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ORIGINAL ARTICLE

The effect of serum biomarkers on the requirement for surgical intervention in tuboovarian abscess

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ABSTRACT

Objective: Tubo-ovarian abscess (TOA) is a complex infectious mass of the adnexa, which is treated by antibiotherapy or surgery. Antibiotherapy failure may occur during TOA treatment. The aim of this study is to assess the effect of TOA size and serum biomarkers on the requirement for surgical intervention.

Material and Methods: Eighty-four patients over five years in our clinic were evaluated. TOA size and laboratory values such as hemoglobin, white blood cell count, lymphocyte, monocyte, platelet, albumin, neutrophil, C-reactive protein (CRP) levels, and if antibiotics were switched to another treatment protocol or changed to a surgical approach, were also reported. Prognostic Nutritional Index (PNI), the platelet-lymphocyte ratio (PLR), neutrophil-lymphocyte ratio (NLR), and monocyte-lymphocyte ratio (MLR) were also used to evaluate medical therapy failure and the requirement for surgery.

Results: Eighty-four patients hospitalized with the diagnosis of TOA, 13 of them required surgery due to antibiotherapy failure and the surgical intervention rate was calculated as 15.47%. Platelet count and TOA size were found to be statistically significantly higher and hospital stay was found to be statistically significantly longer in the surgery group. CRP and other laboratory values did not have a statistically significant difference between groups. Among the indexes, only PLR had a statistically significant prediction value (p=0.020).

Conclusion: TOA volume and PLR were found to be effective predictors in antibiotherapy failure and surgical intervention.

Keywords: Antibiotic failure, surgical intervention, tubo ovarian abscess.

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INTRODUCTION

Tubo-ovarian abscess (TOA) is a complex infectious mass of the adnexa, which is classically characterized by symptoms of fever, pelvic pain, and vaginal discharge, and an increase in vaginal temperature.[1] It is mostly a polymicrobial infection and frequently seen as a complication of untreated pelvic inflammatory disease (PID). The prevalence of PID is 3.6–10%, and 2.3–20% of PID patients may develop TOA.[2] Usually, Chlamydia spp. and Neisseria spp. are isolated in PID, whereas Bacteroides spp., Peptostreptococcus spp., and Peptococcus spp. are isolated from TOA samples.[3] First-line therapy for TOA is antibiotherapy; however, if abscess rupture occurs, the disease can be mortal.[4] While there are varied antibiotic regimens, a combination of clindamycin and gentamicin is used in our clinic as a first-line therapy for TOA.[5]

Antibiotherapy failure may occur during TOA treatment. Resistance to antibiotherapy is also a problem in the treatment of TOA, as well as other diseases. The most common resistance mechanisms are modifying the production of hydrolase enzymes, ribosomal protection, and target site mutation.[2] Antibiotherapy failure, rupture of the abscess, and sepsis are the main indications for surgery. Approximately 25% of patients with unruptured TOA require surgery.[6] The goal of surgery for TOA treatment is the drainage of the abscess and to lessen the infectious burden through peritoneal lavage.[7] It is recommended to place a drain in the abdomen to help continue the drainage. There is not enough data for a definite way to determine which patients will have success with antibiotherapy and which will require surgery according to guidelines; the aim of this study is to show the parameters that can help predict the requirements for surgery in patients.

MATERIAL AND METHODS

This protocol has been reviewed and approved by the Clinical Researches Ethics Committee of the Hospital (approval number: 2022/0214). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

In this retrospective study, we reviewed 84 patients who underwent treatment with gentamicin plus clindamycin for TOA between 01.01.2017 and 25.03.2022 in our Obstetrics and Gynecology clinic. Files of these patients were examined, and age, gravida, parity, abortus, methods of delivery, comorbidities, hospital stay length, TOA size, and laboratory values such as hemoglobin (Hmg), white blood cell count (WBC), lymphocyte (Lym), monocyte (Mon), platelet (Plt), albumin (Alb), neutrophil (Neut), and C-reactive protein (CRP), change of antibiotherapy, and if surgery had been necessitated for treatment of TOA are reported. The day of hospitalization of the patient is accepted as 'day 1'. Laboratory examinations were recorded on 'day 1' and 'day 7'.

In this study, inclusion criteria include symptomatic TOA patients who apply to our clinic. Exclusion criteria are patients whose data were incomplete, pathology results being incompatible with TOA or the presence of another malignant disease, and the requirement for blood transfusion. Patients with ruptured TOA were also excluded since it is a known indication for surgical intervention.

Abscess size was calculated using the ellipsoid formula, where two dimensions are taken of the abscess: the widest single line in the abscess (W) and the perpendicular measurement to that measurement (L) by twisting the ultrasound probe, which is how abscess sizes are calculated in our hospital. The final formula was found to be Volume (mm^3)=$0.5 \times L \times W^2$.[8,9]

The Prognostic Nutritional Index (PNI), which is calculated as serum albumin (g/dL)+5× total lymphocyte count (10^9/L), is used in patients undergoing surgery to predict the prognosis of patients. This parameter was also used in gastric and mammary cancer patients.[10,11]

The platelet-lymphocyte ratio (PLR) was used to evaluate the inflammatory state of the body and predict cardiovascular events. This value is calculated in a complete blood count and does not have an extra cost. We used this test to evaluate the inflammatory response in our patients.[12]

The neutrophil-lymphocyte ratio (NLR) and lymphocyte-monocyte ratio (LMR) were also used to discern the inflammatory status of the body, as different types of leukocytes have different roles. These ratios were included in this study to understand if they are linked with antibiotherapy failure or were higher in the surgery group.[13,14] We used day 1 results to calculate abscess size, PNI, PLR, NLR, LMR.

Statistical Analysis

Statistical analyses were performed using the SPSS 22.0 statistical package. In the descriptive findings section, categorical variables were presented with numbers and percentages, and continuous variables with mean±standard deviation and median value (smallest, largest value). Pearson's Chi-square test was used to compare categorical variables; the Kolmogorov-Smirnov test was used to examine the suitability of the data for normal distribution in the comparison of variables specified by the measurement. The Paired t-test was used to compare two repetitive measurements suitable for normal distribution. The statistical significance level was set at $p<0.05$ in the analysis.

RESULTS

A total of 84 patients were hospitalized with the diagnosis of TOA. The group that did not require surgery (No-Surgery Group, NSG) consisted of 71 patients, and the surgery group (SG) consisted of 13 patients. The surgical intervention rate was calculated as 15.47%. Our results are presented in the tables below. In Table 1, general demographic values and clinical data were examined, along with the average TOA size of the patients.

In Table 2, the laboratory results were compared between SG and NSG. While the Hemoglobin (Hmg) value was found to be statistically significantly lower, the platelet (Plt) count and TOA size were found to be statistically significantly higher, and hospital stay was found to be statistically significantly longer in SG. White blood cell (WBC), C-reactive protein (CRP), and other laboratory values did not show a statistically significant difference between groups.

In Table 3, we examined the Prognostic Nutritional Index (PNI), Platelet-Lymphocyte Ratio (PLR), Neutrophil-Lymphocyte Ratio (NLR), and Lymphocyte-Monocyte Ratio (LMR). Among these indices, only PLR showed a statistically significant difference between SG and NSG.

Table 1: General demographic values and clinical data

	Average±SD (min; max)
Age (n=84)	39.1±7.2 (19; 58)
Gravida (n=84)	2.6±1.6 (0; 8)
Parity (n=84)	1.6±1.1 (0; 5)
Abortus (n=84)	0.8±1.1 (0; 6)
Method of delivery (n=70)	
NSVB	38 (54.3)
C/S	21 (30.0)
C/S-NSVB	11 (15.7)
Day 1 Hmg (n=84)	11.0±1.7 (6.6; 14.5)
Day 7 Hmg (n=84)	10.7±1.6 (7.3; 14.8)
Day 1 WBC (n=84)	13.7±5.2 (4.2; 31.9)
Day 7 WBC (n=84)	9.1±3.2 (4.4; 24.1)
Day 1 CRP (n=84)	114.9±87.1 (1; 314)
Day 7 CRP (n=84)	41.3±49.8 (0.3; 195)
Toa Size (mm^3) (n=84)	110.0±124.1 (4; 682)
Average hospital stay (day) (n=84)	6.0±3.0 (1; 17)

Min: Minimum; Max: Maximum; NSVB: Normal spontaneus vaginal birth; C/S: Cesarean section; WBC: Blood cell count; CRP: C-reactive protein.

Table 2: Laboratory result comparison between groups

	Surgery group (n=13)	No-surgery group (n=71)	p
Hemoglobin day 1*	9.7±1.7	11.2±1.6	0.003
Neutrophil day 1*	14.7±3.8	13.5±5.4	0.490
CRP day 1**	137.9±74.3	110.7±89.1	0.255
Hemoglogin day 7*	10.4±1.1	10.8±1.7	0.253
Neutrophil day 7*	9.4±3.1	9.1±3.2	0.787
CRP day 7**	49.1±56.2	39.9±48.9	0.290
Alb gr/dl*	3.6±0.6	3.7±0.5	0.443
Lymphocyte**	1.9±0.5	2.2±0.9	0.301
Monocyte**	0.5±0.1	0.6±0.3	0.335
Platelet**	381.9±128.9	300.4±102.7	**0.039**
Antibiotic change			0.372
No	9 (69.2)	57 (80.3)	
Yes	4 (30.8)	14 (19.7)	
Gravida**	2.4±1.5	2.6±1.7	0.471
Parity**	1.6±0.6	1.7±1.1	0.776
Abort**	0.8±1.3	0.8±1.1	0.592
Method of delivery***			0.078
NSVB	8 (61.5)	30 (52.6)	
C/S	1 (7.7)	20 (35.1)	
C/S+NSVB	4 (30.8)	7 (12.3)	
TOA size (mm^3)**	137.1±89.3	105.0±129.4	**0.049**
Hospital stay (days)**	7.7±2.6	5.7±2.9	**0.015**

*: Student t test; **: Mann Whitney U test; ***: Chi Square Test; CRP: C-reactive protein; NSVB: Normal spontaneus vaginal birth; C/S: Cesarean section; TOA: Tubo-ovarian abscess.

DISCUSSION

In this study, we examined multiple parameters to predict the requirement for surgery in TOA patients. Among those diagnosed with TOA, 15.5% of patients required surgery, and no demographic values were associated with the need for surgical treatment. The average hospital stay was found to be 2.1±0.3 days longer, hemoglobin (Hmg) values were lower, and platelet (Plt) counts were higher in SG patients on day 1. TOA volume was found to be larger in patients who required surgery. Additionally, the Platelet-Lymphocyte Ratio (PLR) was higher in SG patients. For the other parameters, there were no statistical differences.

TOA is the most common cause of intraabdominal abscess in premenopausal women.[15] TOA mostly develops from PID, since women have peritoneal perforations in their internal genitalia, which differ from men.[16] Modern treatment for TOA involves hospitalization and IV antibiotics, and treatment failure within 48–72 hours can necessitate surgical intervention. In a study similar to ours involving 350 patients over 8 years, the surgery rate was estimated at 49.8%.[17] In another study with 135 TOA patients, the surgery rate was found to be 35%.[18] Another study reported a surgery rate of 25%.[6] In a further study with ceftriaxone, metronidazole, and doxycycline, 44 out of 174 patients required surgery, and the medical treatment success rate was calculated as 77%.[19] In our population, the requirement for surgery was found to be 15.5%. The reason for the lower surgical rate in our study compared to others may be that patients in our country have easy access to health services and can be treated earlier.

Treatment failure was defined as fever, exacerbation of clinical findings, enlargement of the abscess, increased leukocytosis, and sepsis. Patient age >35, white blood cell count >16000/mm^3, and TOA greater than 70 mm in greatest diameter were identified as risk factors for surgery. Additionally, inadequate antibiotic therapy and bilateral abscess were evaluated as risk-increasing factors for antibiotic failure, leading to the development of a risk scoring system.[17] CRP and TOA size were observed to be risk factors for drainage requirement and longer hospital stay.[19] While the mean diameter of the medically successfully treated TOA was 6.3 cm, a diameter of 7.7 cm was associated with the need for surgery, and each 1 cm increase in diameter increased the hospitalization time by 0.4 days.[18] TOA volume was statistically significantly different between groups, and in the SG group, it was found to be larger. We couldn't draw a specific margin for TOA volume, as we did have to operate on some patients with smaller TOA volumes. However, we can safely conclude that as TOA volume increases, the risk of treatment failure also increases. In the study done by Mizushima et al.,[20] a TOA size larger than 5 cm was associated with an increased risk of antibiotherapy failure.

Table 3: Values compared between surgery group and no surgery group

	Surgery group	No-surgery group	p
Prognostic Nutritional Index	13.4±2.9	15.0±4.7	0.279
Neutrophil/lymphocyte ratio	7.8±2.7	7.2±4.6	0.157
Platelet/lymphocyte ratio	207.7±95.6	157.4±91.8	**0.020**
Lymphocyte/monocyte ratio	3.8±1.5	4.0±2.3	0.887

Mann Whitney U test.

In the indices we examined, PNI, LMR, and NLR did not show a statistically significant difference between groups. Among these indices, only the PLR ratio had a statistically significant difference between the surgery group (SG) and the no-surgery group (NSG). Although more randomized controlled trials are needed, we can conclude that as the ratio increases, the risk of antibiotherapy failure also increases.

PNI is especially used in oncologic and rheumatologic patient populations to assess prognosis. We did not find this index being used in TOA patients, nor did we find a statistically significant difference with PNI being lower in the surgery group. We believe this is due to the fact that the main parameter of PNI, albumin, is affected more in chronic processes. A larger population should be analyzed to assess the effectiveness of PNI.

In the study, NLR levels higher than 4.15 were predictive for TOA with 95.2% sensitivity and 99.4% specificity. The PLR cutoff value was 164.37 with 86.7% sensitivity and 92% specificity for TOA.[21] In another study, NLR and PLR levels were used for assessing the success of medical treatment, and 55% of the patients required surgical intervention. In the surgery group, abscess volume, platelet count, and PLR were found to be higher, similar to our results. WBC count was also higher in the surgery group. The cutoff for NLR was 6, and the cutoff for PLR was 165.[22] In a study that included 285 TOA cases, WBC, CRP, NLR, LMR, and PLR were significantly higher in the surgery group. It has been stated that NLR may be an independent marker for antibiotherapy failure.[23] Another study identified risk factors for antibiotherapy failure as age 41.5, BMI 26.72 kg/m², CRP 143.6 mg/L, and abscess diameter of 62.5 mm.[24] In our study, NLR levels were above the cutoff value in both of our groups, however, PLR was statistically significantly higher in the surgery group.

The average hospital stay was longer by 2.1±0.3 days, hemoglobin values were lower, and platelet counts were lower in SG patients on day one. These changes may be related to the severity of the TOA and systemic infection. Day-seven values were no longer statistically significantly different, indicating treatment success. The length of hospital stay can also be associated with the surgical intervention itself, as we routinely observe patients for 48 hours after laparotomy or for 24 hours after a laparoscopy procedure.

There are two important populations when surgery is considered for TOA patients. The first group consists of young adults who wish to preserve fertility, and the second group includes older patients with completed fertility but with advanced age and multiple comorbidities. In the first group of patients, we aim to avoid surgery if possible to minimize interventions to the ovaries. In older patients, we seek to avoid infectious complications as they usually have multiple comorbidities, and delaying surgery might negatively affect their prognosis. In this aspect, we have two special groups: the first group where we try to avoid operation, and the second group where we want to operate as soon as possible if surgery is required.

Our study has multiple limitations; we did not have the course of vitals during the patients' stay in our hospital, which could be useful to determine if surgery is needed for a TOA patient. This study also did not include whether the patients had an intrauterine device present, although the study done by Ginsburg et al.[25] did not reach a definitive conclusion related to antibiotherapy failure.

To conclude, we believe that TOA volume is the most important predictor of antibiotherapy failure, with PLR also playing a significant role in prognosis. Hemoglobin and platelet levels are also important in patients; however, it is challenging to draw a conclusive line for these laboratory levels as they are affected by multiple factors. More prospective trials are needed on this subject.

Statement

Ethics Committee Approval: The Göztepe Training and Research Clinical Research Ethics Committee granted approval for this study (date: 13.04.2022, number: 2022/0214).

Author Contributions: Concept – CSÖ, ED; Design – AK, CSÖ; Supervision – ODY; Materials – AK; Data Collection and/or Processing – AK; Analysis and/or Interpretation – MÇ; Literature Search – CSÖ; Writing – CSÖ, AK; Critical Reviews – AT.

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REFERENCES

1. Kairys N, Roepke C. Tubo-Ovarian abscess. StatPearls Publishing; 2023.
2. Tang H, Zhou H, Zhang R. Antibiotic resistance and mechanisms of pathogenic bacteria in tubo-ovarian abscess. Front Cell Infect Microbiol 2022;12:958210.
3. Landers DV, Sweet RL. Tubo-ovarian abscess: Contemporary approach to management. Rev Infect Dis 1983;5:876–84.
4. Pedowitz P, Bloomfield RD. Ruptured adnexal abscess (tuboovarian) with generalized peritonitis. Am J Obstet Gynecol 1964;88:721–9.
5. Curry A, Williams T, Penny ML. Pelvic inflammatory disease: Diagnosis, management, and prevention. Am Fam Physician 2019;100:357–64.
6. Wiesenfeld HC, Sweet RL. Progress in the management of tuboovarian abscesses. Clin Obstet Gynecol 1993;36:433–44.
7. Jones HW, Rock JA. Te linde operatif jinekoloji. 11th ed. Wolters Kluwer; 2017.
8. Euhus DM, Hudd C, LaRegina MC, Johnson FE. Tumor measurement in the nude mouse. J Surg Oncol 1986;31:229–34.

9. Tomayko MM, Reynolds CP. Determination of subcutaneous tumor size in athymic (nude) mice. Cancer Chemother Pharmacol 1989;24:148–54.
10. Xishan Z, Ye Z, Feiyan M, Liang X, Shikai W. The role of prognostic nutritional index for clinical outcomes of gastric cancer after total gastrectomy. Sci Rep 2020;10:17373.
11. Chen L, Bai P, Kong X, Huang S, Wang Z, Wang X, et al. Prognostic nutritional index (PNI) in patients with breast cancer treated with neoadjuvant chemotherapy as a useful prognostic indicator. Front Cell Dev Biol 2021;9:656741.
12. Balta S, Ozturk C. The platelet-lymphocyte ratio: A simple, inexpensive and rapid prognostic marker for cardiovascular events. Platelets 2015;26:680–1.
13. Park MG, Kim MK, Chae SH, Kim HK, Han J, Park KP. Lymphocyte-to-monocyte ratio on day 7 is associated with outcomes in acute ischemic stroke. Neurol Sci 2018;39:243–9.
14. Huang Y, Liu A, Liang L, Jiang J, Luo H, Deng W, et al. Diagnostic value of blood parameters for community-acquired pneumonia. Int Immunopharmacol 2018;64:10–5.
15. Zeger W, Holt K. Gynecologic infections. Emerg Med Clin North Am 2003;21:631–48.
16. Dulin JD, Akers MC. Pelvic inflammatory disease and sepsis. Crit Care Nurs Clin North Am 2003;15:63–70.
17. Fouks Y, Cohen A, Shapira U, Solomon N, Almog B, Levin I. Surgical intervention in patients with tubo-ovarian abscess: Clinical predictors and a simple risk score. J Minim Invasive Gynecol 2019;26:535–43.
18. Dewitt J, Reining A, Allsworth JE, Peipert JF. Tuboovarian abscesses: Is size associated with duration of hospitalization & complications? Obstet Gynecol Int 2010;2010:847041.
19. Habboub AY. Middlemore Hospital experience with tubo-ovarian abscesses: An observational retrospective study. Int J Womens Health 2016;8:325–40.
20. Mizushima T, Yoshida H, Ohi Y, Ishikawa M, Hirahara F. Evaluating the risk factors for developing resistance to parenteral therapy for tubo-ovarian abscess: A case-control study. J Obstet Gynaecol Res 2013;39:1019–23.
21. 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.
22. Aydın F, Biler A, Taner CE, Ertas IE. Do pre-treatment neutrophil/lymphocyte and platelet/lymphocyte ratios predict success of medical treatment in patients with tubo-ovarian abscess? Kocaeli Tıp Derg [Article in Turkish] 2018;7:165–71.
23. Segal R, Zilberman A, Cohen Y, Yahya HH, Rofe G. Evaluation of cell ratios in routine laboratory tests as a prognostic factor for surgical intervention in tubo-ovarian abscess. J Minim Invasive Gynecol 2020;27:S121.
24. Akselim B, Karaşin SS, Demirci A, Üstünyurt E. Can antibiotic treatment failure in tubo-ovarian abscess be predictable? Eur J Obstet Gynecol Reprod Biol 2021;258:253–7.
25. Ginsburg DS, Stern JL, Hamod KA, Genadry R, Spence MR. Tubo-ovarian abscess: A retrospective review. Am J Obstet Gynecol. 1980;138:1055–8.