ARAŞTIRMA MAKALESİ/ ORIGINAL ARTICLE

Kocaeli Med J 2018; 7; 3:165-171

Tubo-Ovaryan Apse Tanılı Olgularda Tedavi Öncesi Nötrofil/Lenfosit ve Platelet/Lenfosit Oranları Medikal Tedavi Başarısını Predikte Eder mi?

Do Pre-treatment Neutrophil/Lymphocyte and Platelet/Lymphocyte Ratios Predict Success of Medical Treatment in Patients with Tubo-ovarian Abscess?

Fatma Aydın, Alper Biler, Cüneyt Eftal Taner, İbrahim Egemen Ertaş

Sağlık Bilimleri Üniversitesi,Tepecik Eğitim ve Araştırma Hastanesi, Kadın Hastalıkları ve Doğum Kliniği, İzmir, Türkiye

ÖZ

GİRİŞ ve AMAÇ: *Tubo-ovaryan apse (TOA) tanılı hastalarda enflamasyon belirteçlerinin medikal tedavi başarısındaki prediktif değerlerini analiz etmektir.*

YÖNTEM ve GEREÇLER: *Tepecik Eğitim ve Araştırma Hastanesi Kadın Hastalıkları ve Doğum Kliniği'nde 2008-2016 yılları arasında medikal ve cerrahi olarak tedavi edilmiş TOA tanılı 180 hasta retrospektif olarak değerlendirildi. Klinik, demografik, laboratuvar ve operasyon verileri hastaların tıbbi kayıtları incelenerek sağlandı. Medikal ve cerrahi tedavi uygulanan hastaların tedavi öncesi ve sonrası dönemde tam kan sayımı, C-reaktif protein (CRP) ve eritrosit sedimantasyon hızı (ESR) ölçümleri için kan örnekleri alınarak sonuçları karşılaştırıldı. Tam kan sayımı parametreleri olarak; lökosit sayısı, nötrofil, lenfosit, hemoglobin, hematokrit ve platelet değerleri ile nötrofil/lenfosit oranı (NLR) ve platelet/lenfosit oranları (PLR) incelendi.*

BULGULAR: *Antibiyotik tedavisinin başarısız olmasından dolayı 99 (%55) hastaya cerrahi tedavi uygulandı. Hastaların ortalama yaşı, ortalama apse boyutu, tedavi öncesi ortalama lökosit sayısı, nötrofil sayısı, trombosit sayısı, NLR ve PLR oranları ile CRP değerleri cerrahi olarak tedavi edilen grupta daha yüksekti (p<0.001). Medikal tedavi başarısını öngörmede ROC eğrisi incelendiğinde, NLR için 6 cut-off değeri istatiksel olarak anlamlı bulundu (p<0.001, eğri altındaki alan [AUC=0.77], %95 güven aralığı: 0.698-0.843, sensitivite %71, spesifisite %74). PLR için AUC değeri 0.74 idi. ROC analizine göre, PLR için medikal tedavi başarısını öngörmedeki cut-off değeri 165 idi (%74.7 sensitivite ve %65.4 spesifite).*

TARTIŞMA ve SONUÇ: *NLR ve PLR sistemik enflamatuvar hastalıkların prognozuyla korelasyon gösterebilen ucuz ve kolay hesaplanabilen indekslerdir. Preoperatif NLR ve PLR değerleri TOA'da medikal tedavinin başarısını öngörmede katkıda bulunabilir.*

Anahtar Kelimeler: *tuboovaryan apse, nötrofil/lenfosit oranı, platelet/lenfosit oranı*

ABSTRACT

INTRODUCTION: *To analyze the predictive value of inflammatory markers for medical treatment success in patients with tubo-ovarian abscess (TOA).*

METHODS: *Patients with TOA between January 2008 and December 2016 were retrospectively reviewed at Tepecik Training and Research Hospital, Obstetrics and Gynaecology Department. A total of 180 patients were enrolled the study. Patients were compared on the basis of TOA size, demographic characteristics, and laboratory findings. As complete blood count parameters, white blood cell, neutrophil, lymphocyte, and platelet counts, hemoglobin, hematocrit, neutrophil/lymphocyte ratio (NLR), and platelet/lymphocyte ratio (PLR) were analysed.*

RESULTS: *A total of 99 (55%) patients underwent surgical treatment due to unsuccessful medical treatment. Patients who required surgery had larger abscess size, higher mean age, higher mean white blood cell, neutrophil, lymphocyte, and platelet counts, and higher mean C-reactive protein level, NLR, and PLR (p<0.001). In reciever operating characteristic (ROC) analysis, the area under the curve (AUC=0.77) was statistically significant for NLR (p<0.001) with a cut-off value of ≥6 (95% CI 0.698-0.843, sensitivity 71%, specificity 74%). The positive predictive value of NLR was 78%, and the negative predictive value was 67.4% (p<0.001). The recommended threshold for PLR was 165 (AUC: 0.74, 95% CI 0.670-0.818, sensitivity 74.7%, specifity 65.4%).*

DISCUSSION and CONCLUSION: *NLR and PLR are inexpensive and easily determined indexes that correlate with prognosis in systemic inflammatory diseases. Preoperative NLR and PLR values may facilitate prediction of medical treatment success in TOA.*

Keywords: *tuboovarian abscess, neutrophil to lymphocyte ratio, platelet to lymphocyte ratio*

İletişim / Correspondence:

Dr. Alper Biler
Sağlık Bilimleri Üniversitesi,Tepecik Eğitim ve Araştırma Hastanesi, Kadın Hastalıkları ve Doğum Kliniği, İzmir, Türkiye
E-mail: bileralper@gmail.com
Başvuru Tarihi: 22.02.2018
Kabul Tarihi: 06.05.2018

INTRODUCTION

Tubo-ovarian abscess (TOA) is an inflammatory disease characterized by the formation of a mass involving the fallopian tube, ovary, and sometimes the surrounding pelvic organs (1). TOA is usually a complication of pelvic inflammatory disease (PID). One-third to one-half of patients have a history of PID. However, TOA can also develop due to direct spread via lymphatic or hematogenous routes in patients with complicated diverticulitis, Crohn's disease, and perforated appendicitis (2). It is most commonly seen in the third and fourth decades (3).

TOA is a potentially life-threatening condition. Before broad-spectrum antibiotics and modern surgical procedures, TOA-associated mortality was reported to be approximately 50% or higher (4,5). Today, surgical intervention is necessary in 25-30% of TOA patients (6,7).

Although there is a lack of consensus regarding the optimal management of TOA, treatment consists of broad-spectrum antibiotics, minimally invasive surgical drainage procedures, invasive surgical procedures (laparotomy or laparoscopy), or a combination of these (6,8).

Various clinical, laboratory, and ultrasonographic parameters have been used in the literature to predict the need for surgical treatment (9). Risk factors for requiring surgical treatment are advanced age; high leukocyte, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) levels; neutrophil/lymphocyte ratio (NLR); and TOAs larger than 6.5 cm (4,10-12). However, it has not been clearly determined which of these parameters is the best indicator (9).

NLR is a simple, inexpensive, and broadly applicable marker of inflammatory response (13). This simple test can be used to assess disease severity in patients with severe systemic inflammation. Zahorec et al. demonstrated the correlation between disease severity and the degree of neutrophilia and lymphopenia (14). Like NLR, platelet/lymphocyte ratio (PLR) is also among the leukocyte indices recommended as inflammatory markers (15). Recent studies have also shown that NLR and PLR values are easily assessed and reliable prognostic factors for malignancies such as ovarian cancer, colorectal cancer, breast cancer, and non-small cell lung cancer (16-19).

In this study, we aimed to investigate whether pre-treatment NLR and PLR values predicted outcomes of medical treatment in patients with TOA.

METHODS

The medical records of 180 patients who underwent medical or surgical treatment for TOA between January 2008 and December 2016 in the Obstetrics and Gynecology Department of Sağlık Bilimleri (Health Sciences) University Tepecik Education and Research Hospital were retrospectively reviewed. The study was conducted in accordance with the Declaration of Helsinki and approved by the hospital ethics committee.

TOA diagnosis was based on the presence of classic PID findings and detection of the characteristic mass (complex cystic mass with irregular walls, septa, and internal echoes with no peristalsis) (20) on ultrasound (USG). PID findings were abdominal pain, cervical and adnexal tenderness on vaginal examination, and one or more minor criteria: temperature ≥38 °C, leukocyte count >10,000/mL, and ESR >15 mm/h (21). If ultrasound examination was inconclusive, computerized tomography (CT) or magnetic resonance imaging (MRI) was performed. Patients with non-inflammatory masses or malignancies were excluded from the study. The study included patients diagnosed with TOA who were admitted to our hospital and complied with treatment and regular follow-up.

Blood samples were collected from all patients before and after treatment for complete blood count, CRP, and ESR measurement. Complete blood count was performed with a Coulter LH 750 instrument (Beckman Coulter, Brea; CA, USA). Analyzed parameters in complete blood count were white blood cell (WBC), neutrophil, lymphocyte, and platelet counts, hemoglobin level, and hematocrit value. Intrauterine devices (IUD) were removed 24-48 hours after the start of treatment.

In our center, patients with TOA were initially treated with clindamycin (900 mg 3 times daily) and gentamicin (2 mg/kg loading dose, 1.5 mg/kg 3 times daily as maintenance) or ceftriaxone (1 g twice daily) and metronidazole (500 mg 3 times daily). Antibiotics were administered intravenously for at least 4 days. Intravenous administration was continued for 48 hours after body temperature returned to normal, then treatment was continued with 100 mg doxycycline every 12 hours for 14 days.

Failure to respond to treatment was defined as persistence of fever for 72 hours despite antibiotic therapy, or positive peritoneal findings continuing after 48 hours of treatment. Patients with failed medical treatment were treated surgically by laparotomy with unilateral salpingo-oophorectomy (USO), total abdominal hysterectomy and USO, and/or bilateral salpingo-oophorectomy (BSO).

Clinical, demographic, laboratory, and surgical data were obtained from the patients' medical records. Age, pre- and post-treatment blood count parameters, surgery type, methods applied, and postoperative histopathological diagnosis were recorded.

NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count; PLR was determined by dividing the absolute platelet count by the absolute lymphocyte count.

The data were analyzed using SPSS 20.0 statistics software package. Numeric variables were tested for normal distribution using Shapiro-Wilk test. Categorical variables were expressed as frequency and percentage; numerical variables were expressed as mean, standard deviation (SD), and minimum-maximum values. Relationships between pairs of categorical variables were evaluated using chi-square test. Independent means were compared using Student's t-test and independent medians were compared using Mann-Whitney U test. P <0.05 was accepted as a statistically significant result. The ability of NLR, PLR, and CRP values to facilitate diagnostic decisions in predicting treatment choices for TOA patients was evaluated using receiver operating characteristic (ROC) curve analysis. For significant cut-off values, the sensitivity, specificity, positive predictive value, and negative predictive value were calculated. When evaluation of the area under the ROC curve resulted in a Type I error level below 5%, the test was interpreted as having significant diagnostic value.

RESULTS

In total, 180 patients who met the study inclusion criteria were treated for TOA in our clinic between 2008 and 2016. The mean age of the patients was 37.6 years and mean gravidity was 2.6 (Table 1). Of the 180 patients, 81 (45%) received medical treatment and 99 (55%) were treated surgically. Details of the surgeries performed in the surgical treatment group are shown in Table 2. The demographic characteristics of the patients in the medical and surgical treatment groups are compared in Table 1. Mean age was 34.4 years in the medical treatment group and 40.1 years in the surgical treatment group (p<0.001). No significant differences were observed between the medical and surgical treatment groups in terms of gravidity, parity, prior pelvic surgery, and IUD use (p=0.297, p=0.442, p=0.367, p=0.558).

Table 1. Socio-demographic data of patients (n=180)

Characteristic	Value		
Age[a]	37.6 (16-74)		
Gravida[a]	2.6 (0-10)		
Parity[a]	2.06 (0-7)		
History of pelvic surgery (%)	15		
IUD (%)	24		
	Medical treatment (n=81)	**Surgical treatment (n=99)**	**P**
Age[b]	34.4 (7.5)	40.1 (8.7)	**<0.001**
Gravida[b]	2.5 (1.9)	2.7 (1.7)	0.297
Parity[b]	1.9 (1.3)	2.1 (0.9)	0.442
History of pelvic surgery (%)	12.3	17.2	0.367
IUD (%)	20.3	24	0.558
TOA diamater[b] (cm)	4.5 (1.8)	6.5 (2.6)	**<0.001**

IUD: intrauterine device
[a] Values are given as mean and minumum - maximum.
[b] Values are given as mean and SD.

Table 2. The details of the operations in the surgical group (n=99)

Characteristic	N
USO	29 (%29.2)
BSO	4 (%4)
TAH+USO	4 (%4)
Subtotal hysterectomy+USO	4 (%4)
TAH+BSO	10 (%10.1)
Drainage	48 (%48.4)
Appendectomy	7 (%7)

USO: Unilateral salpingo- oophorectomy; BSO: Bilateral salpingo-oophorectomy; TAH: Total abdominal hysterectomy

Mean pre-treatment leukocyte count was significantly higher in the surgical treatment group than in the medical treatment group (17.59±6.33 × 103 /mL vs. 12.51±4.29 × 103 /mL, p<0.001). Mean pre-treatment neutrophil, platelet, and CRP values were also significantly higher in the surgical treatment group (p<0.001 for all) (Table 3). There was no statistically significant difference in the mean post-treatment leukocyte counts of the two groups (p=0.352). However, mean post-treatment neutrophil, platelet, and CRP values were significantly higher in the surgical treatment group (p=0.030, p<0.001, p<0.001).

Table 3. Descriptive statistics of values obtained from the participants

		Tedavi şekli	Ortalama	Standart sapma	P
Pre-treatment	Leukocyte, ×10³/µl	Medical	12.5	4.2	**<0.001**
		Surgical	17.5	6.3	
	Neutrophil, ×10³/µl	Medical	9	4.5	**<0.001**
		Surgical	14.5	6	
	Platelet, ×10³/µl	Medical	287	93.5	**<0.001**
		Surgical	396.3	179.5	
	CRP, mg/dl	Medical	60.7	86.4	**<0.001**
		Surgical	134.2	112.1	
	NLR	Medical	6.1	7.8	**<0.001**
		Surgical	9.6	5.4	
	PLR	Medikal	166.4	152.3	**<0.001**
		Surgical	256.2	136.2	
Post-treatment	Leukocyte, ×10³/µl	Medical	8.6	2.6	0.352
		Surgical	8.9	2.7	
	Neutrophil, ×10³/µl	Medical	5.1	2.3	**0.030**
		Surgical	5.9	2.5	
	Platelet, ×10³/µl	Medical	297.8	124	**<0.001**
		Surgical	376.3	138.7	
	CRP, mg/dl	Medical	13.1	33.6	**<0.001**
		Surgical	32.1	32.8	
	NLR	Medical	2.6	3.6	0.174
		Surgical	3.2	2.1	
	PLR	Medical	135.6	82.2	**<0.001**
		Surgical	201.8	110.4	

CRP: C-reaktif protein; NLR: Neutrophil / lymphocyte ratio; PLR: Platelet/ lymphocyte ratio

Analysis of the groups' pre- and post-treatment NLR and PLR values showed that the surgical treatment group had significantly higher preoperative NLR and PLR (p<0.001 for both). The relationship between the surgical and medical treatment groups' post-treatment PLR values was statistically significant, whereas the relationship between NLR values was not significant (p<0.001 and p=0.174, respectively).

The ROC curve data demonstrating the utility of NLR and PLR in the prediction of surgical treatment in TOA patients is presented in Table 4. Figure 1. Area under the ROC curves for NLR and PLR. An NLR cut-off value of 6 was identified in ROC analysis as statistically significant (p<0.001, area under the curve [AUC=0.77], 95% confidence interval: 0.698-0.843, sensitivity 71%, specificity 74%). The AUC value for PLR was 0.77. According to ROC analysis, the PLR cut-off value predicting surgical treatment was 165 (p<0.001, 95% confidence interval: 0.670-0.818, sensitivity: 74.7%, specificity: 65.4%).

Table 4. Use of NLR and PLR values in predicting TOA medical treatment

	Cut-off	Sensitivity	Specificity	AUC	P
NLR	6	71.7	74.4	0.77	**<0.001**
PLR	165	74.7	65.4	0.74	**<0.001**

TOA: tubo-ovarian abscess; NLR: : Neutrophil / lymphocyte ratio; PLR: Platelet/ lymphocyte ratio; AUC: Area under the curve

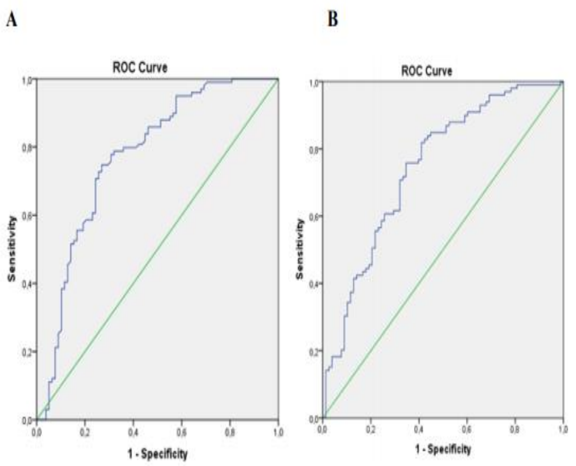

Figure 1. ROC values for (A) NLR and (B) PLR

NLR: Neutrophil / lymphocyte ratio; PLR: Platelet/ lymphocyte ratio; ROC: Receiver operating characteristic

DISCUSSION

In this retrospective study, the clinical, laboratory, and ultrasound findings of 180 TOA patients were analyzed to determine their predictive value in terms of TOA treatment outcomes. Age, TOA size, pre-treatment leukocyte, neutrophil, and platelet counts, CRP level, NLR, and PLR were found to be risk factors for surgical treatment. The present study clearly showed that preoperative NLR value of 6 or higher and PLR value of 165 or higher were predictive of medical treatment failure with sensitivity and specificity values of 71.7% and 74.4% for NLR and 74.7% and 65.4% for specificity.

TOA is an advanced stage of acute PID and can cause long-term mortality and morbidity (22). The most common symptoms are abdominal pain and pelvic pain.

It is often accompanied by fever and leukocytosis. TOA is diagnosed with a complete physical and pelvic examination followed by the necessary laboratory and imaging modalities. Early diagnosis and treatment is important to minimize disease-related morbidity and mortality (22).

Broad-spectrum antibiotic therapy is the first-line treatment unruptured TOA (6,8). Despite there being no recommended specific intravenous antibiotic regimen, broad-spectrum intravenous antibiotics followed by long-term oral antibiotics are effective for most pelvic abscesses (8). Although response to antibiotherapy is high in TOA, approximately 25% of patients require surgery or drainage (1).

Analyses of the sociodemographic risk factors for TOA medical treatment failure found in the literature report contradictory results. Some studies reported that advanced age, greater number of pregnancies, past pelvic surgery, menopausal status, and presence and duration of IUD use were risk factors (6,8,9,12). However, these did not emerge as significant risk factors in other studies (7,8). In the present study, the only sociodemographic difference between the groups was that the surgical treatment group was significantly older than the medical treatment group.

Larger TOA size has been associated with increases in the number of complications, length of hospital stay, and need for surgical treatment or drainage (24-26). Reed et al. reported that surgical treatment was required by 60% of patients with a TOA greater than 10 cm in diameter, compared to 20% of patients with a TOA less than 5 cm in diameter (24). Consistent with these findings, another study showed that laparotomy was required in 72% of patients when the abscess diameter was larger than 10 cm, and 26% when it was less than 5 cm (25). Güngördük et al. determined that TOA diameter >6.5 cm predicted the need for surgical treatment with 77.6% sensitivity and 65% specificity (8). In our study, we also found the mean TOA diameter was 4.5±1.8 cm in the medical treatment group and 6.5±2.6 cm in TOA diameter in the surgical treatment group ($p<0.001$), consistent with the literature.

There are many laboratory tests that demonstrate inflammation and are used in the diagnosis, treatment, and follow-up of TOA. Leukocytosis and elevated CRP and ESR values are well-known laboratory parameters (27). Recently, NLR and PLR values have also been shown to be inexpensive, easily assessed, and widely used markers of inflammatory response (13). The acute inflammatory process and bacterial infection increase neutrophil production and inflammatory infiltration (28). Bone marrow progenitor cells are transformed into granulocytes by interleukin (IL)-3, IL-6, IL-11, and granulocyte colony stimulating factor. During the inflammatory process, neutrophils are the first cells to reach the tissue (29). As a result, there may be an increase in neutrophils and a relative decrease in lymphocytes in the peripheral circulation. This manifests as an elevated peripheral NLR ratio. This process is an important parameter in detecting a systemic inflammatory response. Because the life span of neutrophils is short, the NLR value falls when the infection regresses or resolves. This allows NLR value to be used for evaluation of treatment response.

Like NLR, PLR is also among the leukocyte indices recommended as an inflammatory marker (15). In addition to their role in hemostasis, platelets also play an active role in tissue repair, inflammation, and antimicrobial host defense. Megakaryopoiesis is inhibited in acute infection, but active megakaryopoiesis in chronic infection results in reactive thrombocytosis (30). In addition, recent studies have shown that NLR and PLR are convenient and reliable prognostic factors in diseases such as ovarian cancer, colorectal cancer, breast cancer, and non-small cell lung cancer (16,17). Yıldırım et al. compared 136 TOA patients with 176 healthy women and showed that NLR and PLR values were better predictors of TOA diagnosis (12). NLR had 95.2% sensitivity and 99.4% specificity, while PLR had 86.7% sensitivity and 92% specificity. The authors also showed that NLR and PLR remained high in TOA patients despite normal leukocyte counts.

In our study, the results of ROC analysis showed that an NLR of 6 and PLR of 165 had diagnostic value in predicting medical treatment failure in patients with TOA (71.7% sensitivity, 74.4% specificity for NLR; 74.7% sensitivity, 65.4% specificity for PLR). The main limitation of our study is the retrospective design.

In conclusion, we determined in this study that pre-treatment NLR and PLR values of TOA patients were highly predictive of the success of medical treatment. In the pre-treatment clinical management of patients diagnosed with TOA, we believe NLR and PLR may be inexpensive complementary laboratory parameters that can guide the choice of medical or surgical treatment and are also useful in predicting the success of medical treatment. However, these findings need to be supported by prospective studies determining the discriminatory properties of these tests.

REFERENCES

1. Granberg S, Gjelland K, Ekerhovd E. The management of pelvic abscess. Best Pract Res Clin Obstet Gynaecol 2009; 23:667-8.

2. Chappell CA, Wiesenfeld HC. Pathogenesis, diagnosis, and management of severe pelvic inflammatory disease and tuboovarian abscess. Clin Obstet Gynecol 2012;55:893–903.

3. Vermeeren J, Te Lınde Rw. Intraabdominal rupture of pelvic abscesses. Am J Obstet Gynecol 1954; 68:402.

4. Pedowıtz P, Bloomfıeld Rd. Ruptured Adnexal Abscess (Tuboovarıan)With Generalızed Perıtonıtıs. Am J Obstet Gynecol 1964; 88:721.

5. Rosen M, Breitkopf D, Waud K. Tubo-ovarian abscess management options for women who desire fertility. Obstet Gynecol Surv 2009; 64:681.

6. Kinay T, Unlubilgin E, Cirik DA, et al. The value of ultrasonograhic tubo-ovarian abscess morphology in predicting whether patients will require surgical treatment. Int J Gynaecol Obstet 2016;135:77–81.

7. Topcu HO, Kokanali K, Guzel AI, et al. Risk factors for adverse clinical outcomes in patients with tubo-ovarian abscess. J Obstet Gynaecol 2015;35:699–702.

8. Gungorduk K, Guzel E, Asicioglu O, et al. Experience of tubo-ovarian abscess in western Turkey. Int J Gynecol Obstet 2014;124:45–50.

9. Inal ZO, Inal HA, Gorkem U. Experience of Tubo-Ovarian Abscess: A Retrospective Clinical Analysis of 318 Patients in a Single Tertiary Center in Middle Turkey. Surg Infect (Larchmt). 2018;19:54-60.

10. Oktem O., The Ovary Anatomy and Function throughout Human Life, Ann. N.Y. Acad. Sci. 1127: 1–9 (2008). New York Academy of Sciences.doi: 10.1196/annals.1434.009.

11. Saladin K., Human Anatomy, Second Edition, ISBN 978–0–07–294368–9, MHID 0–07–294368–8,2008,S:736-767.

12. Yildirim M, Turkyilmaz E, Avsar AF. Preoperative Neutrophil-to-Lymphocyte Ratio Has a Better Predictive Capacity in Diagnosing Tubo-Ovarian Abscess. Gynecol Obstet Invest. 2015;80:234-9.

13. Bolat D, Topcu YK, Aydogdu O, et al. Neutrophil to Lymphocyte Ratio as a predictor of early penile prosthesis implant infection. Int Urol Nephrol 2017;49:947–53.

14. Zahorec R: Ratio of neutrophil to lymphocyte counts rapid and simple parameter of systemic inflammation and stress in critically ill. Bratisl Lek Listy 2001; 102: 5–14.

15. Kurtipek E, Bekci TT, Kesli R, et al. The role of neutrophil-lymphocyte ratio and platelet-lymmphocyte ratio in exacerbation of chronic obstructive pulmonary disease. J Pak Med Assoc 2015;65:1283-7.

16. Ertas IE, Gungorduk K, Akman L, et al. Eur J Obstet Gynecol Reprod Biol. 2013 Nov;171(1):138-4.

17. Gungorduk K, Ertaş IE, Ozdemir A, et al. Prognostic Significance of Retroperitoneal Lymphadenectomy, Preoperative Neutrophil Lymphocyte Ratio and Platelet Lymphocyte Ratio in Primary Fallopian Tube Carcinoma: A Multicenter Study. Cancer Res Treat. 2015;47(3):480-8.

18. Paramanathan A, Saxena A, Morris DL: A systematic review and meta-analysis on the impact of pre-operative neutrophil lymphocyte ratio on long term outcomes after curative intent resection of solid tumours. Surg Oncol 2014; 23: 31–9.

19. Williams KA, Labidi-Galy SI, Terry KL, et al. Prognostic significance and predictors of the neutrophil-to-lymphocyte ratio in ovarian cancer. Gynecol Oncol 2014; 132: 542–50.

20. Chappell CA, Wiesenfeld HC. Pathogenesis, d,agnosis, and management of severe pelvic inflammatory diease and tuboovarian abcess. Clin Obster Gynecol 2012;55(4):893-903.

21. Varras M, Polyzos D, Perouli E, et al. Tubo-ovarian abscesses:spectrum of sonographic findings with surgical and pathological correlations: Clin Exp Obstet Gynecol 2003;30(2-3):117-21.

22. Seshadri S, Kirwan J, Neal T: Perimenopausal pneumococcal tubo-ovarian abscess – a case report and review. Infect Dis Obstet Gynecol 2004; 12: 27–30.

23. Topcu HO, Kokanali K, Guzel AI, et al. Risk factors for adverse clinical outcomes in patients with tubo-ovarian abscess. J Obstet Gynaecol 2015;35:699–702.

24. Reed SD, Landers DV, Sweet RL (1991) Antibiotic treatment of tuboovarian abscess: comparison of broad-spectrum β-lactam agents versus clindamycin-containing regimens. Am J Obstet Gynecol 164:1556–62.

25. Doganay M, Iskender C, Kilic S, et al. Treatment approaches in tubo-ovarian abscesses according to scoring system. Bratisl Lek Listy. 2011;112(4):200-3.

26. Dewitt J, Reining A, Allsworth JE, et al. Tuboovarian abscesses: is size associated with duration of hospitalization & complications? Obstet Gynecol Int. 2010;2010:847041.

27. Akkurt MO, Yalcin SE, Akkurt I, et al. The evaluation of risk factors for failed response to conservative treatment in tubo-ovarian abscesses. J Turk Ger Gynecol Assoc 2015; 16:226–30.

28. Ear T, McDonald PP. Cytokine generation, promoter activation, and oxidant-independent NF-kappaB activation in a transfectable human neutrophilic cellular model. BMC Immunol. 2008;9:14.

29. Kolaczkowska E, Kubes P. Neutrophil recruitment and function in health and inflammation. Nat Rev Immunol. 2013;13:159-75.

30. Klinger Mh, Jelkman W. Role of blood platelets in infection and. İnflamation. J Interferon Cytokine Res. 2002;22:913-22.