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The Relationship Between Complete Blood Count Parameters and Pregnancy Outcomes in Women Who Wanted to Become Pregnant

Gebelik İstemi Olan Kadınların Tam Kan Sayımı Parametreleri ile Gebelik Sonuçları Arasındaki İlişki

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ABSTRACT

Background: Oxidative stress due to inflammatory processes in women who want to become pregnant affects the chance of pregnancy success. In our study, we aimed to evaluate the effect of the platelet/lymphocyte ratio (PLR) and neutrophil/lymphocyte ratio (NLR), which are indicators of systemic inflammation and are assessed in the complete blood count parameters, on the pregnancy success of women who desire pregnancy.

Materials and Methods: The data of 170 patients who applied to Giresun Gynecology and Obstetrics outpatient clinic requesting pregnancy between December 2022 and December 2024 were retrospectively analyzed, and the data of 94 patients who met the inclusion and acceptance criteria were evaluated. Demographic data, ovarian reserve test data, thyroid stimulating hormone data, prolactin data, neutrophil data, lymphocyte data, platelet data, NLR, data PLR data of these patients were compared between pregnancy and non-pregnancy groups.

Results: Lymphocyte count and PLR were higher in the group with biochemical pregnancy (p=0.048 and p=0.046). PLR was significantly higher in the group with clinical pregnancy (p=0.020). There was no statistical difference in ovarian reserve tests, and other parameters between the groups, with and without biochemical and clinical pregnancy.

Conclusion: While PLR and high lymphocyte count were significant for predicting biochemical pregnancy occurrence, other parameters had no effect on pregnancy occurrence.

Keywords: Inflammation, platelet/lymphocyte ratio, pregnancy

ÖZ

Amaç: Gebelik istemi olan kadınlarda enflamatuvar süreçlere bağlı meydana gelen oksidatif stres gebelik başarı şansını etkilemektedir. Çalışmamızda gebelik istemi olan kadınların tam kan sayımı parametrelerinde değerlendirilen ve sistemik enflamasyonun göstergesi olan platelet/lenfosit oranı (PLO) ve nötrofil/lenfosit oranının (NLO) gebelik başarısı üzerinde etkisini değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Giresun Kadın Hastalıkları ve Doğum polikliniğine Aralık 2022-2024 tarihleri arasında enfertilite nedeni ile başvuran 170 hastanın verileri retrospektif olarak incelendi. Dışlama ve kabul edilme kriterlerine uygun 94 hastanın verileri değerlendirildi. Bu hastaların demografik verileri, over rezerv testleri, troid stümülan hormon, prolaktin, nötrofil, lenfosit, platelet, NLO, PLO verileri değerlendirildi. Bu veriler biyokimyasal, klinik gebeliği olan ve gebelik oluşmayan hastalar olmak üzere iki grup halinde karşılaştırıldı.

Bulgular: Gruplar arasında lenfosit sayısı ve PLO biyokimyasal gebeliği olan grupta daha yüksek saptandı (p=0,048 ve p=0,046). Klinik gebeliği olan grupta PLO anlamlı şekilde yüksek saptandı (p=0,020). Over rezerv testleri ve diğer parametreler, biyokimyasal ve klinik gebeliği olan ve olmayan gruplar arasında benzer saptandı.

Sonuç: PLO ve lenfosit sayısının yüksek olması biyokimyasal gebelik oluşumu açısından anlamlı iken, diğer paramatrelerin gebelik oluşumu açısından bir etkisinin olmadığı saptandı.

Anahtar Kelimeler: Inflamasyon, platelet/lenfosit oranı, gebelik

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Introduction

Infertility is defined as the inability of couples to conceive despite one year of regular intercourse (1). Women who desire pregnancy can be evaluated, and pregnancy can be achieved with ovulation induction under appropriate conditions. Causes of infertility include poor ovarian reserve, male factor, uterine causes, and unexplained infertility where no cause is found after all these have been investigated. When couples are investigated, approximately 30% do not have an identifiable cause for infertility and this group is referred to as unexplained infertility (2).

One of the most important factors causing infertility is implantation failure. The immunological and inflammatory processes that occur during fertilization and implantation of the embryo play an important role in pregnancy. Implantation of the embryo depends on the interaction and compatibility of the trophoblast with the epithelial cells of the endometrial villi. The period between days 20-24 of the menstrual cycle, when the endometrium is favorable for implantation, is called the implantation window. This period is the time when secretory glands enlarge, and superficial protrusions called pinopods, and microvillus structures are seen (3). The density of endometrial integrins, steroid hormone levels, and cyclooxygenase 2 levels are also important for implantation. Suppression of maternal lymphocyte function and lack of fetal antigen presentation to maternal lymphocytes play a role in the development of fetomaternal immune tolerance during implantation. During pregnancy, the number of B lymphocytes does not change; the number of cluster of differentiation 4 (CD4) T lymphocytes decreases, while the number of CD8 T lymphocytes increases. In the progression of inflammatory processes, platelet count and function are also significant in addition to lymphocytes, with local effect (4). Neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) are important hematologic parameters for demonstrating systemic inflammatory status (5).

In a study where NLR and PLRs were evaluated in the diagnosis of premature ovarian insufficiency, inflammatory processes were blamed although the etiology was not clearly established. It was revealed that the NLR may be important for the diagnosis (6). In another study, it was shown that NLR, as an indicator of inflammation, was associated with the development of spontaneous abortion (7).

Neutrophil count, platelet count, NLR and PLR can be easily evaluated from a complete blood count, which is an inexpensive test to evaluate the systemic inflammatory response in women who want to have children. In our study, we retrospectively analyzed these parameters in women who wanted to have children in order to reveal the effect of these parameters on pregnancy.

Materials and Methods

Data from 170 patients who applied to our center due to infertility between 01.12.2022 and 01.12.2024 were retrospectively analyzed. The patients' age, obstetric history, treatments administered, complete blood count results, and beta (β) human chorionic gonadotropin (hCG) results were analyzed through the hospital system. Patients between the ages of 18-45 years, with no male factor and at least one year of infertility, were included in the study. Women with body mass index (BMI) >30 kg/m^2, follicle-stimulating hormone (FSH) >25 mIU/mL, known chronic diseases (hypertension, diabetes mellitus, chronic liver failure, chronic renal failure, etc.), were excluded.

In our clinic, a complete blood count is performed at the patients' first admission, to determine whether there is any abnormality without any treatment. Venous blood samples of the patients are collected in tubes containing ethylenediaminetetraacetic acid and then are studied in automatic blood analyzers. Neutrophil, lymphocyte, platelet values, NLR, and PLR were analyzed, and their effects on pregnancy were evaluated. Clinical pregnancies of the patients were recorded by assessing the β hCG value taken 14 days later. Those with a positive fetal heartbeat on ultrasonography were recorded as having a confirmed pregnancy.

Demographic information, BMI, treatment protocols, duration of infertility, menstrual patterns, basal hormone levels; FSH, luteinizing hormone (LH) estradiol (E2) and thyroid stimulating hormone (TSH), prolactin (PRL) levels taken during follow-up were recorded.

Ethics committee approval was obtained from the Giresun Training and Research Hospital Ethics Committee (approval number: 25.12.2024/04, dated: 25.12.2024) for the study.

Statistical Analysis

Statistical Package for Social Sciences for Windows (SPSS 20, Chicago, IL, USA) was used for analysis. Kolmogorov-Smirnov test was used to assess the normality of the data distribution. According to the test results, Student's t-test was used for normally distributed groups, and Mann-Whitney U test was used for non-normally distributed groups. A cut-off value will be established through receiver operating characteristic curve analysis, conducted on variables found to be statistically significant. For statistical significance, $p<0.05$ was considered significant.

Results

Patients between the ages of 18-45 years, with no male factor and at least one year of infertility were included

in the study. Women with BMI >30 kg/m^2, FSH >25 mIU/mL, and known chronic diseases (hypertension, diabetes mellitus, chronic liver failure, chronic renal failure, etc.) were excluded. Of the 170 patients screened, 45 had at least one known chronic disease, 14 had uterine anomalies, and 17 had infertility due to male factor. These patients were not included in the study. A total of 94 patients with unexplained infertility who met the inclusion criteria were included in the study.

A total of 94 patients who were receiving infertility treatment and met the inclusion criteria were included in our study. Data from 94 patients were analyzed retrospectively. There were 24 patients with positive β hCG and 8 patients with positive fetal heartbeat.

Age, BMI, FSH, LH, E2, TSH, prolactin, and antimüllerian hormone (AMH) values were similar between β hCG-positive patients (Table 1) and fetal heartbeat-positive (Table 2) and negative patients.

The biochemical pregnancy rate according to β-hCG value was 26.6%. Hematologic data of the patients showed that hemoglobin, neutrophil, platelet, and NLR did not affect biochemical pregnancy. β hCG positivity was found to be higher in patients with low lymphocyte count (p=0.048). Patients with higher PLR had a higher incidence of biochemical pregnancy positivity (p=0.046) (Table 3).

Clinical pregnancy was detected in 8.5% of the patients by fetal heartbeat positivity. Hemoglobin, neutrophil, lymphocyte, platelet, and neutrophil/lymphocyte counts had no effect on clinical pregnancy success. The clinical pregnancy rates were found to be higher in patients with a higher PLR (p=0.020) (Table 4).

A PLN ratio above 164.071 predicted hCG positivity with 50% sensitivity and 85% specificity (p=0.046), while a PLN ratio above 144.098 predicted fetal heartbeat positivity with 100% sensitivity and 68% specificity (p=0.020) (Table 5).

Discussion

This study showed that a high PLR was useful in predicting a higher biochemical and clinical chance of pregnancy success, whereas the NLR had no effect. Following fertilization, the endometrium and the embryo need to recognize and interact with each other for a healthy pregnancy. In the endometrium, macrophages, cyclo-oxygenases, and various immunologic factors play a role in preparing a favorable environment for implantation. This is achieved by development of maternal immune tolerance to the embryo (8).

Chronic inflammation is known to have a negative impact on other characteristics such as oocyte quality, folliculogenesis, hormone production, disease recovery, and fertility (9). However, the effects of these markers on the occurrence of pregnancy in women who want to become pregnant have not been adequately studied. Pre-pregnancy assessment of inflammatory processes and parameters in women who want to become pregnant can be used to predict the chances of pregnancy success.

Studies have shown that inflammatory markers and oxidative stress biomarkers in maternal blood are significantly increased in early pregnancy loss and preeclampsia (10). In contrast to a study in which NLR and PLR were found to be higher in pregnant women with miscarriage compared to normal pregnant women, our study found that the high PLR rate, measured before pregnancy, was significant in terms of clinical and biochemical pregnancy occurrence. Studies have shown that platelets play a role in immunity and/or inflammatory processes (11). NLR and PLR in peripheral blood are markers of systemic inflammatory response (12).

Table 1. Comparison of demographic characteristics and ovarian reserve test results according to β hCG value

	β hCG (n=94, %100)		p-value
	Positive (n=24, 25.6%) Mean + SD (median)	Negative (n=70, 74.4%) Mean + SD (median)	
Age (years)	30.92±5.3 (30.00)	29.30±5.0 (28.00)	0.301
BMI (kg/m^2)	25.09±3.84 (25.00)	25.11±3.24 (25.20)	0.820
FSH (mIU/L)	7.19±3.81 (6.85)	6.08±195 (6.71)	0.862
TSH (mIU/L)	1.95±0.79 (1.80)	2.05±1.34 (1.95)	0.696
LH (mIU/L)	6.38±2.91 (5.88)	7.15±3.66 (6.50)	0.640
PRL (ng/mL)	16.85±9.19 (13.35)	19.90±9.62 (19.25)	0.192
E2 (pg/mL)	38.50±12.60 (36.50)	47.73±16.11 (44.50)	0.068
AMH (ng/mL)	4.55±3.21 (3.69)	4.15±2.38 (3.70)	0.845

Mann-Whitney U test, Student t-test, p<0.05. AMH: Antimüllerian hormone, BMI: Body mass index, E2: Estrodiol, FSH: Follicle stimulating hormone, LH: Luteinizing hormone, PRL: Prolactin, SD: Standard deviation, TSH: Thyroid stimulating hormone, β hCG: Beta human chorionic gonadotropin

Inflammatory processes occurring during miscarriage may cause changes in platelet, neutrophil, and lymphocyte counts. The difference between PLR and NLR ratios evaluated during normal pregnancy and pre-pregnancy, and PLR and NLR ratios evaluated during miscarriage, is the inflammatory processes occurring during miscarriage.

In our study, lymphocyte count was lower in women with positive pregnancy, while platelet count was similar between the groups. When inflammation occurs, the reason for a high NLR is an increase in the number of neutrophils and platelets and a decrease in the number of lymphocytes in the bloodstream (13). Although the decrease in the number of lymphocytes, which is one of the physiologic and inflammatory changes occurring in pregnancy, is similar to this study in the literature. The fact that the number of neutrophils and lymphocytes was similar in both groups is different from the results of this study. The reason for this is that immune system changes in pregnancy, occur through a different mechanism than acute inflammatory processes.

In a study conducted in patients with myocardial infarction, it was revealed that platelet aggregation increased, while platelet count decreased. The neutrophil to lymphocyte ratio also increased due to the inflammatory process that intensified during recovery (14). In our study, similar platelet counts between the groups were found to be insignificant for predicting inflammation. However, the finding that the lymphocyte count was low in hCG positive patients was consistent with the findings of this study (14) and suggested that it could be used as a marker of inflammation.

Although studies suggest that increased PLR and NLR ratios may provide information about inflammatory processes (15), when the numbers of lymphocytes and platelets are considered separately and these values are compared, differences occur in patients. Up to 50% of PLR cases have no clear etiology, but multifactorial conditions such as immunologic, anatomic, genetic, and hematologic disorders are known to cause PLR. It is thought that inflammatory components may cause pregnancy loss through their role

Table 2. Comparison of demographic characteristics and ovarian reserve test results according to fetal heartbeat

	Fetal heartbeat (n=94, 100%)		p-value
	Positive (n=8, 8.6%) Mean + SD (median)	Negative (n=86, 91.4%) Mean + SD (median)	
Age (years)	26.75±2.5 (26.50)	29.92±5.1 (28.50)	0.285
BMI (kg/m^2)	24.95±3.39 (25.00)	25.12±3.38 (25.20)	0.932
FSH (mIU/L)	8.27±1.91 (7.75)	6.70±2.11 (6.55)	0.114
TSH (mIU/L)	1.82±0.82 (1.75)	2.04±1.26 (1.95)	0.783
LH (mIU/L)	6.72±1.62 (6.50)	7.00±3.61 (6.45)	0.877
PRL (ng/mL)	19.27±8.45 (21.9)	19.19±9.69 (17.25)	0.960
E2 (pg/mL)	30.60±12.54 (35.50)	46.85±15.44 (44.00)	**0.046***
AMH (ng/mL)	3.73±0.89 (3.69)	4.28±2.66 (3.70)	0.945

Mann-Whitney U test, Student t-test, p<0.05*. AMH: Antimüllerian hormone, BMI: Body mass index, E2: Estrodiol, FSH: Follicle stimulating hormone, LH: Luteinizing hormone, PRL: Prolactin, SD: Standard deviation, TSH: Thyroid stimulating hormone, β hCG: Beta human chorionic gonadotropin

Table 3. Comparison of complete blood count parameters according to β hCG value

	β hCG (n=94, 100%)				p-value
	Positive (n=24, 25.6%)		Negative (n=70, 74.4%)		
	Min.-max. (median)	Mean + SD	Min.-max. (median)	Mean + SD	
Hemoglobin (gr/dL)	9.3-14.4 (12.4)	12.8±1.49	9.2-14.9 (12.4)	12.6±1.48	0.991
Neutrophil (x10^3/mL)	2.84-10.19 (6.19)	5.86±2.61	2.49-21.6 (6.22)	5.6±3.32	0.786
Lymphocyte (x10^3/mL)	0.61-3.0 (1.72)	1.81±0.67	1.06-3.62 (2.17)	2.25±0.66	**0.048***
Platelet (x10^3/mL)	143-353 (267)	273±62	145-476 (273)	251±89	0.891
Neutrophils/lymphocytes	1.62-15.9 (4.38)	3.17±3.82	0.83-6.26 (2.91)	2.82±1.18	0.208
Platelet/lymphocyte	102.00–286.24 (174.51)	158.57±64.42	50.51-413.91 (135.66)	124.86±63.64	**0.046***

Mann-Whitney U test, Student t-test, p<0.05*. Min.-max.: Minimum-maximum, SD: Standard deviation, β hCG: Beta human chorionic gonadotropin

Table 4. Comparison of complete blood count parameters according to fetal heartbeat

	Fetal heartbeat (n=94, 100%)				p-value
	Positive (n=8, 8.5%)		Negative (n=86 – 91.5%)		
	Min.-max. (median)	Mean + SD	Min.-max. (median)	Mean + SD	
Hemoglobin (gr/dL)	9.3-13.6 (11.2)	11.00±1.80	9.2-14.9 (12.5)	12.75±1.41	0.135
Neutrophil (x10^3/mL)	2.84-10.19 (6.95)	7.38 ±3.16	2.49-21.6 (6.1)	5.52±3.17	0.450
Lymphocyte (x10^3/mL)	1.09-2.33 (1.67)	1.63±0.64	0.61-3.62 (2.11)	2.11±0.68	0.236
Platelet (x10^3/mL)	286-353 (325)	331±32	140-476 (268)	251±85	0.122
Neutrophils/lymphocytes	2.61-5.53 (4.14)	4.22±1.28	0.83-15.9 (3.18)	2.82±2.19	0.099
Platelet/lymphocyte	150.64-256.24 (213.56)	208.69±65.43	50.51-413.91 (138.88)	126.13±62.59	**0.020***

Mann-Whitney U test, Student t-test, p<0.05*. Min.-max.: Minimum-maximum, SD: Standard deviation

Table 5. Evaluation of value cut off

		AUC	p-value	Cut off	Sensitivity	Specificity
PLR	**hCG**	0.692	**0.046***	≥164.071	0.50	0.85
	Fetal heartbeat	0.854	**0.020***	≥144.098	1.00	0.68

AUC: Area under curve, hCG: Human chorionic gonadotropin, PLR: Platelet/lymphocyte ratio

in implantation (16). In a study, a relationship was found between complete blood count parameters and pregnancy loss in patients with threatened miscarriage (17). In addition, the NLR, which is presented as a marker of inflammation, is similar between patient groups; this similarity may mislead the clinician to use it to predict clinical pregnancy success.

The fact that there was no difference in age, BMI, FSH, LH, TSH, prolactin, and AMH between the pregnant and non-pregnant groups suggests that there is no difference in ovarian reserve between them and that these parameters have no effect on pregnancy.

The small number of patients evaluated in our study is one of our limitations. Increasing the number of patients may increase the power of the study.

Conclusion

After excluding other factors, the evaluation of complete blood count parameters, which is a simple and inexpensive test, may be useful in predicting the chances of pregnancy success in women trying to conceive.

Ethics

Ethics Committee Approval: Ethics committee approval was obtained from the Giresun Training and Research Hospital Ethics Committee (approval number: 25.12.2024/04, dated: 25.12.2024) for the study.

Informed Consent: Consent was obtained from the patients.

Footnotes

Authorship Contributions

Surgical and Medical Practices: D.T., Concept: O.A., Design: D.T., Data Collection or Processing: O.A., Analysis or Interpretation: D.T., Literature Search: O.A., Writing: D.T., O.A.

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