Predictors of Treatment Failure of Medical Management Among Patients with Pelvic Inflammatory Disease with Tubo-ovarian Abscess Admitted in a Tertiary Hospital

Ma. Sheryl Lyle M. Santos, MD, FPOGS and Stella Marie L. Jose, MD, MHPEd, FPOGS
Department of Obstetrics and Gynecology, Section of Infectious Diseases, Philippine General Hospital, University of the Philippines Manila

Objective: This study aimed to identify the predictors for treatment failure of medical management among admitted female patients diagnosed with pelvic inflammatory disease with tubo-ovarian abscess.
Methods: This was a retrospective nested case-control study, using chart review of all cases of pelvic inflammatory disease with tubo-ovarian abscess/complex (N = 49) admitted at the Department of Obstetrics and Gynecology, Philippine General Hospital from January 1, 2014 to December 31, 2018.
Results: Medical treatment failure was observed to be significantly higher (51.9%) among patients 40 years old and above as compared to patients less than 40 years old (13.6%). The risk of patients ≥40 years for failed management was 14x higher than those <40 years old (OR=14.00; 95% CI=1.06 to 185.5;p=0.04). The failed management group has significantly higher TOA size of 7.8 (7.8 ± 1.6) as compared to only 5.8 (5.8 ± 1.4) for medical treatment alone group. Correspondingly, those who failed have a significantly bigger volume of 120.4 ml (120.4 ± 84.5) as compared to only 55.2 ml (55.2 ± 40.6) for medical treatment alone group. Other predictive factors such as parity, admitting White blood cell count(WBC), C-Reactive Protein (CRP), and neutrophil-lymphocytic ratio(NLR) were all not significant.
Conclusion: Tubo-ovarian abscess size of more than or equal to 7 cm, or a volume of more than or equal to 120 ml and advanced age of >40 were all predictive of failed response to medical treatment. Early recognition and intervention whether surgery or drainage may be beneficial to reduce morbidity and long-term sequelae of PID.

Keywords: C-reactive protein, neutrophil to lymphocyte ratio, pelvic inflammatory disease, tubo-ovarian abscess, tubo-ovarian complex

Introduction

Pelvic inflammatory disease (PID) is a result of an ascending infection involving the uterus, fallopian tubes, ovaries, and other pelvic organs. It may result in endometritis, salpingitis, oophoritis, peritonitis, perihepatitis and tubo-ovarian abscess (TOA).[1]

A tubo-ovarian abscess is a serious complication of untreated or inadequately treated pelvic inflammatory disease. It is an inflammatory mass containing pus affecting the fallopian tubes and ovaries. Women in the reproductive age are commonly affected and nearly 60% are nulliparous.[2] The risk factors are similar to PID and include reproductive age(15-49 years old), Intrauterine device insertion, early sexual debut, multiple sexual partners, a history of prior PID, diabetes and immunocompromised state.[3,4] The diagnosis is made when the clinical findings such as abdominal pain, pelvic mass on examination and fever are associated

with elevated inflammatory markers and radiologic findings revealing a mass.[5] TOA has a high morbidity. It may be a life-threatening condition especially if it ruptures or when associated with severe systemic sepsis. Delayed treatment could result in long term sequelae such as chronic pelvic pain, recurrent PID, distorted pelvic anatomy, infertility, and ectopic pregnancies.[6,7]

Treatment modalities for TOA include antibiotic therapy, minimally invasive drainage procedures, invasive surgery or a combination of these. Historically, treatment of TOA required a pelvic clean-up (total hysterectomy with bilateral salpingooophorectomy), but in the advent of newer and better antibiotics, medical management with broad-spectrum intravenous (IV) antibiotics is now considered as the initial management of unruptured TOAs, with a success rate of 75% to 85%. The remaining 25% needed surgery or drainage.[8]

There are new studies using neutrophil to lymphocyte ratio (NLR) as a predictor of medical treatment failure. NLR is the ratio of absolute neutrophil count to the absolute lymphocyte count. The normal NLR values in an adult, non-geriatric and healthy population are between 0.78 and 3.53.[9] It is an inexpensive and convenient marker of systemic inflammatory response and stress.[10] This simple test can be used to evaluate and identify the severity of the disease.

At present, as a predictor of treatment failure, there is no universal tubo-ovarian abscess size/ volume cut-off that determines which set of patients will undergo medical therapy alone or warrants immediate surgical intervention. This study aimed to determine the predictors of treatment failure of medical management of patients with a tubo-ovarian abscess as to age, parity, admitting white blood cell count (WBC), C-reactive protein (CRP), tubo-ovarian abscess size and neutrophil to lymphocyte ratio(NLR) that may be beneficial to reduce morbidity and long-term sequelae of PID.

Methods

This is a retrospective nested case-control study through a chart review of all cases of pelvic inflammatory disease with tubo-ovarian abscess/ complex admitted at the Department of Obstetrics and Gynecology, Philippine General Hospital from January 1, 2014 to December 31, 2018. Those who fulfilled at least 1 minimum criteria for PID namely presence of cervical motion tenderness, uterine tenderness, and adnexal tenderness, with additional criteria of fever, abnormal vaginal/ cervical discharge, leukocytosis, elevated ESR (>15mm/hour), elevated CRP and an ultrasound or CT-scan findings of tubo-ovarian abscess/complex were included. Excluded were 1) patients who had TOA but without radiologic/sonologic confirmation of tubo-ovarian abscess/ abscesses; 2) patients who underwent drainage/surgery upon admission; 3) or who were initially admitted as a case of PID but was later diagnosed with tuberculous salpingitis or endometrioma; 4) immunocompromised patients (HIV positive patients, diabetics, patients on steroids); and 5) patients with pelvic abscess other than tubo-ovarian abscess.

After the approval of the University of the Philippines Manila Research Ethics Board (UPMREB) was obtained, the retrieval of charts and the initiation of data collection ensued. The sociodemographic data, medical history, radiologic/ ultrasound findings of a tubo-ovarian abscess, white blood cell (WBC) count on admission, neutrophil and lymphocytic count were recorded. In cases where bilateral TOA/TOCs were identified, the larger sized TOA/TOCs were used for the analysis. All chart handling and reviews were done at the Medical Records section only following the hospital's memorandum on Data Privacy.

The charts of 128 patients with an admitting diagnosis of pelvic inflammatory disease, tubo-ovarian abscess/complex were recorded from the master list from January 1, 2014 to December 31, 2018, but only 82 charts were retrieved, 46 charts were not found or not in the file (Figure 1).

The data were gathered using case report forms. Patients' identifiers such as name, hospital number, age and address were assigned study code in its place to maintain anonymity. The data gathered were encoded in Excel. Only data related to the study objectives were collected. No data gathered were shared for any purpose other than what was intended for in the study. Confidentiality of the case report forms was maintained through the use of sealed envelopes and locked cabinet as storage to make it inaccessible to unauthorized persons

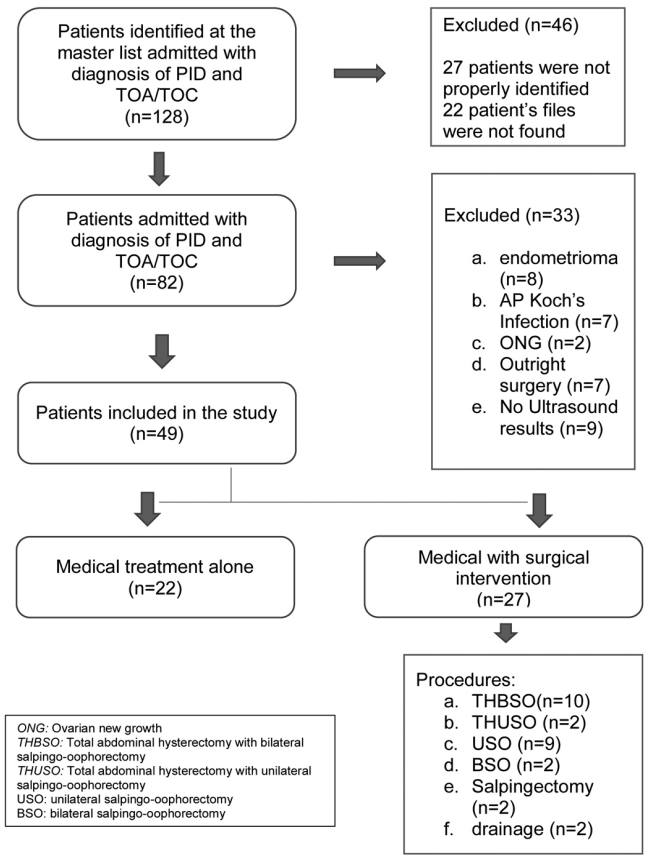

Figure 1. Flowchart of patients included in the study.

located at the OB-IDS office. Excel file format of the data gathered was password protected and changed regularly. This was under the guidelines for privacy and confidentiality as stated in the Data Privacy Act of 2012 and the 2017 National Ethical Guidelines for Health-Related Research (NEGHHR).

The data were retrospectively reviewed and gathered from 82 patients who were admitted with the diagnosis of PID, TOA. Out of the 82 patients, 33 (40%) were excluded, eight patients were later diagnosed with endometrioma, seven had abdominopelvic Koch's infection, two had an ovarian new growth, seven had an outright surgery and nine had no ultrasound result. The data of 49 (60%) patients were further analyzed in the study (Figure 1).

The patients were classified into 2 groups: the medical treatment group and the medical with surgical intervention group. The medical treatment group was comprised of 22 (45%) out of 49 patients who responded to antibiotic therapy alone and the medical with surgical intervention group who comprised of 27 (55%) who did not respond to antibiotics alone and needed surgical intervention or drainage.

Data gathered were encoded and tallied statistically using Medcalc statistical software version 19.1 was used to carry out statistical calculations. Descriptive statistics such as mean and standard deviation was mainly used to describe continuous variables while frequency and percentage for categorical data while t-test or Mann Whitney U test for continuous data. Logistic regression was also used in determining predictors of failed medical treatment. The level of significance is 5%.

Results

A total of 49 patients with pelvic inflammatory disease with tubo-ovarian abscess were included in the study. They were classified into 2 groups: 22 (44.9%) under the successful medical management group and 27 patients under the medical with surgical intervention group where the incidence of failed medical management was 55.1% (95% CI 41.31% to 69.06%). The sociodemographic characteristics of patients in both groups are presented in Table 1. It showed that age was a significant factor of failure among those who were 40 years old and above. This sub-group of patients with failed medical treatment was significantly more (51.9%) than those who were young (13.6%). Civil status turned out to be statistically the same (p=.0581), where most of the patents in medical treatment alone were single (68.2%) while those who failed were mostly married (59.3%). Additionally, gravidity (p=.9444) and parity (p=.9322) turned out to be the same between the two groups. Moreover, the age of first coitus (p=.1396) and the number of sexual partners (p=.3028) also turned out to be not significantly different between those who failed and those who did not. Laboratory investigation presented in Table 2 shows that no significant difference existed between those who underwent medical treatment alone from those who had surgery in terms of most of the laboratory parameters upon admission. Specifically, the two groups had the same mean WBC Count, neutrophil, lymphocytic, NLR, and CRP. After day 3, laboratory parameters were also

obtained, and it turned out that patients who received medical treatment and surgery have significantly higher mean WBC count (14.6) and higher mean neutrophil count (83.6) as compared to those who only received medical treatment. On the other hand, those who received medical treatment alone have a significantly higher mean lymphocytic count of 21.4. The sonologic examination results presented in Table 3 were also compared. The sub-group with failed medical management had a bigger TOA size (7.8 cm) as compared with the sub-group of medical treatment alone (5.8 cm). Similarly, those who have failed medical management have a significantly bigger volume of abscess of 120.4 ml as compared to only 55.2 ml for medical treatment alone group. After 3 days, the two groups turned out to have the same sonologic examination findings. Univariate logistic regression was run and Table 4 shows that those who were 40 years and above were 14 times more likely to end up to be a treatment failure as compared to those aged 17 to 19 years old. On the other hand, parity, WBC, NLR and CRP were not a significant predictor of treatment failure. Lastly, results showed that the size of TOA was significant, where every additional size of TOA increased the odds of treatment failure by 2.55 times. Thus, a bigger TOA would mean more risk of treatment failure.

Table 1. Sociodemographic characteristics of subjects between the two groups.

Sociodemographic Characteristics	Medical Treatment Alone (n=22) n (%)	Medical Treatment + Drainage/Surgery (n=27) n (%)	p value
Age			
17-19 years	3 (13.6)	1 (3.7)	0.0260*†
20-29 years	10 (45.5)	6 (22.2)	
30-39 years	6 (27.3)	6 (22.2)	
> 40 years	3 (13.6)	14 (51.9)	
Civil Status			
Single	15 (68.2)	11 (40.7)	0.0581ns†
Married	7 (31.8)	16 (59.3)	
Widow	0 (0.0)	0 (0.0)	
Reproductive history			
Gravidity			
0	7 (31.8)	7 (25.9)	0.9444 ns†
1 - 2	9 (40.9)	10 (37.0)	
3 - 4	5 (22.7)	8 (29.6)	
>5	1 (4.5)	2 (7.4)	
Parity			
0	7 (31.8)	7 (25.9)	0.9322 ns†
1 - 2	10 (45.5)	12 (44.4)	
3 - 4	4 (18.2)	7 (25.9)	
>5	1 (4.5)	1 (3.7)	
Age of first coitus			
≤18 years old	12 (54.5)	9 (33.3)	0.1396 ns†
≥19 years old	10 (45.5)	18 (66.7)	
Number of sexual partners			
≤2	19 (86.4)	19 (70.4)	0.3028 ns‡
≥3	3 (13.6)	8 (29.6)	

*significant, ns not significant Data presented as frequency (%) †Chi-square test;‡Fisher Exact test

Discussion

Pelvic inflammatory disease is one of the most frequent and notable infections seen in non-pregnant reproductive-aged women associated with major clinical and public health problems. It is associated with significant sequelae that have a great adverse impact on the general and reproductive health of young women. The long-term sequelae develop in approximately 25% of women with acute PID. These include infertility, ectopic pregnancy, and chronic pelvic pain.[11]

Intravenous broad-spectrum antibiotics are the initial treatment management for patients with unruptured TOA with stable vital signs. It can be effective in up to 70% of patients[12] but is associated with a high recurrence rate among adolescents who have inadequately treated or untreated sexual partner and recurrent lower genital tract infection.[13] The majority of TOA respond to antibiotic therapy alone. However, there are approximately 25% of cases wherein surgery or drainage is indicated.[14] In this study, 55% of patients had failed medical management requiring surgical intervention. This is contrary to most previous studies done. Factors that may contribute to the deviation of the results were, first, the relative decrease in the number of TOA cases admitted from the last 5 years. This

Table 2. Comparison of laboratory measurements between the two groups.

Day	Laboratory	Medical Treatment Alone (n=22)	Medical Treatment + Drainage Surgery (n=27)	p-value*
Day 1	CBC			
	WBC count	12.08 ± 4.81	15.00 ± 6.00	0.07 (NS)§
	Neutrophil count	74.27 ± 11.63	77.48 ± 10.43	0.31 (NS)§
	Lymphocyte count	17.14 ± 9.15	14.37 ± 8.36	0.27 (NS)§
	Platelet count	433.59 ± 139.83	368.33 ± 147.32	0.12 (NS)§
	NLR	6.74 ± 5.65	8.21 ± 6.76	0.42 (NS)§
	CRP			
	<6	3 (13.6%)	1 (3.7%)	1.00 (NS)‡
	>12	9 (40.9%)	3 (11.1%)	(among those
	No CRP	10 (45.5%)	23 (85.2%)	w/CRP only)
	Laboratory	Medical Treatment Alone (n=17)	Medical Treatment + Drainage Surgery (n=21)	p-value*
Day 3	CBC			
	WBC count	8.67 ± 3.74	14.58 ± 4.54	0.0001 (S)§
	Neutrophil count	67.77 ± 13.88	83.57 ± 11.31	0.0004 (S)§
	Lymphocyte count	21.41 ± 10.51	10.14 ± 9.04	0.001 (S)§
	Platelet count	374.94 ± 84.29	368.91 ± 126.26	0.87 (NS)§
	NLR	9.46 ± 22.75	15.99 ± 19.29	0.34 (NS)§
	CRP			
	<6	2 (11.8%)	1 (4.8%)	0.42 (NS)‡
	>12	4 (23.5%)	0	(among those
	No CRP	11 (64.7%)	20 (95.2%)	w/CRP only)

* p>0.05- Not significant; p ≤0.05-Significant
Data presented as Mean ± SD, (medians) were computed as needed; or as frequency (%)
‡Fisher Exact test; §T-test; ᴵᴵMann Whitney U test

Table 3. Radiologic examination results between the two groups.

Laboratory Investigation	Medical Treatment Alone (n=22) n (%)	Medical Treatment + Drainage/Surgery (n=27) n (%)	p value
Upon Admission			
Ultrasound	22 (100.0)	27 (100.0)	-
CT Scan	0 (0.0)	0 (0.0)	
MRI	0 (0.0)	0 (0.0)	
Results			
TOA	9 (40.9)	17 (63.0)	0.1278^{ns}
TOC	13 (59.1)	10 (37.0)	
Size	5.8 ± 1.4	7.8 ± 1.6	0.0001*
Volume	55.2 ± 40.6	120.4 ± 84.5	0.0018*
Unilateral	10 (45.5)	14 (51.9)	0.6592^{ns}
Bilateral	12 (54.5)	13 (48.1)	
Day 3			
Ultrasound	6 (100.0)	4 (100.0)	-
CT Scan	0 (0.0)	0 (0.0)	
MRI	0 (0.0)	0 (0.0)	
Results			
TOA	3 (50.0)	3 (75.0)	0.5714^{ns}
TOC	3 (50.0)	1 (25.0)	
Size	21.9 ± 37.8	7.0 ± 1.7	0.4608^{ns}
Volume	64.4 ± 32.0	130.4 ± 86.1	0.1185^{ns}
Unilateral	2 (33.)	4 (100.0)	0.0762^{ns}
Bilateral	4 (66.7)	0 (0.0)	

*significant, ns not significant,
Fisher Exact test (Categorical data), Student t test (Continuous data)

Table 4. Predictors of failed medical treatment among patients with pelvic inflammatory disease with tubo-ovarian abscess.

Variable	Odds Ratio	95% CI	p value
Age			
17 to 19		Reference	
20 to 29	1.80	0.15 to 21.48	0.6422^{ns}
30 to 39	3.00	0.24 to 37.67	0.3948^{ns}
≥40	14.00	1.06 to 185.5	0.0453*
Parity			
0		Reference	
1 - 2	1.20	0.31 to 4.59	0.7901^{ns}
3 - 4	1.75	0.35 to 8.79	0.4969^{ns}
>5	1.00	0.05 to 19.36	1.0000^{ns}
WBC on Admission	1.11	1.0 to 1.3	0.0842
CRP on Admission			
No CRP		Reference	
<6	0.14	0.0 to 1.6	0.1120^{ns}
>12	0.14	0.0 to 0.7	0.0118*
NLR	1.04	0.94 to 1.15	0.4164^{ns}
PLR	1.00	0.98 to 1.0	0.7707^{ns}
Size of TOA	2.55	1.43 to 4.52	0.0014*

*significant, ns not significant
Univariate Logistic Regression

may be attributed to the successful and adequate antibiotic management at the outpatient. Second, PGH mostly catered complicated PID with TOA cases that were referred to and initially managed by other hospitals and lying-in clinics. This explained the increase in failed medical management in the current study as compared to previous literature.

There were several studies evaluated that identified the TOA size, admitting WBC count, CRP, age, and parity were risk factors of antibiotic treatment failure.

The higher incidence of TOA in the older group was studied by Halperin, et al. and Mizushima, et al. They retrospectively studied women's age as a risk factor for failed response to conservative treatment with tubo-ovarian abscess. According to Dr. Halperin,[15] et al. the mean age of the patient who did not respond to conservative treatment was 45.3 ± 6.615 and in Dr. Mizushima, et al. a mean age of 40.4 ± 10.1 was reported.[16] This finding was similar to the current study. More of the sub-group of older women (51.9%) had failed medical management, as compared to 13.6% in the sub-group of younger women. The risk of patients ≥40 years for failed management was 14x higher than those <40 years old (OR=14.00; 95% CI=1.06 to 185.5;p=0.04). The possible explanations are the older group of patients had a more aggressive disease likely explained by more aggressive microorganisms and the low index of suspicion among physicians dealing with abdominal pain in the older age group women. Other possible explanations are: poorer immune system in older women as compared to younger women and errors in the management of patients.[15] Since dysuria is a common complaint in patients with Neisseria gonorrhea, some patients are managed as urinary tract infection (UTI). This leads to delay in management and worsening of the PID leading to development of TOA.

A large TOA size was cited in various literature as one of the predictors of failed medical management. It was associated with a decreased ability of the antibiotic to penetrate in a large abscess. Dewitt, et al. reviewed 373 patient charts, 135 had a TOA and 31% required management with drainage and/or surgery. The average abscess size for those treated successfully with conservative management was 6.3 cm and 7.7 cm for those who required drainage and/or surgery.[17] Greenstein, et al. noted that the mean TOA size in the medical group was 4.4 cm as compared to 7.3 cm in the surgical group.[18] Chan, et al. reviewed 136 patient charts and were classified into 2 groups: successful medical treatment with intravenous antibiotics and failed medical treatment requiring invasive intervention. One hundred eleven (81.6%) patients were successfully treated with a conservative medical approach using intravenous antibiotics; 25(18.4%) required invasive intervention. Failed medical management was predicted by a cut-off of TOA size ≥ 7.4 cm with every 1 cm increase in size associated with a 1.28 times increased risk for invasive intervention.[19] Comparable with the previous literature, this study showed that those who failed had significantly higher TOA Size of 7.8 (7.8 ± 1.6) as compared to only 5.8 (5.8 ± 1.4) for medical treatment alone group. Correspondingly, those who failed have a significantly bigger volume of 120.4 ml (120.4 ± 84.5) as compared to only 55.2 ml(55.2 ± 40.6) for medical treatment alone group.

There were new studies using neutrophil to lymphocyte ratio (NLR) as a predictor of medical treatment failure. NLR is the ratio of absolute neutrophil count to the absolute lymphocyte count. This simple test can be used to evaluate and identify the severity of the disease. It was related to the inflammatory process of antimicrobial defense wherein a decreased number of lymphocytes in the circulation as a result of the redistribution of lymphocytes in the lymphatic system with increased apoptosis, thereby increased the number of neutrophils in the blood stream.[20] A study done by Yildirim, et al.[21] compared NLR between TOA patients and healthy controls. NLR was statistically significant with a cut-off value of >4.15 (95% CI 0.97-1.00, sensitivity 95.2%, specificity 99.4%), median NLR was significantly lower in healthy patients compared to TOA patients at 1.9 and 9.3 rates, respectively. Studies done by Alay, et al.[22] and Aydin, et al.[23] showed that NLR is significantly higher in patients that failed in medical management and concluded that it could be used as a novel marker in the prediction of medical treatment failure in TOA patients. In this study, NLR was elevated in the medical with surgical intervention group (16.0 ± 19.3) as compared to the medical treatment group (9.5 ± 22.8). however, it was not clinically significant to predict treatment failure.

Contrary to the other previous studies,[16,18,24,25] there was no significant association between the failed medical management and parity, admitting WBC count and CRP.

Limitations

There were several limitations identified in this study. First, being a retrospective study, this study was based on chart review and only relied on what was written and present in the charts. Some charts were incomplete, with no laboratory parameters and lacked the ultrasound report that led to its exclusion causing a small sample size. Contributory to the small sample size, 46 charts were not found. The second limitation is a possible selection bias. The decision for immediate surgical intervention was driven by the clinician's personal clinical judgment and experience, and was not based on protocol.

Conclusion

In conclusion, tubo-ovarian abscess size $\geq$ 7 cm, or a volume $\geq$ 120 ml and advanced age of >40 were all predictive of failed response to medical treatment. Early recognition and intervention whether surgery or drainage may be beneficial to reduce morbidity and long-term sequelae of PID.

In this study, Neutrophil-Lymphocytic Ratio (NLR) was not significantly predictive of treatment failure. But in other reported studies, it can serve as parameter to help the clinician choose between medical management alone or an early surgical intervention. A prospective study with a good sample size is recommended to determine the discriminatory properties of this test.

References

1. Beigi RH. Management and complication of tubo-ovarian abscess. Sharp HT, Marrazzo J, Falk SJ (Eds). UpToDate. Waltham, MA: UpToDate Inc. https://www.uptodate.com (Assessed on November 21, 2018)
2. Rosen M, Breitkopf D, Waud K. Tubo-ovarian abscess management options for women who desire fertility. Obstet Gynecol Surv 2009;64:681–9.
3. Chappell CA and Wiesenfeld HC. Pathogenesis, diagnosis and management of severe pelvic inflammatory disease and tubo ovarian abscess. Clin Obstet Gynecol 2012; 55(4): 893–903.
4. Straub T, Reynaud M and Yaron M. Intrauterine device and pelvic inflammatory disease: Myth or reality? Gyne cologie Obstetrique Fertilite & Senologie 2018; 46(4): 414–8.
5. Kairys N, Roepke C. Tubo-Ovarian Abscess. StatPearls. NCBI bookshelf.pdf. https://www.ncbi.nlm.nih.gov/books/NBK448125/. 2017
6. Chayachindaand C, Rekhawasin T. Reproductive outcomes of patients being hospitalised with pelvic inflammatory disease. J Obstet Gynaecol 2016; 1–5.
7. Trent M, Bass D, Ness RB and Haggerty C. Recurrent PID, subsequent STI, and reproductive health outcomes: Findings from the PID evaluation and clinical health (PEACH) study. Sexually Transmitted Diseases 2011; 38 (9): 879–81.
8. Perez-Medina T, Huertas MA and Baja JM. Early ultrasound-guided transvaginal drainage of tubo-ovarian abscesses: a randomized study. Ultrasound Obstet Gynecol 1996; 7: 435–8.
9. Forget P, Khalifa C, Defour JP, latinne D, Van Pel MC, De Kock M. What is the normal value of the neutrophil-to-lymphocyte ratio?. BMC Res Notes 2017; 10:12. DOI 10.1186/s13104-016-2335-5
10. 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.
11. Sweet R, Gibbs R. Pelvic Inflammatory Disease. Infectious Disease of the Female Genital Tract 5th edition (pp. 220-244) Philadelphia: Lippincott Williams and Wilkins; 2009.
12. 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. Ultrasound Obstet Gynecol 2007; 29: 65–9.
13. Trent M, Haggerty CL, Jennings JM, et al. Adverse adolescent reproductive health outcomes after pelvic inflammatory disease. Arch Pediatr Adolesc Med 2011; 165: 49.
14. Granberg S, Gjelland K and Ekerhovd E. Best practice and research. Clin Obstet Gynaecol 2009; 23 (5): 667–8.
15. 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? Gynecol Obstet Invest 2003; 55(4): 211–5. doi:10.1159/000072076
16. 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 Gynecol Res 2013; 39(5): 1019-23.
17. DeWitt J, Reining A, Allsworth JE, Peipert JF. Tuboovarian abscesses: is size associated with duration of hospitalization and complications? Obstet Gynecol Int 2010; https://doi.org/10.1155/ 2010/847041.
18. Greenstein Y, Shah AJ, Vragovic O, et al. Tuboovarian abscess. Factors associated with operative intervention after failed antibiotic therapy. J Reprod Med 2013; 58(3-4): 101–6.

19. Chan GMF, Fong YF and Ng KL. Tubo-ovarian abscesses: Epidemiology and predictors for failed response to medical management in an Asian population. Infect Dis Obstet Gynecol 2019, Article ID 4161394, 8 pages, 2019. https://doi.org/10.1155/2019/4161394.
20. Orfanu AE, Popescu C, Leus tean A, et al. The importance of haemogram parameters in the diagnosis and prognosis of septic patients. J Crit Care Med (Targu Mures) 2017 Aug 19; 3: 105–10.
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. doi: 10.1159/000371762
22. Alay I, Kaya C, Karaca I, Eren E, Hosgoren M, Aslanova F, Cengiz H, Ekin M and YaSar L. The effectiveness of neutrophil to lymphocyte ratio in prediction of medical treatment failure for tubo-ovarian abscess. J Obstet Gynaecol Res 2019; 45: 1183-9. doi:10.1111/jog.13946
23. Aydin 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 Med J 2018; 7;3: 165-71.
24. Farid H, Lau TC, Karmon AE, Styer AK. Clinical characteristics associated with antibiotic treatment failure for tuboovarian abscesses. Infect Dis Obstet Gynecol 2016. Article ID 51202.
25. Akkurt MÖ, Yalçın SE. Akkurt l_ 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.