

# Evaluation of Plateletcrit and Neutrophil/Lymphocyte, Monocyte/Lymphocyte and Platelet/Lymphocyte Ratios in Endometrial Polyp

## Endometriyal Polipte Plateletkrit, Nötrofil/Lenfosit, Monosit/Lenfosit ve Platelet/Lenfosit Oranlarının Değerlendirilmesi

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### ABSTRACT

**Introduction:** To evaluate the association between endometrial polyp (EP) and inflammatory markers such as neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), monocyte/lymphocyte ratio (MLR) and plateletcrit (PCT).

**Methods:** In this retrospective and comparative case series, a total of 137 patients who had undergone endometrial biopsy due to various causes were included. Forty-eight of these patients were diagnosed with EP and classified as the patient group. Eighty-nine patients were diagnosed with proliferative/secretory endometrium and classified as the control group. The groups' PCT, NLR, PLR and MLR values were compared as statistically.

**Results:** There was no significant difference between the EP and control groups in terms of the NLR, PLR and MLR and the PCT value.

**Conclusion:** This is the first study in the literature evaluating the relationship between NLR, PLR and MLR and PCT value and EP. Further large-scale studies are essential to determine the exact role of NLR, PLR and MLR and PCT value on EPs.

**Keywords:** Endometrial diseases, polyps, blood cell count

### ÖZ

**Amaç:** Endometriyal polip (EP) ile nötrofil/lenfosit oranı (NLO), platelet/lenfosit oranı (PLO), monosit/lenfosit oranı (MLO) ve plateletkrit (PCT) gibi enflamasyon belirteçleri arasındaki ilişkiyi değerlendirmektir.

**Yöntemler:** Bu retrospektif karşılaştırmalı olgu serisine, çeşitli nedenlerle endometriyal biyopsi yapılan toplam 137 hasta dahil edildi. Bu hastaların 48'i EP tanısını alarak hasta grubu olarak sınıflanırken 89 hasta proliferatif/sekretuar endometrium tanısı alarak kontrol grubu olarak sınıflandı. Grupların NLO, PLO, MLO ve PCT değerleri istatistiksel olarak karşılaştırıldı.

**Bulgular:** EP ve kontrol grupları arasında NLO, PLO, MLO ve PCT değerleri açısından anlamlı fark saptanmadı.

**Sonuç:** Bu çalışma; NLO, PLO, MLO ve PCT değerleri ile EP arasındaki ilişkiyi irdeleyen ilk çalışmadır. NLO, PLO, MLO ve PCT değerlerinin EP'deki rolünü belirlemek için geniş katımlı çalışmalara ihtiyaç vardır.

**Anahtar Kelimeler:** Endometriyal hastalıklar, polipler, kan hücresi sayımı

### Introduction

Endometrial polyp (EP) is a frequent disease of the endometrium, characterised by a localised hyperplastic over growth of endometrial glands and stroma around a vascular core and the presence of inflammatory cells in the stroma (1). Although the etiopathogenesis has not been fully elucidated, oestrogen and progesterone, apoptosis, growth factors, metabolism and ageing, selective oestrogen receptor modulators, hormone replacement therapy, Ki-67 and also endometrial inflammation may play a role in its etiopathogenesis (2,3).

Although many EPs are asymptomatic, abnormal uterine bleeding is the most common symptom of EP. Even though transvaginal ultrasonography (TVUSG) provides reliable data for the diagnosis of EP, hysteroscopy is the gold standard diagnostic procedure that is also simultaneously used for treatment.

Neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), monocyte/lymphocyte ratio (MLR) and plateletcrit (PCT) in peripheral blood are values that are simple to calculate, have a very low cost and can reveal the systemic inflammation.



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There is no study in the literature that evaluates the relationship between NLR, PLR and MLR and PCT value and EP. In this study, we aimed to investigate the association between symptomatic EPs without ultrasonographic EP-compatible views and inflammation markers (NLR, PLR, MLR and PCT).

## Methods

In this retrospective and comparative case series, a total of 137 patients who had undergone endometrial biopsy due to various causes between June 2017 and March 2019 at Zonguldak Maternity and Child Health Hospital were evaluated. This study was approved by the Clinical Research Ethics Committee of Zonguldak Bülent Ecevit University, Turkey (protocol no: 2019-75-08/05, date: 08.05.2019). Patients' consent was not obtained because the study was retrospective. Forty-eight of these patients were diagnosed with EP and classified as the patient group. EP-compatible views such as dilated glands filled with proteinaceous fluid or a hyperechogenic lesion with regular contours were not detected on ultrasonography prior to the endometrial biopsy. Eighty-nine patients were diagnosed with proliferative/secretory endometrium and classified as the control group. Patient with a history of malignancy, pelvic inflammatory disease, severe liver, kidney and cardiac disease, chronic inflammatory disease and those who received hormone replacement therapy were excluded. Patients' demographic characteristics, pathology results and laboratory values were extracted from the automation system of the hospital. PCT, neutrophil count, lymphocyte count, monocyte count, platelet count values were obtained from complete blood cell count parameters within a month before the endometrial biopsy. PLR value was calculated by dividing the platelet count by the number of lymphocytes. NLR value was calculated by dividing the neutrophil count by the number of lymphocytes and MLR value was calculated by dividing the monocyte count by the number of lymphocytes. The groups' PCT, NLR, PLR and MLR values were compared statistically.

## Statistical Analysis

IBM SPSS 22.0 (IBM SPSS Statistics, IL, USA) was used for all the statistical analyses. Data distribution was determined using the Kolmogorov-Smirnov test. Continuous variables were expressed as means  $\pm$  standard deviations and categorical variables as frequencies and percentages. Continuous variables were compared by an independent sample t-test or Mann-Whitney U test.  $p < 0.05$  was considered significant for all the tests.

## Results

The mean age of the 48 patients diagnosed as EP was  $45.5 \pm 8.9$  and the mean age of the 89 patients diagnosed as proliferative/secretory endometrium was  $43.4 \pm 6.3$ . There was no significant difference in the terms of age between the two groups ( $p = 0.158$ ). Endometrial biopsy was performed in 39 patients with abnormal uterine bleeding, 3 patients with postmenopausal increased endometrial thickness, 4 patients with endometrial irregularity and 2 patients with postmenopausal bleeding in the EP group. In the control group, all the patients had undergone endometrial biopsy due to abnormal uterine bleeding. The blood cell count data of the EP and control groups are shown in Table 1. Neutrophil, lymphocyte, monocyte and platelet count of the groups were not significantly different. NLR, PLR and MLR of the EP group was  $2.32 \pm 1.46$ ,  $137.14 \pm 66.40$  and  $0.20 \pm 0.13$  and in the control group was  $2.72 \pm 3.58$ ,  $135.05 \pm 62.44$  and  $0.20 \pm 0.26$ , respectively. The PCT value in the EP group was  $0.22 \pm 0.05$  and in the control group was  $0.22 \pm 0.05$ . There was no significant difference between the two groups in terms of the NLR, PLR and MLR and PCT value ( $p = 0.458$ ,  $p = 0.856$ ,  $p = 0.995$ ,  $p = 0.963$ ) (Table 1).

## Discussion

EP is one of the causes of abnormal uterine bleeding. They are usually benign, but can have premalignant or malignant tissue variations. Polyps are rare before 30 years and peak in the postmenopausal period (4). Increased fibrotic tissue compared to the normal endometrium, thick-walled blood vessels and inflammatory cells like polymorphonuclear leucocytes, lymphocytes and plasma cells in the stroma are pathologic features of EP (1).

The etiopathogenesis of EP remains unclear. Some studies reported that cytokines like cyclooxygenase, interferon-gamma, aromatase and matrix metalloproteinases can cause EP by causing angiogenesis and cell proliferation (5,6). Some investigators showed that EP is formed as a result of an imbalance in the expression of oestrogen and progesterone receptors (7,8) and deficient apoptosis through the loss of the regulation of Bcl-2 and Ki-67 (9,10). The endometrial inflammatory state can stop the apoptosis in the endometrium and may cause EPs. Endometritis, endometriosis, adenomyosis are examples of pro-inflammatory states (2).

NLR, PLR, MLR and PCT are systemic inflammatory response markers and are associated with several diseases such as peripheral vascular

**Table 1. Neutrophil, lymphocyte, monocyte, platelet and PCT count, NLR, PLR and MLR values in the endometrial polyp and control groups**

|                       | Endometrial polyp  | Control group      | p     |
|-----------------------|--------------------|--------------------|-------|
| Neutrophil ( $\mu$ L) | $0.36 \pm 0.14$    | $0.35 \pm 0.15$    | 0.294 |
| Lymphocyte ( $\mu$ L) | $2.13 \pm 0.91$    | $2.06 \pm 0.70$    | 0.635 |
| Monocyte ( $\mu$ L)   | $4.11 \pm 2.07$    | $4.72 \pm 1.73$    | 0.805 |
| Platelet (K/ $\mu$ L) | $250.21 \pm 66.10$ | $254.20 \pm 62.10$ | 0.728 |
| PCT (%)               | $0.22 \pm 0.05$    | $0.22 \pm 0.05$    | 0.963 |
| NLR                   | $2.32 \pm 1.46$    | $2.72 \pm 3.58$    | 0.458 |
| PLR                   | $137.14 \pm 66.40$ | $135.05 \pm 62.44$ | 0.856 |
| MLR                   | $0.20 \pm 0.13$    | $0.20 \pm 0.26$    | 0.995 |

PCT: Plateletcrit, NLR: neutrophil/lymphocyte ratio, PLR: platelet/lymphocyte ratio, MLR: monocyte/lymphocyte ratio

disease, coronary artery disease, malignancies, rheumatoid arthritis and ulcerative colitis (11-15).

Recurrent pregnancy loss is defined as 3 consecutive pregnancy losses prior to 20 weeks of gestation. The aetiology of 50% of recurrent pregnancy loss is unexplained, but inflammation and coagulation disorders play a significant role. In a study with 208 patients who had 2 or more first trimester spontaneous abortions; white blood cell, platelet, lymphocyte and neutrophil count, red cell distribution width, PCT and NLR in the recurrent pregnancy loss group were significantly higher than in the control group (16).

Nasal polyp is characterised by progressive inflammation with eosinophil, T-cell, neutrophil and plasma cell. The study by Atan et al. (17) included 105 patients diagnosed as nasal polyp. In the nasal polyp group, the mean NLR value was significantly ( $p=0.001$ ) higher than in the control group, while there was no significant difference in the mean PLR value.

Endometriosis is identified using ectopic endometrial tissue. It is a chronic inflammatory condition associated with findings related to inflammation like dyspareunia, dysmenorrhoea and chronic pain. Aydın (18) (187 patients), Kim et al. (19) (219 patients) and Yavuzcan et al. (20) (33 patients) reported that there is no relationship between NLR and endometrioma. On the other hand, in studies by Cho et al. (21) including 231 patients and Tokmak et al. (22) including 467 patients, NLR was found to be elevated in endometriosis cases. Furthermore, in Aydın's (18) study, PLR value in the endometrioma group was higher than in the benign cyst group, but in another study (23), there was no difference in PLR value between the two groups.

EP typically appears as cystic spaces corresponding to dilated glands filled with proteinaceous fluid or a hyperechogenic lesion with regular contours on TVUSG. EP can also be seen as a focal mass or nonspecific thickening. These findings are not specific to EP. The addition of power Doppler can enhance the diagnostic efficacy of TVUSG. Saline infusion sonography improves the diagnostic accuracy. Hysteroscopic-guided biopsy provides the highest sensitivity and specificity for the diagnosis of EP (24). Although blind endometrial biopsy has a high sensitivity and positive pressure ventilation, this technique can cause polyp fragmentation and the inaccurate diagnosis of EP (25).

EPs are generally asymptomatic. In a population-based Danish study, EP was significantly more frequent in asymptomatic women compared to women with abnormal uterine bleeding (26). Abnormal uterine bleeding is the most common symptom for the symptomatic EP (24). In a study by Kanthi et al. (27), 75.6% of premenopausal women and 47.7% of postmenopausal women with polyps had abnormal uterine bleeding. In another study, 20% of postmenopausal women with polyp and 76.3% of premenopausal women were symptomatic with abnormal uterine bleeding (28).

In our study, we evaluated the association between the NLR, PLR and MLR and PCT value and symptomatic EP without ultrasonographic EP-compatible views. These patients were diagnosed by endometrial biopsy, but blind endometrial biopsy is inaccurate in diagnosing EP. If we could find a significant relationship between the two groups; NLR,

PLR and MLR and PCT value, which are simple to calculate and cheap, could have been effective in evaluating the diagnosis of EP before biopsy. Thus, additional tests such as saline infusion sonography, Doppler ultrasonography and hysteroscopy before blind biopsy can be done.

## Conclusion

There are inconsistent conclusions in the literature about NLR, PLR and MLR and PCT value in various diseases. Also, to the best of our knowledge, this is the first study in the literature appraising the association between NLR, PLR and MLR and PCT value and EPs. In our study, there was no significant difference between the symptomatic EPs without ultrasonographic EP-compatible views group and the control group in terms of the NLR, PLR and MLR and PCT value. Further large-scale studies are essential to determine the exact role of NLR, PLR and MLR and PCT value on EPs.

## Ethics

**Ethics Committee Approval:** This study was approved by the Local Ethics Committee of Zonguldak Bülent Ecevit University, Turkey (protocol no: 2019-75-08/05, date: 08.05.2019).

**Informed Consent:** Patients' consent was not obtained because the study was retrospective.

**Peer-review:** Externally peer-reviewed.

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