Hong Kong J Gynaecol Obstet Midwifery 2019;19(1):38-43 | https://doi.org/10.12809/hkjgom.19.1.01

Risk factors for failure of antibiotic therapy for tubo-ovarian abscess

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Objective: To assess the risk factors for antibiotic therapy failure and to predict which patients will require surgical drainage for tubo-ovarian abscess.
Methods: We collected data from patients by ICD-9 codes starting with 614.2. We extracted data regarding background information, clinical presentation, laboratory parameters, and ultrasonographic findings. Patients responded to antibiotics alone were compared with patients required surgical drainage. Relative risk of surgical drainage was estimated with logistic regression model.
Result: A total of 126 cases of tubo-ovarian abscess were evaluated, of which 92 were successfully managed with antibiotic therapy alone and 34 required surgical drainage. Age, multiparity, intrauterine device use, fever, maximal white cell count and abscess size were identified to be significant risk factors associated with the need for surgical drainage. The adjusted relative risks of surgical drainage were 2.250 for abscess size ≥8 cm, and 3.162 for fever on admission. The duration of hospitalisation was increased by 23.8% for abscess size ≥8 cm and by 23.7% for fever on admission.
Conclusion: Larger abscesses are associated with increased risk of surgical drainage. However, additional research is required to determine the optimal treatment for large abscesses. It is reasonable to try antibiotic therapy in clinically stable patients irrespective of abscess size.

Keywords: Abscess; Anti-bacterial agents; Drainage; Fallopian tube diseases; Ovarian diseases

Introduction

Tubo-ovarian abscess (TOA) is a severe form of pelvic inflammatory disease and can involve the fallopian tubes, ovaries, and occasionally adjacent pelvic organs (eg, the bowel, bladder, and omentum). The mortality rate of TOA could approach 50% before the era of broad-spectrum antibiotics and modern surgical drainage[1]. Mortality is rare for uncomplicated TOA, but if TOA is complicated with systemic sepsis or rupture of abscess, the mortality rate can be as high as 5% to 10%[2]. Management options for TOA include antibiotics with or without surgical drainage that is performed immediately or subsequently after suboptimal response to antibiotics. Antibiotic therapy is commonly used; the rate of surgical drainage is 25%. Abscess size, white cell count (WCC), fever, and age are common predictors of surgical drainage[3,4]. In critically ill patients (with signs of sepsis and peritonitis), prompt surgical drainage and antibiotics and appropriate resuscitation are preferable. In clinically stable patients, a combined regimen of broad-spectrum antibiotics is the primary treatment option and is effective in up to 70% of cases[3]. The chosen antibiotics should cover the commonest causative pathogens, have high abscess cavity penetration power, and have a low local resistance rate. The British Association for Sexual Health and HIV provides guidance on possible antibiotic choices, but the local units should develop their own protocols with input from microbiologists.

In the gynaecology unit of Tuen Mun Hospital, patients with suspected TOA are examined by ultrasonography of the pelvis, and diagnosis is made when an infected complex adnexal mass is observed. All such patients are treated as inpatients initially: unstable patients undergo surgical drainage immediately, whereas stable patients are treated with intravenous antibiotics, most commonly (80%) with intravenous levofloxacin and metronidazole, which is recommended by gynaecology

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consultants and local microbiologists in Tuen Mun Hospital, based on previous treatment performance and the bacterial resistance profile. Additional antibiotics or alteration to the regimen is based on clinical response and sensitivity results. Patients are closely monitored for vital signs and laboratory parameters (especially WCC) for 48 hours after treatment. Surgical drainage by laparoscopy or laparotomy is considered if no significant clinical improvement. Image-guided drainage is seldom performed in our unit, owing to limited support from interventional radiology services. For patients with significant clinical improvement after 48 hours, antibiotics are switched to oral route and patients can be discharged from the hospital according to their progress. A ward follow-up session is arranged within 4 to 6 weeks to confirm resolution of the TOA with ultrasonography.

Local data in TOA treatment outcomes are lacking. This retrospective study aimed to identify the risk factors of failed antibiotic therapy in a local population so as to predict which patients require surgical drainage and which factors affect treatment success.

Methods

Case notes of women diagnosed with TOA admitted to Tuen Mun Hospital from 1 January 2012 to 31 December 2016 were retrospectively reviewed. Potential subjects were selected based on ICD-9 codes starting from 614.2 (ie, salpingitis and oophoritis not specified as acute, subacute, or chronic). Only clinically stable patients treated initially with antibiotics were included. Critically ill patients who underwent immediate surgical drainage were excluded, as were those who were initially misdiagnosed as having other diseases and later correctly diagnosed as having TOA during operation. A total of 126 patients with TOA were included in the final analysis.

Clinical characteristics were extracted and categorised into background information, clinical presentation, laboratory parameters, and ultrasonographic findings. Background information included age, parity, presence of immunocompromised condition (eg, diabetes mellitus, autoimmune disease, or long-term steroid use), history of pelvic inflammatory disease, history of hydrosalpinx or ovarian cyst, history of major abdominal surgery, presence of intrauterine device, condom usage, and history of invasive gynaecological procedure within 6 weeks (eg, hysteroscopy or endometrial aspiration). Clinical presentation included presenting symptoms (ie, fever, vomiting or nausea, pain, or vaginal discharge) and duration of symptoms. Laboratory parameters included WCC on admission, maximal WCC during hospitalisation, and presence of positive culture. Pelvic ultrasonography by transvaginal and transabdominal route was the major imaging modality used in our unit. Ultrasonography was performed to quantify abscess size and any bilateral lesions. Abscess size was defined as the maximal dimension of the mass on ultrasonography. If bilateral abscesses were present, the larger of the two was used to quantify abscess size.

Outcome measures included the success rate with antibiotics alone and the duration of hospitalisation. Successful antibiotic treatment was defined as no emergency surgical procedures for TOA were needed within 12 weeks of presentation.

Non-parametric methods were used owing to the non-normal nature of the data and small sample size. Fisher's exact test was used for categorical variables for comparing the distribution of surgical drainage and antibiotics alone group. Wilcoxon rank-sum test was used for continuous variables for comparing the two groups. Relative risks (RRs) and 95% confidence intervals (CIs) of variables were estimated from the logistic regression of surgical drainage with robust error variance[5]. Poisson regression with robust error variance was used to estimate the regression coefficients for length of hospitalisation.

Results

Of 126 patients, 92 (73.0%) responded to antibiotics alone and 34 (27.0%) required surgical drainage. Of 126 patients, 104 (82.5%) were initially treated with intravenous levofloxacin and metronidazole: 31 of 34 patients in the surgical drainage group and 73 of 92 patients in the antibiotics group (91% vs 79.3%, p=0.1851, Table 1). 22 patients were treated with other antibiotic regimens, including intravenous cefuroxime, metronidazole, and doxycycline (n=12), intravenous Augmentin and metronidazole (n=5), and intravenous cefuroxime and metronidazole (n=2).

In total, 34 patients had suboptimal response to initial antibiotics treatment, necessitating surgical drainage through laparotomy (n=16) or laparoscopy (n=17). Only one patient underwent computed tomography–guided drainage performed by an interventional radiologist.

Table 1. Antibiotic regimen*

	All patients (n=126)	Patient responded to antibiotics alone (n=92)	Patient required surgical drainage (n=34)
Levofloxacin + metronidazole	104 (82.5)	73 (79.3)	31 (91)
Other regimens	22 (17.5)	19 (20.7)	3 (9)
Cefuroxime + metronidazole + doxycycline	12	12	0
Augmentin + metronidazole	5	5	0
Cefuroxime + metronidazole	2	2	0
Taxobactam + piperacillin	1	0	1
Ceftriaxone + doxycycline	1	0	1
Clindamycin + metronidazole	1	0	1

* Data are presented as No. (%) of patients

The mean time interval between diagnosis and drainage was 4.3 days (median, 3 days); 33 patients underwent drainage during the same admission. The remaining one patient was discharged from the hospital after a 14-day course of antibiotics with good response, but she later complained of persistent pelvic pain. Ultrasonography during the ward follow-up session showed persistent TOA. Laparoscopic drainage was performed 26 days after the initial presentation.

The mean age of patients was 40.8±10.7 years; 42 (33%) patients were nulliparous; 9 (7%) patients were considered to have an immunocompromised condition; 26 (20.6%) patients had a history of pelvic inflammatory disease; 50 (39.7%) patients had major abdominal operations before; 17 (13.5%) patients were using intrauterine device for contraception; and 10 (7.9%) patients had invasive gynaecological procedures within 6 weeks prior to presentation. The most common symptom on presentation was abdominal pain (100%), followed by fever (50.8%). The mean maximal WCC was 14.7±6.2 per mm^3. The mean abscess size was 6.2±1.9 cm; 48 (35.7%) patients had bilateral abscesses. The mean duration of hospitalisation was 6.5±3.4 days.

Of 36 (28%) patients with positive culture results, the most common pathogen yielded was *Escherichia coli* (n=14), followed by *Staphylococcus aureus* (n=6), chlamydia (n=5), *Streptococcus milleri* (n=4), and *Streptococcus agalactiae* (n=4). Four (11.1%) cultures showed resistance to antibiotics (three in the surgical drainage group from peritoneal swabs and one in the antibiotics group, in which the regimen was changed to Augmentin and metronidazole.

Compared with the surgical drainage group, the antibiotic group were younger (39.4±11.0 years vs 44.3±9.5 years, p=0.0156) and had a higher prevalence of nulliparity (39% vs 17.6%, p=0.0323), a lower (not significantly) prevalence of intrauterine device use (9.8% vs 23.5%, p=0.074), a lower prevalence of fever on admission (35.9% vs 91.2%, p<0.0001), a lower maximal WCC during hospitalisation (13.9±5.7 vs 17.0±7.0, p=0.0108) but similar WCC on admission (13.6±5.7 vs 14.3±6.5, p=0.7312), smaller abscesses (5.7±1.8 cm vs 7.5±1.8 cm, p<0.0001) but similar in the prevalence of bilateral abscesses (32.6% vs 44.1%, p=0.2953), and a shorter duration of hospitalisation (5.2±2.5 days vs 9.9±3.2 days, p<0.0001) [Table 2].

The adjusted RR of surgical drainage of each clinical variable was estimated in a logistic regression model, with abscess size dichotomised to ≥8 cm and <8 cm. Surgical drainage was associated with abscess size ≥8 cm (adjusted RR=2.250, 95% CI=1.149-3.119) and fever on admission (adjusted RR=3.162, 95% CI=2.002-3.581).

Table 2. Patient characteristics, presenting symptoms, blood parameters, and ultrasonographic features*

	All patients (n=126)	Patient responded to antibiotics alone (n=92)	Patient required surgical drainage (n=34)	P value
Mean age, years	40.8±10.7	39.4±11.0	44.3±9.5	0.0156
Nulliparous	42 (33.3)	36 (39)	6 (17.6)	0.0323
With immunocompromised condition	9 (7.1)	6 (6.5)	3 (8.8)	0.7015
History of pelvic inflammatory disease	26 (20.6)	22 (23.9)	4 (11.8)	0.2137
History of hydrosalpinx	10 (7.9)	8 (8.7)	2 (5.9)	0.7279
History of ovarian cyst	12 (9.5)	6 (6.5)	6 (17.6)	0.0845
History of major abdominal surgery	50 (39.7)	34 (37.0)	16 (47.1)	0.3136
Presence of intrauterine device	17 (13.5)	9 (9.8)	8 (23.5)	0.074
Not using condom	109 (86.5)	77 (83.7)	32 (94.1)	0.1535
Having invasive gynaecological procedure within 6 weeks	10 (7.9)	6 (6.5)	4 (11.8)	0.4569
Fever >38°C on admission	64 (50.8)	33 (35.9)	31 (91.2)	<0.0001
Vomit/nausea	12 (9.5)	7 (7.6)	5 (14.7)	0.3035
Abdominal pain	126 (100)	92 (100)	34 (100)	1.0000
Vaginal discharge	31 (24.6)	24 (26.1)	7 (20.6)	0.6437
Duration of symptoms before admission, days	5.5±7.98	5.0±6.3	6.9±11.4	0.5962
White cell count on admission, per mm^3	13.8±5.9	13.6±5.7	14.3±6.5	0.7312
Maximal white cell count during hospitalisation, per mm^3	14.7±6.2	13.9±5.7	17.0±7.0	0.0108
Positive pathogen culture	36 (28)	22 (23.9)	14 (41.2)	0.0754
Abscess size, cm	6.2±1.9	5.7±1.8	7.5±1.8	<0.0001
Bilateral involvement	45 (35.7)	30 (32.6)	15 (44.1)	0.2953
Hospitalisation stay, days	6.5±3.4	5.2±2.5	9.9±3.2	<0.0001

* Data are presented as mean±standard deviation or No. (%) of patients

The association between clinical variables and duration of hospitalisation was estimated using the Poisson regression model. After controlling for confounders, the duration of hospitalisation increased by 23.8% for abscess size ≥8 cm (p=0.045), by 0.86% for 1 year older (p=0.02), by 23.7% for fever on admission (p=0.01), and by 1.2% for 1 day longer duration of symptoms (p=0.01).

Discussion

Results of our study are consistent with those in other studies[6-8]. In a retrospective review of TOA, 65.6% of patients responded to antibiotics and 34.4% of patients required surgical or image-guided drainage; the mean TOA size was larger in those with surgical drainage (4.4 cm vs 7.3 cm, p<0.0001); and a higher risk of surgery was associated with higher maximal leukocyte count, older age, and more parity[6]. In a cross-sectional study of TOA, 74% of patients responded to antibiotic treatment; compared with patients with surgical drainage, those with antibiotic treatment had shorter hospitalisation (6.32 days vs 12.75

days, p=0.021) and smaller TOA (53.6 mm vs 67.9 mm, p=0.036)[7]. In a retrospective review, 69% of patients responded to antibiotic treatment and 31% of patients required surgical drainage; the mean TOA size was larger in those with surgical drainage (6.3 cm vs 7.7 cm, p=0.02); a 1-cm increment in abscess size was associated with an increase in hospitalisation of 0.4 days (p=0.01)[8].

In our study, 73% of patients responded to antibiotic treatment and 27% of patients required surgical drainage. Patients requiring surgery were older; were more likely to be multiparous, having a higher maximal WCC, having a bigger abscess, having longer duration of hospitalization, and more likely to use intrauterine device for contraception.

Larger abscesses and surgical drainage lead to a longer hospitalisation[7,8]. In a retrospective study, patients with TOA of ≥8 cm were hospitalised longer than those with TOA of <8 cm (7.71 days vs 5.97 days, p<0.029)[9]. In our study, hospitalisation was longer in surgical drainage group than antibiotic group (9.9 days vs 5.2 days, p<0.0001). Duration of hospitalisation was 23.8% longer for patients with abscess size ≥8 cm (p=0.01). In addition, older age and longer duration of symptoms also increased length of hospitalisation.

Abscess size is a risk factor of surgical drainage. A management algorithm proposed that patients with TOA of ≥8 cm should receive ultrasound-guided drainage or surgery with concomitant intravenous antibiotics to shorten hospitalisation and decrease hospital costs[9]. Nonetheless, surgical complications, readmission rate, and fertility preservation should be considered. Surgical drainage should be offered when medical treatment fails. In our study, 45% (10/22) of patients with abscess size ≥8 cm responded to antibiotic treatment. We suggest primary treatment with antibiotics for all clinically stable patients with TOA provided that patients are closely monitored for TOA complications and surgical drainage is promptly performed when indicated.

Limitations of our study include an inability to completely control confounders such as virulence of pathogens, and no study of long-term complications (recurrence, chronic pelvic pain, fertility) of antibiotic treatment and surgical drainage. Randomised controlled trials are needed to provide evidence regarding optimal treatment of TOA patients with different risk factors. Nonetheless, the sample size of our study was large (n=126) despite TOA being an infrequent pelvic inflammatory disease complication. Relative risks of the clinical variables were estimated with a regression model.

Conclusion

Larger abscesses are associated with increased risk of surgical drainage. However, additional research is required to determine the optimal treatment for large abscesses. It is reasonable to try antibiotic therapy in clinically stable patients irrespective of abscess size.

Declaration

The authors have no conflict of interest to disclose.

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