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Value of hematological indices NLR, PLR, and MPV to determine the clinical outcome of placental abruption in women regarding stillbirth

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ABSTRACT

OBJECTIVE: This study was conducted to elucidate the predictive value of hematological indices, the neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), and mean platelet volume (MPV), to determine the clinical outcome of placental abruption in women regarding stillbirth.

METHODS: This retrospective review of medical charts was performed in a tertiary center experienced for maternal, fetal, and neonatal care, including 89 pregnant women with placental abruption with or without stillbirth. The results of the hemogram tests with hematological indices, including the NLR, PLR, and MPV, which are the routinely obtained parameters both at admission and 4 h postoperatively, were correlated with other clinical parameters.

RESULTS: The findings showed that although there were remarkable changes in some of the clinical features of women with placental abruption with or without stillbirth, in general, the study groups were found comparable regarding these variables. The values of NLR, PLR, and MPV in women with stillbirth presented remarkable changes when hemogram tests were used as pre-operative and post-operative laboratory examinations, although these changes did not correlate with each other meaningfully.

CONCLUSION: Stillbirth is one of the most important complications of placental abruption requiring rapid diagnosis and regular follow-up after its surgical management. To fine-tune emergent management of placental abruption in women with stillbirth, the indices of NLR, PLR, and MPV calculated at the first admission as well as during follow-up of the patients have clinical value as easily obtainable laboratory findings like other hematological parameters.

Keywords: Mean platelet volume; neutrophil to lymphocyte ratio; placental abruption; platelet to lymphocyte ratio; stillbirth.

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The term placental abruption is a definition that refers to the minimal to complete separation of the placental tissue from the underlying myometrium, often spontaneously, in pregnancies in which the fetus is viable. It is a frequent etiology of emergent bleeding vaginally in the second half of pregnancy [1–3]. Placental abruption develops in 0.4–1% of pregnant women, and at the time of presentation, the placenta is often significantly separated, and the fetus is affected [4]. Risk factors for placental abruption include multiparity, smoking, alcohol consumption, premature rupture of membranes, drug use (such as cocaine), hypertension in pregnancy, fetal growth restriction, prior history of placental abruption, in vitro fertilization, and thrombophilia [5, 6]. Prior placental abruption is considered a strong risk factor that increases its incidence 10–30 times in current pregnancy. The other most common risk factors are smoking and hypertension during pregnancy [7].

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Placental abruption with significant complications, such as disseminated intravascular coagulopathy (DIC), uncontrolled blood loss, or emergency hysterectomy, may lead to various maternal, fetal, and neonatal morbidities and mortality when diagnosed late or managed in health centers with limited resources [8]. Major fetal complications include fetal growth restriction, unreliable fetal heart rate, and stillbirth [9]. Important neonatal complications are composed of preterm birth and neonatal death [10].

The term "stillbirth" refers to the delivery of a fetus ≥20 weeks of gestation with no signs of life. Worldwide, the stillbirth rate has been falling from approximately 35 deaths per 1000 live births in 1980 to approximately 15 deaths per 1000 live births in 2015 [11]. Stillbirth can be an end result of various maternal, fetal, and placental disorders. Abruptio placentae occur in approximately 1% of pregnancies but account for between 10% and 20% of all stillbirths [12].

To decrease complications of placental abruption, there is a need for proper use of laboratory tests, especially hematological ones. These tests are required for baseline evaluation and during follow-up of patients postoperatively. There is a meaningful correlation between the clinical severity of placental abruption and the hematological status of the patients. There are not enough data about the importance of hematological parameters at baseline and follow-up laboratory assessment [13, 14]. Obstetrically, abruption severity is mainly encountered during ultrasound examination before delivery [15]; however, if the placenta is located posteriorly and placental abruption is mild, the diagnostic accuracy of ultrasonographic examination is relatively suboptimal [16]. Inadequate diagnosis causing insufficient assessment of the severity of placental abruption may lead to the delay of obstetrical management, which can be dangerous for the lives of the mother and newborn dyads.

Although the previous studies revealed several findings of placental abruption to determine the severity of disease and no laboratory test can definitively help perform the differential diagnosis of sudden placental abruption, multiple laboratory tests are needed in the clinical management of these cases. A full blood cell count may not be reliable to estimate acute blood loss and determine the current hemodynamic situation in patients with placental abruption. This may be, in part, because the hematocrit level is more reliably lowered several hours after acute hemorrhage and inadvertently lowered by oversupplying crystalloid fluids for resuscitation in emergency care. Within this perspective, no studies specifically evaluated the place of hematological indices, the neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), and mean platelet volume (MPV), in the work-up of diagnosis of placental abruption with or without stillbirth in obstetric emergency conditions [13], since they have merit in determining the severity of placental abruption earlier than hemoglobin and hematocrit levels. This study aimed to assess the value of hematological indices NLR, PLR, and MPV to determine the clinical outcome of placental abruption in women regarding stillbirth.

Highlight key points

- Placental abruption in women with stillbirth is an important cause of both maternal morbidity and neonatal morbidity and mortality. Prompt diagnosis and treatment can reduce these risks.
- The NLR, PLR, and MPV values measured at the first admission and during follow-up of the patients who were diagnosed with placental abruption in women with stillbirth can provide important clues to choose required treatment modalities for obstetricians according to the severity of condition.
- To fine tuning of acute management of placental abruption in women with stillbirth, the NLR, PLR, and MPV values measured at the first admission as well as during follow-up of the patients have clinical value as fastly obtainable laboratory findings like hematological indices.

MATERIALS AND METHODS

This retrospective study reviewed medical charts was performed in a center for maternal, fetal, and neonatal medicine in Haseki Training and Research Hospital, with 89 pregnant women admitted with placental abruption. There were 7077 pregnant women who were delivered between 2016 and 2020 in the study period. The approval of the Haseki Training and Research Hospital Clinical Research Ethics Committee was obtained for this study (date: August 04, 2021, number: 62-2021) and the valid Helsinki Declaration. At the first admission, the diagnosis of placental abruption was confirmed primarily on ultrasonographic examination or one or more of the following clinical features, including uterine tenderness, abdominal pain, and vaginal bleeding or with or without abnormal fetal heart activity. Placental abruption was reconfirmed during cesarean delivery by local examination of the placenta for separation and the presence of a retroplacental hematoma. The suspected placenta was sent to the Pathology Laboratory to confirm the presence of the abruption.

Table 1. Selected clinical characteristics of women with placental abruption with or without stillbirth

	Stillbirth		
	No (n=72)	Yes (n=17)	p
Age (years)	29.1±7.3	30.8±5.4	0.36
Gravidity	2 (1–7)	3 (1–9)	0.25
Parity	1 (0–3)	2 (0–3)	0.12
Mode of delivery			0.35
No delivery	20 (27.8%)	4 (23.5%)	
Vaginal delivery	31 (43.1%)	5 (29.4%)	
Cesarean delivery	21 (29.2%)	8 (47.1%)	
Related complaints			
Pelvic pain	14 (19.4%)	1 (5.9%)	
Vaginal bleeding	35 (48.6%)	8 (47.1%)	
Pelvic pain and vaginal bleeding	4 (5.6%)	6 (35.3%)	
History of trauma	1 (1.4%)	0 (0%)	
Acute fetal distress during labor	13 (18.1%)	1 (5.9%)	
History of eclampsia	5 (6.9%)	1 (5.9%)	
Comorbidities			
Hypertension	19 (26.4%)	7 (41.2%)	
Diabetes mellitus	1 (1.4%)	0 (0%)	
Epilepsy	1 (1.4%)	0 (0%)	
Familial Mediterranean fever	1 (1.4%)	0 (0%)	
Hypothyroidism	2 (2.8%)	1 (5.9%)	
Placental insertion			0.20
Anterior	39 (54.2%)	13 (76.5%)	
Posterior	23 (31.9%)	2 (11.8%)	
Lateral	10 (13.9%)	2 (11.8%)	
Abnormality of placental location			
Low lying placenta	3 (4.2%)	1 (5.9%)	
Placenta previa	2 (2.8%)	1 (5.9%)	
Ultrasonographic sign of placental abruption	26 (36.1%)	11 (64.7%)	0.03
Ratio of abrupted placental area	30 (10–100%)	80 (15–100%)	0.001

Data were presented as mean with standard deviation, median with interquartile range, or number (%) as appropriate.

Medical charts of the study participants for this period were screened for baseline clinical, obstetric and ultrasonographic features, presence of stillbirth, pre-and post-delivery laboratory results, required transfusion and its amount, and neonatal outcomes of women with placental abruption with or without stillbirth were collected. A composite poor maternal outcome was recorded if any of the following features were present: hemorrhagic shock and DIC. The results of the hemogram tests, which are the targeted parameters of the study and routinely applied both at admission and 4 h postoperatively, were recorded. Exclusion criteria included clinical conditions, including known acute or chronic maternal infections, hematological disorders (disorders affecting thrombocyte function and hematological cancers), and chronic systemic disorders affecting the results of complete blood count.

Statistical Analysis

Statistical analysis was performed with the IBM SPSS v23 software (USA). Descriptive statistical results were as mean (standard deviation), median (interquartile range), and count (percentage). The normality of the continu-

TABLE 2. Obstetrical parameters of the women with placental abruption with or without stillbirth

	Stillbirth		
	No (n=72)	Yes (n=17)	p
Transfusion	0 (0–11)	1 (0–9)	0.001
Couvelaire sign			0.003
No	68 (94.4%)	12 (70.6%)	
Yes	4 (5.6%)	5 (29.4%)	
Composite poor maternal outcome	1 (1.4%)	4 (23%)	
Gestational age at delivery (weeks)	35 (23–42)	32 (27–39)	0.068
Birth weight (g)	2309.1±861.9	1828.8±840.8	0.041
Neonatal gender			0.59
Female	39 (54.2%)	8 (47.1%)	
Male	33 (45.8%)	9 (52.9%)	
Apgar score			
1 min	5.9±2.7		
5 min	7.6±2.2		
Need for NICU admission	52 (73.2%)		
Stay in NICU (days)	6.5 (0–366)		

Data were presented as mean with standard deviation, median with interquartile range, or number (%) as appropriate. NICU: Neonatal intensive unit.

ous variables was checked with the Kolmogorov–Smirnov normality test. For the non-parametric variables, the Mann–Whitney test was used and for the parametric data, the t-test was used. For the pre-and post-operative hematological parameters, paired t or Wilcoxon rank tests were used as appropriate. For categorical variables, the Chi-square test was used. P<0.05 was considered a statistically significant difference of percentages.

RESULTS

In the present study, we collected clinical and hematological data of 89 women with placental abruption. Of these women, 17 had a stillbirth and 72 had no stillbirth. Table 1 presents the selected clinical findings of women with placental abruption with or without stillbirth. The mean ages of women with or without stillbirth were similar (30.8±5.4 vs. 29.1±7.3; p>0.05). The median gravidities and parities of women with or without stillbirth were comparable (3 [1–9] vs. 2 [1–7] and 2 [0–3] vs. 1 [0–3], respectively; p>0.05). There were no significant differences between the rates of vaginal and cesarean deliveries of women with or without stillbirth (5 [29.4%] vs. 31 [43.1%] and 8 [47.1%] vs. 21 [29.2%], respectively; p>0.05). The most common complaints of women with or without stillbirth were vaginal bleeding and pelvic pain. Hypertension was the most common comorbidity of women with or without stillbirth. The rates of anterior, posterior, and lateral placental insertions were comparable (13 [76.5%] vs. 39 [54.2%], 2 [11.8%] vs. 23 [31.9%], and 2 [11.8%] vs. 10 [13.9%], respectively; p>0.05). Seven women had an abnormality of placental location. The rate of ultrasonographic signs of placental abruption in the women with stillbirth was significantly higher than without stillbirth (64.7% vs. 36.1%; p<0.05). The ratio of the abrupted placental area was significantly higher in the women with stillbirth than without stillbirth (80 [15–100%] vs. 30 [10–100%]; p<0.05).

Table 2 shows the obstetric findings of women with placental abruption with or without stillbirth. The number of transfused blood units in the women with stillbirth was significantly higher than that of the women without stillbirth (1 [0–9] vs. 0 [0–11]; p<0.05). The presence of the Couvelaire sign in women with stillbirth was significantly higher than the women without stillbirth (5 [29.4%] vs. 4 [5.6%], respectively; p<0.05). The ratios of composite poor maternal outcome were 23% (n=4) versus 1.4% (n=1) in the women with stillbirth and without stillbirth, respectively. There was no significant difference between the study groups regarding the median gestational age at delivery (p>0.05).

TABLE 3. Hematological findings of the women with placental abruption with or without stillbirth

	Stillbirth							
	No (n=72)			Yes (n=17)				
	Preoperative	Postoperative	p (preoperative-postoperative)	Preoperative	Postoperative	p (preoperative-postoperative)	p Preoperative	p Postoperative
WBC (10^3 uL)	13.2±5.1	13.7±4.2	0.04	13.1±3.0	10.3±3.1	0.45	0.94	0.002
RBC (10^6 uL)	3.9±0.6	3.5±0.4	0.001	3.6± 0.7	3.3±0.5	0.04	0.03	0.052
Hb (g/dL)	10.9±1.7	9.8±1.3	0.001	10.6±2.1	9.7±1.4	0.10	0.52	0.53
Hct (%)	32.5±4.9	29.3±3.7	0.001	30.5±7.1	28.1±4.6	0.11	0.16	0.25
PLT (10^3 uL)	221.1±104.6	219.7±130.0	0.86	166.7±74.7	189.3±81.0	0.37	0.04	0.37
MCV (fL)	82.5±7.7	82.7±9.0	0.64	79.8±14.7	85.8 ±6.0	0.09	0.28	0.09
MCH (pg)	27.6±3.0	27.7 ±2.8	0.36	29.8±2.8	29.9±2.0	0.83	0.008	0.002
MCHC (g/dL)	33.5 (30.5–38.1)	33.4 (28.3 – 36.6)	0.94	33.9 (13.6–37.1)	34.9 (32.0–37.3)	0.58	0.02	0.001
RDW (%)	14.7±1.9	14.8±2.0	0.001	14.3±2.4	14.8±1.8	0.001	0.51	0.85
NEU (10^3 uL)	10.3±4.9	11.4±4.2	0.25	10.0±4.0	7.8±2.9	0.97	0.78	0.002
LYM (10^3 uL)	2.1±0.8	1.6±0.6	0.11	1.7±0.8	1.7±0.6	0.95	0.10	0.58
EO (10^3 uL)	0.1 (0–1.6)	0.1 (0–0.5)	0.23	0.1 (0–1.0)	0.2 (0–0.6)	0.20	0.97	0.013
MONO (10^3 uL)	0.7 (0.1–2.1)	0.6 (0.1–1.7)	0.77	0.7 (0–1.5)	0.6 (0.2–1.4)	0.16	0.56	0.18
BASO (10^3 uL)	0.0 (0–0.1)	0.01 (0–0.1)	0.002	0 (0–0.1)	0.02 (0.01–0.1)	0.90	0.83	0.25
NEU% (10^3 uL)	76.7±8.8	81.2±8.1	0.004	78.8±7.8	75.2±6.6	0.21	0.35	0.006
LYM% (10^3 uL)	17.17±7.9	12.8±6.2	0.001	15.1±8.1	17.1±5.3	0.41	0.32	0.01
EO% (10^3 uL)	0.69 (0–3.9)	0.69 (0–3.6)	0.51	0.60 (0–2.2)	1.77 (0.1–6.2)	0.016	0.71	0.003
MONO% (10^3 uL)	5.3 (1.3–11.2)	5.1 (0.7–11.2)	0.63	5.9 (2.6–9.7)	5.5 (2.4–1)	0.57	0.23	0.73
BASO% (10^3 uL)	0.1 (0–0.5)	0.1 (0–0.4)	0.03	0.2(0–0.6)	0.25 (0.1–1.5)	0.49	0.90	0.01
PCT (%)	0.5±2.2	0.2±0.1	0.29	0.2±0.1	0.1±0.1	0.92	0.56	0.3
PDW (fL)	14.5 (10.2–19)	13.1 (5.9–17.5)	0.001	13.0 (10.5-17.3)	12.3 (9.3-16.6)	0.10	0.12	0.02

Data were presented as mean with standard deviation or median with interquartile range as appropriate. WBC: White blood cell count; RBC: Red blood cell count; Hb: Hemoglobin; Hct: Hematocrit; PLT: Platelet; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; RDW: Red cell distribution width; NEU: Neutrophils; LYM: Lymphocytes; EO: Eosinophils; MONO: Monocytes; BASO: Basophils; PCT: Platelet crit; PDW: Platelet distribution width.

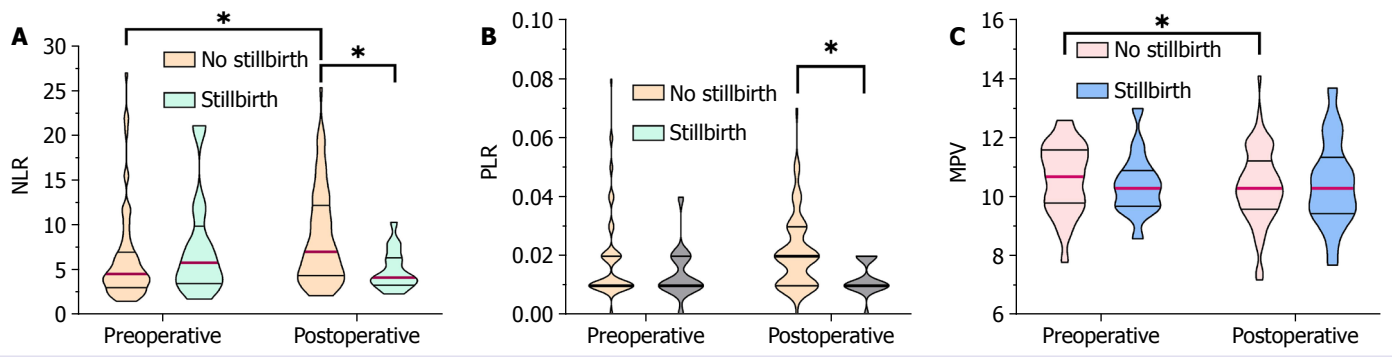

FIGURE 1. **(A)** Median NLR values of the women with placental abruption with or without stillbirth. Data were expressed as median with interquartile range and analyzed with Mann–Whitney and Wilcoxon rank test as appropriate. *p<0.05. **(B)** Median PLR values of the women with placental abruption with or without stillbirth. Data were expressed as median with interquartile range and analyzed with Mann–Whitney and Wilcoxon rank test as appropriate. *p<0.05. **(C)** Median MPV values of the women with placental abruption with or without stillbirth. Data were expressed as median with interquartile range and analyzed with Mann–Whitney and Wilcoxon rank test as appropriate. *p<0.05.

The mean birth weight of women with stillbirth was significantly lower than that of the women without stillbirth (1828.8±840.8 vs. 2309.1±861.9; p<0.05). The ratio of female newborns was similar in the women with or without stillbirth (8 [47.1%] vs. 39 [54.2%]; p>0.05). In the women without stillbirth, the median Apgar scores 1 and 5 min were 5.9±2.7 versus 7.6±2.2, the rate of need for NICU admission was 73.2% and the median stay in NICU was 6.5 (0–366) days.

Table 3 displays the hematological findings of women with placental abruption with or without stillbirth. We found notable changes in hematological parameters (p<0.05); however, no significant alterations were present, implicating a meaningful trend (p>0.05).

Figures 1 present the median NLR, PLR, and MPV values of women with placental abruption with or without stillbirth. The median post-operative NLR value of women with placental abruption without stillbirth was significantly higher than women with placental abruption with stillbirth (p<0.05). In the women with placental abruption without stillbirth, the median post-operative NLR value was significantly higher than the median pre-operative NLR value (p<0.05). The median post-operative PLR value of women with placental abruption without stillbirth was significantly higher than the women with placental abruption with stillbirth (p<0.05). In the women with placental abruption without stillbirth, the median post-operative MPV value was significantly higher than the median pre-operative MPV value (p<0.05).

DISCUSSION

In this study population, we collected clinical and hematological findings of women with or without stillbirth with placental abruption. The most common morbidity in the population was hypertension, and the ratio of abrupted placenta area was more pronounced in women with stillbirth. The women with stillbirth had noticeably more transfusion needs, a Couvelaire sign, and less mean birth weight. In the mother without stillbirth, the Apgar score at 1 and 5 min were mildly low and NICU admission was considerably higher in these newborns. Although hematological parameters revealed meaningful changes, these were not consistent among the participants. The NLR, PLR, and MPV values in women with placental abruption with stillbirth presented remarkable changes.

Since the placenta is vital for fetal growth and development and plays a crucial role in regulating all aspects of pregnancy, placental abruption is one of the remarkable obstetric emergencies, and it usually develops rapidly. Prompt diagnosis and management from the patient's admission can partially reduce poor maternal and fetal outcomes. Current evidence supports the long-term adverse impact condition for both the mother and child [13].

Patients with placental abruption causing perinatal high-risk conditions require close follow-up and delivery should be performed promptly. It is important to treat these mothers in tertiary care centers that can accept life-threatening patients and have maternal and neonatal intensive care facilities to reduce mortality and morbidity. In a recent study, including 62 women admitted with pla-

cental abruption, the authors examined the relationship of etiological factors and clinical outcomes of those cases [10]. They found that the leading factors included preeclampsia and premature rupture of the membrane in a decreasing frequency. In that study population, abdominal pain and vaginal bleeding were prominent as the classical findings of the condition. However, the clinical presentation varied from asymptomatic, in which the diagnosis is made by inspection of the placenta at delivery, to massive abruption leading to fetal death and severe maternal morbidity. They performed emergency cesarean sections in 45 cases (73%). In their study population, fetal complications were stillbirth (4.8%), neonatal asphyxia, and neonatal death. The authors suggested that early diagnosis, prenatal follow-up, and urgent cesarean delivery improve the maternal and fetal prognosis by reducing severe morbidities with the help of prompt and tailored maternal care [10].

Alfandari et al. [6] investigated the value of the hematological indices NLR and PLR obtained by hematological tests performed during the first half of pregnancy to predict the development of placental abruption later in pregnancy. They found no meaningful difference between the women with or without placental abruption regarding NLR and PLR values. The results of their findings can be considered to support the value of hematological indices used in our study settings, including measurements of hematological indices in the acute stage of placental abruption.

Boisramé et al. [17] performed a retrospective study, including 100 pregnant women with placental abruption. They found that 67 of them gave birth prematurely and that, among those, 50 patients delivered before 34 weeks of gestational age. In that study, perinatal mortality was 19%, with stillbirth (12.4%) and three neonatal deaths (2.8%). They highlighted that joint medical care of obstetricians and intensivists was often required to reduce perinatal mortality, mainly as stillbirth [17].

Pils et al. [18] evaluated routine laboratory parameters in women with and without placental abruption, and 417 women were included in that retrospective cohort study in a tertiary-care center. Their study revealed that placental abruption was associated with slightly but significantly increased CRP levels. They found that significantly increased CRP levels were present in women with placental abruption and that the lack of a difference in CRP between bleeding and non-bleeding cases was in line with the theory of a chronic process being associated with placental abruption. However, they concluded that CRP did not help distinguish placental abruption [18].

Arlier et al. [14] investigated the role of MPV and platelet distribution width (PDW) in predicting placental abruption before cesarean section. In that study, pre- and post-operative MPV and PDW presented meaningful differences regarding placental abruption. Their results suggested that the MPV and PDW values provided reasonable accuracy as a marker of placental abruption.

Su et al. [13] assessed the predictive value of pre-delivery routine laboratory parameters, including hematological tests for the severity of placental abruption and maternal and neonatal outcome of cases. Those parameters changed significantly with the increasing severity of the condition. They concluded that those laboratory findings could be predictors of the degree of this condition [13].

In a systematic review, the authors stated that several biophysical and biochemical tests performed on first- and second-trimester pregnancies had been proposed to predict stillbirth, but their predictive ability remains unclear. They evaluated 71 studies, including stillbirth data, and noted that clinical and laboratory tests do not have enough power to be used in clinical practice [19]. In the present study, the study population was mainly in the third trimester, and this study focuses on the diagnostic value of hematological indices in women with placental abruption-caused stillbirth.

Inflammatory markers, such as MPV and PLR, obtained using hemogram parameters, are thought to be important in the prediction and diagnosis of various diseases [20]. As stated above, some studies focused on hematological variables in the management of placental abruption, and according to their results, there are meaningful contributions of those variables to the diagnosis and follow-up of their participants. In our study, we observed that it is possible to determine the severity of placental abruption as presented by a stillbirth with the hemogram test. Despite some changes in the hemogram parameters, those did not reach statistical significance.

This study has its inherent limitations, especially with retrospective research, including a low sample size. All health records of the participants were screened twice for quality assurance to detect possible errors and increase the reliability of study parameters. We thought that this condition prevented the detection of meaningful differences in some of the hematological variables. It might be possible to draw useful conclusions when serial follow-up of hematological indices is performed.

Conclusion

Stillbirth is one of the most important complications of placental abruption, requiring rapid diagnosis and conscientious follow-up after emergent cesarean section. During the management, the hemogram test considerably helps with varied hematological parameters and indices in women with placental abruption. Therefore, according to the results of this study, the values of NLR, PLR, and MPV measured at the first admission and during follow-up of the patients with placental abruption complicated with stillbirth may help determine the severity and course of the condition underlying stillbirth, especially when used during the hospitalization.

Ethics Committee Approval: The Haseki Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 04.08.2021, number: 62-2021).

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Authorship Contributions: Concept – FYG, AC; Design – FYG, AC; Supervision – FYG, AC; Materials – ME, BSA; Data collection and/or processing – FYG, AC, ME, BSA; Analysis and/or interpretation – FYG, AC, ME, BSA; Literature review – FYG, AC, ME, BSA; Writing – FYG, AC; Critical review – FYG, AC.

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