



ORIGINAL ARTICLE

Importance of Inflammatory Markers in Ovarian Torsion

✉ Emin Erhan Dönmez¹, ✉ Gülizar Özbilen², ✉ Fisun Vural²

¹Department of Gynecologic Oncology, Koc University Hospital, Istanbul, Türkiye

²Department of Obstetrics and Gynecology, University of Healty Sciences, Haydarpaşa Numune Training and Research Hospital, Istanbul, Türkiye

Abstract

Introduction: Early diagnosis is important for the preservation of ovarian function and fertility after ovarian torsion. In this study, we aimed to investigate the usability of inflammatory markers in the diagnosis of ovarian torsion.

Methods: Data of 120 patients who had been operated for ovarian torsion (60) and benign adnexal mass (60) between 2013 and 2019 were analyzed retrospectively. The final C-reactive protein (CRP) value and hemogram parameters of the patients in the preoperative period were recorded. Laboratory and clinical comparisons were made between both groups.

Results: When the torsion group and the control group were compared, neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), white blood cell (WBC), and CRP values were found to be statistically higher in the torsion group ($p=0.000$, $p=0.003$, $p=0.000$, $p=0.028$). When the cutoff value for NLR was >2.95 , sensitivity was 79.2%, specificity was 90.3%, when the cutoff value was >169.7 for PLR, the sensitivity was 49.0%, and specificity was 84.6%. For WBC >8.58 , sensitivity and specificity were 73.58% and 78.85%, respectively, and for CRP >0.47 , sensitivity and specificity were 90.6% and 88.5%, respectively.

Discussion and Conclusion: According to the results of this study, these markers can be used as inflammatory markers in the diagnosis of ovarian torsion.

Keywords: C-reactive protein; leukocyte; neutrophil-lymphocyte ratio; ovarian torsion; thrombocyte-lymphocyte ratio.

Adnexal torsion may occur as because of the total or partial rotation of the adnexa on the vascular axis. Due to the torsion of the tissues, the venous system and the lymphatic system are obstructed first. Subsequently, ovarian enlargement, edema, and interstitial hemorrhage can be encountered due to this obstruction of venous return. Ischemia and hemorrhagic necrosis may develop because of occlusion in the arterial system in the progressive process^[1]. Nonspecific findings may be observed in patients ranging from mild to severe depending on the degree of ischemia, such as lower abdominal pain, nausea-vomiting, fever, leukocytosis, and pelvic tenderness, which do not respond to medical treatment. Adnexal torsion is usually unilateral. Although it is most common in the population between the ages of 20 and 30, it can be observed in any age group. Imaging methods, such as gray-scale ultrasonography,

Doppler ultrasonography, and magnetic resonance imaging, can be used for the diagnosis of adnexal torsion^[2]. However, in 33% of cases with ovarian torsion, venous circulation was not detected with imaging methods, but arterial circulation was observed^[3]. Possible delays due to diagnostic difficulties may result in loss of ovarian function and infertility^[4]. Adnexal torsion has no specific clinical or laboratory findings. However, recent studies have shown that inflammatory markers can be used in diagnosis^[4-7]. The leukocyte count white blood cell (WBC) increases due to any kind of inflammation in the body. Accordingly, many studies have shown that the WBC count increases due to inflammation that arises from ischemia during adnexal torsion^[8]. It has also been shown that markers, such as the neutrophil/lymphocyte ratio (NLR), as well as the platelet/lymphocyte ratio (PLR) and mean platelet volume (MPV),

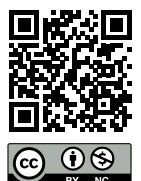
Correspondence: Emin Erhan Dönmez, M.D. Department of Gynecologic Oncology, Koc University Hospital, Istanbul, Türkiye

Phone: +90 506 885 67 62 **E-mail:** eminerhan@gmail.com

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can be utilized as markers in diagnosis and prognostic analysis of many systemic inflammatory diseases, gynecological diseases, cardiovascular diseases, and malignancies^[9-12]. In a limited number of studies, C-reactive protein (CRP) has also been studied as a marker.

When the literature is examined, to our knowledge, there is no study in which WBC, NLR, PLR, MPV, and CRP markers used in the diagnosis of ovarian torsion are evaluated together and compared concerning sensitivity. Thus, the present study aims to investigate the use of inflammatory markers (WBC, NLR, PLR, MPV, and CRP) in the pre-diagnosis of adnexal torsion by evaluation of the laboratory test results and clinical presentations of surgically confirmed adnexal torsion cases.

Materials and Methods

This retrospective case–control study was conducted by Haydarpaşa Numune Training and Research Hospital gynecology and obstetrics clinic. It was carried out in cases operated between July 2013 and April 2019. Ethics committee approval was obtained for the study. Study data were extracted from the hospital computer data and patient files. Patients operated for 60 torsion and 60 benign adnexal masses with matching age groups were included in the study. Of these patients, 48 patients who fulfilled the study conditions were included in the torsion group and 52 patients in the control group (benign ovarian mass) (Fig. 1).

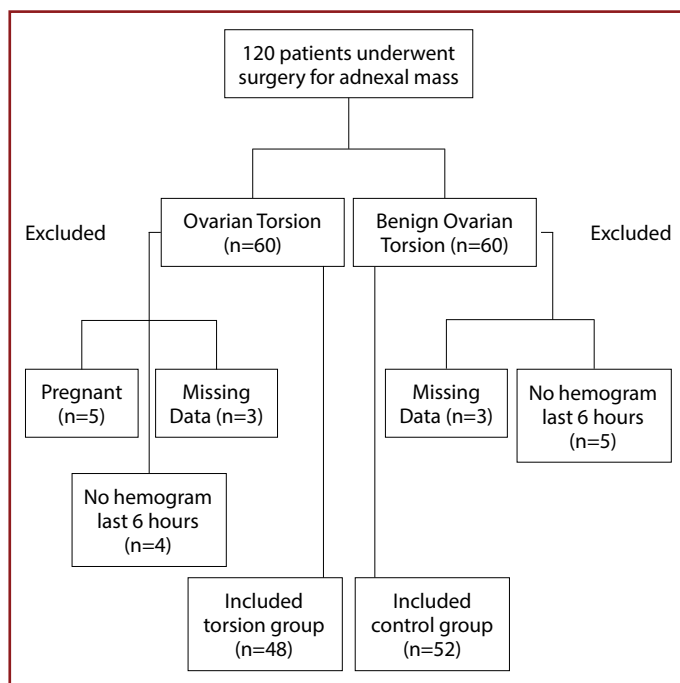


Figure 1. Scheme of the patients included in the study.

Inclusion Criteria in the Study

Pathologically diagnosed benign ovarian masses, patients who were operated with a diagnosis of torsion, those with complete hospital records, those with a hemogram result taken just before surgery (within 6 h).

Reasons for Exclusion

Those who have pelvic inflammatory disease, tuboovarian abscess, bilateral ovarian mass, presence of malignancy, pregnancy, obesity, diabetes, thyroid dysfunction, polycystic ovary syndrome, rheumatological, hematological or systemic disease history, and those who used medication for any reason. Inflammatory markers: Inflammatory markers are NLR, PLR, MPV, and CRP. Complete blood count was measured with an automated hematology analyzer. WBC, Neutrophil, platelet, lymphocyte count, and MPV were recorded from the hemogram results. NLR and PLR values were found by dividing the neutrophil and platelet counts into lymphocytes. CRP value was measured by turbidimetric method (reference range: up to 5 mg/L for adult population 0.5 mg/dL).

Statistical Analysis

When evaluating the findings obtained in the study, IBM SPSS Statistics 22 for statistical analysis (SPSS IBM, Türkiye) programs was used. While evaluating the study data, the compliance of the parameters to the normal distribution was evaluated with the Shapiro–Wilk’s test. While evaluating the study data, besides descriptive statistical methods (mean, standard deviation, and frequency), Student t-test was used for comparing normally distributed parameters between two groups, and Mann Whitney U-test was used for comparing parameters that did not show normal distribution between two groups. Chi-square test, Fisher’s exact test, Fisher Freeman Halton test, and Continuity (Yates) correction were used for the comparison of qualitative data. The most appropriate cutoff point was chosen based on receiver operating characteristic (ROC) curve analysis. Significance was evaluated at the $p < 0.05$ level.

Results

The demographic characteristics of the torsion group and the control group are summarized in Table 1. The mean age was 27.1 ± 7.0 in the torsion group, in the control group 31.0 ± 7.7 ($p = 0.008$), gravida was 0.7 ± 1.2 to 1.8 ± 1.9 , parity was 0.5 ± 0.8 to 1.4 ± 1.4 . All cases with ovarian torsion are in the premenopausal period and 19 (35.8%) of them were virgo. In the torsion group, 5 patients also had pregnancy. 28 (57.1%) of the torsion cases were in the follicular phase, their mean endometrial thickness was 7.65 ± 2.8 mm.

Table 1. Demographic and clinical findings of the torsion and control group

Characteristics	Torsion group	Control group	p
Age	27.15±7.06	31.08±7.7	^a 0.008*
Gravidity	0.77±1.2	1.85±1.94	^b 0.001*
Parity	0.51±0.85	1.85±1.94	^b 0.001*
Menopause n (%)			
Yes	0	0	-
No	53 (100)	52 (100)	
Virgo n (%)			
Yes	19 (35.8)	9 (17.3)	^c 0.055
No	34 (64.2)	43 (82.7)	
Pregnancy status n(%)			
Yes	5 (9.4)	52 (100)	^d 0.057
No	48 (90.6)		
Menstrual cycle n(%)			
Follicular	28 (57.1)	27 (51.9)	^e 0.599
Luteal	21 (42.9)	25 (48.1)	
Endometrial thickness (mm)	7.65±2.82	6.59±2.67	^b 0.017*
Tumor size (cm)	7.58±2.93	9.54±13.23	^b 0.941
Cyst localization n (%)			
Right	33 (62,3)	26 (50)	² 0.285
Left	20 (37.7)	26 (50)	

*p<05 was considered significant; ^aStudent t-test. ^bMann Whitney U-test. ^cContinuity (Yates) correction. ^dFisher's exact test. ^eKi-Kare test.

Laparotomy was performed in 15 (28.3%) of 53 torsion cases and laparoscopy was performed in 38 (71.7%) of them. Sixteen (30.2%) cases underwent detorsion alone, 4 (7.5%) cases oophorectomy, and 33 (62.3%) cases detorsion and cyst extirpation. The mean time between admission to the hospital and operation was 19.5±34.2 h, and the number of torsion was 1–6 rounds (mean 2.5±1.1). When

the pathology results of the patients were examined, mature cystic teratoma was found in 35.1% (n=13), serous cystadenoma (n=7), simple serous cyst (n=7), and corpus luteum cyst (n=7) were found in 18.9% and mucinous cystadenoma was detected at the rate of 9.1 (n=3).

The comparison of the hematological parameters of the groups is shown in Table 2. The mean WBC, NLR, PLR, and

Table 2. Evaluation of study parameters between groups

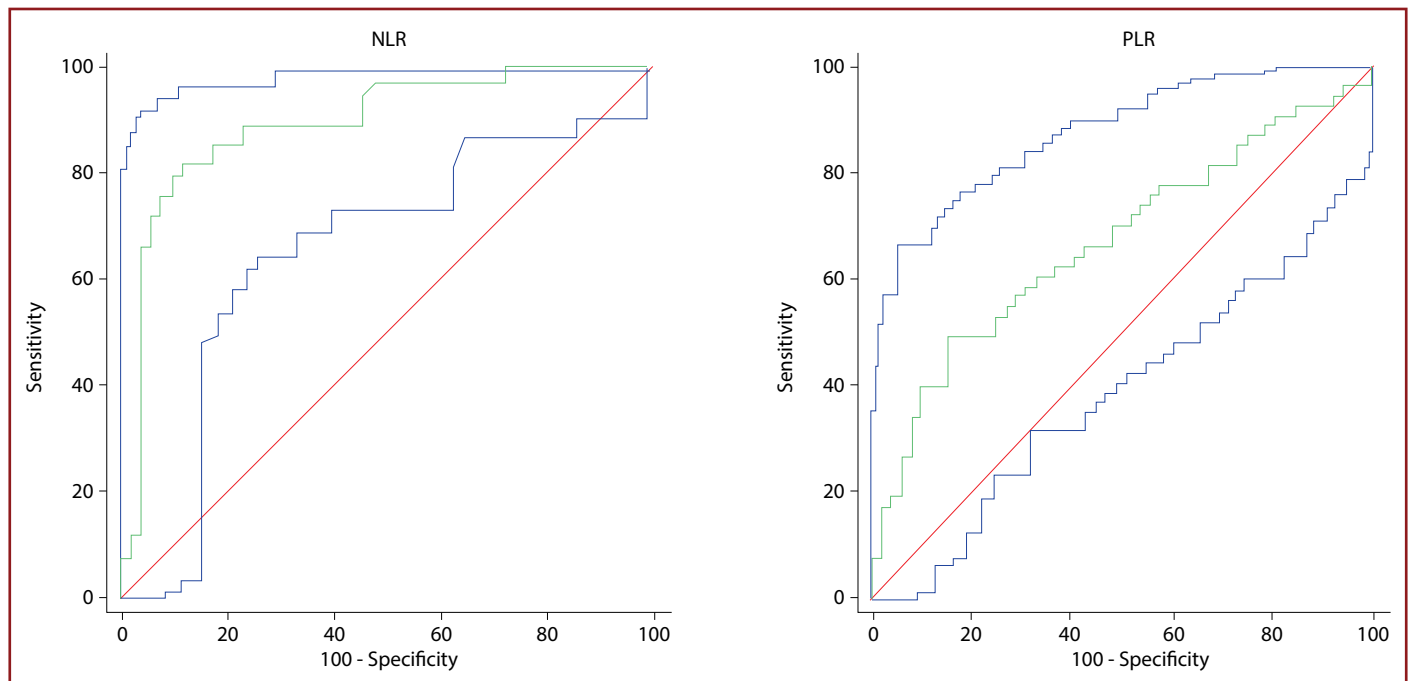
	Torsion Group		Control group		p
	Min-Max	Mean±SS	Min-Max	Mean±SS	
WBC (meiyan)	5860–34030	11417.55±4820.09 (9780)	4400–20600	7698.13±2876.03 (7090)	^a 0.000*
Nöeutrophil (median)	4.01–30	9.17±4.61 (7.9)	2.05–16.8	4.67±2.62 (4)	^a 0.000*
Nöeutrophil (%)	8.01–94	77.1±14.3 (80.6)	42.8–83.14	58.41±9.26 (58.2)	^a 0.000*
Lymphocyte	0.2–4.1	1.62±0.79	0.98–3.5	2.26±0.64	^b 0.078
Lymphocyte (%)	2.31–37	15.61±8.53	4.76–46.45	31.5±8.62	^b 0.027*
HB	8.21–14.6	11.72±1.44	9.26–14.8	12.2±1.35	^b 0.086
HCT	27.4–43.5	35.21±4.12	29.8–45	36.93±3.7	^b 0.783
Platelet	26–521	260.26±80.89	172–475	285.29±66	^b 0.028*
MPV (median)	6.03–88	10.05±11.01 (8.9)	4.8–13.3	8.58±1.69 (8.2)	^a 0.068
CRP (median)	0.16–26.6	1.58±3.82 (0.7)	0–4.14	0.38±0.56 (0.3)	^a 0.000*
RDW (median)	11.7–22.6	14.68±2.29 (14.1)	11.9–45.5	16.19±5.2 (14.9)	^a 0.003*
NLR (median)	1.4–40.95	7.74±6.8 (5.9)	0.92–17.14	2.41±2.69 (1.7)	^a 0.000*
PLR (median)	44.07–1105	208.1±165.98 (156.4)	67.98–402.04	137.62±60.84 (123.5)	^a 0.000*

^aStudent t-test. ^bMann Whitney U-test. *p<05 was considered significant. WBC: White blood cell, HB: Haemoglobin, HCT: Hematocrit, MPV: Mean platelet volume, CRP: C-reactive protein, RDW: Red cell distribution width; NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet to lymphocyte ratio.

Table 3. The diagnostic value of serum inflammatory markers and ROC curve results for torsion

	Diagnostic scan					ROC curve		
	Cut off	Sensitivity	Spesificity	Positive predictive value	Negative Predictive value	Area	95% Confidence interval	p
WBC (/uL)	>8580	73.58	78.85	78.00	74.55	0.819	0.732–0.887	0.000*
PLR	>169.75	49.06	84.62	76.47	61.97	0.667	0.569–9.756	0.002*
NLR	>2.95	79.25	90.38	89.36	81.03	0.894	0.818–0.945	0.000*
CRP (mg/dL)	>0.47	90.6	88.5	84.2	68.7	0.914	0.850–0.977	0.000*

*p<05 was considered significant; WBC: White blood cell; NLR: Neutrophil to lymphocyte ratio; PLR: Platelet to lymphocyte ratio; CRP: C- reactive protein.

**Figure 2.** Receiver operating characteristic curve for NLR and PLR. (a) Roc curve for NLR, (b) ROC curve for PLR.

CRP were significantly higher in the torsion group ($p<0.05$). No significant difference was found for platelet, MPV, and RDV ratios ($p=0.86$, $p=0.783$, $p=.068$). Furthermore, hematocrit and lymphocyte count were significantly lower in the torsion group ($p<0.05$).

Cutoff values were determined for NLR, PLR, and WBC levels (Table 3). The cutoff point determined for NLR in the diagnosis of torsion was >2.95 and the sensitivity was 79.25%, the specificity was 90.38%, positive predictive value was 89.36% and negative predictive value was 81.03% for this value. ROC analysis for NLR is shown in Figure 2a and the area under the curve is 0.894, its standard error is 0.03. The area under the ROC curve was found to be significantly higher than 0.5 ($p=0.000$; $p<0.05$).

The cutoff point determined for PLR is >169.75 . The sensitivity of this value was 49.06%, the specificity was 84.62%,

positive predictive value was 76.47%, and negative predictive value was 61.97%. ROC analysis for PLR is shown in Figure 2b and the area under the curve was determined as 0.667.

For CRP with a cutoff point >0.47 , the sensitivity was 90.6% and the specificity was 88.5%. The area under the curve was determined as 0.914 ($p<0.000$).

Discussion

Ovarian torsion is a gynecological emergency that may progress with loss of fertility when the diagnosis cannot be made at the right time. Although ultrasonography is used in addition to the evaluation of clinical findings, the success of additional diagnostic methods is not sufficient. Thus, other tools are needed to guide the clinicians in diagnosis. The possible usability and role of inflammatory markers in

the diagnosis of ovarian torsion were investigated in this study. The findings obtained in this study showed that the success of inflammatory markers (NLR, PLR, WBC, and CRP) in the diagnosis of torsion cases was high and statistically significant.

Ovarian torsion accounts for 2.7% of all gynecological emergencies. With this ratio, it ranks fifth in commonness among them all^[13]. Given that the clinical findings are nonspecific, the clinical presentation is variable among the patients, and the additional methods in the diagnosis do not have sufficient sensitivity and specificity, makes the development of novel diagnostic methods in the diagnosis of ovarian torsion essential. The reliability of ultrasonography in diagnosis is controversial, and its sensitivity was found between 23% and 66% in studies. It is among the limitations of ultrasonography that it is a real-time method and depends on the experience of the person performing it. Pena et al.^[14] found the total loss of blood flow or decreased blood flow in only 40% of torsion cases using Doppler ultrasonography and reported that blood flow evaluation was normal in 60% of the cases. Therefore, in clinical practice, while the presence of torsion findings in Doppler ultrasonography helps in diagnosis, normal Doppler ultrasonography findings do not rule out ovarian torsion^[15]. Possible delays due to difficulties in the diagnosis of torsion may lead to ovarian loss and infertility^[16]. In our study, we determined the average duration between admission to the hospital and surgery as 19.5 h (2–216 h).

Ovarian masses are blamed in the etiology of torsion. For example, the presence of a mass of at least 5 cm has been shown as a primary risk factor^[17]. In the literature, the most common pathology found in ovarian torsion cases was reported as mature cystic teratoma with a rate of 32%^[18]. Similarly, in our study, we encountered mature cystic teratoma, most commonly among our patients (35%).

The role of inflammatory markers has been investigated in many fields of medicine in recent years. Hematological parameters, such as NLR, PLR, and MPV, can be used in the diagnosis and follow-up of many systemic inflammatory diseases, cardiovascular diseases, and malignancies^[9,19,20].

In patients with myocardial infarction (MI), the increase in the neutrophil count has been found to be associated with larger areas of infarction^[21]. Neutrophil count increases as an inflammatory response due to several biochemical mechanisms in response to tissue damage may result from infarction. Similarly, a decrease in lymphocyte count due to stress caused by an increase in endogenous cortisol was observed in cases with MI^[22]. Thus, the rise in the

NLR further increases the strength of diagnostic prediction based on the two WBC subtypes^[23]. As a consequence of ovarian torsion, the ovarian blood supply is impaired and an ischemic process progresses over time. Since a pathophysiological mechanism similar to that in MI cases is observed in ovarian torsion, inflammatory markers may also be valuable in the diagnosis of it. However, there are a limited number of studies on this subject in the literature. To our knowledge, our research is the first study investigating NLR, PLR, WBC, MPV and CRP parameters simultaneously.

Ercan et al.^[5] reported in 2015 that NLR value over 3 (>3) might be helpful in the diagnosis of torsion cases with 88.9% sensitivity and 100% specificity. In a study conducted in 2016, Yilmaz et al.^[24] found the NLR value significantly higher in the torsion group compared to the control group ($p=0.001$). On the other hand, Soysal et al.^[25] found NLR to be significant in the differential diagnosis of ovarian torsion and ovarian cyst. However, they did not find a significant difference in the differential diagnosis of ovarian torsion and ovarian cyst rupture. Bacanakgil et al.^[26] found that the probability of NLR to be 3.10 and above was 33 times higher in the torsion group compared to the control group (ODDS ratio 33.657 [95% CI: 11.742–96.470]). Tas et al.^[27] also found significantly higher NLR values in ovarian torsion cases ($p<0.05$). Similarly, in our study, the cut-off value was 2.95 in the ROC analysis for NLR. In the analysis, the sensitivity value of the NLR value was 79.25%, and the specificity value was 90.38%. Ercan et al. evaluated only WBC and NLR parameters in their study. In their aforementioned study, they found the sensitivity as 74.1% and specificity as 83.3% for the cut-off value of WBC >8800/uL. Consistent with previous studies, Tas et al. also found WBC significantly higher in torsion cases ($p=0.035$). They also associated ovarian torsion with increased neutrophil count and decreased lymphocyte count. Similarly, in our study, the neutrophil count was significantly higher and the lymphocyte count was significantly lower in the torsion group compared to the control group ($p=0.000$, $p=0.000$). In addition, the sensitivity value for WBC >8580/uL in the differential diagnosis of ovarian torsion was 73% and the specificity value was 78.85%.

Platelets play a role in endothelial damage, angiogenesis, and hypoxia, which occur in ovarian torsion pathogenesis. Therefore, it was considered that the PLR parameter could also be used in the differential diagnosis of ovarian torsion. Tas et al.^[27] found that the PLR and Platelet count values in the torsion group were significantly higher than the control group ($p\leq 0.001$, $p=0.008$). On the other hand, Bacanakgil et al.^[26] found no statistical difference in PLR values for

the torsion group in their study ($p=0.910$). In this study, we found that PLR was significantly higher in the torsion group ($p=0.003$). However, when the platelet count parameter was compared, we found no statistically significant difference between the two groups ($p=0.086$).

Tobiume et al.^[8] found that CRP was higher in torsion cases, which progressed with necrosis compared to the control group ($p<0.05$). When the cut-off limit of CRP positivity was determined as $>0.3\text{mg/dL}$, they found the sensitivity as 83% and the specificity as 35%. In 2015, Bakacak et al.^[28] found that plasma high-sensitivity CRP (hs-CRP) levels were significantly higher in the torsion group compared to the control group in their study conducted on rats ($p<0.001$). Similarly, in our study, we found significantly higher CRP values in the torsion cases ($p=0.028$). When the cut-off value was taken as >0.47 in the ROC analysis for the CRP parameter, the sensitivity was 90.6%, and the specificity was 88.5%. However, this value is in the normal range ($0\text{--}0.5\text{ mg/dL}$) for our hospital laboratory. When the cut-off value for CRP was taken as $>4\text{ mg/dL}$, the sensitivity was determined as 22.6% and the specificity was 100%.

MPV is the most commonly used hematological parameter to evaluate platelet function. Like other markers, it has been reported that MPV can be a significant indicator of many inflammatory diseases^[29]. Conflicting opinions have been proposed for ovarian torsion. Tas et al.^[27] found that the MPV value in the torsion group was significantly lower than the control group ($p<0.001$). On the other hand, there are studies reporting that there are no statistically significant different MPV values for ovarian torsion cases^[4,25,30]. In our study, there was no significant difference between the groups in MPV and Red cell distribution width parameters ($p=0.783$). These results may be due to MPV acting as an acute phase reactant or negative phase reactant in different inflammatory processes.

The limitation of this study is its retrospective design. However, in our study, data recorded in a prospective manner, only then were analyzed retrospectively. Also, only the hemogram results obtained within the last 6 h were included in the evaluation. All these strengthen the reliability of the study results. To our knowledge, this is the first study to evaluate all markers together in the literature.

In our clinic, complete blood count tests are routinely performed on all hospitalized patients. Inflammatory markers can also be calculated easily from these complete blood count tests without any additional cost. Therefore, they should be utilized in the early diagnosis of ovarian torsion cases.

Conclusion

In conclusion, early diagnosis is critical for the preservation of ovarian function and fertility in cases of ovarian torsion. Inflammatory markers can be used in early diagnosis. Among all inflammatory markers, WBC, NLR, PLR and CRP are the markers with the strongest diagnostic value. The availability of the measurement tests of these markers without additional treatment costs may help clinicians in the diagnosis of ovarian torsion cases.

Ethics Committee Approval: Haydarpasa Numune Training and Research Hospital Ethics And Clinical Investigation Committee-HNEAH-KAEK 2017/57 (HNEAH-KAEK 2017/KK/57).

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