An evaluation of factors that are predictive of the success of antibiotic treatment in tubo-ovarian abscess cases

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Original Article

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ABSTRACT

Objective: To assess which factors were predictive of the success of antibiotics in treating tubo-ovarian abscess (TOA) cases

Design: Retrospective clinical research

Setting: Tertiary university hospital in Istanbul, Turkey

Subjects: One hundred and eight patients aged between 27-70 diagnosed with TOA between January 2014 and August 2018.

Interventions: The first group comprised patients who had successfully been treated with antibiotics (Group A). The second group comprised patients who had received antibiotics but who underwent surgery for TOA due to antibiotic treatment failure (Group B).

Main outcome measures: A comparison was conducted of the pre- and post-treatment patient parameters.

Results: The hemoglobin levels were higher in the group in whom antibiotic treatment was successful (Group A; 11.1±1.4 g/dL) compared to the group who had to undergo surgery due to unsuccessful antibiotic treatment (Group B; 10.5±1.7 g/dL). The median TOA size was 5.5 cm in Group A (successful antibiotic treatment) and 6.4 cm in Group B (surgery in response to unsuccessful antibiotic treatment) when assessed using ultrasound . The median TOA size was 5.0 cm for Group A and 6.2 cm for Group B using computed tomography (CT). The median duration of hospitalization was 8 and 10 days for groups A and B, respectively. The cut-off levels that were predictive of the successful antibiotic treatment of TOAs were 6.7 cm using ultrasound and 6.6 cm using CT.

Conclusion: TOA size was a good indicator of the likelihood of successful antibiotic treatment.

KEY WORDS: Adnexitis, Antibiotics, treatment failure.

INTRODUCTION

Pelvic inflammatory disease (PID) is a genital infection that covers a large spectrum of conditions, ranging from endometritis to tubo-ovarian abscess (TOA) formation [1].

PID is seen in 10% of reproductive women [2]. Although *Neisseria gonorrhoeae* and *Chlamydia trachomatis* are usually implicated in PID, bacterial vaginosis-associated pathogens, including anaerobes, *Gardnerella vaginalis, Haemophilus influenzae,* enteric Gram-negative rods, and *Streptococcus agalactiae* are also associated with it [3]. Younger age of coitarche, multiple sexual partners, nonuse of barrier contraception, and infection with chlamydia or gonorrhea are the risk factors that have been identified for development of PID[4]. Although there is a concern about whether intrauterine device (IUD) insertion or use increases the risk of PID, evidence shows that the risk of PID is low among IUD users[5,6].

Infertility, ectopic pregnancy, chronic pelvic pain and recurrent PID are long term complications of PID which can be decreased with prompt diagnosis and treatment. Delay in diagnosis and treatment of PID can lead to the postinflammatory sequelae of the upper genital tract.Therefore, women at risk for sexually transmitted diseases who are experiencing pelvic or lower abdominal pain with cervical motion tenderness, uterine tenderness, or adnexal tenderness should be empirically treated for PID after exclusion of other illnesses[7].

TOA formation is a complication of PID and is seen in 10–15% of cases [8]. TOAs are generally managed using antibiotics and drainage. Successful treatment with antibiotics, without the need for drainage, is achieved in 70% of cases [9-12]. The current study objective was to assess which factors were predictive of the success of antibiotics in treating TOAs.

SUBJECTS AND METHODS

A retrospective study was performed to determine the risk factors for TOA and identify which were predictive of antibiotic efficacy in treating patients with TOA who presented at a single tertiary university hospital in Istanbul, Turkey. Approval to conduct the study was granted by the local ethics committee of the hospital. The medical records of 108 patients (aged 27-70 years) diagnosed with TOA between January 2014 and August 2018 were reviewed. TOA diagnosis was made according to the classic PID findings of abdominopelvic pain, cervical and adnexal sensitivity to a bimanual examination, along with one or more minor criteria, such as fever, leukocytosis, a high erythrocyte sedimentation rate and the presence of an adnexal lesion (*i.e.*, a complex adnexal mass without peristalsis and with thick, well-formed walls) using ultrasound. Routine CT imaging was performed to exclude other adnexal mass etiologies. Patients who underwent both the initial ultrasonography and computed tomography (CT) were included in the study.

Exclusion criteria were uncertainty of diagnosis, the absence of CT, a co-existing malignancy or pregnancy, patients who underwent surgery on admission, and those who refused antibiotic treatment. Data of interest obtained from the records included the patient demographics (age, gravidity, and parity), medical history (*e.g.*, hypertension, diabetes mellitus, and surgery), current symptoms (vaginal discharge, abdominal pain, and fever), site of the abscess (left, right, or bilateral), and maximum abscess diameter using ultrasound and CT.

White blood cell (WBC) count, platelet count, hemoglobin levels, neutrophil to lymphocyte ratio (NLR), red blood cell distribution (RDW), serum C-reactive protein (CRP), and the procalcitonin levels of patients were recorded on admission to hospital and at discharge. Duration of hospital stay, change in the size of abscess after antibiotic use, urine test results, blood tests results, and the results of the cervicovaginal and abscess cultures (only for the surgically treated patients) were also obtained.

All of the patients received 900 mg of intravenous (IV) clindamycin every eight hours with an IV loading dose (2 mg/kg) of gentamicin, followed by a maintenance dose (1.5 mg/kg) of gentamicin every eight hours as the antibiotic treatment, according to the Centers for Disease Control and Prevention guidelines [1].

One hundred and eight patient records were reviewed. Twelve, two and four patients were excluded because they had not undergone CT, had a co-existing malignancy, and because of uncertainty of diagnosis, respectively. One patient refused surgical treatment and was also excluded from the study. The patients were grouped according to treatment modality. The first group comprised patients who had successfully been treated with antibiotics (Group A). The second group comprised patients who had received antibiotics but who underwent surgery for TOA due to antibiotic treatment failure (Group B).

Antibiotic failure was defined as the lack of a decrease in abscess size within 48–72 hours of the treatment. The surgery was performed using laparoscopy or laparotomy. Hysterectomy and bilateral salpingo-oophorectomy were carried out in postmenopausal patients. The type of surgery was adjusted from abscess drainage to bilateral salpingectomy depending on whether or not patients of reproductive age wished to bear children.

Statistical Analysis

The descriptive statistics were expressed as the mean ± standard deviation or median and interquartile range. The distribution of the variables was analyzed using histogram graphics and the Kolmogorov-Smirnov test. The comparisons of the quantitative values were carried out using the Independent samples T test for normally distributed data and Mann-Whitney U test for non-normally distributed data. Receiver operating characteristic (ROC) curve analysis was used to determine the cut-off levels for successful antibiotic treatment. A *P*-value of <.050 was considered to be statistically significant. All the statistical analyses were carried out on a personal computer with SPSS, version 15.0 analysis software (IBM Corporation, New York, USA).

RESULTS

Eighty-nine patients were diagnosed with TOA during the study period. Of these, 37 (42%) were successfully treated with antibiotics, while the remainder (n = 52, 58%) required surgery after the failure of antibiotic treatment. The difference in median age, gravidity status, and parity status of the patients was similar between the two groups (Table 1). Twenty-nine patients in Group A and 39 patients in Group B were premenopausal. Pelvic pain was the most common symptom in both groups (Group A: 87% vs. Group B: 81%). Only 5% of the patients in Group A and 12% of the patients in Group B were febrile. The differences in symptoms, menopausal state, and the medical history of the patients (data not shown) were without statistical significance.

The difference in the localization of abscess formation and bilateral involvement between the treatment groups was not statistically significant. Blood culture positivity was not detected in either group following analysis. Genital cultures were obtained (Group A: n=21, 57%; Group B: n=27, 52%; *P*=>.050). Two of the cultures were positive (*G. vaginalis* [n=1], *Staphylococcus aureus* [n=1]) in Group A, and five of them were positive in Group B (*S. agalactiae* [n=2], *Enterococcus* spp. [n=2], *G. vaginalis* [n=1]). The difference in the positive genital cultures was not significant between the two groups. Abscess aspiration cultures were obtained from 25 patients (48%) in Group B. *Bacteroides fragilis* (32%) was the most isolated microorganism.

The blood test results of the patients were evaluated in the first day of hospitalization. Hemoglobin levels were higher in the group in whom antibiotic treatment was successful (Group A; 11.1±1.4 g/dL) compared to the group who had to undergo surgery due to unsuccessful antibiotic treatment (Group B; 10.5±1.7 g/dL) (*P*=<.050). The differences in WBC, platelet count, CRP and procalcitonin levels, RDW, and NLR between the groups were without statistical significance (Table 2). The blood test results prior to discharge from the hospital were also evaluated. There was no significant difference in CRP, procalcitonin levels, RDW, and WBC count between the groups. The hemoglobin levels were lower at discharge from hospital in the Group B subjects (10.6±1.1 vs. 10.0±1.2 g/dL) compared to the Group A subjects (P=<.050). This finding is consistent with blood loss during surgery. Similarly, the NLR (2.0) and platelet count (3717.6±1048.8) was higher in Group B compared to Group A (respective figures of 3.2 and 4285.8±1275.0), which can be attributed to inflammatory changes due to surgical stress (P=<.050).

The groups were evaluated with respect to lesion size and duration of hospitalization. The median TOA size in the first day of hospitalization was 5.5 cm and 6.4 cm using ultrasound (P=.003), and 5.0 cm and 6.2 cm using CT for Groups A and B, respectively (P=.002). A more substantial decrease in the size of the lesion was observed within 48–72 hours of treatment in Group A compared to Group B (P=<.001). The median length of stay in hospital was 8 and 10 days for Groups A and B, respectively (P=<.001) (Table 3).

ROC curve analysis was used to define the size of the lesions in relation to their ability to predict antibiotic failure based on the ultrasound and CT findings (Figure 1). The ROC curve indicated cut-off points of 6.7 cm (ultrasound) and 6.6 cm (CT) in predicting the successful antibiotic treatment of cases of TOA (Table 4).

DISCUSSION

TOA is a late complication of PID and contributes significantly to the admission to hospital of patients with genital infections [7]. TOA treatment usually comprises the administration of antibiotics and surgery. The current study aim was to define factors that were predictive of the success of antibiotic treatment (i.e., without the need for surgery).

The treatment modalities for TOA differ. Twenty-nine (25%) of the 119 patients evaluated in the study by Reed et al. underwent surgery after antibiotic treatment [13]. A poor prognosis was attributed to 87 (80%) of the patients (who were managed surgically or discharged after 7 days of antibiotic therapy) in the study by Topçu *et al*, and 85 of them were treated with surgery [14]. Twenty-five percent of antibiotic-treated patients (n=61) required an additional intervention in the study by Farid *et al*[15]. The current study finding in this regard was that 59% of the TOA cases required surgical treatment.

TOA cases are usually associated with polymicrobial infection by anaerobic, aerobic, and facultative organisms. *Escherichia coli, B. fragilis, Peptostreptococcus* spp., *Peptococcus* spp.,and anaerobic *Streptococcus* are the most commonly isolated organisms in TOA patients [9,10]. In another Turkish study, the most commonly isolated microorganism was *E. coli* [14]. In our study, *B. fragilis* was the most frequently identified microorganism in the abscess cultures.

There are conflicting results about the effect of age on the success of antibiotic treatment. It has been reported that older age is poorly prognostic of successful antibiotic treatment in TOA cases [16-18]. Elsewhere, an age-related difference was not found in relation to TOA prognosis [14,15,19]. In the current study, age was not predictive of antibiotic success.

Bilateral TOA lesions were found to be a predictor of antibiotic failure in TOA in previous studies [14,16,20]. In contrast, unilaterality of TOA was not shown to be a predictor of antibiotic success by Farid *et al* [15]. The location site and bilateral TOA involvement were not predictive of the success of antibiotic treatment in TOA in our study.

There are conflicting results on the use of inflammatory markers in TOA to predict antibiotic success. Increased WBC count has been demonstrated in patients who underwent surgery compared to those in whom antibiotic treatment was successful [14-16,20]. Conversely, a difference in WBC count was not observed between the groups treated with antibiotics and those treated with surgery in other studies [17,19]; supported by the current study finding.

CRP levels have also been evaluated in TOA. Although elevated CRP levels have been shown to be a poor prognostic factor for antibiotic treatment success elsewhere [14,16,19,20], a significant difference in CRP levels between Groups A and B was not seen in the present research.

TOA diameter has been demonstrated to be an important predictor of antibiotic treatment failure; specifically, a large TOA diameter was associated with the need for a surgical intervention [7,14,15,17,19,21]. A similar finding was observed in the current study.

Different cut-off levels have been proposed in various studies to predict antibiotic success. A diameter of 5.2 cm was identified as the cut-off point for antibiotic treatment success in a study that used multiple imaging (ultrasound, CT, and magnetic resonance imaging) [15]. Elsewhere, this value was reported to be 6.5 cm [16,19]. In a different study, a diameter of 4.8 cm was shown to be a poor prognostic factor for TOA [14]. Cut-off values of 6.6 cm and 6.7 cm were ascertained in the current study using CT and ultrasound, respectively, to predict antibiotic success in TOA.

Other parameters, such as serum procalcitonin levels, NLR, RDW, and platelet count were not predictive of the successful antibiotic treatment of TOA in the present research, a finding that is in conflict with that of a previous study [16].

The retrospective study design and absence of data related with the long term complications, like recurrence of the disease, tubal infertility and chronic pelvic pain were the major limitations in this study. Study strengths included the large sample size and the use of two imaging modalities to diagnose TOA.

CONCLUSION

A TOA diameter of ≤6.6 cm (using CT) and 6.7 cm (using ultrasound) were predictive of the successful use of antibiotic treatment in the current study. Other parameters, such as age, CRP, WBC, procalcitonin levels, platelet count, RDW, and NLR did not effectively predict the successful treatment of TOA with antibiotics.

ACKNOWLEDGMENT

We thank Abdullah Sarioz for his support in performing data and statistical analysis of the patients.

Author contributions: All authors contributed to the design of the study, data collection, statistical analysis and final version of the paper submitted.

Disclosure Statement: The authors declare no conflicts of interest.

Funding Sources: The authors have no funding to declare.

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Table 1: Age, gravidity, parity status of the groups

Age and Parity	**Group A Median (IQR)**	**Group B Median (IQR)**	**p value**
Age	38.4±9.5	40.6±8.8	0.265[a]
Gravida	2.0 (1.0-3.0)	3.0 (1.0-4.0)	0.369[b]
Parity	2,0 (1.0-3.0)	2.0 (1.0-3.0)	0.676 [b]
Abortion	0.0 (0.0-0.0)	0.0 (0.0-0.5)	0.333 [b]
Cesarean Section	0.0 (0.0-1.0)	0.0 (0.0-0.0)	0.586 [b]

[a] t test in independent groups, [b] Mann whitney u test

Table 2: Blood test results of two groups in the first day of hospitalization

Blood Markers	**Group A Median (IQR)**	**Group B Median (IQR)**	**p value**
CRP (mg/dL)	139.0 (101.0-179.0)	172.0 (96.0-257.0)	0.143 [a]
N/L ratıo	6.9 (4.6-10.4)	8.0 (5.0-14.6)	0.287 [a]
Procalcitonin (ng/mL)	0.0 (0.0-0.0)	0.0 (0.0-0.3)	0.090 [a]
RDW (g/dL)	14.6 (13.5-16.0)	14.8 (13,4-16.1)	0.977 [a]
WBCx100 (µl/ml)	138.1±55.8	154.1±55.3	0.185 [b]
HB (g/dL)	11.1±1.4	10.5±1.7	**0.047 [b]**
Platelet $x10^2$	3322.4±995.8	3624.0±1314.2	0.243 [b]

[a] Mann whitney u test, [b] t test in independent groups

Table 3: Lesion size in ultrasound and CT and hospitalization periods

Lesion Size and Hospitalization Period	Group A Median (IQR)	Group B Median (IQR)	p value*
Size in ultrasound (cm)	5.5 (4.3-6.4)	6.4 (5.5-8.1)	**0.003**
Size in CT	5.0 (4.0-6.0)	6.2 (5.0-9.0)	**0.002**
Decrease in size (cm)	2.0 (2.0-3.0)	0.0 (0.0-0.0)	**<0.001**
Hospitalization time (day)	8.0 (6.0-9.0)	10.0 (8.0-15.0)	**<0.001**

*Mann whitney u test

Table 4: ROC curve analysis results for cut off levels for prediction of success in treating tubo-ovarian abscess with antibiotics

Imaging modality	Cut Off (cm)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC	%95 CI	
							Lower limit	Upper limit
Ultrasound	6.7	86.5	46.2	53.3	82.8	0.682	0.571	0.794
CT	6.6	81.1	46.2	51.7	77.4	0.695	0.586	0.803

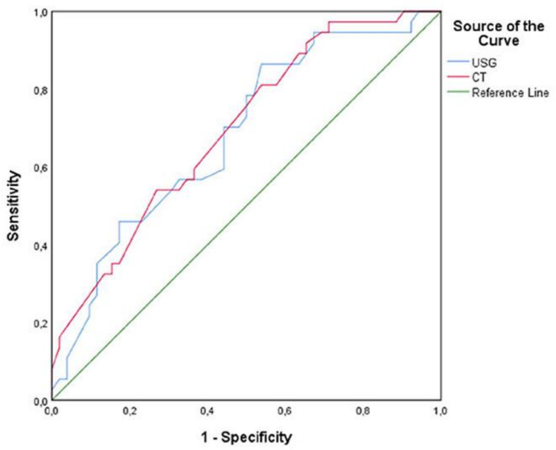

Fig. 1: ROC curve for cut off levels of the lesion in ultrasound and CT for prediction of treatment of tubaovarian abscess without surgery