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ORIGINAL ARTICLE

Evaluation of first-trimester hematological indices in preeclampsia: A retrospective observational case-control study

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ABSTRACT

Objective: Preeclampsia (PE) is one of the leading major causes of maternal and neonatal mortality and morbidity. Improving the outcome for preeclampsia necessitates early prediction of the disease to identify women at high risk. Evaluation of hematological parameters might provide prognostic and diagnostic clues to diseases. The purpose of this study is to investigate hematological changes in early pregnancy using complete blood counts in order to determine whether these measurements may provide useful information for the early diagnosis of preeclampsia.

Material and Methods: This retrospective observational case–control study was conducted at a tertiary referral center between August 2020 and February 2022. Medical records of women with preeclampsia and healthy controls were compared regarding clinical characteristics and first-trimester hematological parameters. Receiver operating characteristic curve analysis was performed to identify the optimal white blood cells level predicting preeclampsia.

Results: The white blood cells (WBC) values were significantly higher in the preeclampsia group compared with the control group ($p<0.049$). There were no significant differences in other hematological parameters between the groups. For WBC, the values of area under the curve were 0.605, and the p-value for this parameter statistically differed ($p=0.049$).

Conclusion: This study showed that WBC may be a useful marker in the prediction of preeclampsia in early pregnancy.

Keywords: Neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, preeclampsia, white blood cells.

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INTRODUCTION

Preeclampsia (PE) is a significant complication that involves 2-8% of pregnant women and can lead to maternal and neonatal morbidity and mortality. It is a major cause of maternal death in developing countries, primarily due to eclampsia resulting from untreated preeclampsia.[1]

The cause of PE is placental dysfunction and hypoxia, which triggers immunological factors.[2–4] Despite extensive research, the root causes of the excessive systemic inflammation response in normal pregnancy and PE remain unclear.

The immune system can be assessed through a simple and cost-effective test named complete blood count (CBC). This test displays different cellular components of blood and their distribution, which is valuable in evaluating various obstetric complications such as PE.[5] Hematologic parameters derived from CBC can provide diagnostic and prognostic clues to diseases.[6–8]

While many studies have examined hematologic parameters in preeclampsia, uncertainty remains regarding their predictive value of first-trimester CBC parameters in PE. Early prediction of PE is crucial to improve outcomes and identify women at high risk. Therefore, this study was to compare CBC indices between preeclamptic and healthy pregnant women during the first trimester.

MATERIAL AND METHODS

This retrospective observational case-control study was carried out by primiparous singleton pregnant women aged 18-40 years and delivered at a tertiary hospital from August 2020 to February 2022. Our study was granted by the Ethics Committee (23.03.2022/39) and follows the tenets of the Declaration of Helsinki.

Women were stratified into two groups: a healthy control group and a group with PE, as determined by the American College of Obstetrics and Gynecology guidelines.[9] The healthy control group was randomly selected from patients with uncomplicated pregnancies hospitalized during the same period.

Patients with chronic systemic diseases, autoimmune disease, renal or hepatic diseases, cardiovascular disease, malignancies, thyroid disorders, any medication use, Body Mass Index ≥30 kg/m², a history of recurrent miscarriages or infertility, history of thrombophilia or any other medical condition requiring chronic drug treatment, the use of acetylsalicylic acid, complicated pregnancies, multiple gestations, inflammatory bowel diseases, smoking, anemia, hepatitis infections, ruptured membranes, or any active local or systemic infection which could affect maternal complete blood count results were excluded.

Sociodemographic information, obstetric, clinical characteristics, and laboratory results were extracted from electronic medical records. We collected the blood tests for all patients during the first trimester. When multiple CBC results were available, the result closest to 6 weeks of gestation was selected. The NLR and PLR were computed by dividing neutrophils and platelets by lymphocytes, respectively.

Statistical Analysis

Statistics were analyzed with SPSS v. 25.0. The variables were presented as mean±standard deviation. We utilized Chi-square test, Student's t-test, and the Mann-Whitney U test, when necessary.

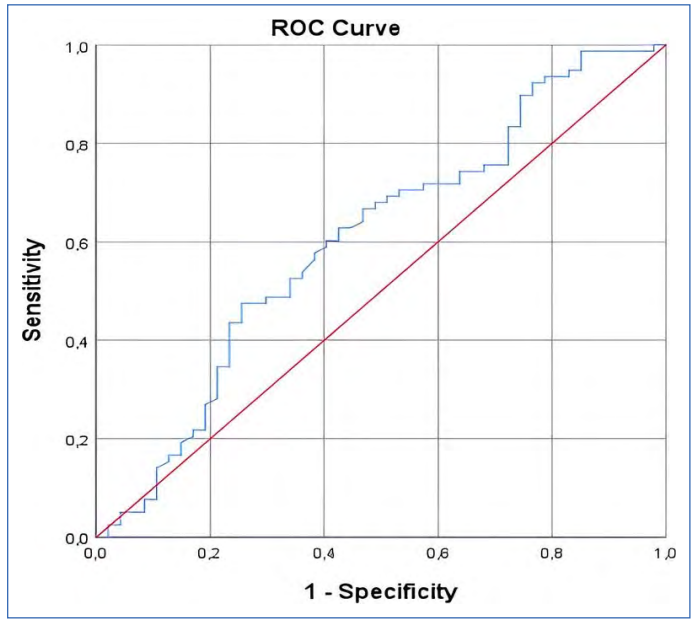

Figure 1: Area under the receiver operating characteristic curve for white blood cell measurement for predicting preeclampsia. The area under the curve was 0.605 (95% confidence interval 0.500–0.710).

Receiver operating characteristic (ROC) curves were constructed to determine the cut-off values, sensitivity, and specificity. Statistical significance was considered as $p<0.05$.

RESULTS

Seventy-eight pregnant women with PE and 47 healthy controls were enrolled in the study. The maternal age and gestational week at blood sampling did not differ between groups. The PE group had higher mean blood pressures and lower APGAR scores at 1- and 5-minute than the healthy control group (all p=0.001).

Hemoglobin, lymphocyte count, neutrophil count, platelet count, red blood cell distribution width (RDW), and MCV during the first trimester were comparable between the two groups. The first-trimester white blood cells (WBC) counts for the PE group were significantly higher in comparison to those of the healthy control group (p=0.049). NLR and PLR values were not significantly different between groups (Table 1).

ROC curves indicated that the cut-off point for WBC was 9.7×10^3/µL, exhibiting a sensitivity of 62.8% and a specificity of 57.4%. ROC curve analysis revealed an AUC of 0.605 (95% CI 0.500–0.710) (Fig. 1).

DISCUSSION

The study found that women with preeclampsia had higher levels of WBC in comparison to the healthy controls. Other hematologic parameters did not differ between groups. NLR and PLR are easily calculated, cost-effective inflammatory indexes. Evidence concerning the association between NLR and PLR values and preeclampsia is contradictory.[1,10–12] While Gogoi et al.[13] observed significantly higher values of NLR and PLR in women with PE, the present study found no differences in these indices between groups. These results were in agreement with those of Örgül et al.,[14] who also concluded that

Table 1: Comparison of demographic, clinical characteristics and hematological results of preeclampsia group and the control group

	Preeclampsia group (n=78) Mean±SD	Control group (n=47) Mean±SD	p*
Maternal age (years)	29.9±5.8	28.8±5.1	0.326
Gestational age at delivery (weeks)	36.2±4.0	38.5±2.5	0.001
Neonatal birth weight (g)	2576.0±857.6	3131.7±686.4	0.001
APGAR Score 1-minute	6.9±1.3	7.7±0.7	0.001
APGAR Score 5-minute	8.5±0.8	8.9 ±0.5	0.001
Systolic blood pressure (mmHg)	140.8 ±19.8	116.6 ±15.5	0.001
Diastolic blood pressure (mmHg)	90.4 ±14.0	76.8 ±21.6	0.001
Gestational age at blood sampling (weeks)	14.2±4.3	14.4 ±4.1	0.810
Hemoglobin	12.1±1.2	14.0 ±3.9	0.275
White blood cells	10.6±3.0	9.8 ±3.7	**0.049**
Neutrophils (10^3/mm–3)	7.8±2.9	15.2±10.7	0.208
Lymphocytes (10^3/mm–3)	3.1±0.5	2.0±0.6	0.532
Platelets (10^3/mm–3)	259.9±66.5	254.1±67.4	0.638
Mean corpuscular volume (MCV) (fL)	9.5±1.2	9.3±0.9	0.623
Red cell distribution width (RDW)	13.9±1.6	14.3±2.3	0.994
Neutrophil to lymphocyte ratio	4.1±2.5	5.0±5.4	0.723
Platelet to lymphocyte ratio	138.6±76.4	137.2±49.7	0.889

*: P-value≤0.05 statistically significant difference between pre-eclampsia group and control group.

NLR and PLR are not significant predictors in preeclampsia. Similarly, Yavuzcan et al.[15] did not observe a significant increase in NLR in women with PE compared to healthy pregnant women. It should be noted, however, that the insignificant results in this research may be attributed to the small sample size.

Anemia has been shown to have no association with PE, according to a recent systematic meta-analysis,[16] and our study also found no differences in anemia parameters between the preeclamptic and healthy controls. Red blood cell distribution width (RDW), another parameter that is measured during CBC tests, has been associated with inflammation. It has been established that increased RDW levels during pregnancy were related to the occurrence and severity of PE.[1,17] However, in contrast to previous studies, our findings did not show significant differences in RDW values between groups.

This study indicated that women with PE had higher WBC counts in comparison to the controls. In addition, a WBC count >9.7×10³/μL was associated with PE. These findings were comparable to those of Örgül et al.,[14] who also concluded that an increased first-trimester WBC count is linked to early-onset PE. However, no difference was observed with regard to eosinophils, basophils, monocytes, and lymphocytes. It has been suggested that the increased WBC levels in the first trimester are caused by endothelial dysfunction in PE.

Our study has some limitations due to its single-center design and small sample size. However, it is worth noting that the dataset collected during the study is one of the few rigorously collected datasets regarding PE. Further multicenter research is necessary to confirm the changes in hematological values that occur during the first trimester of pregnancy that is complicated by PE. These findings may contribute to the development of effective diagnostic tools and therapeutic interventions for PE.

CONCLUSION

The present study found that first-trimester increased WBC levels were associated with PE, while other inflammation markers did not exhibit any significant differences between groups.

Statement

Ethics Committee Approval: The Istanbul Zeynep Kamil Maternity and Children's Diseases Health Training and Research Center Clinical Research Ethics Committee granted approval for this study (date: 23.03.2022, number: 39).

Author Contributions: Concept – EK, LK, PK, ZK; Design – EK, LK, PK, ZK; Supervision – EK, LK, PK, ZK; Resource – LK, ZK; Materials – LK, ZK; Data Collection and/or Processing – LK, ZK; Analysis and/or Interpretation – PK; Literature Search – EK, LK, PK, ZK; Writing – EK, LK, PK, ZK; Critical Reviews – EK, LK, PK, ZK.

Conflict of Interest: The authors have no conflict of interest to declare.

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