

Inflammatory hematological indices in early partial hydatidiform mole: A retrospective case-control study

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Ethics Committee Approval

The study was approved by the Necmettin Erbakan University Ethics Committee for Non-Drug and Non-Medical Device Research (approval date: January 23, 2026; approval number: 2026/6286). All research procedures were conducted in accordance with the Declaration of Helsinki. Because of the retrospective design and use of anonymized clinical and laboratory data, the ethics committee waived the requirement for informed consent.

Conflict of Interest

No conflict of interest was declared by the authors.

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Previous Presentation

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Abstract

Background/Aim: Early differentiation of partial hydatidiform mole from missed abortion remains challenging because clinical and ultrasonographic findings may overlap during the first trimester. The contribution of systemic inflammatory response to this diagnostic process is unclear. This study aimed to compare inflammatory hematological indices derived from routine complete blood counts among patients with partial hydatidiform mole, missed abortion, and uncomplicated early pregnancy, and to assess whether these parameters provide clinically meaningful diagnostic discrimination during early gestation.

Methods: Electronic medical records of patients presenting to a university hospital between January 1, 2020, and December 31, 2025, were reviewed retrospectively. Patients with histologically confirmed partial hydatidiform mole (n = 32) were compared with patients with missed abortion (n = 35) and uncomplicated early pregnancy (n = 40). Neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), systemic immune-inflammation index (SII), and systemic inflammatory response index (SIRI) were calculated from complete blood counts obtained at initial presentation.

Results: Age did not differ significantly among groups ($P = 0.860$), whereas gestational age differed significantly ($P < 0.001$). No significant differences were observed among groups for NLR, PLR, MLR, SII, or SIRI ($P = 0.740$, $P = 0.290$, $P = 0.110$, $P = 0.850$, and $P = 0.680$, respectively). Gestational age was not significantly correlated with NLR, PLR, MLR, SII, or SIRI ($P = 0.154$, $P = 0.524$, $P = 0.238$, $P = 0.371$, and $P = 0.781$, respectively). Receiver operating characteristic analysis showed poor discriminatory performance for all indices, with AUC values ranging from 0.522 to 0.639.

Conclusion: Complete blood count-derived inflammatory indices did not provide sufficient diagnostic discrimination to support their use as standalone biomarkers for differentiating partial hydatidiform mole from missed abortion during early gestation. Larger prospective studies are needed to clarify the role of systemic inflammation in this clinical setting.

Keywords: hydatidiform mole, gestational trophoblastic disease, inflammation, neutrophils, lymphocytes, first trimester

Introduction

Hydatidiform mole is a gestational disorder resulting from abnormal fertilization and characterized by atypical trophoblastic proliferation. It is the most common benign entity within the spectrum of gestational trophoblastic disease and is classified as complete or partial hydatidiform mole based on genetic and histopathological features [1, 2].

Despite advances in ultrasonography and beta-human chorionic gonadotropin (beta-hCG) testing, early diagnosis, particularly of partial hydatidiform mole, remains challenging. Sonographic findings and beta-hCG levels may have limited diagnostic accuracy during the first trimester, and partial moles are frequently misclassified because their clinical and imaging features overlap with those of other early gestational conditions [3-5]. Missed abortion, a common form of early pregnancy loss, may show similar ultrasonographic features, making early differentiation from partial hydatidiform mole difficult in routine practice [6]. Nevertheless, this distinction is clinically important because molar pregnancies require post-evacuation beta-hCG surveillance and specialized follow-up because of the risk of gestational trophoblastic neoplasia. Some partial molar pregnancies may also continue to later gestational weeks if they are not recognized early [6, 7].

Molar pregnancy may alter maternal immune and inflammatory responses through abnormal trophoblastic proliferation and placental development. Increased expression of inflammatory mediators and placental factors in molar gestational tissue suggests that systemic inflammatory changes may accompany molar pregnancy [8].

Hematological indices derived from routine complete blood counts, including the neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), and systemic inflammatory response index (SIRI), have been investigated as accessible markers of systemic inflammation in various obstetric and medical conditions [9-11]. Because these indices reflect different components of the systemic inflammatory response, they have attracted interest as potential diagnostic and prognostic biomarkers in diverse clinical settings.

However, evidence regarding the diagnostic value of these inflammation-based hematological indices for distinguishing partial hydatidiform mole from missed abortion remains limited. This distinction is particularly relevant because the two conditions often present with similar clinical and ultrasonographic findings during early pregnancy but differ substantially in subsequent management and follow-up.

Therefore, this study aimed to compare inflammatory hematological indices among patients with partial hydatidiform mole, missed abortion, and uncomplicated early pregnancy and to determine whether these routinely available indices provide meaningful diagnostic discrimination, particularly between partial hydatidiform mole and missed abortion.

Materials and methods

This retrospective case-control study was conducted in the Department of Obstetrics and Gynecology, Faculty of Medicine, Necmettin Erbakan University, Konya, Türkiye.

Electronic medical records of patients evaluated for early pregnancy between January 1, 2020, and December 31, 2025, were reviewed. Patients with complete clinical and laboratory data were eligible for inclusion.

Three groups were defined. Patients with partial hydatidiform mole confirmed by histopathological examination constituted the first group. Patients with missed abortion, diagnosed according to the accepted ultrasonographic criteria for early pregnancy loss during first-trimester evaluation [12], constituted the second group. In accordance with routine institutional practice, products of conception obtained after uterine evacuation in the missed abortion group were also submitted for histopathological examination. The control group comprised patients evaluated during the first trimester whose pregnancies progressed without complications and resulted in term live birth. Pregnancy outcomes were verified from hospital delivery records. To ensure complete outcome ascertainment, the uncomplicated early pregnancy group was selected retrospectively only from pregnancies with completed delivery records confirming term live birth.

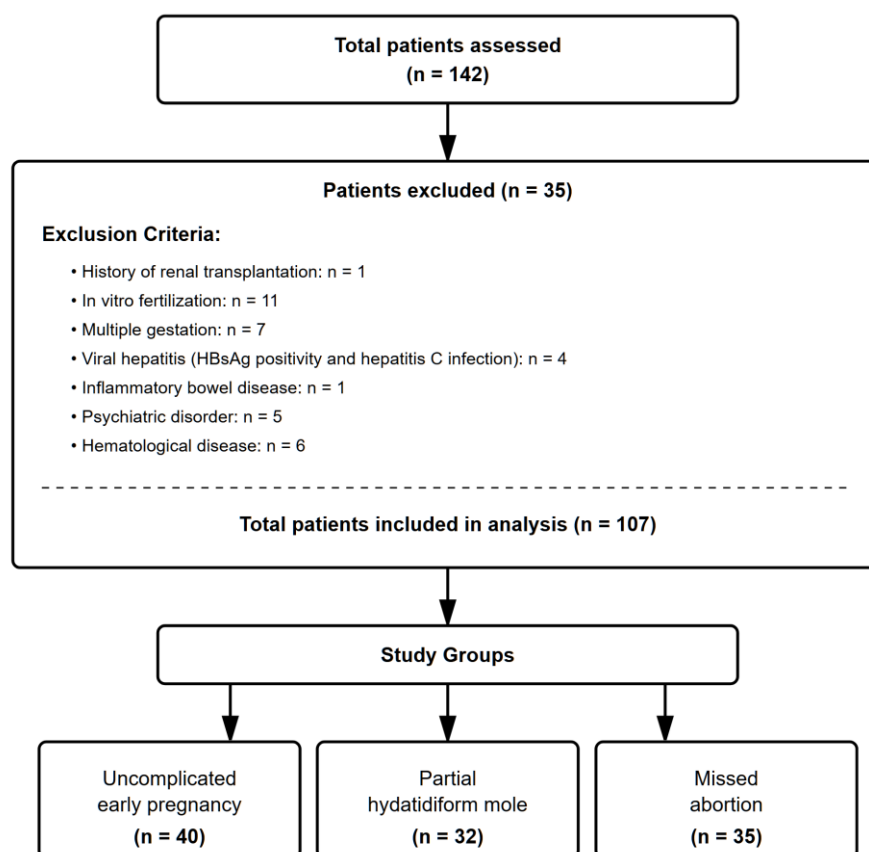
The missed abortion group was selected as the most clinically relevant comparison group because partial hydatidiform mole frequently mimics missed abortion during first-trimester evaluation. The uncomplicated early pregnancy group was included to provide reference values for inflammatory hematological indices during normal early gestation. Gestational age was determined from the last menstrual period and confirmed by first-trimester ultrasonographic measurements.

Patients with a history of renal transplantation, pregnancies conceived through in vitro fertilization, multiple gestations, viral hepatitis (hepatitis B surface antigen positivity or hepatitis C infection), inflammatory bowel disease, psychiatric disorders, hematological diseases, or clinical evidence of acute infection were excluded. A total of 142 patients were initially assessed during the study period. After 35 patients were excluded according to the predefined criteria, 107 patients remained for analysis: 32 with partial hydatidiform mole, 35 with missed abortion, and 40 with uncomplicated early pregnancy. The patient selection process is shown in Figure 1.

Partial hydatidiform mole was diagnosed by routine histopathological examination of products of conception. A single pathologist performed the histopathological evaluations, and p57 immunohistochemical staining was used in all cases as an ancillary aid to diagnostic classification. Ploidy analysis was not routinely performed. No equivocal cases requiring additional ploidy analysis or genotyping were encountered during the study period. Inflammatory hematological indices, including NLR, PLR, MLR, SII, and SIRI, were calculated from routine complete blood count parameters.

Calculations used absolute neutrophil, lymphocyte, monocyte, and platelet counts obtained by automated complete blood count analysis; leukocyte percentages were not used. The same hematology analyzer system was used throughout the study period (2020-2025). SII was calculated as (neutrophil count $\times$ platelet count)/lymphocyte count, and SIRI was calculated as (neutrophil count $\times$ monocyte count)/lymphocyte count.

Demographic data were obtained from patient records, and laboratory parameters were derived from complete blood

Figure 1. Flow diagram of patient selection and group allocation

Among 142 patients assessed for eligibility, 35 were excluded according to predefined exclusion criteria. A total of 107 patients were included in the final analysis and classified into three groups: partial hydatidiform mole (n = 32), missed abortion (n = 35), and uncomplicated early pregnancy (n = 40). Abbreviations: HBsAg: hepatitis B surface antigen.

counts obtained during the first trimester. All hematological measurements were based on blood samples collected at initial admission and before any medical or surgical intervention. Acute infection was excluded through medical record review for a documented clinical diagnosis or recorded fever at presentation.

The study protocol was approved by the Necmettin Erbakan University Ethics Committee for Non-Drug and Non-Medical Device Research (approval date: January 23, 2026; approval number: 2026/6286). The study was conducted in accordance with the Declaration of Helsinki. Because of the retrospective design and use of anonymized clinical and laboratory data, the ethics committee waived the requirement for informed consent. Patient confidentiality was maintained throughout data extraction and analysis. This study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed with the Shapiro-Wilk test. Normally distributed variables are presented as mean (SD), and non-normally distributed variables are presented as median (minimum-maximum).

Age, which was normally distributed, was compared among the three groups using one-way analysis of variance. Continuous variables without normal distributions were compared using the Kruskal-Wallis test. When an overall difference was statistically significant, pairwise comparisons were performed using the Mann-Whitney U test with Bonferroni correction.

To assess potential confounding by gestational age, associations between gestational age and inflammatory hematological indices were examined using Spearman's rank correlation analysis. Multivariable adjusted analyses were not performed because of the relatively limited sample size.

Receiver operating characteristic (ROC) curve analyses were performed to evaluate the ability of inflammatory hematological indices to distinguish partial hydatidiform mole from missed abortion. The area under the curve (AUC) and 95% confidence interval (CI) were calculated for each marker.

A P -value < 0.05 was considered statistically significant for all analyses.

Results

A total of 107 patients were included. Demographic characteristics, gestational age, and inflammatory hematological indices are summarized in Table 1. Age did not differ significantly among the groups (one-way analysis of variance, $P = 0.860$).

Table 1. Demographic characteristics and inflammatory hematological indices of patients

Variable	Uncomplicated early pregnancy (n = 40)	Missed abortion (n = 35)	Partial hydatidiform mole (n = 32)	P-value
Age (years)	29.9 (4.5)	30.0 (5.5)	29.3 (5.9)	0.860
Gestational age (weeks)	12 (6-13) ^a	10 (7-13) ^b	8.5 (5-13) ^c	<0.001
NLR	2.92 (1.2-7.1)	3.01 (0.7-6.1)	2.65 (1.76-8.09)	0.740
PLR	130.6 (63.1-210.9)	118.4 (66.4-266.4)	133.45 (67-272.7)	0.290
MLR	0.24 (0.14-0.41)	0.22 (0.11-0.49)	0.26 (0.17-0.81)	0.110
SII	746.93 (262.8-1672.5)	803.83 (153.3-1740.9)	790.07 (314.9-2427.3)	0.850
SIRI	1.493 (0.6-3.8)	1.53 (0.4-4.6)	1.53 (0.9-7.3)	0.680

Abbreviations: NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio, MLR: monocyte-to-lymphocyte ratio, SII: systemic immune-inflammation index, SIRI: systemic inflammatory response index, SD: standard deviation. Data are presented as mean (SD) or median (range). Different superscript letters indicate statistically significant pairwise differences after Bonferroni-corrected Mann-Whitney U testing. $P < 0.05$ was considered statistically significant.

Gestational age differed significantly among the groups (Kruskal-Wallis test, $P < 0.001$). Bonferroni-corrected post hoc comparisons showed significant differences between partial hydatidiform mole and uncomplicated early pregnancy (adjusted $P < 0.001$), between missed abortion and uncomplicated early pregnancy (adjusted $P < 0.001$), and between partial hydatidiform mole and missed abortion (adjusted $P = 0.030$).

No statistically significant group differences were observed in NLR, PLR, MLR, SII, or SIRI (Kruskal-Wallis test; $P = 0.740$, $P = 0.290$, $P = 0.110$, $P = 0.850$, and $P = 0.680$, respectively). The distributions of all indices showed broad overlap across the groups, with no consistent pattern suggesting greater systemic inflammation in partial hydatidiform mole.

Spearman's rank correlation analysis showed no significant associations between gestational age and NLR ($\rho = 0.139$, $P = 0.154$), PLR ($\rho = 0.062$, $P = 0.524$), MLR ($\rho = -0.115$, $P = 0.238$), SII ($\rho = 0.087$, $P = 0.371$), or SIRI ($\rho = -0.027$, $P = 0.781$) (Table 2).

ROC curve analyses showed poor discrimination between partial hydatidiform mole and missed abortion for all evaluated indices (Table 3). AUC values ranged from 0.522 to 0.639. MLR had the highest AUC (0.639, 95% CI 0.507-0.772; $P = 0.050$), but none of the markers achieved clinically meaningful diagnostic accuracy.

Table 2. Correlation between gestational age and inflammatory hematological indices

Variable	Spearman rho	P-value
NLR	0.139	0.154
PLR	0.062	0.524
MLR	-0.115	0.238
SII	0.087	0.371
SIRI	-0.027	0.781

Abbreviations: rho: Spearman correlation coefficient, NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio, MLR: monocyte-to-lymphocyte ratio, SII: systemic immune-inflammation index, SIRI: systemic inflammatory response index.

Table 3. Receiver operating characteristic analysis of inflammatory hematological indices for differentiating partial hydatidiform mole from missed abortion

Marker	AUC	95% CI	P-value
NLR	0.558	0.418-0.698	0.415
PLR	0.610	0.475-0.745	0.123
MLR	0.639	0.507-0.772	0.050
SII	0.522	0.383-0.662	0.754
SIRI	0.537	0.396-0.678	0.607

Abbreviations: AUC: area under the curve, CI: confidence interval, NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio, MLR: monocyte-to-lymphocyte ratio, SII: systemic immune-inflammation index, SIRI: systemic inflammatory response index, ROC: receiver operating characteristic.

Discussion

Although several studies have reported differences in systemic inflammatory markers between molar and normal pregnancies [13, 14], early pregnancy is itself a physiologically pro-inflammatory state in which systemic inflammatory indices may be elevated [15]. This background may obscure pathological inflammation associated with molar pregnancy, particularly in partial moles, in which trophoblastic proliferation is less pronounced than in complete moles. It remains uncertain whether inflammation in partial hydatidiform mole exceeds the inflammatory milieu of early gestation. The absence of group differences in NLR, PLR, MLR, SII, and SIRI in this study suggests that complete blood count-derived inflammatory indices have limited value for distinguishing partial hydatidiform mole from missed abortion or uncomplicated early pregnancy.

Several factors may explain the difference between the present findings and earlier reports of inflammatory changes in molar pregnancy. First, many previous studies combined complete and partial molar pregnancies or predominantly included complete

moles, which have more pronounced trophoblastic proliferation and may produce a stronger systemic inflammatory response [16]. In contrast, this study focused specifically on partial hydatidiform mole, which may be associated with subtler inflammatory changes. Second, early pregnancy and pregnancy loss are both accompanied by physiological and pathological inflammatory changes that may reduce the contrast between groups [17, 18].

The evaluated hematological indices are also broad, nonspecific markers of systemic inflammation and may be influenced by physiological stress, vaginal bleeding, subclinical infection, and chronic medical conditions [19]. These factors may have limited the ability of routine complete blood count-derived indices to detect disease-specific inflammatory changes in partial hydatidiform mole.

NLR and PLR values in patients with missed abortion and uncomplicated early pregnancy were similar, consistent with some previous reports [9, 10]. In a systematic review and meta-analysis, Hantoushzadeh et al. [11] reported higher NLR and PLR values in recurrent pregnancy loss and spontaneous abortion. However, the included studies involved heterogeneous populations with different abortion subtypes and did not consistently control for potential confounders such as infection, chronic inflammatory conditions, and gestational age. Differences in patient selection and the timing of blood sampling relative to pregnancy failure may therefore account for the inconsistent findings.

Direct comparison of partial hydatidiform mole with missed abortion showed no differences in inflammatory hematological indices. ROC curve analyses supported this finding by demonstrating poor discrimination for all evaluated indices. Although MLR had the highest AUC, its diagnostic accuracy remained modest and below a clinically useful level. Routine inflammation-based hematological indices are therefore unlikely to serve as reliable standalone markers for differentiating partial hydatidiform mole from missed abortion during early gestation.

Both pathological conditions may produce similar inflammatory response patterns during early gestation. Under the conditions of this study, complete blood count-derived inflammatory indices did not meaningfully distinguish the groups. Whether this similarity reflects a shared pathway of placental dysfunction or the common inflammatory background of early pregnancy remains unclear. Direct comparisons of partial hydatidiform mole and missed abortion in early gestation remain scarce, limiting the interpretation of these findings.

From a clinical perspective, partial hydatidiform mole and missed abortion constitute the most relevant differential diagnostic comparison because they may present similarly during early pregnancy evaluation and often lead to uterine evacuation. The uncomplicated early pregnancy group primarily provided reference values for inflammatory hematological indices during normal early gestation.

The principal clinical implication is that routine complete blood count-derived inflammatory indices should not be used to determine whether a suspected early pregnancy loss represents partial hydatidiform mole. Although NLR, PLR, MLR, SII, and SIRI are inexpensive and readily available, neither group comparisons nor ROC curve analyses showed clinically meaningful discrimination. Histopathological examination of

products of conception therefore remains essential for definitive diagnosis and appropriate post-evacuation beta-hCG surveillance.

Gestational age differed among the groups. Partial molar pregnancies were identified earlier, whereas uncomplicated pregnancies were evaluated at later gestational ages, a pattern that may reflect differences in clinical presentation and the timing of routine prenatal care. No association was identified between gestational age and any evaluated inflammatory index. Gestational age alone is therefore unlikely to fully explain the absence of group differences, although residual confounding cannot be excluded.

The simultaneous comparison of partial hydatidiform mole with both missed abortion and uncomplicated early pregnancy is a strength of this study. Age distributions were comparable, reducing the likelihood of confounding by age. The cohort was restricted to early gestation, when diagnostic uncertainty is greatest and pre-evacuation discrimination is most clinically relevant. Multiple indices reflecting different components of systemic inflammation were assessed. Because these indices are derived from routine complete blood counts, they are inexpensive and widely available.

This study contributes clinically relevant negative evidence: routine complete blood count-derived inflammatory indices add little diagnostic value when differentiating partial hydatidiform mole during early gestation, the period in which diagnostic uncertainty is greatest.

Limitations

The retrospective design, single-center setting, and relatively limited sample size are important limitations. In particular, the small number of patients with partial hydatidiform mole may have reduced the statistical power to detect subtle differences in inflammatory hematological indices. No a priori or post hoc power analysis was performed; therefore, a type II error cannot be excluded.

Residual confounding is another limitation. Although major exclusion criteria were applied to minimize factors known to affect inflammatory markers, unmeasured variables may still have influenced the evaluated indices. Gestational age differed among the groups, but multivariable adjusted analyses were not performed because the limited sample size restricted the feasibility and reliability of more complex models. Consequently, confounding by gestational age cannot be completely excluded.

The analyzed hematological parameters are broad and nonspecific markers of systemic inflammation and may be affected by physiological stress, vaginal bleeding, subclinical infection, and other clinical factors that could not be fully controlled in a retrospective study. The analysis was also limited to inflammation-related indices derived from routine complete blood counts; cytokine profiles and other biochemical inflammatory markers were not evaluated. In addition, serum beta-hCG levels were not included because beta-hCG data were not available for all patients owing to the retrospective study design. Beta-hCG is central to the biological behavior, diagnosis, and clinical suspicion of molar pregnancy, the lack of adjustment for beta-hCG is an important limitation.

Other limitations arise from retrospective data collection. Complete blood counts were obtained during routine clinical care, and the timing of blood sampling relative to symptom onset,

vaginal bleeding, or pregnancy failure could not be standardized. This variability may have affected inflammatory marker levels and contributed to interindividual heterogeneity.

Histopathological diagnosis served as the reference standard; however, diagnostic misclassification cannot be completely excluded in a retrospective pathology-based study. All diagnoses were established by routine histopathological evaluation, and p57 immunohistochemical staining was performed in all cases classified as partial hydatidiform mole.

Finally, the uncomplicated early pregnancy group included pregnancies that ultimately resulted in term live birth and therefore represented a selected healthy control population. Although this approach allowed estimation of baseline inflammatory index ranges during early gestation, these controls may not fully represent the heterogeneous population presenting with early pregnancy symptoms in routine practice. The findings should therefore be interpreted within these methodological limitations.

Conclusion

Inflammatory hematological indices did not provide clinically meaningful discrimination between partial hydatidiform mole and missed abortion in this cohort. Histopathological examination of products of conception remains essential for definitive diagnosis and appropriate beta-hCG surveillance. These indices should not be used as standalone diagnostic markers in the differential evaluation of partial hydatidiform mole. Larger prospective studies incorporating complementary biomarkers are needed to define whether systemic inflammation has a clinically useful role in this setting.

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