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Original Article

Systemic immune-inflammation indices and pelvic pain burden in endometriosis: Added value of PIV over conventional ratios

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Abstract

Aim: Endometriosis is an estrogen-dependent gynecologic disorder that often presents with pain. Objective and easily accessible biomarkers for assessing pain remain limited. This study aimed to evaluate the association between systemic inflammatory indices including neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), and pan immune inflammation value (PIV) and pelvic pain in women with endometriosis.

Materials and Methods: This retrospective study included 104 women with surgically and/or radiologically confirmed endometriosis. Patients were categorized according to the presence of clinically significant pelvic pain. Demographic characteristics, complete blood count parameters, inflammatory indices (NLR, PLR, PIV), and revised American Society for Reproductive Medicine (rASRM) scores were compared between groups. A logistic regression model was performed to find predictors of pelvic pain.

Results: Pelvic pain was present in 73 patients (70.2%), while 31 patients (29.8%) reported no pain. Age and absolute neutrophil, lymphocyte, and platelet counts were similar between the groups. Patients with pelvic pain exhibited significantly higher mean NLR (2.01±0.95 vs. 1.56±0.75, p=0.012), PLR (130.6±41.5 vs. 111.1±35.3, p=0.017), and PIV values (421±101.8 vs. 355±114.1, p=0.007). The rASRM score was significantly higher in patients with pelvic pain (17.0±13.2 vs. 5.0±5.3, p<0.001). In multivariable analysis, PLR (OR=1.03, 95% CI: 1.01–1.05, p=0.004), PIV (OR=1.01, 95% CI: 1.00–1.01, p=0.008), and rASRM score (OR=1.16, 95% CI: 1.07–1.26, p<0.001) were identified as independent predictors of pelvic pain, whereas NLR did not.

Conclusion: PLR and PIV are independently associated with pelvic pain in endometriosis, alongside disease severity. These readily available inflammatory markers may serve as adjunctive tools in clinical pain assessment.

Keywords: Disease severity, endometriosis, neutrophil-to-lymphocyte ratio, pan-immune-inflammation value, pelvic pain, platelet-to-lymphocyte ratio

INTRODUCTION

Endometriosis, a chronic, estrogen-dependent gynecologic disease is strongly associated with pelvic pain, dysmenorrhea, dyspareunia, and often infertility, significantly impairing quality of life (1). Despite extensive research into its pathophysiology, pain prediction and management remain clinically challenging (2). Systemic inflammatory mechanisms are increasingly recognized as key contributors to endometriosis-associated pelvic pain, driving interest in routinely accessible inflammatory biomarkers for better symptom assessment and management (3).

The neutrophil-to-lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) are inexpensive, readily derived from complete blood counts, and reflect systemic inflammatory states. Importantly, a recent retrospective study found that patients with endometriosis experiencing pelvic pain had a significantly higher NLR and PLR levels compared to those without pain (4). The study reported moderate diagnostic accuracy, NLR (AUC=0.63, OR=3.06 at cut-off>1.85) and PLR (AUC=0.60, OR=2.84 at cut-off>139.77),suggesting these markers could independently predict both pain presence and disease stage (III–IV) (4).

Another dimension of inflammatory profiling is the Pan immune inflammation value (PIV). PIV has demonstrated promising prognostic performance in oncology and immunotherapy contexts (5). For instance, Chen et al. showed that baseline PIV and its dynamics significantly correlated with prognosis in advanced non-small cell lung cancer (NSCLC) patients undergoing immunotherapy, outperforming conventional indices like NLR and PLR (5). Similarly, in endometrial cancer, Chalabiyev et al. identified high PIV levels as independent predictors of worse overall survival, with elevated PIV linked to increased mortality risk (6).

While these findings underscore the value of NLR, PLR, and PIV in malignant and inflammatory contexts, their roles in benign gynecologic pathologies such as endometriosis remain under-explored (4). Given the strong inflammatory underpinnings of endometriosis related pain, studying these markers may offer novel insights into non-invasive symptom prediction.

Against this backdrop, we conducted a retrospective study to assess associations between NLR, PLR, and PIV and the presence and severity of pelvic pain in endometriosis. By integrating the well established markers (NLR, PLR) with the more comprehensive PIV, our study fills a critical knowledge gap. Demonstrating that PIV and not just NLR or PLR correlates with pain could substantially enhance symptom monitoring, aid personalized management, and support non-invasive risk stratification in contexts where advanced diagnostics may be limited.

This study aims to elucidate whether systemic inflammatory indices especially PIV can serve as adjunctive markers in evaluating pelvic pain burden among patients with endometriosis, with potential implications for optimized symptom driven care.

MATERIALS AND METHODS

The study was approved by the institutional ethics committee of Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital. Approval date: 10 Jul 2025, Number: 2025-07/105. Electronic medical records of women diagnosed with endometriosis between January 2010 and December 2024 were reviewed. The study was reported in line with the STROBE recommendations for observational research.

Eligibility criteria

1. Women aged 18–50 years with a confirmed diagnosis of endometriosis;
2. Availability of laboratory test results;
3. Documentation of pelvic pain status in clinical records.

Exclusion criteria

1. Presence of comorbidities that could influence systemic inflammation (e.g., autoimmune disease, infection, malignancy);
2. Incomplete laboratory data;
3. Pregnancy or postpartum status within the last six months.

Data collection

From eligible patients, the following data were extracted:

- Age at the time of diagnosis;
- Pelvic pain status (presence vs. absence) as documented in clinical records;
- rASRM classification score;
- Laboratory results from CBC at diagnosis.

Biomarker definitions

- NLR (Neutrophil to Lymphocyte Ratio): neutrophil count / lymphocyte count
- PLR (Platelet to Lymphocyte Ratio): platelet count / lymphocyte count
- PIV (Pan Immune Inflammation Value): (neutrophil×platelet×monocyte) / lymphocyte

Timing of laboratory assessment

Complete blood count parameters were obtained at the time of diagnosis or initial clinical evaluation, prior to any surgical or medical treatment for endometriosis. Laboratory measurements and pain assessment were derived from the same clinical encounter or closely related visits documented in the medical records.

Definition of pelvic pain

In routine clinical practice, pelvic pain was recorded as present or absent based on patient-reported symptoms documented during outpatient visits. Clinically significant pelvic pain was defined as patient-reported pelvic pain requiring clinical attention, including symptoms such as dysmenorrhea, non-cyclic pelvic pain, or dyspareunia, as documented in medical records. No standardized pain scoring system or validated pain intensity scale was routinely used due to the retrospective nature of the study. Disease severity was assessed using the revised American Society for Reproductive Medicine (rASRM) classification system. rASRM scores were obtained from operative reports and imaging-based documentation when available and reflect the extent, location, and depth of endometriotic lesions, as well as the presence and severity of adhesions. Higher rASRM scores indicate more advanced disease.

Outcomes

The primary outcome was the presence of pelvic pain (yes/no) rather than pain intensity or severity in patients with endometriosis.

Statistical analysis

Continuous variables were summarized as mean±SD, and categorical variables as counts and percentages. Comparisons

between patients with and without pelvic pain were performed using independent samples t-tests for continuous variables. A logistic regression analysis was made for predicting factors of pelvic pain, including NLR, PLR, PIV, and rASRM score. Analyses were performed with standard statistical software (SPSS v25.0, IBM Corp., Armonk, NY).

RESULTS

A total of 104 women with a diagnosis of endometriosis were retrospectively analyzed. Among them, 73 patients (70.2%) reported clinically significant pelvic pain, whereas 31 patients (29.8%) did not experience pain at the time of evaluation. The comparison of demographic, hematologic, and inflammatory parameters between the two groups is presented in Table 1.

The mean age was comparable between groups (33.0±10.0 vs. 34.0±13.0 years, p=0.704). No statistically significant differences were observed in absolute neutrophil, lymphocyte, or platelet counts (p=0.108, p=0.198, and p=0.577, respectively).

Patients with pelvic pain had significantly higher NLR compared to those without pain (2.01±0.95 vs. 1.56±0.75, p=0.012). Platelet to lymphocyte ratio was also elevated in the pelvic pain group (130.6±41.5 vs. 111.1±35.3, p=0.017). The pan immüne inflammation value was significantly increased in women reporting pelvic pain (421±101.8 vs. 355±114.1, p=0.007). In addition, the revised American Society for Reproductive Medicine (rASRM) score was substantially greater in the pain group compared with the pain-free group (17.0±13.2 vs. 5.0±5.3, p<0.001).

To identify independent predictors of pelvic pain, a multivariable logistic regression model was constructed including NLR, PLR, PIV, and rASRM score (Table 2). In this analysis, PLR (OR=1.03, 95% CI: 1.01–1.05, p=0.004), PIV (OR=1.01, 95% CI: 1.00–1.01, p=0.008), and rASRM score (OR=1.16, 95% CI: 1.07–1.26, p<0.001) were identified as independent predictors of pelvic pain, while NLR did not retain statistical significance (p=0.430). The overall discriminative capacity of the model was strong, with an AUC of 0.864. Variance inflation factor (VIF) analysis demonstrated values below 2 for all predictors, excluding relevant multicollinearity.

Table 1. Baseline characteristics and laboratory findings in patients with and without pelvic pain

Variables	Total Median Mean±SD	Pelvic Pain (n=73) Mean±SD	No Pelvic Pain (n=31) Mean±SD	p-Value
Age	34.0 ±10.0	33.0±10.0	34.0±13.0	0.704
Neutrophils (10^3/µL)	4.13±1.15	4.21±1.31	3.70±1.51	0.108
Lymphocytes (10^3/µL)	2.11±0.85	2.09±0.87	2.37±1.05	0.198
Platelets (10^3/µL)	271.0±93.0	273.0±95.0	263.5±71.4	0.577
NLR	1.95±1.12	2.01±0.95	1.56±0.75	0.012
PLR	128.4±41.2	130.6±41.5	111.1±35.3	0.017
PIV	411±105.4	421±101.8	355±1141	0.007
rASRM score	11.0±15.5	17.0±13.2	5.0±5.3	<0.001

NLR: Neutrophil-to-Lymphocyte Ratio, PLR: Platelet-to-Lymphocyte Ratio, PIV: Pan-Immune-Inflammation Value rASRM: Revised American Society for Reproductive Medicine classification score

Table 2. Multivariable logistic regression analysis of predictors of pelvic pain in endometriosis

Variable	Odds Ratio (OR)	95% CI for OR	p-value
NLR	1.39	0.61–3.15	0.430
PLR	1.03	1.01–1.05	0.004
PIV	1.01	1.00–1.01	0.008
rASRM score	1.16	1.07–1.26	<0.001

NLR: Neutrophil-to-Lymphocyte Ratio, PLR: Platelet-to-Lymphocyte Ratio, PIV: Pan-Immune-Inflammation Value rASRM: Revised American Society for Reproductive Medicine classification score

DISCUSSION

In this retrospective observational study, we demonstrated that PLR and PIV are significantly associated with the presence of pelvic pain in women with endometriosis. Although NLR, PLR, and PIV were all elevated in patients with pelvic pain on univariate analysis, multivariable modeling revealed that only PLR and PIV, together with disease severity measured by the rASRM score, independently predicted pelvic pain. These findings reinforce the concept that composite inflammatory markers better capture the complex immüne inflammatory mechanisms underlying endometriosis-associated pain.

Endometriosis is a chronic inflammatory process rather than a condition limited to ectopic endometrial implants (7,8). Persistent inflammation within the peritoneal environment leads to immune cell recruitment, cytokine release, angiogenesis, and neurogenesis, all of which contribute to nociceptive sensitization and chronic pelvic pain (9,10). Importantly, pain severity does not consistently correlate with lesion size or anatomical extent, suggesting that inflammatory and neuroimmune factors play a central role in symptom generation (9,11).

Our work demonstrated significantly higher NLR, PLR, and PIV values in patients reporting pelvic pain, despite no differences in absolute neutrophil, lymphocyte, or platelet counts. This observation highlights the importance of immune balance rather than isolated cell counts in reflecting clinically relevant inflammation. Previous studies have similarly demonstrated elevated NLR and PLR in symptomatic endometriosis. Gorun et al. reported that both markers were associated with pelvic pain and advanced stage disease, albeit with modest discriminatory performance (4). Our univariate findings are concordant with these results.

However, in multivariable analysis, NLR did not retain independent significance, whereas PLR did. This finding may reflect the limited ability of NLR alone to capture the multidimensional inflammatory response involved in endometriosis related pain. Platelets are increasingly recognized as active participants in inflammatory signaling, angiogenesis, and neuroinflammation (12,13). Activated platelets release cytokines, chemokines, and growth factors that promote vascular proliferation and sensitize peripheral nociceptors, providing a plausible biological explanation for the independent association between PLR and pelvic pain observed in our cohort (13-15).

The most novel and clinically relevant finding of this study is the independent association between PIV and pelvic pain. PIV integrates neutrophils, platelets, monocytes, and lymphocytes into a single index, offering a comprehensive reflection of systemic immune–inflammatory status. While PIV has been extensively studied in oncology where it consistently outperforms NLR and PLR as a prognostic and predictive biomarker (5,16,17)—its role in benign inflammatory gynecologic diseases has remained largely unexplored. To our knowledge, this is one of the first studies to demonstrate a significant relationship between PIV and pelvic pain in endometriosis.

Composite systemic inflammatory indices such as SII have shown clinical utility across various gynecologic conditions, including infectious, premalignant, malignant, and symptomatic disorders. These data support the broader relevance of integrated inflammatory markers in gynecology. Accordingly, the independent association between PIV and pelvic pain in endometriosis is biologically plausible and consistent with prior evidence (18-21).

The biological rationale supporting PIV's relevance in endometriosis is strong. Monocytes and macrophages play a central role in sustaining chronic inflammation within endometriotic lesions, while neutrophils contribute to cytokine release and oxidative stress (14,15). Lymphocyte dysregulation reflects impaired immune surveillance, and platelet activation enhances angiogenesis and neurogenic inflammation (12,13). By integrating these components, PIV may better capture the persistent inflammatory milieu that drives pain perception and chronicity in endometriosis, explaining its independent predictive value in our multivariable model.

Consistent with prior literature, the rASRM score emerged as a strong independent predictor of pelvic pain (4,22). Nevertheless, it is well established that disease stage alone fails to fully explain pain heterogeneity in endometriosis (2). The persistence of PLR and PIV as independent predictors after adjustment for rASRM score suggests that systemic inflammation provides additive information beyond anatomical classification. This supports growing calls for adjunctive biomarker-based approaches to complement traditional staging systems (23).

From a clinical standpoint, our findings suggest that PLR and particularly PIV both derived from inexpensive and widely available laboratory tests may serve as non-invasive adjunctive tools for identifying patients at higher risk of pelvic pain. This could aid in early symptom stratification, closer clinical monitoring, and personalized management strategies, especially in resource-limited settings where advanced imaging or invasive diagnostics may not be readily accessible.

Several limitations should be acknowledged. The retrospective design and single-center nature of the study may limit generalizability. Pelvic pain was assessed as a binary outcome rather than using validated pain severity scales, precluding evaluation of dose–response relationships. Additionally, inflammatory markers were measured at a single time point, and longitudinal changes were not assessed. In addition, the long study period may have introduced heterogeneity related to diagnostic practices, documentation standards, and clinical assessment of pelvic pain over time. Although efforts were made to ensure consistency by relying on documented clinical records, this temporal variability should be considered when interpreting the results. Accordingly, our findings should be interpreted as reflecting the presence of pelvic pain rather than

its intensity. Despite these limitations, the study's strengths include standardized laboratory evaluation, adjustment for disease severity, and the novel application of PIV in the context of endometriosis-related pain.

CONCLUSION

Our study demonstrates that PLR and, notably, PIV are independently associated with pelvic pain in women with endometriosis. These findings should be interpreted as evidence of association rather than predictive or causal inference. Prospective, large-scale studies incorporating longitudinal biomarker assessment and standardized pain measures are warranted to validate these results and further clarify the role of PIV in symptom driven care.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that there is no financial support.

Ethical Approval
The study protocol received approval from the Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital. Approval date: 10 Jul 2025, Number: 2025-07/105.

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