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WHEN THE SURGICAL TREATMENT IS SUGGESTED IN PATIENTS WITH TUBO-OVARIAN ABSCESS?

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ABSTRACT

To assess the risk factors for medical treatment failure and requirement of surgical treatment for tubo-ovarian abscess (TOA). The patients with tubo-ovarian abscess were recruited between 2012 and 2014, retrospectively. Age, obstetric history, menopausal status (non-menopausal vs menopausal), clinical and sonographic presentation, pelvic inflammatory design risk factors, antibiotic therapy, surgical treatment, time interval between hospitalization and surgery, presence of complications, laboratory results, and length of hospital stay were examined. We detected 52 patients with prediagnosis of tubo-ovarian abscess were hospitalized. After hospitalization, TOA was ruled out in 11 patients. 41 patients were reviewed. Ten (24, 3%) patients underwent surgical treatment because of failed antibiotic therapy. Thirty-one (75, 7%) patients treated successfully with parenteral antibiotic. The mean age of surgically treated patients was significantly higher than medically treated patients (p=0.048). Number of gestations and abortions were higher in patients who needed surgery (p=0,032 and p=0,037). It was also seen that abscess volume, C-reactive protein (CRP) levels and erythrocyte sedimentation rate (ESR) were also higher in surgically treated patients (p=0,004; p=0,010 and p=0,036, respectively). Mean duration of hospitalization was significantly longer in patients treated surgically (p=0,017). According to the ROC analysis, CRP level, abscess volume and abscess size are useful to predict the outcome of TOA treatment with antibiotics. Medical treatment failure and need of surgery are more common in patients who have large abscess (volume:>60 cm^3 or size: >5cm), elevated CRP levels (>6,7 mg/L) and high ESR (>50 mm/hr).

Key words: Medical treatment, Risk factor, Surgical treatment, Tubo-ovarian abscess.

INTRODUCTION

Pelvic inflammatory disease (PID) is an infection of the upper genital tract [1]. Tubo-ovarian abscess (TOA) is the most serious complication of PID [2]. 15% of all PID cases are complicated by TOA (Dewitt et al., 2010). Treatment of TOA classically consists of intravenous (iv) antibiotics followed by oral antibiotics [3]. The response rate to antimicrobial treatment is about 70% [4]. The antimicrobial approach fails in about 25% of all cases and surgical intervention becomes necessary [5]. Mortality associated with TOA has decreased dramatically over the last 50 years. However, the morbidity of TOA like infertility, ectopic pregnancy, chronic pelvic pain, pelvic thrombophlebitis, and ovarian vein thrombosis, remains significant [6]. Several studies show that features of TOA are associated with an increase in duration of hospitalization and an increase in need for drainage or surgery [7, 8].

The objective of our retrospective study was to assess the risk factors for medical treatment failure and requirement of surgical treatment for tubo-ovarian abscess. If the failure of antibiotic therapy can be predicted according to the clinical findings, early surgical intervention can be expected.

MATERIALS AND METHODS

All patients with the diagnosis of TOA who were hospitalized in the Department of Obstetrics and Gynecology in Ankara Training and Research Hospital between January 2012 and December 2014 included in this study. There were 52 patients who were hospitalized for

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suspected TOA were reviewed. After hospitalization, TOA was ruled out in 10 patients. Therefore, 42 patients were reviewed. The study protocol was approved by the institution's review board.

Abdominal pain, adnexal and cervical tenderness on vaginal examination and one or more of the minor criteria were used to diagnose the TOA. Minor criteria's are: fever (38ºC or more); leukocyte count of more than 10000/ml; erythrocyte sedimentation rate (ESR) of more than 15 mm/hour; and presence of a sonographic mass [3].

As suggested in the literature, the patients were initially treated with clindamycin and gentamicin or with ceftriaxone and metronidazole. The intravenous antibiotic treatment was applied for at least 4 days; parenteral treatment was discontinued 24-48 hours after clinical improvement. Oral therapy with 100 mg doxycycline every 12 hours to complete 14 days of treatment was used as complementary in these patients. In patients who did not responded to medical treatment (persistence of fever, positive peritoneal signs) after 48 hours surgical intervention was performed (unilateral or bilateral salpingectomy, salpingoophorectomy, and total abdominal hysterectomy).

Demographic and clinical datas were reviewed and recorded via medical file and computer based screening. Specifically, age, obstetric history, menopausal status (non-menopausal vs menopausal), clinical and sonographic presentation, PID risk factors, antibiotic therapy, surgical treatment, time interval between hospitalization and surgery presence of complications, laboratory results, and length of hospital stay were analyzed.

The average volume of the TOAs was calculated by the ellipsoid volume formula (volume=height×width×length×0, 52). Analyses were conducted by using the SPSS 17.0 for Windows. Whether the distributions of continuous and discrete variables were normal or not was determined by using the Kolmogorov-Smirnov test. Standard deviation, mean and median were utilized as descriptive statistics for discrete and continues variables whereas absolute and relative sample sizes are utilized for categorical variables. Whether the means of the groups are different were investigated by using Student's t test. The Mann Whitney U test was utilized to check if medians of the groups were significantly different. The descriptive statistics of categorical variables were analyzed by using Pearson's Chi Square and Fisher's exact test. Relative risks (RRs) with 95% confidence intervals (CIs) were calculated. P value of 0.05 was considered to indicate statistical significance. To assess cut-off, sensitivity, and specificity values, we used a receiver operating characteristic (ROC) curve.

RESULTS

We detected 52 patients prediagnosed tubo-ovarian abscess between January 2012 and December 2014 in Ankara Training and Research Hospital. After hospitalization, TOA was ruled out in 11 patients. Forty-one patients were reviewed. Composition of total patient population was presented in figure1. Ten (24,3%) patients underwent surgical treatment because of failed antibiotic therapy. In 31 (75,7%) patients parenteral antibiotic treatment was successful. The mean age of medically treated patients was 37,4 ±7,9 years and the mean age of surgically treated patients was 43,5 ±9,3 years. The mean age of surgically treated patients was significantly higher than medically treated patients (p=0.048).

Body mass index, number of gestations, delivery, abortion, abscess volume, c-reactive protein level, white blood cell count, the sedimentation rate and body temperature at hospitalization were analyzed using the Mann Whitney U test. The results indicated that number of gestations and abortions were higher in patients needed surgery (p=0,032 and p=0,037). Some of the demographic characteristics of the patients were summarized in table 1. It was also seen that abscess volume was increased in surgically treated patients (p=0,004). C-reactive protein (CRP) levels and erythrocyte sedimentation rate (ESR) were also higher in surgically treated patients (p=0,010 and p=0,036, respectively). Clinical characteristics of the patients were summarized in table 2.

The Pearson Chi-square test was used to identify whether there was a relationship between surgical treatment and smoking, alcohol use, the choice of contraception, previous pelvic surgery and history of curettage. The results of the chi-squared showed no significant association between these factors and the need for surgery.

Most of the TOA that treated surgically were localized on the left side of the patient (n=7; 70%). But there was no significant association between localization of TOA and surgery (p=0,235)

In the patients treated surgically, meantime between hospitalization and surgery was 4,3 ±4,49 days (min:0-max: 15 days). Immediate surgery was performed in one patient (10%) due to suspicion of rupture of the abscess. The most commonly performed surgical procedure was total abdominal hysterectomy and bilateral salpingo-oophorectomy (n=5). Surgical interventions performed in patients who failed medical treatment were presented in figure 2.

Mean duration of hospitalization was significantly longer in patients treated with surgically (p=0,017). Hospital stay was 3,93 ±1,57 for medically and 8,1 (±5,53) days for surgically treated patients.The areas under the ROC curves (AUC) for age, CRP levels, ESR, WBC count, abscess volume and mean abscess size were 0.82, 0.74, 0.68, 0.81, and 0,81 respectively. According to the ROC analysis; CRP level, abscess volume and mean abscess size were useful to predict the outcome of TOA treatment with antibiotics. ROC curves of CRP levels, abscess volume and mean abscess size were presented in

figure 3. The sensitivity, specificity and AUC of CRP, abscess size and abscess volume were summarized in table 3.

Logistic regression analysis was conducted to predict medical treatment failure using CRP and abscess volume. A test of full model against a constant only model was statistically significant indicating that the predictors as a set reliably distinguished between successfully treated with antibiotics and failed patients (chi-square: 9,18, p<0.05, df: 2). Nagelkerke R^2 of 0,365 indicated a moderately strong relationship between prediction and grouping. Prediction success overall was 88,6 (96,4% for successful medical treatment and 57,1% for failure). The Wald criterion demonstrated that only CRP level made a significant contribution to prediction (p<0.05, Odds ratio: 9,9; 95% CI: 1,24-78,9).

DISCUSSION

Tubo-ovarian abscess is a serious complication of PID. It carries significantly higher morbidity and mortality than uncomplicated pelvic infections [9]. First line treatment of TOA is antibiotics. Center of Disease Control (CDC) recommends at least 24 hours of inpatient observation in these cases (CDC, 2010). However, in the case of TOA, both oral and parenteral medical treatment may not ensure expected progress. Even with modern antibiotic therapy, 25-50% of women with pelvic abscesses require surgery [10-12]. If the failure of antibiotic therapy can be predicted based on clinical findings, early surgical intervention can be expected and the duration of hospitalization can be shortened.

There is not a consensus on the major risk factors causing medical treatment failure in TOA. In the current literature, there are studies reporting that older age, menopausal state, high gravidity and parity, diseases such as diabetes mellitus, low socio-economic status are the main epidemiologic risk factors for medical treatment failure [5, 6]. Halperin *et al*. reported that the mean age of the patients who were successfully treated with parenteral antibiotics was significantly lower than the patients who did not respond to medical treatment (45, 3 vs 39,6) [13]. Greenstein *et al*. reported that older age and higher parity were associated with significantly higher risk of surgery [6]. A retrospective study from Taiwan showed that patients with TOA who underwent surgical intervention were more likely in multiparous women [5]. However, there is not an exact cut off point for age for medical treatment failure. Although there were significant differences in age, still mean ages of the patients who were treated medically or surgically were close to each other. In this study, similarly we also found that the mean ages of the patients in two groups were significantly different from each other and patients who failed to respond medical treatment were older (37,4 years for medical treatment vs and 43,5 years for surgically treated patients). The cut point for age was 40 years for medical treatment failure with a sensitivity of 60% and a specificity of 65% (AUC: 70,8; p=0.05; 95% CI: 0,52-0,89). Increased number of gestations and abortions were also associated with medical failure in this report but there are controversies in the literature. There are studies supporting this finding and some do not.

Our results showed that there was no relationship between medical treatment failure and BMI, smoking, alcohol use, and choice of contraception, previous pelvic surgery, and history of curettage. Like our study, Gungorduk *et al.* and Kuo *et al*. reported that previous pelvic surgery and use of IUD were not different in surgically treated patients. However, Halperin *et al*. found that there was a significantly lower incidence of previous pelvic surgery in surgically treated patients [14]. On the other hand, Terao *et al*. reported that open gynecological surgery was associated with poor clinical course.

Table 1. Socio-demographic characteristics of patients

	Medical (n=31) Mean±SD	Surgical (n=10) Mean±SD	P value
Age (years)	37,4 ±7,9	43,5 ±9,3	**0,048**
BMI (kg/m2)	25,9 ±3,54	24,4 ±3,13	0,395
Gravidity	3,1 ±2,02	4,4 ±1,71	**0,032**
Parity	2,5 ±1,63	2,6 ±0,69	0,514
Abortion	0,25 ±0,57	1,1 ±1,45	**0,037**
Smoking			
No	22 (71,0%)	7 (70%)	0,953
Yes	9 (29,0%)	3 (30%)	
Alcohol use			
No	30 (96,8%)	10 (100%)	0,565
Yes	1 (3,2%)	0 (0%)	
Contraception			
None	18(58,1%)	9 (90%)	
IUD	7 (22,6%)	1 (10%)	0,293
OCS	5 (16,1%)	0 (0%)	

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Condom	1 (3,2%)	0 (0%)	
Previous pelvic surgery **None** **Cesarean** **Appendectomy** **Hysteroscopy** **Laparoscopy**	 18 (58,1%) 6 (19,4%) 3 (9,7%) 1 (3,2%) 3 (9,7%)	 8 (80%) 0 (0%) 2 (20%) 0 (0%) 0 (0%)	0,347
History of curettage **No** **Yes**	 22 (71%) 9 (29%)	 6 (60%) 4 (40%)	0,517

BMI: body mass index; IUD: intrauterine device; OCS: Oral contraceptive.

Table 2. Clinical characteristics of the patients

	Medical (n=31)	**Surgical (n=10)**	**P value**
Abscess volume (cm^3)(±SD)	48,65 ±35,8	120,27 ±88,21	**0,004**
Abscess size (mm)(±SD)	43,6 ±10,9	59,1 ±14,8	**0,003**
CRP level, mg/L (±SD)	4,3 ±5,93	13,9 ±9,75	**0,010**
ESR (mm/hr) (±SD)	29,5 ±23,01	51,6 ±25,76	**0,036**
WBC count (mcL) (±SD)	12370 ±4379,27	15100 ±5530	0,102
Body temperature (℃) (±SD)	37,2 ±0,76	37,4 ±0,79	0,447
TOA location **Left** **Right** **Bilateral** **Douglas**	 15 (50%) 13 (43,3%) 1 (3,3%) 1 (3,3%)	 7 (70%) 1 (10%) 1 (10%) 1 (10%)	0,235

CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; WBC: White blood cell

Table 3. The sensitivity, specificity and AUC of CRP, Abscess Volume and Abscess Size

Parameter	**Cut-off**	**Sensitivity %**	**Specificity %**	**AUC**	**p value**
CRP	6,67 mg/L	71,4	72,4	81,5	0,011
Abscess Volume	59,51 cm^3	70	70	80,7	0,004
Abscess Size	5 cm	70	73,3	81,2	0,003

AUC: Area under the curve; CRP: C-reactive protein; TOA: Tubo-ovarian abscess.

Fig 1. Composition of total patient population

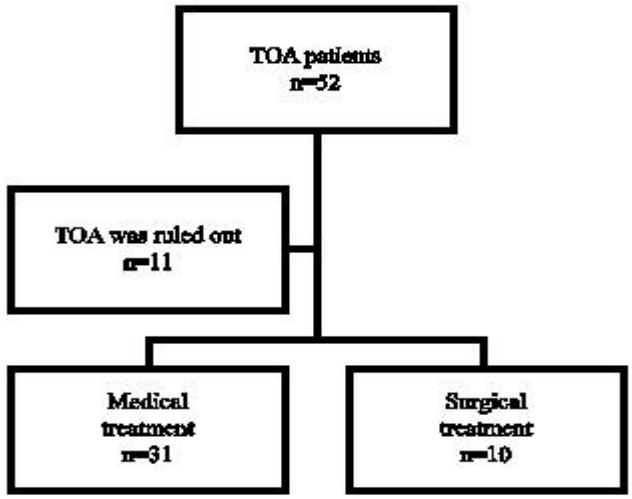

Fig 2. Surgical interventions performed in patients who failed medical treatment

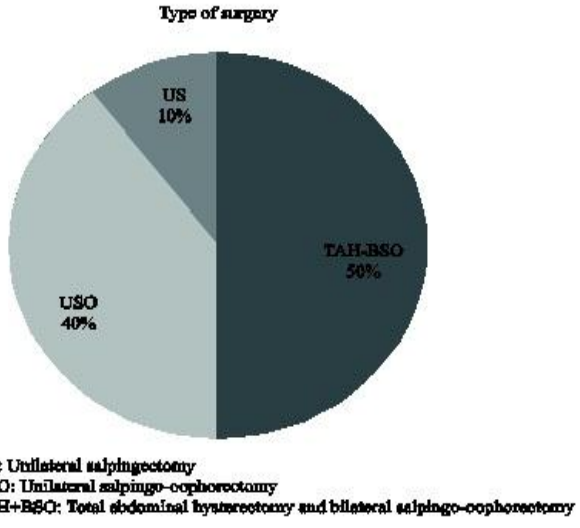

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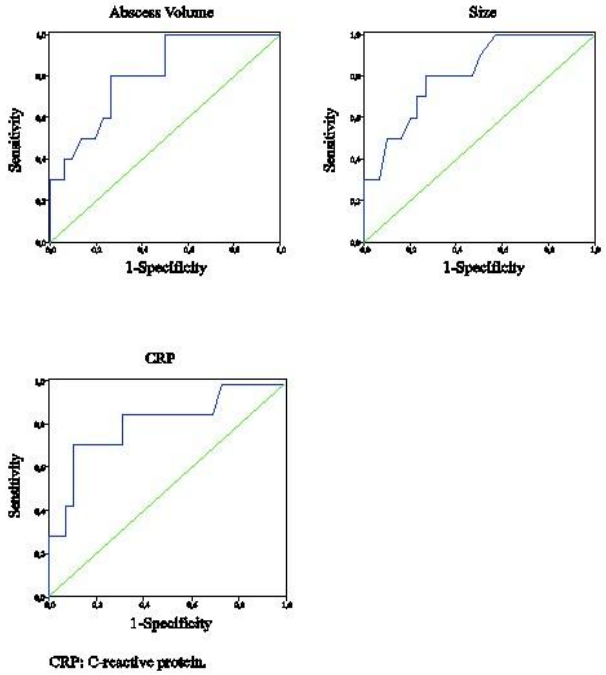
Fig 3. Receiver operating characteristic (ROC) curves of CRP levels, abscess volume and mean abscess size



CRP: C-reactive protein.

The relationship between abscess size and medical treatment failure is the most commonly emphasized and concurred topic in the literature. There are many studies reporting that increased abscess size is correlated with increased need for surgery [4-7]. However, cut off points in these studies are diverse. Reed et al. showed if the size of TOA is larger than 10 cm, surgery will be necessary about in % 60 of patients [15]. Doganay et al. reported that patients with TOA diameter of more than 10 cm, laparotomy was necessary 72 % of patients. Dewitt et al. reported abscess more than 8 cm required drainage or surgery more often than abscess of smaller size [16]. Almost in all studies, successfully treated cases with antibiotics have an abscess smaller than 5 cm. In this report, we also found that both mean abscess volume (48,65 cm^3 ±35,8 vs. 120,27 cm^3 ±88,21) and abscess size (43,6 mm ±10,9 vs. 59,1 mm ±14,8) were increased in surgically treated patients. ROC analysis revealed that cut points for abscess volume and abscess size were 60 cm^3 and 5 cm reciprocally. In our knowledge, there is only one study comparing the abscess volume and the need for imaging guided drainage. In this report they also found that larger TOA volume is a risk factor to failure to antibiotic therapy.

Laboratory evaluation of these patients mostly reveals leukocytosis, elevated CRP level and increased ESR. We also found that increase in WBC, CRP level and ESR was present almost in all patients. However, the counts of WBC were similar in two groups. Several authors have investigated the relationship between laboratory findings and the need for surgery. Gungorduk et al. showed that CRP level and ESR were higher in surgically treated patients. This study reported that an ESR of 63.0 mm/hour or more had a diagnostic value of 83.6%, the specificity and sensitivity values for predicting the need for surgical intervention following failure of antibiotic therapy were 82.7% and 73.7%, respectively. In the same study, CRP more than 21.0 mg/L had a diagnostic value of 80.4%; the respective specificity and sensitivity values were 82.3% and 65. In our study, ROC analysis revealed that CRP level had an AUC of 81, 5 (sensitivity 71, 4%, specificity 72, 4%) that was indicating a good predicting value for medical treatment failure. The cut off point for CRP level was 6, 7 mg/L. It seems that fever and WBC were not as reliable as CRP level and TOA size in the prediction of failure of medical treatment [11, 12]. We concluded that although both fever and WBC levels are important especially for monitoring response to the treatment there is not a relationship between these parameters and medical treatment failure.

In our study, most of the patients treated surgically had a mass on the left side (70%). There were one patient with bilateral involvement (10%). However, there was no significant association between lateralization and medical treatment success. We found two studies in the literature comparing unilateral and bilateral TOA and need for surgery. They also did not find any significant differences.

We found that, as it was expected, the mean duration of hospitalization was significantly longer in patients treated surgically. Hospital stay was 3, 93 days ±1, 57 for medically treated patients and 8, 1 ±5,53 days for surgically treated patients. There are similar results in the literature about the longer duration of hospitalization in surgically treated patient.

In conclusion, medical treatment failure and need of surgery are more common in patients who have larger abscess (volume> 60 cm^3 or size > 5cm), elevated CRP levels (>6, 7 mg/L) and increased ESR (>50 mm/hr). However, it is still hard to claim definitive values for medical treatment failure since the results for all these parameters in the current literature are diverse.

REFERENCES

1. Khan ZE, Rizvi HJ. Pelvic inflammatory disease and pelvic abscesses. *Gynaecol and Perin Pract*, 6, 2006, 185-91.
2. 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. *The journal of obstetrics and gynaecology research*, 39(5), 2013, 1019-23.
3. Gungorduk K, Guzel E, Asicioglu O, Yildirim G, Ataser G, Ark C, et al. Experience of tubo-ovarian abscess in western Turkey. *International journal of gynaecology and obstetrics*, 124(1), 2014, 45-50.

4. Goharkhay N, Verma U, Maggiorotto F. Comparison of CT- or ultrasound-guided drainage with concomitant intravenous antibiotics vs. intravenous antibiotics alone in the management of tubo-ovarian abscesses. *Journal of the International Society of Ultrasound in Obstetrics and Gynecology*, 29(1), 2007, 65-69.
5. Granberg S, Gjelland K, Ekerhovd E. The management of pelvic abscess. *Best practice & research Clinical obstetrics & gynaecology*, 23(5), 2009, 667-78.
6. Dewitt J, Reining A, Allsworth JE, Peipert JF. Tuboovarian abscesses: is size associated with duration of hospitalization & complications. *Obstetrics and gynecology international*, 2010.
7. Kuo CF, Tsai SY, Liu TC, Lin CC, Liu CP, Lee CM. Clinical characteristics and treatment outcomes of patients with tubo-ovarian abscess at a tertiary care hospital in Northern Taiwan. *Journal of microbiology*, 45(1), 2012, 58-64.
8. Greenstein Y, Shah AJ, Vragovic O, Cabral H, Soto-Wright V, Borgatta L, et al. Tuboovarian abscess. Factors associated with operative intervention after failed antibiotic therapy. *The Journal of reproductive medicine*, 58(3-4), 2013, 101-6.
9. Chan Y, Parchment W, Skurnick JH, Goldsmith L, Apuzzio JJ. Epidemiology and clinical outcome of patients hospitalized with pelvic inflammatory disease complicated by tubo-ovarian abscess. *Infectious diseases in obstetrics and gynecology*, 3(4), 1995, 135-139.
10. Demirtas O, Akman L, Demirtas GS, Hursitoglu BS, Yilmaz H. The role of the serum inflammatory markers for predicting the tubo-ovarian abscess in acute pelvic inflammatory disease: a single-center 5-year experience. *Archives of gynecology and obstetrics*, 287(3), 2013, 519-523.
11. Wiesenfeld HC, Sweet RL. Progress in the management of tuboovarian abscesses. *Clinical obstetrics and gynecology*, 36(2), 1993, 433-44.
12. Nelson AL, Sinow RM, Renslo R, Renslo J, Atamdede F. Endovaginal ultrasonographically guided transvaginal drainage for treatment of pelvic abscesses. *American journal of obstetrics and gynecology*, 172(6), 1995, 1926-1932.
13. Halperin R, Levinson O, Yaron M, Bukovsky I, Schneider D. Tubo-ovarian abscess in older women: is the woman's age a risk factor for failed response to conservative treatment. *Gynecologic and obstetric investigation*, 55(4), 2003, 211-215.
14. Reed SD, Landers DV, Sweet RL. Antibiotic treatment of tuboovarian abscess: comparison of broad-spectrum beta-lactam agents versus clindamycin-containing regimens. *American journal of obstetrics and gynecology*, 164(1), 1991, 1556-1561.
15. Doganay M, Iskender C, Kilic S, Karayalcin R, Moralioglu O, Kaymak O, et al. Treatment approaches in tubo-ovarian abscesses according to scoring system. *Bratislavske lekarske listy*, 112(4), 2011, 200-3.
16. Terao M, Koga K, Fujimoto A, Wada-Hiraike O, Osuga Y, Yano T, et al. Factors that predict poor clinical course among patients hospitalized with pelvic inflammatory disease. *The journal of obstetrics and gynaecology research*, 40(2), 2014, 495-500.