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The relationship between endometrioma and systemic inflammation indexes

Endometrioma ve sistemik inflamasyon indeksleri arasındaki ilişki

Mehmet Alican SAPMAZ[1], Murat POLAT[1], Furkan AKIN[1], Mine Büşra BOZKÜRK[2]

[1]Ankara Etlik Şehir Hastanesi, Kadın Hastalıkları ve Doğum Kliniği, Ankara, Türkiye
[2]Ankara Etlik Şehir Hastanesi, Tıbbi Biyokimya Kliniği, Ankara, Türkiye

ABSTRACT

Aim: Recent studies have examined systemic inflammatory markers like C-reactive protein (CRP) and fibrinogen, but the role of comprehensive indices such as the systemic immune inflammation index (SII), systemic inflammation response index (SIRI), and pan-immune inflammation value (PIV) in endometrioma remains unclear. This study aimed to evaluate whether isolated endometrioma stimulates systemic inflammation by assessing SII, SIRI, and PIV.

Material and Methods: A retrospective case-control study was conducted involving 213 patients with endometrioma and 207 controls with no gynecological or systemic diseases. Data collected included age, CA-125, CA 19-9, platelet, neutrophil, lymphocyte, monocyte counts, and inflammatory indices (SII, SIRI, PIV). Statistical analysis was performed using the Student's t-test.

Results: No significant differences were found between the endometrioma group and the control group in terms of SII (970±146.6 vs. 753±471, p=0.121), SIRI (1.73±1.21 vs. 1.39±1.02, p=0.107), or PIV (551±420 vs. 419±313, p=0.100). CA-125 and CA 19-9 levels were significantly higher in the endometrioma group compared to controls (p=0.003 and p=0.020, respectively).

Conclusion: The study did not find significant evidence that isolated endometrioma induces systemic inflammation based on SII, SIRI, and PIV. The findings suggest that endometrioma may primarily cause localized inflammation rather than systemic effects. Limitations include the retrospective design and relatively small sample size, which may affect the generalizability and causality of the results. Further prospective studies with larger cohorts are needed to fully understand the systemic inflammatory implications of endometrioma.

Keywords: Endometriosis, ovarian cysts, inflammation, biomarkers

ÖZ

Amaç: Son çalışmalar C-reaktif protein (CRP) ve fibrinojen gibi sistemik inflamatuar belirteçleri incelemiştir, ancak sistemik immün inflamasyon indeksi (SII), sistemik inflamasyon yanıt indeksi (SIRI) ve pan-immün inflamasyon değeri (PIV) gibi kapsamlı indekslerin endometriomadaki rolü belirsizliğini korumaktadır. Bu çalışmanın amacı, izole endometriomanın sistemik inflamasyonu uyarıp uyarmadığını SII, SIRI ve PIV'yi değerlendirerek değerlendirmektir.

Gereç ve Yöntemler: Endometriomalı 213 hastayı ve jinekolojik veya sistemik hastalığı olmayan 207 kontrolü içeren retrospektif bir vaka-kontrol çalışması yapıldı. Toplanan veriler arasında yaş, CA-125, CA 19-9, trombosit, nötrofil, lenfosit, monosit sayıları ve inflamatuar indeksler (SII, SIRI, PIV) yer aldı. İstatistiksel analiz Student's t-testi kullanılarak yapılmıştır.

Bulgular: Endometrioma grubu ile kontrol grubu arasında SII (970±146.6 vs. 753±471, p=0.121), SIRI (1.73±1.21 vs. 1.39±1.02, p=0.107) veya PIV (551±420 vs. 419±313, p=0.100) açısından anlamlı fark bulunmadı. CA-125 ve CA 19-9 düzeyleri endometrioma grubunda kontrol grubuna kıyasla anlamlı derecede yüksekti (sırasıyla p=0.003 ve p=0.020).

Sonuç: Bu çalışmada, izole endometriomanın SII, SIRI ve PIV'e dayalı sistemik inflamasyona neden olduğuna dair anlamlı kanıt bulunmamıştır. Bulgular, endometriomanın sistemik etkilerden ziyade öncelikle lokalize inflamasyona neden olabileceğini düşündürmektedir. Retrospektif tasarım ve nispeten küçük örneklem büyüklüğü, sonuçların genellenebilirliğini ve nedenselliğini etkileyebilecek kısıtlamalar arasındadır. Endometriomanın sistemik enflamatuvar etkilerini tam olarak anlamak için daha geniş kohortlarla yapılacak prospektif çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Endometriozis, ovaryan kistler, enflamasyon, biyobelirteçler

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Sorumlu Yazar/Corresponding Author: Murat Polat, Ankara Etlik Şehir Hastanesi, Kadın Hastalıkları ve Doğum Kliniği, Ankara, Türkiye
E-mail: dr.muratpolat@hotmail.com

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INTRODUCTION

A cyst formed by the transformation of epithelial cells on the surface of the ovary into endometrial tissue (coelomic metaplasia) or by the inward progression of ectopic endometrial tissue on the surface of the ovary (progressive invagination) forms a mass in the pelvic region. This cyst is a structure known as an endometrioma and called a pseudocyst. Endometrioma is a benign cyst and may be asymptomatic or with symptoms such as dyspareunia, pelvic pain, dysmenorrhoea. Endometriosis is a progressive disease characterised by inflammatory processes in which endometrial tissue may invade the pelvic organs and peritoneum beyond the uterine cavity. This condition usually leads to pelvic pain and infertility. Recent studies investigating the mechanism of inflammation in endometriosis patients have generally focused on inflammatory cells (1). Inflammatory cells such as neutrophils and macrophages, which are related with the primary immune response in endometriosis patients, have been found to show higher chemotactic activity in both proliferative and luteal biopsies compared to normal endometrium (2). On the other hand, it has been found that neutrophil activation responds to certain activation signals only in stage III and IV endometriosis patients, and this is related with the proinflammatory effects of endometriotic tissue (3).

It is a common view that endometrioma creates a more localised inflammation rather than systemic inflammation like endometriosis. In a study, it was observed that the inflammatory environment of ovarian endometriosis remained strongly localised and had less systemic effect (4). In another study in which serum levels of systemic inflammatory parameters were compared in endometriosis and endometrioma, it was found that ovarian endometriosis did not induce a systemic inflammatory response (5). Contrary to the results of these studies, studies showing that endometrioma triggers a systemic inflammatory response have also been performed. In one study, C reactive protein, platelet and fibrinogen levels were found to be higher in the group with endometrioma compared to the control group and it was reported that high coagulation and systemic inflammatory response were triggered due to shortening of thrombin time and prothrombin time (6).

Recently, new indicators such as systemic immune inflammation index (SII), systemic inflammation response index (SIRI) and pan-immune inflammation value (PIV), which are obtained from blood cell counts and considered as comprehensive inflammatory markers, have attracted interest. (7). Calculation of these inflammatory markers is both easy and cost-effective. These inflammatory parameters based on peripheral lymphocyte (Lym), neutrophil (NE) and platelet (PLT) counts have been recognised as a better index to reflect local immune response and systemic inflammation (8). In addition, these markers have been shown to have a high prognostic value in many cancer types, cervical cancer (9), pancreatic cancer (10) and colorectal cancer (11). In a study on systemic inflammatory index in patients with endometriosis, it was considered to be a potentially simple and cost-effective approach to predict disease (12).

The primary aim of our study was to evaluate whether isolated endometrioma stimulates systemic inflammation mechanisms with SII, SIRI and PIV, which have been the subject of recent studies. The main focal points of this study are that the relationship between endometrioma and systemic inflammation is not yet fully understood and the studies of the above-mentioned parameters, which are considered to be related to systemic inflammation, are limited in the literature on endometrioma.

MATERIAL METHODS

The aim of this retrospective case-control study was to investigate whether systemic inflammatory mechanisms are involved in patients with endometrioma. SII, SIRI and PIV levels, which are inexpensive and easy to calculate markers, were investigated in patients diagnosed with endometrioma in Gynaecology and Obstetrics outpatient clinics. The study was conducted in the Department of Obstetrics and Gynecology and included patients diagnosed with endometrioma between 1 November 2022 and 1 August 2024. The study population consisted of all patients diagnosed with endometrioma during the study period. In patients diagnosed with endometrioma, one or more symptoms such as chronic pelvic pain, dysmenorrhea, and dyspareunia were present. Pelvic pain was observed during vaginal examination in patients who had previously given birth or were non-virgins. Ultrasound performed on these patients (transvaginal for non-virgins and suprapubic abdominal ultrasound for virgins) revealed homogeneous cystic structures with a “frozen glass” appearance. The cyst wall was smooth and well-defined, typically with a unilocular structure. The size of the identified endometriomas ranged from 4 cm to 10 cm. The diagnosis of endometrioma was established based on clinical findings, laboratory results (elevated CA-125 levels), and typical cystic features on ultrasound. Patients in the control group were included in the study provided that they had no gynaecological and systemic disease. Patients were excluded if they were under 18 years of age, had pre-existing systemic diseases, history of malignancy, active smoking, alcohol or illicit drug use, HIV, HCV or HBV infection or any pre-existing chronic disease or organ transplantation history.

Data for the study were collected retrospectively from the medical records of eligible patients. These data included patients’ age, ca 125 value, ca 19-9 value, platelet value, neutrophil value,

lymphocyte value, monocyte value and systemic inflammatory index value, systemic inflammation response index value, pan immune inflammation value calculated from these values. According to the calculation formula, SII (Platelet count × Neutrophil count / Lymphocyte count), SIRI (Monocyte count × Neutrophil count / Lymphocyte count) and PIV (Monocyte count × Platelet count × Neutrophil count / Lymphocyte count) were calculated using absolute neutrophil count (×10^9/L), monocyte count (×10^9/L), lymphocyte count (×10^9/L) and platelet count (×10^9/L), respectively.The study included 213 patients with endometrioma and 207 control patients without any gynaecological or systemic disease. The statistical method used in the evaluation of the data was Student-T test.

RESULTS

When the patients were grouped as endometrioma and control group, the mean age of the endometrioma group was 36.5±8.47, while the mean age of the other group was 34.1±11.4 and the difference between them was not significant (p=0.77). CA 125 values were 280±74.5 in the endometrioma group and 26.0±22.5 in the other group and this difference was statistically significant (p=0.003). CA 19-9 values were 80.2±26.0 in the endometrioma group and 15.3±16.2 in the other group and this difference was statistically significant (p=0.020). Platelet values were 311000±83300 and 302000±58500 in the endometrioma and other groups, respectively, and this difference was not significant

Table 1. Comparison of endometrioma (group 1) and other control group (group 2)

	GROUP	AGE	CA 125	CA 19-9	PLT	NEU	MON	LYM	SII	SIRI	PIV
NUMBER OF PATIENT	1	213	213	213	213	213	213	213	213	213	213
	2	207	207	207	207	207	207	207	207	207	207
MEAN	1	36.5	280	80.2	311000	5.81	0.568	2.18	970	1.73	551
	2	34.1	26.0	15.3	302000	5.08	0.542	2.23	753	1.39	419
STANDARD DEVIATION	1	8.47	74.5	26.0	83300	5.24	0.188	0.751	146.6	1.21	420
	2	11.4	22.5	16.2	58500	2.32	0.164	0.690	471	1.02	313
P VALUE		0.77	0.003	0.020	0.22	0.145	0.180	0.646	0.121	0.107	0.100

PLT: Platelet, NEU: Neutrophil, MON: Monocyte, LYM: Lympocyte, SII:systemic immune inflammation index, SIRI: systemic inflammation response index, PIV: pan-immune inflammation value

Table 2. Comparison of demographic characteristics of endometrioma and control group

VARIABLES	ENDOMETRIOMA GROUP (n=213)	CONTROL GROUP (n=207)	P VALUE
GRAVIDY			0.225
0	61 (%28.6)	45 (%21.7)	
1	73 (%34.2)	86 (%41.5)	
≥2	79 (%37.1)	76 (%36.7)	
PARITY			0.427
0	51 (%24.9)	57 (%27.5)	
1	105 (%49.3)	97 (%46.9)	
≥2	57 (%26.8)	53 (%25.6)	
ABORTUS			0.386
0	148 (%69.5)	162 (%78.2)	
1	42 (%19.7)	29 (%14.0)	
≤2	23 (%10.8)	16 (%7.7)	
SMOKING	5 (%2.3)	4 (%1.9)	0.763
CONTRACEPTION			0.952
IUD	89 (%41.7)	81 (%39.1)	
COC	36 (%16.9)	49 (%23.7)	
Condom	53 (%24.9)	48 (%23.2)	
Other	35 (%16.4)	29 (%14.0)	

IUD: Intrauterin Device, COC: Combined Oral Contraceptives

(p=0.22). Neutrophil values of both groups were 5.81±5.24 and 5.08±2.32 , respectively, and this difference was not significant (p=0.145). Monocyte values were 0.568±0.188 and 0.542±0.164 in both groups, respectively, and the difference between them was not significant (p=0.180). Lymphocyte values were 2.18±0.751 and 2.23,±0.690, respectively, and this difference was not significant (p=0.646). SII values were 970±146.6 and 753±471 in the endometrioma and control groups, respectively, and this difference was not statistically significant (p=0.121). SIRI values were 1.73±1.21 and 1.39±1.02 in the two groups, respectively, and the difference between them was not significant (p=0.107). PIV values were found to be 551±420 and 419±313, respectively, and this difference was not statistically significant (p=0.100) (Table1).

There was no significant difference between endometrioma and control groups in terms of gravida, parity, abortion, smoking and contraceptive methods as reported in Table 2.

DISCUSSION

Endometrioma is a type of cyst formed by endometrial cells with haemorrhage and fluid accumulation, which develops in the ovarian regions as a complication of endometriosis pathology. It is usually associated with clinical symptoms such as pelvic pain, dysmenorrhoea and infertility and can cause various health problems in the long term if left untreated. There are studies emphasising that endometrioma is associated with systemic inflammation. In a study conducted by Ding et al., it was demonstrated that increases in C-reactive protein (CRP), platelet and fibrinogen levels, shortening of thrombin time and prothrombin time together with high coagulation and systemic inflammatory response were triggered in women with ovarian endometrioma (6). In another study conducted by Wu et al. (13) on patients with endometrioma, they found that this group had a hypercoagulable state due to altered procoagulant factors and high percentage of activated platelets in the peripheral blood and that this was closely related with systemic inflammation. In another study by Chmaj-Wierzchowska et al., urocortin, ghrelin and leptin levels were higher in the patient group with endometrioma compared to the control group, and the relationship between this and systemic inflammation was mentioned (14). In contrast to endometriosis, the prevailing view is that endometrioma causes inflammation at the site of localisation. The available data on the effects of endometrioma on systemic inflammation generally reveal that endometrioma causes a more localised inflammation and has no significant effect on systemic inflammation. Opøien et al. (5) reported that there was no significant difference in serum cytokine levels between patients with and without endometriosis, indicating that ovarian endometriosis does not cause systemic inflammation and that they did not observe cytokine changes indicating inflammation in precursor follicles adjacent to endometriomas. In a different study by Yland et al. (4) it was stated that the inflammatory effect of endometriomas was strongly localised and had a more limited systemic effect, and that the effect on infertility could not be explained only by increased inflammation.

In recent years, new indicators such as SII, SIRI and PIV, which are derived from blood cell counts and considered as comprehensive inflammatory indicators, have attracted attention. SIRI is known to show the balance between inflammatory response and immune status (15).

In our study, no significant difference was found in terms of systemic inflammation parameters in the endometrioma patient group compared to the control group. It was concluded that endometrioma does not cause systemic inflammation and the effects of inflammation may be localised and localised. This study provides valuable information regarding the prognostic value of systemic inflammation parameters in endometrioma patients. In particular, the findings that endometrioma does not cause systemic inflammation and that the effects of inflammation may be localised contribute to the limited studies available in the literature. It also sheds light on the few previous studies on systemic inflammation in endometrioma patients. SII, SIRI and PIV studies in endometrioma patients are also few in the literature. However, this study has some important limitations and weaknesses. Firstly, the retrospective design of the study has the potential to introduce direct biases related to data collection and patient selection. Retrospective studies are usually observational and limited in terms of controlling for interactive factors. This may cast doubt on the accuracy and validity of the findings of the study.

CONCLUSION

This study provides valuable information regarding the predictive value of systemic inflammatory markers in endometrioma. However, it is important to recognise its limitations. As a retrospective study, it is open to inherent biases related to data collection and patient selection. The relatively small sample size may also limit the generalisability of the findings. Furthermore, the study design does not allow firm conclusions to be drawn about the causality between the observed markers and systemic inflammation of the specific endometrioma.

Conflict of Interest: There is no conflict of interest in our study. There is no financial support in our study

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