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Orijinal Makale

# The Role of Inflammatory Markers in Distinguishing Endometrial Polyp: Single Center Results

## *Endometrial Polipi Ayırt Etmede İnflamatuar Belirteçlerin Rolü: Tek Merkez Sonuçları*

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## Abstract

**Objective:** To investigate the role of inflammatory markers in predicting the presence of endometrial polyps in patients undergoing endometrial sampling due to abnormal uterine bleeding.

**Methods:** The pathology results of patients who presented to Akçakoca State Hospital with abnormal uterine bleeding and underwent endometrial sampling between May 2023 and July 2023 were retrospectively examined. The demographic characteristics of the patients, platelet-lymphocyte, neutrophil-lymphocyte and lymphocyte-monocyte ratios and systemic immune inflammation index were calculated. Patients were categorized into endometrial polyps and other benign pathologies according to the pathological diagnosis. Malignant and premalignant lesions were not included in the study. The examination results and inflammatory markers were compared between these two groups.

**Results:** 89 patients were included in the study. While the pathological finding in 38 patients was an endometrial polyp, other benign pathologies were found in 51 patients. No significant difference was found in terms of hemoglobin, hematocrit, lymphocytes, monocytes, platelets, neutrophils and PDW variables in patients with endometrial polyps ($p>0.05$). PLR (platelet-to-lymphocyte ratio) and SII (systemic immune-inflammatory index) were significantly higher in the endometrial polyp group compared to other benign pathologies ($p<0.05$). NLR (neutrophil to lymphocyte ratio) was higher in the endometrial polyp group and was not significant (p: 0.056). SII was 669884.4±410641.7 in the endometrial polyp group and was higher than other benign pathologies. ($p<0.05$)

**Conclusion:** Endometrial polyps are one of the most important causes of abnormal uterine bleeding. NLR, PLR and SII are parameters of the systemic immune response that can be easily determined with blood tests at no additional cost. SII appears to be an effective and simple test to differentiate endometrial polyps from benign endometrial pathologies.

**Keywords:** abnormal uterine bleeding; endometrial polyps; Systemic immune-inflammatory index

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## Öz

**Amaç:** Anormal uterin kanama nedeniyle endometrial örnekleme yapılan hastalarda endometrial polip varlığını öngörmede inflamatuar belirteçlerin rolünü değerlendirmek.

Yöntem: Mayıs 2023- Temmuz 2023 tarihleri arasında Akçakoca Devlet Hastanesine anormal uterin kanama ile başvuran ve endometriyal örnekleme yapılan hastaların patoloji sonuçları retrospektif olarak tarandı. Hastaların demografik özellikleri, Trombosit-lenfosit, nötrofil-lenfosit ve lenfosit-monosit oranları, sistemik immün inflamasyon indeksi hesaplandı. Hastalar patolojik tanıya göre endometrial polip ve diğer bening patolojiler olmak üzere gruplandırıldı. Malign ve premalign lezyonlar çalışmaya dahil edilmedi. Tetkik sonuçları ve inflamatuar belirteçler bu iki grup arasında karşılaştırıldı.

**Bulgular:** Çalışmaya 89 hasta dahil edildi. 38 hastanın patoloji sonucu endometrial polip iken 51 hastada diğer bening patolojiler saptandı. Endometrial polip olan hastalarda hemoglobin, hemotokrit, lenfosit, monosit, platelet, nötrofil ve PDW değişkenleri açısından anlamlı bir fark saptanmadı (p>0,05). PLR (trombosit-lenfosit oranı) ve SII (sistemik immün-inflamatuar indeks) endometial polip grubunda diğer bening patolojilere göre anlamlı olarak daha yüksek bulundu ( p<0,05). NLR (nötrofil-lenfosit oranı) endometrial polip grubunda daha yüksek olup anlamlı değildi (p: 0,056). SII endometrial polip grubunda 669884,4±410641,7 olup diğer bening patolojilere göre daha yüksekti (p<0,05).

**Sonuç:** Endometrial polip anormal uterin kanamanın önemli sebeplerinden biridir. NLR, PLR ve SII ek bir maliyet gerektirmeksizin kan testleri ile kolayca değerlendirilebilen sistemik immün yanıt parametreleridir. SII bening endometrial patolojiler arasında endometrial polipi ayırt etmede etkili ve basit bir tetkik olarak görünmektedir.


**Anahtar Kelimeler:** anormal uterin kanama; endometrial polip; sistemik immün-inflamatuar indeks

## 1. Introduction

Abnormal uterine bleeding is defined as bleeding that is outside the 5th to 95th percentile of the general population in terms of frequency, duration, regularity and amount of menstrual bleeding, with pregnancy excluded. Menstrual cycles that are shorter than 24 days or longer than 38 days, a difference of more than 9 days between menstrual cycles, cycles that last longer than 8 days, blood loss greater than 80ml, and intermenstrual bleeding are all indicative of abnormal uterine bleeding (1).

Endometrial polyps (EP) are one of the most common causes of abnormal uterine bleeding in both premenopausal and postmenopausal patients. They are defined as benign growths of the endometrial glands and stroma (2,3). Factors such as monoclonal endometrial hyperplasia, overexpression of endometrial aromatase, somatic gene mutations, cytogenetic restructuring, etc. are thought to be responsible for the pathogenesis (4-9). Although the actual incidence is unknown due to asymptomatic cases, it is observed with an incidence between 7.8% and 50%. It is mostly benign and 1-3% malignant transformation can be expected in postmenopausal patients. Recent studies have shown a strong correlation between endometrial polyps and a disturbed inflammatory status of the endometrium (10-16).

There are studies showing that the expression of transforming growth factor alpha-1 (TGF-α1) and vascular endothelial growth factor (VEGF), which are proinflammatory markers that are elevated in chronic inflammatory diseases, is also increased in EPs (3,14,17). In addition, risk factors related to chronic inflammation are among the EP risk factors. Studies showing that gynecologic malignancies, especially pathologies of the cervix and endometrium, are associated with chronic inflammation show us that inflammatory processes may also play a role in the development of endometrial polyps (18-20).

The Systemic Inflammatory Immune Index (SII) is a novel biomarker that reflects the immune response and systemic inflammation. Peripheral blood cell-derived inflammatory indices (NLR, PLR, NML, LMR) have recently attracted much attention and have been studied for many diseases as they are easily measurable and accessible. They have been shown to be a prognostic factor in many different clinical conditions, including coronary heart disease, inflammatory diseases, solid organ tumors, obstetric and gynecologic diseases, endometrial hyperplasia, and endometrial cancer. Our aim in this study was to evaluate the role of inflammatory markers in the prediction of endometrial polyps associated with impaired endometrial inflammatory status.

## 2. Material and Methods

The study protocol was approved by the Ethics Committee of Duzce Unıversity (19/08/2024, #2024/153), and the principles of the Declaration of Helsinki were followed.

For our retrospective cross-sectional observational study, patients who presented with abnormal uterine bleeding to the hospital's gynecology and obstetrics outpatient

clinic and underwent endometrial sampling between May 2023 and July 2023 were recorded via the medical record. Patients with premalignant and malignant lesions on pathology, postmenopausal and obese patients, patients with inflammatory diseases and patients with a history of malignancy were excluded. Demographic characteristics, obstetric and reproductive history, comorbidities, complete blood count and pathology results obtained prior to endometrial biopsy were evaluated. The complete blood count parameters (hemoglobin, hematocrit, platelets, lymphocytes, neutrophils, neutrophils, monocytes, hemoglobin, platelets, lymphocytes, neutrophils, monocytes) obtained from the patients before the procedure were analyzed using the PDW Sysmex CA-600 device. PLR (platelets/lymphocytes), NLR (neutrophils/lymphocytes), NMR (neutrophils/monocytes), LMR (lymphocytes/monocytes) and SII (neutrophils x platelets/lymphocytes) were calculated for the assessment of inflammatory indices and the values were recorded on the patient's follow-up form. The patients were divided into two groups according to the results of the benign pathology: Endometrial polyps and non-endometrial polyps (proliferative endometrium, secretory endometrium, atrophic endometrium, etc.).

**Statistical analysis**

Statistical Package for the Social Sciences -SPSS 22 (SPSS Inc, Chicago, IL) was used for the statistical analysis. The distribution of parameters was tested using the Shapira-Wilk normality test. Data were expressed as mean ± standard deviation and median (min-max). The t-test for independent samples was used for the normally distributed data and the Mann Whitney U-test for the non-normally distributed variables. The, chi-square test or Fisher's exact test was used.to analyse the categorical variables. A total type I error level of 5% was used to derive statistical significance.

## 3. Results

The study population comprised 89 patients who met the pre-established inclusion and exclusion criteria. Histopathology revealed the presence of endometrial polyps in 42% of patients, while 58% exhibited other benign histopathologic findings. Upon analysis of the reproductive characteristics of the patients, no statistically significant difference was observed between the groups in terms of gravida, parity, and abortion history ($p > 0.05$). The mean age of the patients was comparable between the two groups (Table 1). The mean age was 43.5±6.6 years in patients with endometrial polyps and 45.2±7.0 years in patients without endometrial polyps (p=0.278). Upon individual analysis of complete blood count parameters, it was observed that patients with EP exhibited a mean haemoglobin value of 11.9±1.5, which was found to be lower than that of the group without endometrial polyps. Nevertheless, no statistically significant difference was identified between the two groups ($p = 0.335$). The values for lymphocytes, monocytes, thrombocytes and neutrophils were found to be similar between the groups ($p > 0.05$). Upon analysis of the inflammatory indices, it was determined that the PLR was markedly elevated in the EP group. The PLR value was 151.2 ± 56.9 in the EP group and 128.7 ± 39.5 in the group without coexisting endometrial polyp. The NLR value was 2.4±1.8 in the EP group, indicating a higher level than that observed in the group without endometrial polyps (p=0.056). The systemic inflammatory immune index was calculated to be 669884.4±410641.7 in the EP group, exhibiting a significantly higher value in the EP group (p=0.022) compared to the group without endometrial polyps (Table 2).

## 4. Discussion

Recent studies have shown a strong correlation between endometrial polyps and a disturbed inflammatory status of the endometrium. In our study, we found that inflammatory indices were higher in patients with endometrial polyps than in patients without EP, with SII and PLR being statistically significant. Our results show that inflammatory status has an impact on the formation of endometrial polyps.

In the literature, the relationship between inflammatory indices and malignant and premalignant endometrial pathologies has been investigated in studies on inflammatory indices. The fact that chronic inflammation is associated with tissue damage and cellular changes that can lead to proliferation and mutations suggests that inflammation has an important influence on carcinogenesis (21,22). The inflammation associated with

**Table 1.** Comparison of complete blood count parameters between patients with and without coexisting endometrial polyp

| | EP N: 38 | No EP N:51 | p |
|---|---|---|---|
| Age (years) | 43,5±6,6 | 45,2±7,0 | 0,278 |
| Hemoglobin (g/dl) | 11,9±1,5 | 14,1±14,1 | 0,335 |
| Hematocrit (%) | 36,5±3,7 | 37,2±3,3 | 0,326 |
| Lymphocyte (ml) | 2083±770 | 2300±874 | 0,228 |
| Monocyte (ml) | 527±220 | 549±154 | 0,587 |
| Platelet (ml) | 288789±79535 | 274470±70848 | 0,373 |
| Neutrophil (ml) | 4403±1730 | 4056±1178 | 0,264 |
| PDW (fl) | 11,6±1,8 | 12,0±2,1 | 0,414 |

*Data are given as mean ± Standard Deviation (SD).
EP: Endometrial Polyps. No EP: without coexisting endometrial polyp

| **Table 2.** Comparison of inflammation indices between patients with and without coexisting endometrial polyp | | | |
|---|---|---|---|
| | EP N: 38 | No EP N:51 | p |
| Mean platelet volüme (fl) | 10,1±0,8 | 10,3±0,9 | 0,409 |
| Platelet to lymphocyte ratio (PLR) | 151,2±56,9 | 128,7±39,5 | **0,030** |
| Neutrophil to lymphocyte ratio (NLR) | 2,4±1,8 | 1,8±0,6 | **0,056** |
| Neutrophil to monocyte ratio (NMR) | 11,7±20,4 | 7,7±2,8 | 0,176 |
| Lymphocyte to monocyte ratio (LMR) | 4,2±1,6 | 4,2±1,2 | 0,947 |
| SII | 669884,4±410641,7 | 516280,5±196718,7 | **0,022** |
| **Data are given as mean ± Standard Deviation (SD).<br>EP: Endometrial Polyps, No EP: without coexisting endometrial polyp, SII: Systemic immune-inflammatory index | | | |

carcinogenesis occurs mainly in the systemic circulation and in the tumor microenvironment and manifests as neutrophilia, thrombocytosis and lymphocytopenia in the peripheral blood (23). Based on this biological behavior of the tumor and its consequences in the peripheral blood, inflammatory indices have been developed to reflect the inflammatory status in the presence of malignant disease (24). In the study conducted by Cakmak et al., higher NLR and PLR values were found in patients with atypia-hyperplasia than in patients without atypia-hyperplasia and non-hyperplasia (25). Another study reported that SII is an independent risk factor for lymph node metastasis and myometrial invasion in patients with endometrial cancer (26). In a study by Gökulu et al. on the effect of SII on endometrial pathologies, the role of inflammatory indices in predicting endometrial cancer in the presence of atypia-hyperplasia was investigated, but no significant difference was found between the groups. This result was attributed to the fact that the patients had early adenocarcinoma (27). All these studies show the importance of inflammatory status in malignant endometrial pathologies. And they show the impact of a disturbed inflammatory status of the endometrium on the development of malignancy.

The review by Drizi et al. emphasizes the concept of impaired inflammatory status of the endometrium (IISE) and mentions that inflammatory processes have an impact on the pathogenesis of endometrial pathologies, including benign pathologies, and that treatment of IISE with the right anti-inflammatory therapies is important to prevent future pathologies. The elevation of VEGF, TGF alpha 1 (proinflammatory) in patients with endometrial polyps, the presence of risk factors associated with chronic inflammation in EP patients, the barrier effect of the inflammatory state on sperm transport and implantation in EP, and the increase in pregnancy rates after resection, the presence of chronic inflammation in the background of cervical and endometrial malignancies show that the impaired inflammatory state of the endometrium is the cause of many pathologies (28).

In our study, we found that the SII was effective in predicting endometrial polyps, a benign pathology. While the inflammatory indices (PLR, NLR, NMR, SII) were higher in the patient group with endometrial polyps, only SII and PLR were statistically significant. The fact that the study was conducted in a single center and with the same team is one of the strengths of the study. It is the first study to investigate the relationship between endometrial polyps and inflammatory indices. Limitations of the study include the retrospective study design and the limited number of patients. Further studies are needed to uncover the rwlationship between endometrial pathologies and an impaired inflammatory status of the endometrium especially in endometrial pathologies.

**Author contribution**

Study conception and design: BŞ; data collection: BŞ, EY, and FND; analysis and interpretation of results: BŞ and FD; draft manuscript preparation: BŞ, FND, and EY. All authors reviewed the results and approved the final version of the manuscript.

**Ethical approval**

The study was approved by the Duzce University (Protocol no. 2024/153/19.08.2024).

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**Conflict of interest**

The authors declare that there is no conflict of interest.

**Yazar katkısı**

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