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Original Article

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Evaluation of the Neutrophil-Lymphocyte Ratio and Platelet-Lymphocyte Ratio in Patients With Ectopic Pregnancies

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Abstract

Background: The aim of this study was to evaluate hematologic parameters in ectopic pregnancy.

Methods: This retrospective study was conducted at Izmir Katip Celebi University Ataturk Education and Research Hospital between January 2016 and June 2017. The medical records of 97 patients hospitalised for ectopic pregnancy (EP) were summarised. The control group consisted of 112 women at 6 - 8 weeks, healthy, intrauterine gestations as confirmed by ultrasound (positive fetal heart rates). Hematologic parameters including white blood cells, hemoglobin and platelet counts, neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and mean platelet volume (MPV) were compared.

Results: In total, 209 patients were included in the study: 112 with healthy pregnancies and 97 with EPs. There was no statistically significant difference between the groups regarding mean age, gravidity, parity, number of abortions, body mass index, history for previous cesarean deliveries, and previous EPs. The MPV level was lower in the EP group than in the control group. In addition, the mean NLR was higher in the EP group than in the controls.

Conclusions: Considering the sensitivity and specificity, overall, the NLR and MPV has moderate diagnostic potential in patients with ectopic pregnancies.

Keywords: Ectopic pregnancy; Neutrophil-lymphocyte ratio; Platelet-lymphocyte ratio

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Introduction

Ectopic pregnancy (EP) is a clinical condition in which the pregnancy is implanted outside the uterine cavity. Most of the time, gestational material implants in the fallopian tube (98%) [1]. The main risk factors of EP are history of previous EP, tubal damage due to tubal surgery or infection, smoking, and use of assisted reproductive techniques [2]. The pathogenesis depends on changes in the tubal microenvironment and ciliary dysfunction leading to failure of successful transport of the fertilized ovum to the uterine cavity [3]. Early diagnosis and accurate treatment are very important for EP because it may cause intra-abdominal bleeding due to tubal rupture. EP is one of the most common causes of maternal death in the first trimester of pregnancy, accounting for 6-10% of pregnancy-related mortality [1, 4].

In recent studies, the neutrophil-lymphocyte ratio (NLR) has become a commonly used marker of systemic inflammatory response [5]. This ratio is determined with current hematologic parameters without additional costs, by dividing the total neutrophil count by the number of lymphocytes. Also, the platelet-lymphocyte ratio (PLR) and mean platelet volume (MPV) have proved useful as predictive and prognostic markers in various systemic inflammatory diseases, cardiovascular diseases, and malignancies [6, 7]. It has been found that inflammatory cytokine levels are elevated both in the region of inflammation and systemic circulation during EPs [3]. Inflammatory signalling mechanisms (leukocytes guided by cytokines, chemokines and integrins) are also involved in directing and engaging the embryo to the site of implantation [8].

In this study, we evaluated the change in complete blood count parameters in EP.

Materials and Methods

This retrospective study was conducted at Izmir Katip Celebi University Ataturk Education and Research Hospital between January 2016 and June 2017. The Institutional Ethics Committee approved the study (2017/197). The medical records of 97 patients hospitalised for EP and 112 patients at 6 - 8 weeks, healthy, intrauterine gestations as confirmed through an ultrasound examination (positive fetal heart rates) were reviewed. The exclusion criteria were as follows: any findings of rupture of EP such as hemodynamic instability or intra-abdominal bleed-

Table 1. Comparison of Demographic Parameters

Variables	EP group	Control group	P value
Age, years (mean ± SD)	27.43 ± 5.56	30.41 ± 5.452	0.76
Gravida, n (mean ± SD)	2.73 ± 1.49	2.58 ± 1.476	0.77
Parity, n (mean ± SD)	2.12 ± 1.76	1.93 ± 0.21	0.56
Abortion, n (mean ± SD)	0.25 ± 0.64	0.27 ± 0.9	0.49
Gestational age (days) (mean (min - max))	46.4 (32 - 68)	51.6 (41 - 79)	0.82
BMI (mean ± SD)	26.01 ± 4.96	27.28 ± 4.63	0.47
Previous cesarean delivery (n, %)	28 (31%)	34 (30%)	0.76
Previous ectopic pregnancy (n, %)	4 (4.1%)	6 (5.3%)	0.82

EP: ectopic pregnancy; SD: standard deviation; BMI: body mass index.

ing, known chronic inflammatory disease or connective tissue disorders, use of anticoagulants, smoking, acquired or congenital hematologic disorders, and use of any medication that could interfere with platelet (PLT) function and number. We evaluated all complete blood count parameters. Additionally, we recorded the demographic and clinical characteristics of all patients.

We compared the laboratory data including white blood cell (WBC) counts, hemoglobin, human chorionic gonadotropin (hCG), NLR, PLR, MPV, and PLT values of the two groups.

Statistical analyses

The IBM Statistical Package for the Social Sciences (SPSS), version 22, was used for statistical analysis. The Chi-square test was used for categorical variables. Mean and standard deviations (SD) were used for descriptive analysis. The Mann-Whitney test and Student's *t*-test were used for statistical comparisons of the two groups. P values < 0.05 were regarded as statistically significant for all comparisons.

Results

In total, 209 pregnant women were included in the study: 112 with healthy pregnancies (control group) and 97 with EPs. The mean ages of the EP group and control group were 27.4 ± 5.5 years and 26.3 ± 4.6 years, respectively; there was no significant difference between the groups (P > 0.05). Table 1 shows the demographic data of the two groups. There were no statistically significant differences between the groups regarding mean age, gravidity, parity, number of abortions, gestational age, body mass index (BMI), history of previous cesarean deliveries and previous EPs (P > 0.05). When analysing the laboratory data of the two groups, no significant differences were seen between the groups with regards to mean hemoglobin, PLR and PLT values (P > 0.05). The mean WBC level was 11.18 ± 2.87 × 10^9 cells/L in the EP group and 8.18 ± 8.7 × 10^9 cells/L in the control group. The mean WBC level was found to be statistically significantly higher in the EP group than in the control group. The mean hCG level was found to be statistically significantly higher in the control group than in the EP group (P < 0.05). The mean MPV level was 9.29 ± 2.64 fL in the EP group and 11.79 ± 1.44 fL in the control group (P < 0.05). The MPV level was found to be statistically significantly lower in the EP group than in the control group (P < 0.05). In addition, the mean NLR was found to be higher in the EP group than in the control group (P < 0.05). Table 2 shows the comparison of the laboratory variables between the two groups.

Discussion

The present study revealed that the NLR and MPV were higher in EPs. Tubal EP is the implantation of the fertilized ovum in the fallopian tubes due to a defect or variations in the tubal

Table 2. Comparison of Hematologic Variables

Variables	EP group	Control group	P value
WBC (10^3/μL) (mean ± SD)	11.18 ± 2.878	18 ± 8.75	0.016
Hgb (g/dL) (mean ± SD)	11.21 ± 2.16	10.69 ± 1.96	0.58
hCG (mIU/mL) (mean (min - max))	1,542 (327 - 7,244)	3,073 (187 - 14,758)	0.033
NLR (mean ± SD)	4.98 ± 3.39	2.81 ± 5.41	0.038
PLR (mean ± SD)	118.34 ± 64.49	116.84 ± 74.59	0.92
MPV (fL) (mean ± SD)	9.29 ± 2.64	11.79 ± 1.44	0.046
PLT (10^3/μL) (mean ± SD)	193.9 ± 84.6	203.1 ± 64.3	0.64

EP: ectopic pregnancy; WBC: white blood cell; hCG: human chorionic gonadotropin; NLR: neutrophil-lymphocyte ratio; PLR: platelet-lymphocyte ratio; MPV: mean platelet volume; PLT: platelet; SD: standard deviation.

lumen during the transport of the fertilized ovum. The level of inflammatory cytokinesis increased both in the region of inflammation and in the systemic circulation in EP patients [3]. The complete blood count is one of the tests that are routinely checked during the evaluation of all pregnant women. MPV and platelet distribution width (PDW) are PLT indices that are measured in cell counters, which employ impedance and optical effects [9]. MPV is a marker of PLT activation and function. It has become evident that MPV is a reflection of both proinflammatory and prothrombotic conditions, where thrombopoietin and numerous inflammatory cytokines (e.g. interleukin (IL)-1, IL-6, and tumour necrosis factor (TNF)-α) regulate thrombopoiesis. In EP, due to inflammation at the implantation site and alterations in the microenvironment of the fallopian tube, PLT indices such as MPV and PDW should be different from those in controls with viable healthy intrauterine pregnancies [10].

In a recent study, routine blood counts of 138 patients with tubal EP were evaluated and compared with72 healthy pregnant patients, retrospectively. The authors found lower PDW levels and higher monocyte counts in tubal EP and reported that the role of monocyte activation in the pathophysiology of EP could be effective in tubal motility and might dysregulate the microenvironment [11]. In another study, Turgut et al showed higher MPV levels in patients with EP compared with controls [10]. MPV levels, which are a marker of PLT function, were higher in women with EPs because PLTs may participate in the development of endothelial damage, angiogenesis, and hypoxia in EP. Turgut et al concluded that increased PLT activity might contribute to the pathogenesis of EP [10]. On the other hand, a recent study found lower MPV levels in tubal EP [12]. The authors suggested that possible high-grade inflammation in pathology may have led to this result.

The number of leukocytes in the circulation changes during the inflammatory response. The response of leukocytes to stress causes an increase in neutrophils and decreases the lymphocyte count, and thus, the ratio of neutrophils and lymphocytes can be used as a marker of inflammation in intensive care practices [13]. Dogru et al reported elevated NLR levels in ruptured EPs compared with women with unruptured EPs [14]. In the same study, PLR values were similar in the two groups. In our study, both parameters were detected as high in patients with EP. Donmez et al reported that the NLR and PLR inflammatory markers were significantly high in patients with ruptured EPs, but MPV levels were found similar between the groups. There was no difference between patients who were successfully and unsuccessfully treated with methotrexate in terms of NLR and PLR [15]. An important goal in the evaluation of women in early pregnancy is to exclude the possibility of EP because ruptured EP can result in severe hemorrhage and even death. Our study was a retrospective analysis; therefore, the predictive value of NLR and MPV levels for EP is suboptimal. We think that NLR and MVP can be used together for the prediction of patients with EP; however, further studies are needed.

Akkaya et al reported that hematologic parameters could be helpful in the choice of treatment of EP. In their report, they investigated whether hematologic parameters could predict the response to medical treatment in EP and concluded that red cell distribution width (RDW) and MPV values were associated with methotrexate treatment [16]. The major limitation of our study is that we did not analyse the relationship between hematologic parameters and treatment response.

In conclusion, the gold standard for the diagnosis of EP is still the combination of ultrasound and serial measurements of b-hCG. We found that initial MPV and NLR values were higher in patients with EPs. We aimed to facilitate the early prediction of EP with the help of complete blood count parameters that are routinely used in obstetrics clinics with which no additional cost is required. Considering the limitations of the study, overall, the NLR and MPV could be have a diagnostic potential in patients with EP.

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None to declare.

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Conflict of Interest

We confirm that there are no known conflicts of interest.

Informed Consent

Informed consents were obtained from the patients.

Author Contributions

Study conception and design: Gencdal S. Acquisition of data: Aydogmus H, Gencdal Kiziltug N and Gencdal S. Analysis and interpretation of data: Ekmekci E, Aydogmus H and Destegul E. Drafting of manuscript: Gencdal S and Gencdal Kiziltug N. Critical revision: Gencdal S, Gencdal Kiziltug N and Destegul E.

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