

Predictability of Platelets to Lymphocyte and Neutrophil to Lymphocyte Ratios and its Comparison in the First Trimester Missed Abortion at Tertiary Care Center: A Case-Control Study

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Received: 25-07-2024 / Revised: 23-08-2024 / Accepted: 25-09-2024

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Conflict of interest: Nil

Abstract:

Background: The NLR (Neutrophil-to-Lymphocyte Ratio), lymphocyte-to-monocyte ratio (LMR), and PLR (Platelet-to-Lymphocyte Ratio) are indices calculated from a simple complete blood count. The significant potential values of these ratios, which reflect inflammatory status, frequently serve as markers of underlying inflammatory burden in various diseases and pregnancy complications, including missed abortion. This study was conducted with the aim of assessing the role of platelets to lymphocyte and neutrophil to lymphocyte ratios in the first trimester missed abortion at a tertiary care centre.

Materials and Methods: This was a case-control study conducted over a period of 2.5 years involving pregnant women with gestational age <14 weeks who had missed abortion within 1 week. 40 subjects were considered in each group. The age group of the study subjects was between 17 and 42 years.

Results: The mean BMI in cases, 19.64 ± 2.4 , was statistically significantly lower compared to the control group, 22.29 ± 2.5 . The hemoglobin and platelets were found to be statistically significantly lower in the cases compared to the control group. Neutrophils and lymphocytes found to be statistically significantly higher in cases compared to the control group. NLR and LMR found to be statistically significantly higher in cases compared to the control group, and MLR and PLR were statistically significantly lower in cases compared to the control group. With an optimal cut-off value of 4.46 for NLR, AUC was 0.71, with specificity and sensitivity of 96.5% and 81.4%, respectively. With an optimal cut-off value of 63.2 for PLR, the AUC was 0.88, with specificity and sensitivity of 66% and 98%, respectively.

Conclusion: NLR and LMR were found to be statistically significantly higher, while MLR and PLR were statistically significantly lower in those with MA compared to healthy pregnant women. These markers can therefore be utilized in the prediction of a missed abortion in pregnant women with gestational age <14 weeks who are at risk. The optimal cut-off values were 4.46 for NLR and 63.2 for PLR.

Keywords: Neutrophil-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio, Missed Abortion, First Trimester.

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Introduction

Regarding miscarriages, early pregnancy loss is among the most prevalent issues during the reproductive era, accounting for about 26% of all pregnancies. The first 12 weeks of pregnancy account for 80% of miscarriages, with the incidence of miscarriage gradually declining after this week. [1,2] CBC (Complete Blood Count) parameters are rapid, simple and cost-effective indicators of systemic inflammation and immune balance. The NLR (Neutrophil-to-Lymphocyte Ratio), LMR (Lymphocyte-to-Monocyte Ratio), and PLR (Platelet-to-Lymphocyte Ratio) are all indices calculated from a simple complete blood count. Owing to the significant potential values of these ratios reflecting inflammatory status, they are frequently introduced as markers of underlying

inflammatory burden in various diseases and also in various pregnancy complications. Placental dysfunction is considered to be the common factor in the etiopathogenesis of both MA and preeclampsia. In preeclampsia, inflammatory markers rise. Some research has looked into markers including NLR, PLR, and MLR in first trimester MA cases based on this theory. [3,4] However, there has not been a consensus on the optimal cut-off values of these markers to be used. Therefore, this study was conducted with the aim of assessing the role of platelets to lymphocyte and neutrophil to lymphocyte ratios in the first trimester of missed abortion and to elucidate the optimal cut-off values.

Materials and Methods

This was a case-control study conducted over a period of 2.5 years involving pregnant women with gestational age <14 weeks who had missed abortion within 1 week. 40 subjects were considered in each group. The age group of the study subjects was between 17 and 42 years. The study excluded women with comorbidities, those taking glucocorticoids or anti-inflammatory medicines, those with identifiable pathologies such as uterine deformities that were thought to be implicated in the pathophysiology of missed abortions, and those who were pregnant with an embryonic seed. Quantitative variables were expressed in terms of mean and standard deviation

and categorical variables were expressed in terms of percentage. NLR and PLR responses were evaluated by ROC (Receiver Operating Characteristic) analysis. Also, the AUC (Area Under the Curve) value, sensitivity, and specificity values were calculated. A p-value of <0.05 was considered to be significant.

Results

The mean age of cases was 26.25 ± 4.6 years, and control was 25.75 ± 4.4 . There was no statistically significant difference between two groups for age. ($p > 0.05$). The majority of study subjects belonged to the 20–25 year age group in cases and the control group, respectively. (Table 1)

Table 1: Age Distribution

Age (in years)	Cases n (%)	Control n (%)	P-Value
20-25	17 (42.5)	16 (40)	0.65
26-30	16 (40)	15 (37.5)	
31-35	6 (15)	7 (17.5)	
36-40	1 (2.5)	2 (5)	
Total	40 (100)	40 (100)	
Mean \pm SD	26.25 \pm 4.6	25.75 \pm 4.4	

The mean BMI in cases 19.64 ± 2.4 was statistically significantly lower compared to the control group 22.29 ± 2.5 . ($p < 0.001$).

The mean gestational age of MA cases was 53.82 ± 10.54 and controls was 53.12 ± 11.04 days. The mean gravida in MA (Missed Abortion) cases was 1.92 ± 0.72 and in controls was 1.80 ± 0.70 . The mean parity in MA cases was 0.97 ± 0.65 and in the control group was 0.92 ± 0.76 . There was no

statistical difference between the groups in terms of gestational age, gravida, parity, and abortion. ($p > 0.05$).

Hemoglobin and platelets were found to be statistically significantly lower in the cases compared to the control group. Neutrophils and lymphocytes were found to be statistically significantly higher in cases compared to the control group. ($p < 0.001$), as shown in Table 2.

Table 2: Hematologic Parameters

Hematologic Parameters	Cases (Mean \pm SD)	Control (Mean \pm SD)	P-Value
Hemoglobin	10.75 \pm 1.01	11.62 \pm 1.09	<0.001
Hematocrit	32.92 \pm 1.80	33.75 \pm 2.07	0.05
Platelets	1.866 \pm 0.14	2.62 \pm 0.43	<0.001
Leukocytes	11069 \pm 1562	10940 \pm 1804	0.34
Neutrophils	7876.8 \pm 1498	4088 \pm 631.09	<0.001
Monocytes	322.12 \pm 57.21	290.25 \pm 44.83	0.07
Lymphocytes	2972 \pm 758.17	1268.4 \pm 105.45	<0.001

When comparing cases to the control group, it was discovered that NLR and LMR were statistically considerably greater, whereas MLR and PLR were statistically significantly lower. ($p < 0.001$) as shown in Table 3 and Figure 1.

Table 3: Hematologic Ratios

Hematologic Ratios	Cases (Mean \pm SD)	Control (Mean \pm SD)	P-Value
NLR	4.62 \pm 0.54	3.07 \pm 0.30	<0.001
MLR	0.13 \pm 0.22	1.18 \pm 0.11	<0.001
PLR	65.90 \pm 18.60	102.62 \pm 16.03	<0.001
LMR	9.67 \pm 2.79	4.22 \pm 0.81	<0.001

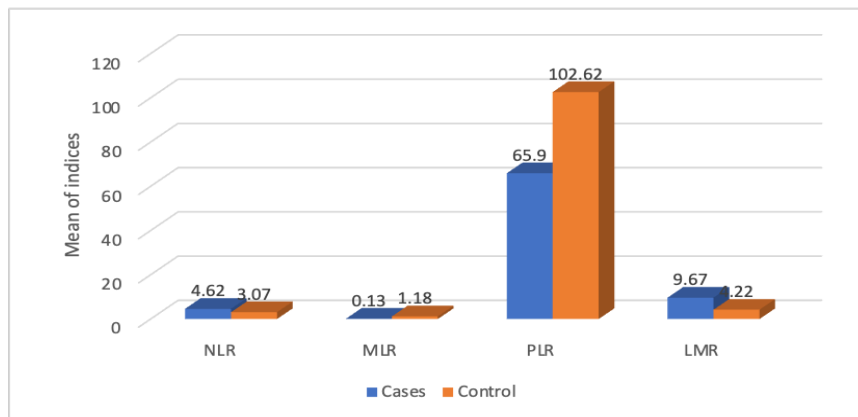


Figure 1: Hematologic Ratios

ROC analysis was performed to determine the diagnostic NLR value for cases (MA). It was concluded that the best predicted value for MA based on AUC was NLR with an optimal cut-off value of 4.46 and AUC of 0.71, with specificity and sensitivity of 96.5% and 81.4%, respectively, as shown in Figure 2.

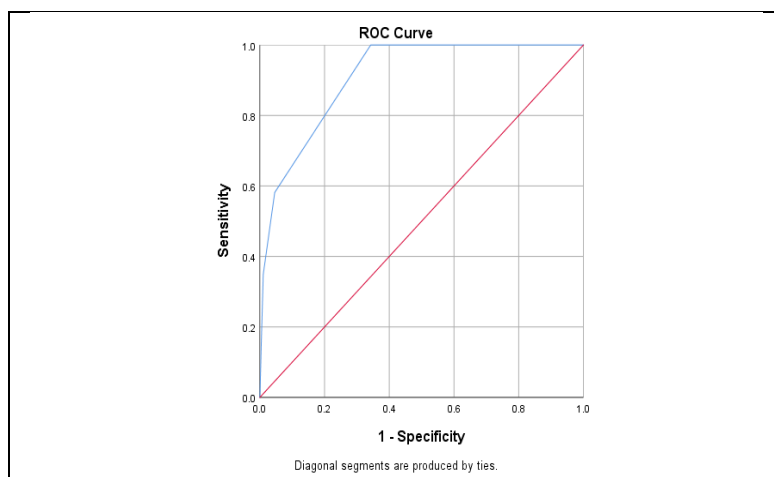


Figure 2: The ROC Curve Analysis for the NLR. The Area Under Curve for the NLR was 0.71 (95% Confidence Interval 0.573-0.847, p=0.00)

ROC analysis determined the diagnostic PLR value for cases (MA). It was concluded that the best predicted value for MA based on AUC was PLR with an optimal cut-off value of 63.2 and AUC of 0.88, with specificity and sensitivity of 66% and 98%, respectively, as shown in Figure 3.

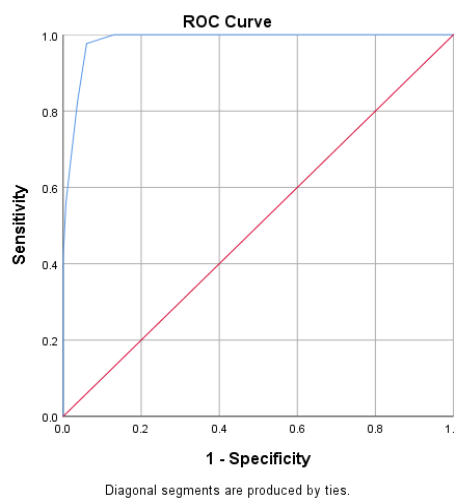


Figure 3: The ROC Curve Analysis for the PLR. The Area Under the Curve for the NLR was 0.88 (95% Confidence Interval 0.763-0.923, p=0.00)

Discussion

A missed abortion is when an embryo loses part of its viability and stays inside the uterus. In 15% of clinical pregnancies, MA is found. [3] Regarding age, there was no statistically significant difference seen between the two groups in this investigation. The mean BMI in cases was statistically significantly lower compared to the control group ($p < 0.001$). This finding was in contrast to studies by Biyik et al., [5] and Erin et al., [6] in which no significant difference ($p > 0.05$) was observed in BMI between the spontaneous abortion and control groups.

There was no statistically significant difference between two groups with respect to gestational age, gravida, parity, and abortion ($p > 0.05$). Similar to our study findings, Onur Yavuz et al., [7] Biyik et al., [6] and Oğlak and Aydın et al., [8] in their studies did not find a difference between the missed abortion and healthy pregnant women with respect to these observations.

In this study, hemoglobin and platelet counts were found to be statistically significantly lower in the cases compared to the control group. It was discovered that the case group had statistically considerably more neutrophils and lymphocytes than the control group. ($p < 0.001$). Leukocyte and neutrophil values were also shown to be statistically substantially higher in the MA group ($p = 0.001$, $p = 0.003$) by Onur Yavuz et al., [5] Nevertheless, Biyik et al., [6] discovered that there was no significant difference ($p > 0.005$) in the groups' haemoglobin, platelet, and neutrophil values. Patients who had missed abortions had decreased haematocrit, MPV, and lymphocyte levels when compared to controls ($p = 0.027$, $p = 0.044$, and $p = 0.025$, respectively). Oğlak and Aydın [7] reported that the neutrophil count was significantly higher ($p < 0.05$) and the lymphocyte count was significantly lower ($p < 0.05$) in the early pregnancy loss group than the control group.

In the present study, NLR and LMR were found to be statistically significantly higher in cases compared to the control group, and MLR and PLR were statistically significantly lower in cases compared to the control group ($p < 0.001$). Similar to our observation, Onur Yavuz et al., [7] found that NLR values were found to be statistically significantly higher in the MA group ($p = 0.02$); though PLR values were higher in missed abortion compared to the control group, they were not statistically significant. MLR values are similar in both missed abortion and control groups. Biyik et al., [5] found that platelet distribution width, NLR, and PLR values were higher in the missed abortion group ($p = 0.043$, $p = 0.038$, and $p = 0.010$, respectively). Erin et al., [6] found that NLR and PLR mean differed significantly across the

spontaneous abortion and control groups ($p = 0.049, 0.039$). Oğlak and Aydın [8] also reported that the NLR and PLR values were significantly higher in the early pregnancy loss group than the control group ($p < 0.05$).

In a retrospective case-control research, Yakıştıran B et al., [9] found statistically significant differences for NLR, SII, and PLR ($p = 0.001$, $p = 0.039$, and $p = 0.000$, respectively). The comparison between elective abortions and healthy pregnancies revealed that only NLR differed statistically ($p = 0.050$). They came to the conclusion that lower PLR and NLR values might be applied as useful and affordable indicators for miscarriage prediction. Süleyman Additionally, Cemil Oğlak et al., [8] discovered that the early pregnancy loss group's NLR and PLR values were considerably greater than those of the control group ($p < 0.05$). High PLR and NLR readings, according to the authors, were powerful indicators for predicting the loss of an early pregnancy.

The neutrophil-to-lymphocyte ratio was investigated by Kim Y et al., [10] to determine its predictive usefulness in cases of early miscarriages. 72 women in group 2 had missed abortions, while 104 women in group 1 had been threatened with one. There was a noteworthy variation in NLR seen between the groups ($p = 0.001$; $p < 0.01$). NLR was the only predictor of an early miscarriage, according to the multivariate analysis (odd ratio [OR], 0.732; 95% confidence interval [CI], 0.612-0.881, $p = 0.001$). The optimum cutoff value was 5.72 ($p < 0.05$), and the area under the receiver-operating characteristic of NLR for differentiating between the missed and threatened abortion groups was 0.792.

On the other hand, Liu et al., [11] retrospective cohort study, which included 400 women-200 of whom had missed an early miscarriage and 200 of whom had a normal pregnancy-found no evidence of a significant difference between the two groups' WBC, RBC, PLT, RDW-SD, PDW, neutrophil, lymphocyte, NLR, and PLR levels ($p > 0.05$). In order to find out how pregnancy outcomes in women who have been threatened with an early abortion relate to factors associated with inflammation, Feng QT et al., [12] undertook a study. They discovered that the pregnancy outcomes for NLR (OR: 0.92, CI 95%: 0.72, 1.17) and PLR (OR: 1.00, CI%: 0.99, 1.01) did not differ significantly from one another.

In this investigation, we found that NLR, with an ideal cut-off value of 4.46 and an AUC of 0.71, along with specificity and sensitivity of 96.5% and 81.4%, respectively, was the best predicted value for MA based on AUC. With an ideal cut-off value of 63.2 and an AUC of 0.88, along with specificity and sensitivity of 66% and 98%, respectively, PLR

was the best predicted value for MA based on AUC. According to Onur Yavuz et al., [7] NLR had the best predicted value for MA based on AUC, with an ideal cut-off value of 4.56 and an AUC of 0.62, along with 52% and 86% of specificity and sensitivity, respectively. Kim et al., [10] study and Wang et al., [4] study both reported that the NLR threshold value used to predict MA was less than 5.72 and less than 2.4. There could be two reasons for the discrepancies between this research and the literature. First, the patients' progesterone admission status could have an impact on the result. Second, the change in blood biomarkers between the moment the patient's MA state manifests and the ultrasound-detected diagnosis cannot be computed.

A PLR score > 123.14 indicated miscarriage with 62.5% sensitivity and 55% specificity, according to Biyik et al., research. [5] According to Uckan et al., [13] ROC analysis findings The PCT, NLR, and PMI areas under the curve were 0.62, 0.85 and 0.61, respectively ($p = 0.24$). A high risk of miscarriage was strongly associated with NLR > 2.99 and PMI > 2430.9 ($p < 0.05$).

Conclusion

Increased maternal systemic inflammatory processes play a role in the estimation of MA. In our study, NLR and LMR were found to be statistically significantly higher, while MLR and PLR were statistically significantly lower in those with MA compared to healthy pregnant women. These markers can therefore be utilized in the prediction of a missed abortion in pregnant women with gestational age less than 14 weeks who are at risk. The optimal cut-off values were 4.46 for NLR and 63.2 for PLR.

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