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Diagnostic Performance of Neutrophil/Lymphocyte Ratio and Platelet/Lymphocyte Ratio in Endometrioma

Endometriomada Nötrofil/Lenfosit Oranı ve Trombosit/Lenfosit Oranının Tanı Performansı

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ABSTRACT

Introduction: To evaluate whether neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) have diagnostic value in endometrioma, which is a chronic inflammatory disease.

Methods: A total of 187 patients who underwent surgery for adnexal mass, 97 patients diagnosed with endometrioma and 90 patients with benign cyst (corpus luteum, serous cysts or functional cysts), were included in this retrospective, comparative case series. NLR and PLR values obtained from preoperative complete blood count parameters were compared between the two groups.

Results: There was no statistically significant difference between endometrioma and benign cyst groups regarding mean age (34.8±8.93 and 34.0±8.59 years, respectively, p=0.88). Fourteen point four percent (n=14) of the endometriomas were bilateral. The mean endometrioma size was 6.0±2.74 cm and 27.8% (n=27) of the endometriomas was found to be smaller than 5 cm. There was no significant difference between the endometrioma and the benign cyst group in terms of median NLR values (1.848 and 1.635, respectively, p=0.124). PLR median values were significantly higher in endometrioma group than in benign cyst group (128.77 and 114.69, respectively, p=0.015). NLR ratio was found to be statistically significantly higher in bilateral endometriomas compared to unilaterals.

Conclusion: Although NLR was not found to be elevated in patients with endometrioma, it was found to be affected from bilaterality. PLR was found to be elevated in patients with endometrioma and not affected by the stage of the disease.

Keywords: Endometrioma, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio

ÖZ

Amaç: Nötrofil/lenfosit oranı (NLR) ve trombosit/lenfosit oranının (PLR) kronik enflamatuvar bir hastalık olan endometriomada tanı değerinin olup olmadığını değerlendirmektir.

Yöntemler: Bu retrospektif, karşılaştırmalı olgu serisine adneksiyel kitle nedeniyle opere edilip patoloji sonucu endometrioma gelen 97 hasta ile kontrol grubu olarak patoloji sonucu benign kist (korpus luteum, seröz kist ya da fonksiyonel kistler) olan 90 hasta dahil edildi. Hastaların preoperatif dönemde hemogram parametrelerinden elde edilen NLR ve PLR değerleri iki grup arasında karşılaştırıldı.

Bulgular: Endometrioma ve benign kist grubu yaş ortalamalarında istatistiksel anlamlı fark yoktu (sırasıyla 34,8±8,93 ve 34±8,59, p=0,88). Endometriomaların %14,4'ü (n=14) bilateraldi. Ortalama endometrioma boyutu 6±2,74 cm olarak belirlendi, %27,8'inin (n=27) 5 cm'den daha küçük olduğu saptandı. Endometrioma ile benign kist grubu arasında ortanca NLR değerleri açısından anlamlı bir fark saptanmadı (sırasıyla 1,848 ve 1,635, p=0,124). PLR ortanca değerleri endometriomada benign kiste göre anlamlı yüksek saptandı (sırasıyla; 128,77 ve 114,69, p=0,015). Bilateral endometriomalarda unilaterallere göre NLR oranının istatistiksel olarak anlamlı yüksek olduğu görüldü.

Sonuç: NLR'nin endometrioma olgularında yüksek saptanmasa da bilateral olma durumundan etkilendiği görüldü. PLR'nin ise endometriomalı hastalarda yüksek olduğu ve hastalığın evresinden etkilenmediği tespit edildi.

Anahtar Kelimeler: Endometrioma, nötrofil/lenfosit oranı, trombosit/lenfosit oranı

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Introduction

Endometriosis is defined as the presence of endometrial tissue outside the uterus and is a common disease seen in 5-10% of women in reproductive age (1). It is a common, chronic inflammatory condition and ectopic endometrial tissue and associated inflammation may cause dysmenorrhea, dyspareunia, chronic pain and infertility. The lysis of erythrocytes by inflammatory cells in hemorrhages in the endometriotic foci formed with hormonal effect during menstrual period results in the formation of pigmented histiocytes and hemosiderin-laden macrophages (2). Although endometriosis is usually seen in the pelvic region, it may be localized to any part of the body. Endometriosis lesions in the pelvis can be categorized as superficial-peritoneal, ovarian and deep infiltrating (3). Ovarian endometriosis is caused by bleeding of ectopic endometrial tissue and it results in a hematoma surrounded by ovarian parenchyma, known as endometrioma (4). One-third of cases are bilateral. Unlike most hemorrhagic physiological ovarian cysts, endometriomas typically have fibrotic walls and surface adhesions, and they are filled with syrup-like chocolate colored material, and are surrounded by over parenchyma (5). In addition, the endometrial epithelium is covered with stroma and glands (6).

Based on the inflammatory response in endometriosis, inflammation markers and lymphocyte counts were studied alone and in combination with cancer antigen 125 (CA 125) for the detection of endometriosis (7,8).

Neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) in peripheral blood are simple systemic inflammatory response markers assessed by blood parameters and are associated with several neoplastic conditions. NLR has diagnostic value in some pathologies characterized by systemic or local inflammatory response such as diabetes mellitus, liver failure, presence and severity of coronary artery disease, ulcerative colitis and inflammatory arthritis (9-13). A relationship was found between elevated PLR and venous thrombosis (14).

We have planned this study to evaluate the role of these markers that are associated with various inflammatory processes in the pathophysiology of endometriosis in which chronic inflammation plays a significant role and to differentiate endometriomas from benign processes.

Methods

A total of 187 patients, who underwent surgery for adnexal mass at Haseki Training and Research Hospital, Obstetrics and Gynecology Clinic between September 2008 and October 2017, were included in this retrospective, comparative case series. Ninety-seven patients diagnosed with endometrioma and 90 patients with benign cysts (corpus luteum, serous cysts or functional cysts) without histopathological findings of endometriosis were included in the study as the patient and the control groups. Ethics committee approval and patient consent were not obtained because the study was retrospective. Non-pregnant women with regular menstrual cycles, with no hormonal treatment for endometriosis, and with normal liver and renal function tests were included in the study. The definitive diagnosis was made histopathologically with laparotomy or laparoscopy. Women with pelvic inflammatory disease, myoma uteri, adenomyosis, endometrial pathology, metabolic and autoimmune disorders or history of malignancy were excluded from the study. Age, complete blood count parameters within a month before surgery, lateralization, size and histopathological definitive diagnosis of endometrioma were obtained from hospital data system for each patient. NLR ratio was obtained by dividing the neutrophil count by lymphocyte count, and PLR was obtained by dividing platelet count by lymphocyte count.

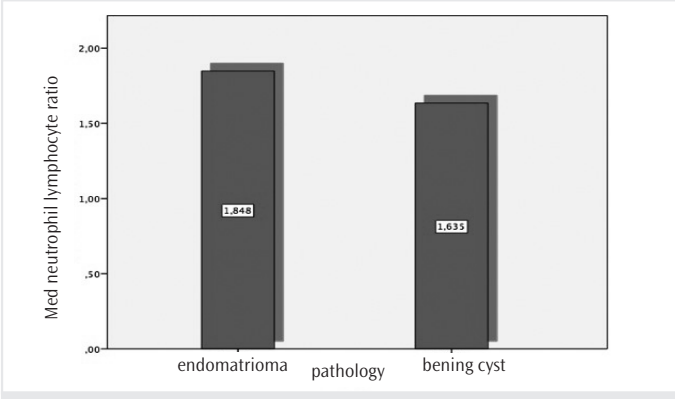
Statistical Analysis

IBM SPSS 22.0 (IBM SPSS Statistics, IL, USA) was used for all statistical analyzes. The NLR and PLR median values were compared using the median test. Continuous variables between the two groups were compared using Student's t-test. $p<0.05$ was considered significant.

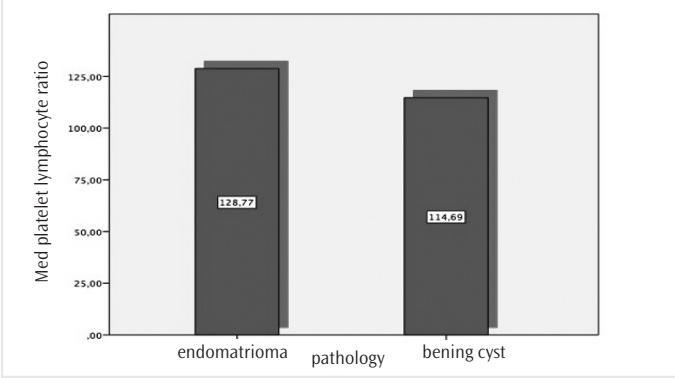
Results

The mean age of 97 patients operated for endometrioma was 34.8±8.93 years and the mean age of 90 patients with benign cyst pathology was 34±8.6 years. There was no statistically significant difference between the two groups in terms of age (p=0.88). Eighty-five point six percent (n=83) of the patients with endometrioma were unilateral and 14.4% (n=14) were bilateral. The mean cyst size in patients operated for endometrioma was 6±2.74 cm. It was detected that 27.8% (n=27) of the endometriomas were smaller than 5 cm.

When the median NLR values of endometrioma and benign cysts were compared, no significant difference was found between the two groups (1.848 and 1.635, respectively, p=0.124). Graphic 1 summarizes the median NLR values of the two groups. However, when the median PLR



Graphic 1. Comparison of median neutrophil/lymphocyte ratio values of cases with endometrioma and benign cyst



Graphic 2. Comparison of median thrombocyte/lymphocyte ratio values of cases with endometrioma and benign cyst

Table 1. Median neutrophil and platelet and p values in endometrioma and benign cyct

	Endometrioma	Benign cyst	p
Median NLR	1.85	1.64	0.124
Median PLR	128.77	114.69	0.015

NLR: neutrophil/lymphocyte ratio, PLR: platelet/lymphocyte ratio

values of both groups were compared, it was found that it was significantly higher in the endometrioma group than in the benign cyst group (128.77 and 114.69, respectively, p=0.015). Graphic 2 shows the median PLR values of the two groups. The median NLR and PLR and p values of the endometrioma and benign cyst groups are shown in Table 1.

When the median NLR and PLR values were compared according to bilaterality in the endometrioma group, there was a statistically significant elevation in NLR in bilateral endometriomas. In patients with unilateral and bilateral endometrioma, the median NLR values were 1.82 (minimum-maximum=0.41-3.84) and 2 (minimum-maximum=1.42-4.30), respectively (p=0.03). However, in patients with unilateral and bilateral endometrioma, median PLR values were calculated as 126.80 (minimum-maximum=60.67-588.33) and 134.85 (minimum-maximum=93.03-208.99), respectively, and there was no statistically signifacant difference between the two groups (p=0.23).

Discussion

Although endometrioma is known for the presence of chocolate colored fluid during surgery, the definitive diagnosis is made by tissue biopsy and histological verification. The combination of signs, symptoms, imaging methods and laboratory is used in the diagnosis. The patient may present with dysmenorrhea, dyspareunia, chronic pelvic pain, and symptoms of infertility and a sensitive cystic mass can be detected in the pelvic examination. The characteristic appearance of endometrioma on transvaginal ultrasound is a cystic ovarian mass with diffuse homogeneous ground-glass echoes. There are no pathognomonic laboratory findings for endometriosis. A number of urinary and endometrial biomarkers have been examined for noninvasive diagnosis of the disease, but none have been clinically useful (15). Although the role of serum CA 125 in primary diagnosis is not defined (5), it may be increased in women with endometriosis (for example more than 35 units/mL) (16,17). However, serum CA 125 concentrations are not routinely tested in women evaluated or treated for endometriosis. This is due to the high concentration of serum CA 125 in other diseases, especially in ovarian cancer.

As a result of studies on the role of inflammation in the pathogenesis of endometriosis, it was seen that macrophages, which account for 85% of peritoneal fluid leukocytes, have increased in the peritoneal fluid of patients with endometriosis. Macrophages have been associated with the onset and development of endometriosis through fibronectin, tumor necrosis factor (TNF)-alpha, cytokines and interleukin production (18-20). Activated macrophages also provide TNF-alpha and endometrial cell proliferation that stimulate collagen synthesis and fibroblast proliferation, thus leading to adhesion formation, and secrete cytokines that stimulate the activation of T and B cell (21). The cytokines detected in the peritoneal fluid of patients with endometriosis are interleukin (IL)-1, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12, IL-13, interferon gamma, TNF-alpha, transforming growth factor (TGF)-beta and vascular endothelial growth factor. TNF-alpha is secreted by activated macrophages, fibroblasts, T and B cells, and its concentration in the peritoneal fluid was positively correlated with the stage of the endometriosis by some authors (22). TGF-beta was also found to be high in the peritoneal fluid of patients with endometriosis in line with the stage of the disease. TGF-beta is most likely involved in endometrial proliferation, angiogenesis, inhibiton of lymphocyte and natural killer cells (23).

In this study, although NLR and PLR values were thought to be effective in the preoperative diagnosis of endometrioma, it was observed that only PLR values are higher in patients with endometrioma than in patients with benign cyct.

In the literature, there are conflicting results with our finding that NLR is not different in endometrioma compared to benign cysts. Similar to our study, Yavuzcan et al. (24) (33 patients) and Kim et al. (25) (219 patents) did not find a relationship between NLR and endometrioma. However, in studies by Cho et al. (26) including 231 patients and by Sayan et al. (27) including 50 patients at any stage, and in studies by Tokmak et al. (28) including 467 patients and by Yang et al. including 197 patients at stage 3-4, NLR was significantly higher in endometriosis cases. In the study with the highest number of cases, the NLR were higher in the endometrioma group (29). When the characteristics of endometrioma cases included in this study were examined, it was observed that 95% of the patients had stage 3-4 endometriosis. In the same study, the bilaterality rate was reported as 26%. It may be thought that this series may have high NLR values because of advanced endometriosis and possibly more peritoneal inflammation. In our study, we found statistically significant elevation in NLR in bilateral endometriomas. Although there was no subgroup analysis in the previous study, the ratio of bilaterality was more than our series and it might be another factor that can explain the elevated NLR.

Thrombocytosis has been associated with various proinflammatory mediators (30). Increased platelet count in response to chronic inflammation due to the nature of endometriosis is also an expected result. In this study, we detected elevated PLR as a result of chronic inflammation of endometriosis. PLR was significantly higher in a study of 197 patients with moderate and severe endometriosis (31). However, in a study in 61 cases of stage 3-4 endometriosis, there was no difference between the endometrioma and the control group in terms of PLR (32). In our study, we also found no relationship between bilaterality and elevated PLR values. Based on this finding, further studies may be conducted to demonstrate that PLR values are not affected by the stage of the disease.

Study Limitations

Our study has some limitations including (a) the stages of endometriosis cannot be reached due to retrospective nature of the study, (b) the control group including only patients operated for a mass, and (c) not including patients being followed up and recevieved medical treatment. However, it is valuable because the number of patients is higher than many studies in the literature and it has a similar control group in terms of age.

Conclusion

In conclusion, NLR was shown to be affected by bilaterality, although it was not found to be elevated in patients with endometrioma. In addition, PLR was found to be elevated in patients with endometrioma and was not affected by the stage of the disease.

Ethics Committee Approval: Retrospective study.

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

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