemoglobin level <11.0 g/dL. According to this definition, participants were divided into anemic and non-anemic groups.

Among women with anemia, exploratory subgroup analyses were also performed according to MCV and RDW values. Normocytic anemia was defined as hemoglobin <11.0 g/dL and MCV ≥80 fL. Microcytic anemia was defined as hemoglobin <11.0 g/dL and MCV <80 fL. In an additional exploratory analysis, microcytic anemia with elevated RDW was defined as hemoglobin <11.0 g/dL, MCV <80 fL, and RDW ≥14.5%.

Assessment of Postpartum Depressive Symptoms: Postpartum depressive symptoms were assessed using the Edinburgh Postnatal Depression Scale (EPDS), a 10-item self-report screening tool with a total score ranging from 0 to 30. The EPDS questionnaire was administered during the routine postpartum follow-up visit at 4–6 weeks postpartum. For the primary analysis, participants were categorized into two groups according to their EPDS score: <10 and ≥10. In addition, the frequency of cases with EPDS ≥13 was reported descriptively (7).

Statistical Analysis

All statistical analyses were conducted using Jamovi software (version 2.6.45.0). Normality was assessed using the Shapiro–Wilk test together with histogram and Q-Q plot inspection. Since most continuous variables were not normally distributed, they were expressed as median (IQR), whereas categorical variables were expressed as n (%). Group comparisons according to EPDS category (<10 vs. ≥10) were performed using the Mann-Whitney U test for continuous variables and the chi-square test or Fisher's exact test for categorical variables. Spearman's rank correlation analysis was used to examine the relationship between EPDS scores and continuous variables. To identify factors associated with EPDS ≥10, univariate and multivariable binary logistic regression analyses were performed. The multivariable model included anemia together with age, body mass index, parity, and mode of delivery. Odds ratios (ORs) with 95% confidence intervals (CIs) were reported, and a p-value <0.05 was considered statistically significant.

Results

A total of 326 term pregnant women were included in the study. The median age was 26.0 years (IQR: 23.0-30.0), the median body mass index was 28.2 kg/m² (IQR: 25.4-31.1), and the median gestational age at delivery was 39.0 weeks (IQR: 38.0-40.0). The median hemoglobin level was 11.6 g/dL (IQR: 10.7-12.5), and anemia was present in 112 women (34.4%). The median EPDS score was 1.0 (IQR: 0.0-4.0), and 32 women (9.8%) had EPDS scores ≥10 (Table I).

Table I: *Baseline maternal and obstetric characteristics of the study population*

Variable	Value
Age, years	26.0 (23.0-30.0)
Body mass index, kg/m²	28.2 (25.4-31.1)
Gravidity	2.0 (1.0-3.0)
Parity	1.0 (0.0-2.0)
Neutrophil count	7.66 (6.19-9.14)
Lymphocyte count	2.19 (1.81-2.57)
NLR	3.50 (2.64-4.36)
Hemoglobin, g/dL	11.6 (10.7-12.5)
MCV, fL	85.1 (80.4-89.8)
RDW, %	14.5 (13.1-15.9)
Platelet count, /μL	234,500 (187,750-281,250)
Gestational age at delivery, weeks	39.0 (38.0-40.0)
Birth weight, g	3280 (3019-3541)
EPDS score	1.0 (0.0-4.0)
Smoking, n (%)	13 (4.0)
Anemia, n (%)	112 (34.4)
EPDS ≥10, n (%)	32 (9.8)
Vaginal delivery, n (%)	245 (75.2)
Cesarean delivery, n (%)	81 (24.8)

Data are presented as median (interquartile range, IQR) or n (%). IQR indicates the range between the 25th and 75th percentiles. MCV: Mean corpuscular volume; NLR: Neutrophil-to-lymphocyte ratio; RDW: Red cell distribution width. MCV was available for 325 participants. EPDS: Edinburgh Postnatal Depression Scale.

When participants were compared according to EPDS category, women with EPDS scores ≥10 had significantly lower hemoglobin levels and higher RDW values than those with EPDS scores <10. Median hemoglobin was 10.2 g/dL in the EPDS ≥10 group versus 11.7 g/dL in the EPDS <10 group (p<0.001), whereas median RDW was 15.45% versus 14.40%, respectively (p=0.020). Anemia was also significantly more frequent among women with EPDS ≥10 (84.4% vs. 28.9%, p<0.001). No significant differences were observed between the groups in terms of age, gravidity, parity, BMI, neutrophil count, lymphocyte count, NLR, MCV, platelet count, gestational age at delivery, birth weight, mode of delivery, or smoking status (Table II).

In Spearman's correlation analysis, the EPDS score showed a significant negative correlation only with hemoglobin level (ρ=-0.221, p<0.001). No significant correlation was observed between EPDS score and age, gravidity, parity, BMI, gestational age at delivery, birth weight, neutrophil count, lymphocyte count, NLR, MCV, RDW, or platelet count (Table III).

In univariate logistic regression analysis, both lower hemoglobin level and the presence of anemia were significantly associated with EPDS scores ≥10. Each 1 g/dL increase in hemoglobin was associated with lower odds of EPDS ≥10 (OR 0.55, 95% CI 0.42-0.72, p<0.001), whereas women with

Table II*: Comparison of maternal and obstetric characteristics according to EPDS category*

Variable	EPDS <10 (n=294)	EPDS ≥10 (n=32)	p
Age, years	26.0	24.0	0.123
Gravidity	2.0	2.0	0.777
Parity	1.0	1.0	0.987
BMI, kg/m²	28.34	27.43	0.381
Neutrophil	7.81	7.17	0.243
Lymphocyte	2.21	2.13	0.836
NLR	3.51	3.47	0.431
MCV, fL	85.40	83.45	0.110
RDW, %	14.40	15.45	0.020
Gestational age at delivery, weeks	39.0	39.0	0.887
Birth weight, g	3280	3295	0.791
Hemoglobin, g/dL	11.70	10.20	**<0.001**
Platelet, /μL	234,000	243,500	0.374
Anemia, n (%)	85/294 (28.9)	27/32 (84.4)	**<0.001**
Vaginal delivery, n (%)	221/245 (90.2)	24/245 (9.8)	0.983
Cesarean delivery, n (%)	73/81 (90.1)	8/81 (9.9)	0.983
Smoking, n (%)	32/313 (10.2)	0/13 (0.0)	0.625*

*Continuous variables were compared using the Mann–Whitney U test and are presented as medians. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. * Fisher's exact test.*

Table III: *Spearman correlation analysis between EPDS score and selected maternal and obstetric variables*

Variable	Spearman's rho	p
Age	-0.072	0.195
Gravidity	0.018	0.750
Parity	0.059	0.285
Body mass index	-0.096	0.084
Gestational age at delivery	0.026	0.634
Birth weight	-0.024	0.663
Hemoglobin	-0.221	**<0.001**
Neutrophil count	-0.066	0.235
Lymphocyte count	0.005	0.934
Neutrophil-to-lymphocyte ratio	-0.060	0.276
Mean corpuscular volume	-0.057	0.304
Red cell distribution width	0.083	0.136
Platelet count	0.064	0.248

EPDS: Edinburgh postnatal depression scale

anemia had markedly higher odds of EPDS ≥10 than non-anemic women (OR 13.28, 95% CI 4.95-35.55, p<0.001). RDW and MCV were not significantly associated with EPDS ≥10, although the estimates suggested a possible trend. Age, BMI, parity, NLR, and mode of delivery were also not significantly associated with EPDS ≥10 (Table IV).

After adjustment for age, BMI, parity, and mode of delivery in the multivariable logistic regression analysis, anemia remained independently associated with EPDS scores ≥10. Women with anemia had approximately 14-fold higher odds of EPDS ≥10 compared with non-anemic women (adjusted OR 13.95, 95% CI 5.06-38.44, p<0.001). Age, BMI, parity, and mode of delivery were not significantly associated with EPDS ≥10 (Table V).

In an exploratory subgroup analysis among women with selected anemia phenotypes, EPDS ≥10 was more frequent in the normocytic anemia group than in the microcytic anemia with elevated RDW group (33.3% vs. 16.7%). This difference was significant in chi-square analysis (p=0.044), but not confirmed by Fisher's exact test (p=0.069), and therefore should be interpreted with caution (Table VI)

Table IV: *Univariate logistic regression analysis for predictors of EDPS ≥10*

Predictor	OR	95% CI	p
Age	0.96	0.89-1.03	0.262
BMI	0.97	0.89-1.06	0.536
Parity	0.99	0.73-1.36	0.972
Hemoglobin	0.55	0.42-0.72	<0.001
RDW	1.11	0.98-1.26	0.087
MCV	0.96	0.92-1.01	0.097
NLR	0.90	0.69-1.18	0.450
Anemia	13.28	4.95-35.55	<0.001
Labor mode	1.01	0.43-2.34	0.983

EPDS: Edinburgh postnatal depression scale; OR: Odds ratio; CI: Confidence interval

Table V: *Predictors of EPDS ≥10 in multivariable logistic regression*

Predictor	Adjusted OR	95% CI	p
Age	1.01	0.93-1.10	0.818
Body mass index	0.99	0.90-1.08	0.806
Parity	0.96	0.67-1.38	0.825
Anemia (yes vs no)	13.95	5.06-38.44	<0.001
Labor mode	0.73	0.28-1.90	0.522

Model fit: AIC=183, McFadden R^2=0.185

Table VI: *Comparison of EPDS ≥10 frequency between normocytic anemia and microcytic anemia with elevated RDW among anemic women*

Outcome	Normocytic anemia (n=48)	Microcytic anemia with elevated RDW (n=60)	p
EPDS <10, n (%)	32 (66.7)	50 (83.3)	0.044*
EPDS ≥10, n (%)	16 (33.3)	10 (16.9)	0.044*
Fisher's exact test			0.069

*EPDS: Edinburgh postnatal depression scale; RDW: Red cell distribution width. *Chi-square test*

Discussion

In this study, an independent relationship was shown between the presence of anemia and postpartum depressive symptoms in term pregnant women. The most striking finding of our study was that the likelihood of having an EPDS score ≥10 was markedly increased in anemic women, and that this relationship remained significant in the multivariable analysis. In addition, the negative correlation between hemoglobin levels and EPDS scores showed that lower hemoglobin levels were associated with more severe depressive symptoms. The more frequent occurrence of postpartum depressive symptoms in women with normocytic anemia in the subgroup analyses suggests that the relationship between anemia and postpartum depression may not be explained only by iron deficiency. In this context, normocytic anemia may be a phenotype related to inflammation and the stress response, and the relationship observed in this study suggests a possible role for these mechanisms; however, confirmatory biochemical data are needed.

Postpartum depression is a mood disorder that occurs during the postpartum period and has a multifactorial etiology. Hormonal changes, especially the rapid decline in estrogen and progesterone levels, activation of the hypothalamic-pituitary-adrenal axis, psychosocial stress factors, and sleep disorders are among the main determinants of this process (8,9). While the prevalence of postpartum depression is about 10-15% in developed countries, this rate may reach up to 20% in developing countries (1). Therefore, routine mental health screening during pregnancy and the postpartum period is recommended to ensure early recognition of postpartum depression and to prevent possible adverse outcomes (10). In our study, the rate of cases with an EPDS score ≥10 was 9.8%. This rate is close to the lower limit of the rates reported in the literature, and this may be because all cases included in our study had term pregnancies, high-risk obstetric conditions were excluded due to the nature of the center where the study was conducted, cases with systemic disease or known psychiatric disorders were excluded from the study and all cases included in our study belonged to a relatively homogeneous population in terms of sociocultural characteristics and access to healthcare services.

In recent years, the role of biological factors in the pathogenesis of postpartum depression, especially neurotransmitter synthesis, oxygen-carrying capacity, and inflammatory processes, has been increasingly emphasized in the literature. In this context, anemia stands out as an important clinical condition that may potentially be associated with postpartum depression. It has been suggested that anemia may contribute to the development of depressive symptoms through neurotransmitter imbalance, and that low hemoglobin levels may also increase the risk of postpartum depression through problems such as chronic fatigue, weakness, and reduced physical capacity; this hypothesis has become a popular research topic in recent years (6).

In our study, the significant relationship between anemia and postpartum depression is also consistent with other studies in the literature. Corwin et al. showed that low hemoglobin levels in the postpartum period were associated with higher depressive symptom scores (11). This finding was also supported by later systematic reviews and meta-analyses, which reported that the risk of postpartum depression was significantly increased in women with anemia during pregnancy or in the postpartum period (4,12). However, not all studies have reported consistent findings. In a prospective study, LaVerde et al. did not find a significant relationship between prepartum anemia and postpartum depression (13). This difference may be explained by the fact that postpartum depressive symptoms were evaluated immediately after delivery (postpartum day 3) in that study. In addition, in our cohort, lower hemoglobin levels were correlated with higher EPDS scores, supporting previous evidence that reduced hemoglobin may be related to increased depressive symptoms during the postpartum period (11,14).

One of the notable findings of our study is that not only the presence of anemia, but also its phenotypic features may be related to postpartum depression. In subgroup analyses, postpartum depression was more common in women with normocytic anemia than in the subgroup characterized by microcytic anemia and high RDW. This finding suggests that the relationship between anemia and postpartum depression may not be explained only by iron deficiency. While microcytic anemia is generally associated with iron deficiency, normocytic anemia may more often reflect conditions such as chronic inflammation, the physiological stress response, or impaired functional iron use. In this context, the stronger relationship between normocytic anemia and postpartum depressive symptoms suggests that inflammatory processes and stress response mechanisms may contribute to the development of these symptoms. Indeed, the important role of low-grade inflammation and immune system activation in the pathogenesis of depression has been increasingly emphasized. Studies have shown that increased levels of proinflammatory cytokines may affect neurotransmitter metabolism and lead to changes in serotonin and dopamine pathways, which may contribute to the development of depressive symptoms (15,16). It has also been emphasized that increased levels of inflammatory markers such as IL-6 and CRP in the postpartum period may be associated with depressive symptoms developing later (17). Women with overt infection were excluded to minimize the possible confounding effect of infection-related inflammatory changes. Despite this, the finding of an association between normocytic anemia, which is often linked to chronic inflammation, and postpartum depression suggests that this relationship cannot be explained only by inflammatory processes related to acute infections. Still, rather than low-grade chronic inflammation, stress response mechanisms may be more important in the pathogenesis of postpartum depressive symptoms. These findings suggest that underlying biological pro-

cesses, in addition to low hemoglobin levels, may play an important role in the development of postpartum depression.

Our study has several important strengths. First, the relationship between postpartum depressive symptoms and hematological parameters was evaluated not only based on the presence of anemia, but also by considering anemia phenotypes. While most studies in the literature have treated anemia as a binary variable, separately evaluating normocytic and microcytic anemia subtypes in this study allowed a more detailed interpretation of the findings. To the best of our knowledge, the number of studies evaluating postpartum depressive symptoms by taking anemia phenotypes into account is very limited. In this respect, our study makes an original contribution to the literature. In addition, the study population of 326 women allowed reliable statistical analysis in a single-center and relatively homogeneous cohort. Including only term pregnancies, excluding deliveries with adverse obstetric outcomes, and excluding women with systemic diseases or a known psychiatric history helped reduce the effect of potential confounding factors and allowed a clearer evaluation. Finally, the relationship between hemoglobin levels and postpartum depressive symptoms was assessed using both correlation analyses and multivariable regression models, which strengthens the statistical consistency of our findings. The use of readily available routine clinical parameters also enhances the clinical relevance of the findings.

Our study also has some limitations. First, the retrospective design precludes causal inference; therefore, the findings should be interpreted as associations rather than causal relationships. Second, the single-center design and the relatively homogeneous study population may limit the broader applicability of the findings. The lack of biochemical parameters related to inflammation and iron metabolism, such as ferritin and CRP, limited a more detailed evaluation of the relationship between anemia phenotypes and the underlying biological mechanisms. The small sample size in the subgroup analyses also requires cautious interpretation of these findings. In routine clinical practice, all women are prescribed oral iron supplementation starting from the 12th week of pregnancy; however, regular use of this treatment could not be confirmed in this retrospective cohort.

Conclusions

This study shows that anemia in term pregnant women is not only a hematological condition, but is also strongly and independently associated with postpartum depressive symptoms. In addition, the phenotypic characterization of anemia suggests that this association extends beyond iron deficiency and may involve more complex biological mechanisms, including inflammatory and neuroendocrine pathways.

These findings suggest that readily available hematological parameters may serve as a useful screening tool for the early identification of women at risk for postpartum depression in routine clinical practice. From a clinical perspective, anemia may need to be considered not only as a correctable laboratory finding, but also as a potential warning sign for postpartum mental health. Larger prospective and mechanistic studies are still needed to clarify the causal nature of this association and its underlying mechanisms.

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from the Ethics Committee of Ege University Medical Research (approval number: 26-4T/71, date: 02.04.2026). The study was conducted in accordance with the Declaration of Helsinki.

Consent to participate: All participants were informed about the study, and written informed consent was obtained from all individuals included in the study.

Consent for publication: Not applicable.

Availability of data and materials: The datasets generated and/or analyzed during the current study are not publicly available because they contain potentially identifiable clinical information but are available from the corresponding author on reasonable request.

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