RESEARCH ARTICLE

Neutrophil lymphocyte ratio, platelet lymphocyte ratio and other haematological parameters as predictive indicators for early pregnancy loss

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ABSTRACT

Introduction: Early pregnancy loss is a common complication, and accurate diagnosis is crucial for appropriate management. While ultrasound is a standard diagnostic tool, hematological parameters, particularly neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), may offer additional insights into pregnancy prognosis.

Objective: This study aimed to evaluate the role of complete blood count inflammatory markers, specifically NLR and PLR, in predicting early pregnancy loss.

Methods: This retrospective case-control study included 90 women (aged 18-41 years) in their first trimester (<12 weeks gestation). The study group comprised 44 women with early pregnancy loss, while the control group included 46 women with healthy pregnancies. Complete blood count data were analyzed, and NLR and PLR were calculated. Statistical analysis was performed to compare the groups.

Results: Women experiencing pregnancy loss had significantly higher NLR (4.25 ± 2.47 vs. 2.81 ± 1.22, p=0.009) and PLR (158.53 ± 72.97 vs. 124.24 ± 39.1, p=0.006) compared to the control group. Conversely, mean corpuscular hemoglobin concentration (MCHC), mean platelet volume (MPV), and platelet distribution width (PDW) were significantly lower in the pregnancy loss group.

Conclusion: Elevated NLR and PLR are strongly associated with early pregnancy loss. These readily available and cost-effective hematological markers, along with MCHC, MPV, and PDW, may aid in predicting early pregnancy complications and facilitate timely intervention.

Key words: : Early pregnancy loss, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), complete blood count, inflammatory markers, pregnancy complications.

INTRODUCTION

A first trimester of pregnancy loss is a pregnancy lost before it reaches viability. Every year, an estimated 23 million first-trimester pregnancy losses occur globally, resulting in 44 pregnancy losses every minute. All recognized pregnancies have a probability of first trimester of pregnancy loss of 15.3%; 95 % confidence interval: 12.5%–18.7%. Younger or older female age, old husband age of more than 40 years, extremely low or very high Body mass index (BMI), black ethnicity, smoking, alcohol, stress, environmental factors like pesticide exposure, air pollution, and working night shifts are all risk factors for the first trimester of pregnancy loss.[1]

Haematological changes, including significant variations in blood volume, occur during pregnancy to meet the needs of the

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growing fetus and placenta. Plasma volume increases by 40 to 45%. This rise is driven by progesterone and estrogen in the kidneys, stimulating the release of renin and activating the renin-angiotensin-aldosterone system. As a result, sodium retention occurs, leading to an increase in total body water.[2]

A healthy pregnancy depends on proper communication between fetal trophoblasts and immune cells at the maternal-fetal interface, including macrophages. Trophoblasts are essential in the early stages of embryonic implantation and pregnancy, as they invade the endometrium to establish the maternal-fetal connection and promote maternal immune tolerance to the fetus. Impaired trophoblast migration disrupts this connection, potentially leading to pregnancy loss.[3]

Red cell distribution width (RDW), mean platelet volume (MPV), plateletcrit (PCT), platelet distribution width (PDW), neutrophil to lymphocyte ratio (NLR), and platelet to lymphocyte ratio (PLR) have all been identified as systemic inflammatory markers.[4] A complete blood count test could determine these blood parameters easily. They chiefly show the presence of inflammatory load and are therefore used as prognostic indicators in many diseases.[5] Pregnancy loss is characterized by an imbalance of pro-inflammatory and anti-inflammatory states. This imbalance is mainly caused by disrupted trophoblast-macrophage communication.[3]

One of the most interesting aspects of reproductive biology is that a healthy woman with a fully functioning immune system can conceive a pregnancy to full term without suffering from immunological rejection. Immunoglobulins, cytokines, hormonal, and other endometrial variables impact local and systemic immune responses. A synergy of these components is essential for successful implantation and subsequent conception.[6]

The neutrophil-lymphocyte ratio is the proportion of total neutrophils to total lymphocytes. It's thought to be a biomarker of the body's immunological response. It is also considered a quick and easy way to detect systemic inflammation and stress. Another marker that rises during thrombosis and inflammation is the platelet lymphocyte ratio.[7]

During the early stages of pregnancy, the human fetus grows in a low-oxygen environment. To maintain a low oxygen concentration, extravillous trophoblasts enter the uterine tissues and form a shell cell barrier into the terminals of the uteroplacental arteries. This barrier shields the placenta from the harmful effects of free oxygen radicals generated due to maternal circulation's early and excessive blood flow. Increased oxygen radicals cause necrosis and apoptosis in the placental villous tree of the trophoblast epithelium.[8]

The PLR is readily available and simple to calculate, but it can be affected by various inflammatory illnesses. As per current studies, a high PLR has been associated with inflammation, atherosclerosis, and platelet activation. Further research is required to determine the potential use of PLR in clinical practice.[9]

The current study aims to evaluate the potential predictive value of haematological markers, especially PLR and NLR, in the first trimester of pregnancy loss.

METHODS

Study design and setting: This case-control study was conducted at the Gynecology and Obstetrics wards of Al-Imamein Al-Kadhimein Medical City from January 2022 to June 2022.

Ethical consideration: The ethical research committee of Al-Karkh Health Directorate and the Institutional Review Board (IRB) of Al-Nahrain Medical College approved the protocol for this study. We took the agreement of the administration of Al-Imamein Al-Kadhimein Medical City to perform the study and to use the records of the patients eligible for participation in this study. Informed written consent was obtained from each participant after explaining the aim and procedure of the study.

Definition of cases, inclusion and exclusion criteria:

Cases: We included 44 women between the ages of 18 and 41 years and less than 12 gestational weeks who were admitted to gynaecology and obstetrics wards during the study period due to first-trimester pregnancy loss. For the sake of the inclusion of patients, early pregnancy loss was defined as the absence of the fetal heartbeat in a pregnant woman below the 12^{th} gestational week, whether or not it had previously been observed or having active vaginal bleeding at least six weeks of pregnancy with an undetected fetal heartbeat. Women with chronic inflammatory illnesses, thyroid disorders, diabetes mellitus, hematologic disorders, history of thrombosis, systemic lupus erythematosus, numerous pregnancies, current infections, other afflictions (such as arthritis), uterine anomalies, molar pregnancy, and antiphospholipid syndrome were excluded from this study. Women with anembryonic pregnancy were also excluded from this study. To calculate the gestational age, we depended on the last menstrual cycle date supported by measuring the crown-rump length (CRL) on an abdominal or transvaginal ultrasound examination. We depended only on the CRL measurement if the last menstrual period was uncertain.

Control: As the control group, we included 46 women with healthy, uncomplicated pregnancies under 12 weeks of gestation. The same exclusion criteria were applied to the cases and control groups. All participants were healthy, without any underlying medical conditions, and were recruited from the outpatient department of Al-Zahraa Primary Care Medical Center.

Sampling: we selected the sample from January 2022 to June 2022 using a convenient sampling technique.

Data collection: the data of all enrolled women were extracted into a predesigned form, and it included demographic data of the women (age, height, body weight, BMI and smoking status), obstetric and gynaecological history of the women, and haematological indices.

Using a syringe, we aspirated 3 ml of blood from the capital vein into a plain test tube and left for 30 min at room temperature. Then, the tubes were centrifuged at 3000 rpm for 15 minutes and stored at -20°C. Biochemical kits from Boisource/ USA were used to measure Kisspeptin, Activin AB, Progesterone, and Human chorionic gonadotropin hormone (HCG) levels. The biochemical kits employed in this research were based on enzyme-linked immunosorbent tissue assay (ELISA), the gold standard of immunoassays with high sensitivity to detect antibodies, antigens, proteins, glycoproteins, and hormones.

The complete blood count (CBC) inflammation markers included white blood cell (WBC), red blood cell (RBC), neutrophil (N), lymphocyte (L), platelets (PLT), mean platelet volume (MPV), neutrophil-lymphocyte ratio (NLR),) and platelet-lymphocyte ratio (PLR), haematocrit (HCT), haemoglobin (HCG), mean cell volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), red cell distribution width (RDW), platelets distribution width (PDW), Plateletcrit (PCT), and platelets large cell ratio (P-LCR) were recorded.

Statistical analysis: SPSS software version 25.0 was used for statistical analysis (SPSS, Chicago). The normality of continuous data was tested (Shapiro Wilk test), and data with a normal distribution were presented as mean and standard deviation and analyzed using a Student t-test. We used median, range, and Mann-Whitney U tests to show data with non-normal distributions and measure its statistical significance.

The Chi-square test was used to examine categorical variables that were reported as numbers and percentages. The predictive usefulness of haematological markers in predicting early pregnancy loss was assessed using the receiver operating characteristic curve (ROC). A statistically significant difference was defined as a p-value less than 0.05.

Table 1 | Demographic data of the study population.

Variables	EPL (n = 44)	Control (n = 46)	P-value
Age (years)			
Mean±SD	28.7±6.83	26.04±6.04	0.058
Range	18-40	18-40	
Height (cm)			
Mean±SD	160.64±7.88	158.87±5.76	0.346
Range	150-180	150-175	
Weight (Kg)			
Mean±SD	68.61±13.24	65.74±12.67	0.395
Range	48-100	46-95	
Body mass index (kg/m²)			
Mean±SD	26.42±3.63	25.8±3.81	0.498
Range	19.98-35.38	19.7-33.2	
Smoking			
Yes	2(4.55%)	2(4%)	0.642
No	42(95.5%)	44(96%)	

Table 2 | Obstetric and gynaecologic history of the study population.

Variables	EPL (n = 44)	Control (n = 46)	P-value
Age at menarche (years)			
Mean±SD	12.96±1.35	13.05±1.28	0.825
Range	11-17	11-17	
Cycle regularity			<0.001
Yes	32(77.73%)	50(100%)	
No	12(27.27%)	0(0%)	
Duration of menstrual cycle (days)			0.037
Mean±SD	5.16±1.51	5.73±0.95	
Range	3-9	3-7	
Gestational age (weeks)			0.189
Mean±SD	8.75±3.71	8.07±3.51	
Range	5-12	4-12	
Number of miscarriages			<0.001
One	13(29.54%)	10(20%)	
More than one	31(70.45%)	36(80%)	
Family history of miscarriage			<0.001
Yes	17(38.64%)	2(4%)	
No	27(61.36%)	44(96%)	
Parity			<0.001
Nulliparous	6(13.64%)	12(24%)	
1-3	23(52.27%)	33(74%)	
≥4	15(34.1%)	1(2%)	

RESULTS

Demographic characteristics of the study population: Women with EPL were slightly older than those without, 28.7±6.83 years vs. 26.04±6.04 years. However, the difference was not significant. Likewise, the two groups had no significant differences in height, weight, BMI, or smoking. See Table 1.

Obstetric and gynecologic history of the study population: The mean age at menarche was 12.96±1.35 years in patients with EPL and 13.05±1.28 years in those without, with a p-value of 0.8. However, menstrual irregularities were observed in 27.27% of the patient group, compared to none in the control group (p<0.001). The mean cycle duration in patients (5.16±1.51 days) was shorter than in controls (5.73±0.95 days, p=0.03). Over two-thirds of patients (70.45%) experienced more than one miscarriage, while none of the controls did (p<0.001). A family history of EPL was more common in patients than controls (38.64% vs. 4%, p<0.001). Additionally, 34.1% of patients had ≥4 parities, compared to 2% of controls (p<0.001). See Table 2.

Haematological parameters: The Hb level, RBC, WBC, neutrophil, lymphocyte, platelet counts, HCT, MCV, MCH, RDW-SD (standard deviation), and RDW-CV (coefficient of variation) have shown no statistical difference between the two groups.

MCHC, MPV, PDW, and PLCR are lower in patients with EPL than those without (p values <0.001, 0.009, 0.06, and 0.012). For details, see Table 3.

Diagnostic Value of MCHC, MPV, PDW, and P-LCR in prediction of EPL: The AUC for MCHC was 0.769, 95% CI= 0.669-0.869, p < 0.001. The test's sensitivity and specificity were 76% and 64%, respectively, at a cut-off value of MCHC= 34.55g/dL.

The AUC for MPV was 0.662, 95% CI= 0.546-0.778, p = 0.011. The test's sensitivity and specificity were 62% and 74%, respectively, at a cut-off value of MPV= 34.95fL.

The AUC for PDW was 0.680, 95% CI= 0.566-0.794, p = 0.005. The test's sensitivity

Table 3 | Blood indices of the study population.

Variables	EPL (n = 44)	Control (n = 46)	P-value
Hb level (g/dl)			0.594
Mean±SD	11.73±1.46	11.87±1.09	
Range	8.2-14.2	8.2-14.1	
RBC count ×10^{12} /L			0.387
Mean±SD	4.28±0.48	4.19±0.46	
Range	3.31-5.79	3.26-5.78	
HCT %			0.212
Mean±SD	34.7±3.63	33.84±2.83	
Range	25.4-41.0	26.8-39.3	
MCV (fl)			0.690
Mean±SD	81.67±7.83	81.03±7.42	
Range	60.4-97.7	57.5-92.5	
MCH (pg)			0.255
Mean±SD	27.74±3.74	28.6±3.30	
Range	18.7-36.2	17.6-32.7	
MCHC (g/dl)			<0.001
Mean±SD	33.75±1.84	35.24±2.01	
Range	28.4-38.2	30.6-40.1	
RDW-SD, fl			0.644
Mean±SD	42.17±3.76	41.84±2.86	
Range	35.8-50.4	35.9-47.8	
RDW-CV, fl			0.487
Mean±SD	14.23±2.15	13.93±1.94	
Range	11.8-20.4	11.5-22.2	
WBC count ×10^{3}/ml			0.761
Mean±SD	8.54±2.12	8.67±2.16	
Range	4.02-15.11	4.6-14.8	
Neutrophil count ×10^{3}/ml			0.974
Mean±SD	5.84±2.02	5.82±1.96	
Range	2.28-11.32	1.7-10.7	
Lymphocyte count ×10^{3}/ml			0.399
Mean±SD	2.02±0.64	2.12±0.51	
Range	0.61-3.2	1.2-3.1	
Platelet count ×10^{3}/ml			0.381
Mean±SD	268.16±76.01	256.62±69.03	
Range	128-549	116-430	
MPV (fl)			0.009
Mean±SD	10.56±1.23	11.24±1.1	
Range	6.8-13.8	8.8-13.4	
PDW (fl)			0.006
Mean±SD	13.39±2.42	14.9±2.49	
Range	8.3-20.6	10.6-21.5	
PCT (ng/ml)			0.470
Mean±SD	0.28±0.08	0.29±0.07	
Range	0.15-0.55	0.15-0.46	
PLCR (%)			0.012
Mean±SD	30.53±8.4	35.45±9.14	
Range	14.1-54.1	16.6-54.5	

Hb = Haemoglobin; RBC = Red blood cell; HCT = Haematocrit; MCV = Mean corpuscular volume; MCH = Mean corpuscular haemoglobin; MCHC = Mean corpuscular haemoglobin concentration; RDW-SD = Red cell distribution width - standard deviation; RDW-CV = Red cell distribution width - coefficient of variation; WBC = White blood cells; MPV = Mean platelet volume; PDW = Platelet distribution width; PCT=Plateletcrit, PLCR = Platelet large cell ratio.

Table 4 | NLR and PLR of the study population.

Variables	EPL (n = 44)	Control (n = 46)	P-value
Neutrophil/lymphocyte ratio			**0.009**
Mean±SD	**4.25±2.47**	**2.81±1.22**	
Median	**3.73**	**2.4**	
Range	**1.5-10.42**	**0.85-6.31**	
Platelet/lymphocyte ratio			0.006
Mean±SD	158.53±72.97	124.24±39.1	
Median	142.85	120.55	
Range	48.48-428.8	59.5-268.75	

and specificity were 62% and 62%, respectively, at a cut-off value of PDW= 13.85 fL.

The AUC for P-LCR was 0.654, 95% CI= 0.537-0.771, p = 0.015. The test's sensitivity and specificity were 60% and 57%, respectively, at a cut-off value of P-LCR = 31.6. For details see **Figure 1**.

Derived blood parameters: The data for NLR and PLR were found to be non-normally distributed. Therefore, these values were presented as median and range and analyzed using the non-parametric Mann-Whitney U test. The median NLR in patients with EPL was 3.73 (range 1.5-10.42), which was significantly higher than that of the controls (median 2.4, range 0.85-6.31). Likewise, the median PLR

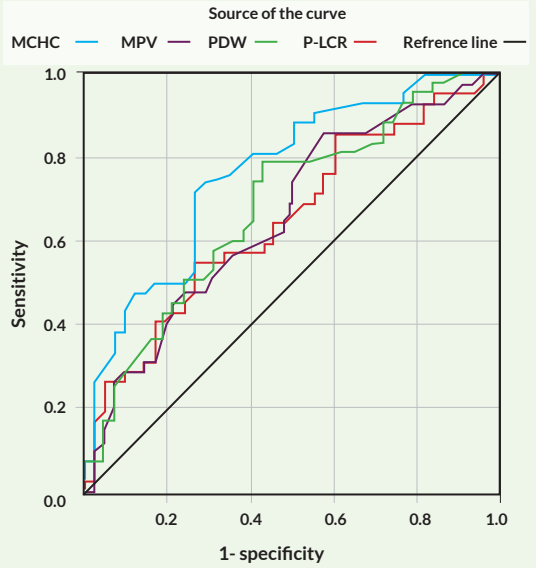

Figure 1 | Receiver operating characteristic curve of MCHC, MPV, PDW, and P-LCR in the context of discrimination between patients with EPL and controls

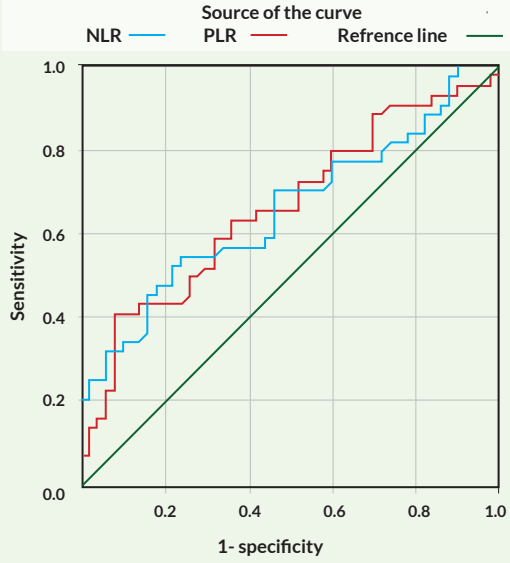

Figure 2 | Receiver operating characteristic curve for NLR and PLR in predicting EPL

was significantly higher in patients (142.85, range 48.48-428) compared to the controls (median 120.55, range 59.5-268.75), as shown in **Table 4**.

Predictive Value of NLR and PLR for EPL: To evaluate the sensitivity and specificity of NLR and PLR, the receiver operating characteristic (ROC) curve was employed. For NLR, the area under the curve (AUC) was 0.675 (95% CI = 0.544–0.769, p = 0.009), with sensitivity and specificity values of 71% and 54%, respectively, at a cutoff of NLR = 2.48. For PLR, the AUC was 0.663 (95% CI = 0.552–0.775, p = 0.006), with sensitivity and specificity values of 64% and 62%, respectively, at a cutoff of PLR = 129.42, as shown in **Figure 2**.

DISCUSSION

During pregnancy, various haematological changes occur as the fetus continuously develops. These changes return to normal after the postpartum period. However, they are essential to meet the metabolic needs of the mother while ensuring sufficient oxygen supply to the fetus. The extent of these haematological modifications can influence the outcome of the pregnancy. Therefore, monitoring haematological markers throughout pregnancy is crucial to optimize outcomes.[9]

The connection between PLR and NLR levels and abnormal early intrauterine pregnancies has been investigated to determine if they could serve as diagnostic markers for EPL. It was thought that the destruction of fetal organs and/or the negative fetal pole would lead to distinct PLR and NLR levels in EPL patients compared to those with normal intrauterine pregnancies.[10] PLR has been previously examined in pregnancy-related issues such as gestational diabetes, preeclampsia, pancreatitis and early premature rupture of membranes (PPROM).[5]

In the present study, the level of NLR and PLR in EPL patients was significantly higher compared to women with normal pregnancy (P<0.009 and P<0.006, respectively). Also, we found that the PLCR was significantly lower in the patients relative to the controls (30.53±8.4 versus 35.45±9.14). Similarly, MPV was significantly lower in the patients when compared to the controls (10.56±1.23 fl versus 11.24±1.1 fl). As well as the PDW and MCHC were lower in the patients (13.39±2.42 fl and 33.75±1.84 respectively) when compared to (14.9±2.49 and 35.24± 2.01 fl respectively) of the controls with significant differences. These findings are in agreement with the results obtained by Biyik et al, who found that serum NLR and PLR levels are high in women with missed abortion, pointing to a faulty placentation in the pathogenesis of early pregnancy loss.[11] also in line with the results of Ata et al., who found that MPV, RBCs, and PLR levels were linked to miscarriage in the first trimester. These blood indices, which are both inexpensive and simple to use, can be used to forecast fetal losses.[5] Aiob et al. notice that due to continuing trophoblastic development, molar pregnancies may generate a stronger inflammatory reaction than missed abortion. However, the amount of the change was insignificant and useless for making a diagnosis.[12]

Conversely, Christoforaki et al. found that NLR levels did not differ significantly between pregnant women who had a live delivery

and those who experienced a miscarriage. However, NLR levels greater than 5.8 were exclusively observed in the miscarriage group with a statistically significant finding.[13]

Dan Liu et al. claim that NLR and PLR are ineffective predictors of miscarriage. MPV should be considered in the first trimester pregnancy loss.[14]

Kale et al. reassure that high NLR levels obtained from the hemogram results in the first trimester were associated with miscarriage. They think that NLR can be useful in predicting pregnancy evolution because of its cost-effectiveness and non-invasiveness.[15]

Bas et al. discovered that inflammation markers in blood tests such as white blood cell count (WBC), neutrophil, lymphocyte, NLR, PLR, and MPV were evaluated at the sixth gestational week and can be used to assess the risk of early pregnancy loss. They discovered that the abortion groups had lower MPV and PLR levels and higher neutrophil, lymphocyte, and NLR levels than the control group. WBC, neutrophil, lymphocyte, and NLR were positive predictive indicators. In contrast, MPV and PLR were shown to be a negative predictive signal for the evaluation of spontaneous abortion, but with limited sensitivity and specificity.[16] This observation was reconfirmed by Erdem et al.'s study, which found that CBC parameters such as high MPV, RDW, PCT, and MCHC could be considered as a crucial predictor of recurrent miscarriage, their study showed that Complete blood count (CBC) inflammatory indicators such as NLR, PLR, Platelets, neutrophil, lymphocyte, WBC, and MPV showed a difference between the abortion and control groups. When compared to the control group, the abortion groups had lower MPV and PLR, and higher neutrophil, lymphocyte, and NLR levels. WBC, neutrophil, lymphocyte, and NLR were revealed to be positive predictive indicators with low sensitivity and specificity. In contrast, MPV and PLR were shown to be negative predictive markers for spontaneous abortion.[17]

Kale et al. found that the demographic characteristics and the first-trimester hemogram results of the miscarriage and the control group were compared in both groups and had similar ages and BMIs. In terms of basophil, neutrophil, eosinophil, lymphocyte, monocyte, platelets, RBC, haemoglobin, hematocrit, MCV, MCH, MCHC, RDW, MPV, PCT, and PDW, there was no statistically significant difference between the two groups. In contrast, leukocyte and neutrophil counts were statistically significantly higher in the miscarriage group.[15]

CONCLUSION

Haematological parameters such as PLR, NLR, MPV, RDW, PCT, and MCHC could serve as important predictors of first-trimester pregnancy loss, making them promising markers for the early detection of missed abortions. To better understand the relationship between these blood cell function indicators and early pregnancy loss, further prospective studies with larger patient populations are needed to support our findings.

REFERENCES

1. Quenby S, Gallos ID, Dhillon-Smith RK, Podesek M, Stephenson MD, Fisher J, et al. Miscarriage matters: the epidemiological, physical, psychological, and economic costs of early pregnancy loss. *Lancet*. 2021 May 1;397(10285):1658-67. doi: 10.1016/S0140-6736(21)00682-6. Epub 2021 Apr 27. PubMed PMID: 33915094.
2. Gebreweld A, Bekele D, Tsegaye A. Hematological profile of pregnant women at St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia. *BMC Hematol*. 2018 Dec;18(1):1-7. doi: 10.1186/s12878-018-0108-y. PubMed PMID: 30518322; PubMed Central PMCID: PMC6289803.
3. Gao P, Zha Y, Wei L, Zhou X, Zhu S, Zhang H, et al. G-CSF: A vehicle for communication between trophoblasts and macrophages which may cause problems in recurrent spontaneous abortion. *Placenta*. 2022 Jul;121:164-72. doi: 10.1016/j.placenta.2022.05.002. Epub 2022 May 7. PubMed PMID: 35533775.
4. Oglak SC, Aydın MF. Are neutrophil to lymphocyte ratio and platelet to lymphocyte ratio clinically useful for the prediction of early pregnancy loss? *Ginekol Pol*. 2020 Sep;91(9):524-7. doi: 10.5603/GP.a2020.0088. PubMed PMID: 33057057.
5. Ata N, Kulhan M, Kulhan NG, Turkler C. Can neutrophil-lymphocyte and platelet-lymphocyte ratios predict threatened abortion and early pregnancy loss? *Ginekol Pol*. 2020 Apr;91(4):210-5. doi: 10.5603/GP.a2020.0028. PubMed PMID: 32368202.
6. Hao F, Zhou X, Jin L. Natural killer cells: functional differences in recurrent spontaneous abortion†. *Biol Reprod*. 2020 Mar 1;102(3):524-31. doi: 10.1093/biolre/ioz214. PubMed PMID:

31783450.

7. Biyik I, Albayrak M, Keskin F. Platelet to lymphocyte ratio and neutrophil to lymphocyte ratio in missed abortion. *Rev Bras Ginecol Obstet*. 2020 May;42(5):235-9. doi: 10.1055/s-0040-1708194. Epub 2020 Apr 27. PubMed PMID: 32343030.
8. Huppertz B, Gauster M, Orendi K, König J, Moser G. Oxygen as modulator of trophoblast invasion. *J Anat*. 2009 Jul;215(1):14-20. doi: 10.1111/j.1469-7580.2009.01089.x. PubMed PMID: 19445632; PubMed Central PMCID: PMC2736080.
9. Obeagu E, Adepoju OJ, Okafor CJ, Obeagu GU, Ibekwe AM, Okpala PU, et al. Assessment of Haematological Changes in Pregnant Women of Ido, Ondo State, Nigeria. *J Res Med Dent Sci*. 2021;9(4):145-8.
10. Tolunay HE, Eroglu H, Varlı EN, Aksar M, sahin D, Yücel A. Evaluation of first-trimester neutrophil-lymphocyte ratio and platelet-lymphocyte ratio values in pregnancies complicated by intrauterine growth retardation. *Turk J Obstet Gynecol*. 2020;17(2):98-104. doi: 10.4274/tjod.galenos.2020.02156. PubMed PMID: 32661811; PubMed Central PMCID: PMC7364367.
11. Hantoushzadeh S, Gargar OK, Jafarabady K, Rezaei MM, Asadi F, Eshraghi N, Panahi Z, Shirdel S, Mirzamoradi M, Ghaemi M. Diagnostic value of neutrophil to lymphocyte and platelet-to-lymphocyte ratio to predict recurrent pregnancy loss and abortion; a systematic review and meta-analysis. *Immunity, Inflammation and Disease*. 2024 Mar;12(3):e1210.
12. Aiob A, Naskovica K, Zilberfarb IA, Sharon A, Bornstein J, Lowenstein L. Complete blood count parameters, neutrophil-to-lymphocyte ratio, and platelet-to-lymphocyte ratio in hydatidiform mole versus missed abortion. *Eur J Gynaecol Oncol*. 2022;43(2):175-8. PubMed PMID: 35355173.
13. Christoforaki V, Zafeiriou Z, Daskalakis G, Katasos T, Siristatidis C. First trimester neutrophil to lymphocyte ratio (NLR) and pregnancy outcome. *J Obstet Gynaecol*. 2020 Jan;40(1):59-64. doi: 10.1080/01443615.2019.1634443. Epub 2019 Jul 11. PubMed PMID: 31295591.
14. Liu D, Huang X, Xu Z, Chen M, Wu M. Predictive value of NLR and PLR in missed miscarriage. *J Clin Lab Anal*. 2022 Mar;36(3):e24250. doi: 10.1002/jcla.24250. Epub 2022 Jan 25. PubMed PMID: 35072536.
15. Kale I, Helvacıoglu Ç, Mugurtay TE. Evaluation of complete blood count parameters in the first trimester: an early indicator of miscarriage? *J Turk Ger Gynecol Assoc*. 2021 Jun 30;22(2):110-5. doi: 10.4274/jtgga.galenos.2020.2020.0089. PubMed PMID: 34234933; PubMed Central PMCID: PMC8268844.
16. Bas FY, Tola EN, Sak S, Cankaya BA. The role of complete blood inflammation markers in the prediction of spontaneous abortion. *Pak J Med Sci*. 2018 Nov;34(6):1381-5. doi: 10.12669/pjms.346.15814. PubMed PMID: 30574132; PubMed Central PMCID: PMC6295222.
17. Erdem ZS, Cayir Y, Kosan Z, Erdem HB. Is There Any Relation Between Recurrent Miscarriage and Complete Blood Count Values? A Case-Control Study. *Konuralp Med J*. 2020;12(1):82-6. doi: 10.18521/kmj.711970. PubMed PMID: 32292693; PubMed Central PMCID: PMC7162222.

Abbreviations list: Area under the curve (AUC), Body mass index (BMI), Complete blood count (CBC), Confidence interval (CI), Crown-rump length (CRL), Enzyme-linked immunosorbent tissue assay (ELISA), Femtolitre (fL), Haematocrit (HCT), Haemoglobin (HCG), Human chorionic gonadotropin hormone (HCG), Institutional Review Board (IRB), Lymphocyte (L), Mean cell volume (MCV), Mean corpuscular haemoglobin (MCH), Mean corpuscular haemoglobin concentration (MCHC), Mean platelet volume (MPV), Nanogram (ng), Neutrophil (N), Neutrophil to lymphocyte ratio (NLR), Picogram (PG), Platelet distribution width (PDW), Platelet to lymphocyte ratio (PLR), Plateletcrit (PCT), Platelet-lymphocyte ratio (PLR), Platelets (PLT), Platelets distribution width (PDW), Platelets large cell ratio (P-LCR), RDW-CV (coefficient of variation), RDW-SD (standard deviation), Receiver operating curve (ROC), Red blood cell (RBC), Red cell distribution width (RDW), Statistical Package for Social Sciences (SPSS), United State of America (USA), White blood cell (WBC), .

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