

Tubal ectopic pregnancy in acute abdominal presentation: A case control analysis

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ABSTRACT

BACKGROUND: The aim of the study was to evaluate the demographic data, clinical findings, ectopic pregnancy (EP) localization (left or right-sided), and treatments versus clinical presentation of tubal pregnancies (TP) with or without acute abdomen.

METHODS: Pregnants with a diagnosis of TP, selected for acute abdomen or not, were evaluated and compared, concerning EP localization (right/left), age, parity, symptoms (menstrual delay, vaginal bleeding, and groin pain), initial β -hCG value, endometrial thickness, presence of rupture, and treatment type (methotrexate and surgery).

RESULTS: On a total of 122 pregnant with TP, 32 showed acute abdomen, 45 had a TP located in the right tube and 32 in the left tube. In the acute abdomen group, parity, initial β -hCG level, and endometrial thickness were greater than non-acute abdomen group. In addition to this, the frequency of bleeding complaints, right-sided TP, rupture, and need for surgery were higher, than to the non-acute abdomen group. The frequency of the previous EP and methotrexate treatment was higher in those with the left-sided TP compared to those with the right-sided TP.

CONCLUSION: EP rate, in patients with TP who applied to the emergency department with acute abdominal symptoms, was mostly located in the right tube with greater frequency of salpingectomy in open surgery.

Keywords: Acute abdomen; ectopic pregnancy; methotrexate; salpingectomy; tubal pregnancy.

INTRODUCTION

The ectopic pregnancies (EPs) are characterized by the location of gestational sac outside the uterus. They are one of the most common life-threatening emergencies encountered in early pregnancy.^[1] In about 1% of fertilizations, the fertilized ovum is located outside the uterine cavity and almost all EPs settle in the fallopian tube (98%), creating a clinical anomaly and the tubal pregnancy (TP).^[2] Typical clinical findings occur 6–8 weeks after the last menstruation date, but symptoms may be delayed if pregnancy is located outside of the tube. The most common clinical finding of EP is abdominal pain and/or vaginal bleeding in the first trimester.^[3] These findings may occur together with the patients' admission into the emergency department and they could be confused with an

acute abdomen, in both non-ruptured cases and also those that progress into rupture.^[4]

Serum human chorionic gonadotropin (hCG) levels and transvaginal ultrasound (TVS) examination are always recommended in suspected cases. Today, more than 80% of EPs can be diagnosed without rupture development.^[5] The approach to EPs includes methotrexate (MTX) administration or surgical intervention. The preference is personalized according to each patient's clinical characteristics, EP localization, and serum β -hCG values.^[6]

In theoretical practice, it is assumed that there is an equal ovulation possibility from both ovaries.^[7] However, there is an increasing evidence that ovulation occurs frequently from

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the right ovary.^[8] In addition, it has been shown that patients who underwent *in vitro* fertilization and embryo transfer (IVF-ET) demonstrate higher response rates in the right ovarian ovulation than left.^[9] Based on the hypothesis that TP likelihood may be greater on the side where ovulation is more frequent, we aimed to evaluate the demographic data, clinical findings, and treatment characteristics of patients who were diagnosed with the right- or left-sided TP, and to compare patients with and without acute abdomen at admission.

MATERIALS AND METHODS

A cross-sectional study was carried out by a retrospective scanning of the medical records of patients treated for TP between October 2016 and October 2020. Ethical approval for the study was granted by the Local Institutional Review Board with the following decision number: 2020-9-100.

The diagnosis of EP was made by serial β -hCG measurements and TVS findings. It was also supported by histopathological evaluation of endometrial curettage specimens in appropriate cases. The study exclusion criteria were the following: patients with TP who were older than 18 years of age and did not have a history of cancer, obesity, polycystic ovary syndrome, and metabolic or syndromic diseases were excluded from the study. Patients with any EP type other than TP, such as ovarian pregnancy (three cases), cervical pregnancy (two cases), and cesarean scar pregnancy (four cases), were excluded from the study. Moreover, women who had a single fallopian tube left (after salpingectomy for any reason) were not included in the analyses.

During the medical records examination, the following data were recorded: patients' age, clinical features, obstetric history, admission complaints, examination findings, β -hCG values, TVS findings, and treatment methods that had been applied.

All patients were divided in two groups, respecting to their preliminary condition at hospital admission and enrolment: Those with acute abdomen and those without acute abdomen.

Pregnants were treated with MTX or surgical intervention. Patients receiving MTX treatment had these clinical criteria: Initial β -hCG values of $<10,000$ mIU/mL, TP size below 4 cm of diameter, non-ruptured TPs without fetal cardiac activity, non-active hepatic, or renal disease. They received a single intramuscular MTX injection^[10] and its success was defined as a 15% or greater decrease in serum β -hCG value on the 4th and 7th days after the treatment and a decrease of β -hCG value below 15 mIU/mL until the 35th day after injection.^[11]

Surgical treatment (salpingectomy or salpingostomy), through laparoscopy or laparotomy, was applied to patients who did not meet any of the criteria for MTX treatment, or non-re-

sponder to MTX treatment, or those who developed tubal rupture.

Statistical Analysis

The statistical analyses of study data were performed using the IBM SPSS Statistics version 21.0 software (IBM Corp., Armonk, NY). Descriptive statistics (mean, median, standard deviation, minimum, maximum, number, and percentage) were used to depict data. The Mann-Whitney U test was used to compare non-normally distributed quantitative variables between two groups, and the Student's t-test was used for comparison of quantitative variables with normal distribution. In comparison of qualitative data, Pearson Chi-square test and Yates Chi-square (Continuity Correction) test were used. $P \leq 0.05$ was accepted to demonstrate statistical significance.

RESULTS

A total of 122 patients diagnosed for TP, in 5 years analysis, received medical and/or surgical treatment. Thirty-two were admitted with acute abdomen, while the remaining 90 women were admitted without acute abdomen. Patient's evaluation for parity, menstrual delay and vaginal bleeding, initial β -hCG value, endometrial thickness, presence of right tubal ectopic focus, presence of tubal rupture, open surgery, and salpingectomy rates showed higher values in patients hospitalized for acute abdomen ($p=0.02$, $p=0.01$, $p<0.01$, $p<0.01$, $p<0.01$, $p<0.01$, $p<0.01$, and $p<0.01$), as reported in Table 1.

In the non-acute abdomen group, the rate of MTX administration was higher ($p<0.01$), so as the success rate of MTX treatment in this group was 72.5%, whereas, overall success rate, in all patients diagnosed for TP, was 67.2%.

Evaluating the side of TP localization, it was detected EP mainly in the right tube (45 patients) than in the left tube (32 patients). It was recorded a more frequent left-sided TP, so as initial MTX treatment was more commonly administrated in patients with the left-TP (Table 2). However, the success rate of MTX treatment in this group was 50%.

DISCUSSION

The worldwide hospital women urgent admission reported EP delayed diagnosis as one of the leading causes of maternal deaths in the early weeks of pregnancy.^[12] In recent years, the incidence of EP appears to increase in parallel with increased frequency of infertility, particularly among patients with abdominopelvic surgeries and pelvic inflammatory disease.^[13] Although women with EP diagnosis can be clinically recovered with different complaints, ranging from minor symptoms to severe events, the most common complaints include three signs: Menstrual delay, abdominal pain, and vaginal bleeding. Nevertheless, EP may develop and progress silently in some patients, while in others can show severe symptoms in the

Table 1. Characteristics of women with tubal ectopic pregnancies

	Acute abdomen (+) (n=32)	Acute abdomen (-) (n=90)	p-value
Age (years)	33.2±5.5	32.3±5	0.47
Parity	1 (0-5)*	1 (0-5)	0.02*
Admission compliant			0.01*
None	4 (12.5)	38 (42.2)	
Menstrual delay	11 (34.4)	19 (21.1)	
Vaginal bleeding	13 (40.6)	20 (22.2)	
Groin pain	4 (12.5)	13 (14.4)	
Previous EP	10 (31.2)	28 (31.1)	0.98
Initial β-hCG (mIU/mL)	5346±3482	2053±1833	<0.01*
Endometrial thickness	9.2±2.0	7.1±2	<0.01*
Localization			<0.01*
Unknown	5 (15.6)	40 (44.4)	
Right	19 (59.4)	26 (28.9)	
Left	8 (25)	24 (26.7)	
Presence of rupture	27 (84.4)	16 (17.8)	<0.01*
Initial MTX treatment	4 (12.5)	51 (56.7)	<0.01*
Treatment attempt			
MTX and follow-up	0	37 (41.1)	<0.01*
Laparoscopy	12 (37.5)	39 (43.3)	
Laparotomy	20 (62.5)	14 (15.6)	
Final treatment			
MTX and follow-up	0	37 (41.1)	<0.01*
Salpingostomy	5 (15.6)	26 (28.9)	
Salpingectomy	27 (84.4)	27 (30)	

β-hCG: β-human chorionic gonadotropin; EP: Ectopic pregnancies; MTX: Methotrexate. Data presented as mean±standard deviation, median (minimum-maximum), n (%).

early stages, progressing to acute abdomen and even shock. In this study, the majority of patients were diagnosed and treated before the possible occurrence of acute abdominal symptoms. However, in most studies from developing countries, it was stated that more than half of the cases had rupture findings at diagnosis.^[14] The increased frequency of rupture can be attributed to patients' late admission or limitations in early diagnosis.

In a study, Fukuda et al. showed that more than half of the ovulations in women were from the right ovary (55%) and such data could promote the anatomy of the ovarian arteries and veins assessing, respecting to their possible effects relating to EP. While the right ovarian vein drains into the vena cava, the left ovarian vein drains into the left renal vein and this anatomical feature may have a role in the decreased

Table 2. Characteristics of women with left sided and right sided of tubal pregnancy

	Left sided TP (n=45)	Right sided TP (n=32)	p-value
Age (years)	34.9±5	32.6±5.4	0.61
Parity	1 (0-5)	1 (0-5)	0.60
Admission compliant			
None	11 (24.4)	8 (25)	0.90
Menstrual delay	11 (24.4)	8 (25)	
Vaginal bleeding	17 (37.8)	10 (31.2)	
Groin pain	6 (13.3)	6 (18.8)	
Previous EP	8 (17.8)	15 (46.9)	<0.01*
Initial β-hCG (mIU/mL)	4206±3350	3138±2687	0.08
Presence of acute abdominal symptoms	19 (42.2)	8 (25)	0.11
Endometrial thickness	8.3±2.2	8.3±2.5	0.99
Presence of rupture	19 (42.2)	14 (43.8)	0.89
Initial MTX treatment	7 (15.6)	12 (37.5)	0.02*
Treatment attempt			
MTX and follow-up	6 (13.3)	6 (18.8)	0.71
Laparoscopy	20 (44.4)	15 (46.9)	
Laparotomy	19 (42.2)	11 (34.4)	
Final treatment			
MTX and follow-up	6 (13.3)	6 (18.8)	0.54
Salpingostomy	13 (28.9)	6 (18.8)	
Salpingectomy	26 (57.8)	20 (62.5)	

β-hCG: β-human chorionic gonadotropin; EP: Ectopic pregnancies; MTX: Methotrexate. Data presented as mean±standard deviation, median (minimum-maximum), n (%).

ovulation likelihood of the left ovary. In fact, a study of Xia et al.^[15] stated that pooling of blood in the left ovary – possibly due to anatomical characteristics – could cause a temperature increase in the left ovary, subsequently decreasing the potential fertility of oocytes on the left side. Thus, they emphasized that EP is more frequently located in the right fallopian tube, rather than the left tube. Another study reported that the left ovarian (or adnexal) torsion was less common due to the proximity of the left sigmoid colon.^[16] However, endometriomas mostly develop in the left ovary, which was emphasized to be associated with the fact that peritoneal fluid flow rate was slower in the left hemipelvis due to the sigmoid colon.^[17]

Xia et al.^[15] stated that the right tubal blood flow was greater than that of the left tube, and therefore, right-sided TPs break more frequently. The authors argued that, in clinical practice, tubal ruptures are thought to be more common in the left TPs, due to low β-hCG level and delayed clinical diagnosis.

In this study, although tubal rupture was more common in the left-sided TPs than the right-sided TPs, the difference was not significant (43.8% vs. 42.2%). In fact, β -hCG levels were higher in the right-sided TPs at the time of admission, than in the left TPs (although statistical significance was not reached), believing that β -hCG levels at admission were not directly associated with tubal rupture. In addition, the tubal muscular elasticity can be an important factor in the development of rupture.

The study strengths included a 5-year analysis in a single-center, involving related physicians on this topic with a holistic view of the data of the EP cases, dynamically reviewing the treatment modalities and displaying the appropriate approach to the patient.

The study limitation included the retrospective study and a small number of cases. The results of this hospital-based study may be liable to recall bias and selection bias. The asymmetry of some other factors would be missed for lacking the data, such as gestation age and post-operative serum β -hCG level. This is a retrospective and observational study and further studies are needed to validate our findings and explore the mechanism.

Conclusion

The overall evaluation of pregnant admitted and treated for TP during the 5-year study period demonstrated that 32 of these had an acute abdomen, EP was located in the right tube in 45 patients and in the left tube in 32 patients. When patients had acute abdomen for TP, it was more frequent on the right tube, generally submitted to salpingectomy by open surgery. Moreover, it was observed that repetitive EPs mostly occurred in the left tube and, although the great majority of patients with left-sided TP received MTX treatment, the success rate was only the 50%. The literature needs more high-volume prospective analysis and authors recommend to enlarge the cohort of enrolled patients.

Ethics Committee Approval: This study was approved by the Amasya University Non-interventional Clinical Research Ethics Committee (Date: 03.09.2020, Decision No: 2020-9-100).

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REFERENCES

1. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins-Gynecology. ACOG practice bulletin no. 193: Tubal ectopic pregnancy. *Obstet Gynecol* 2018;131:91–103. [CrossRef]
2. Nama V, Manyonda I. Tubal ectopic pregnancy: diagnosis and management. *Arch Gynecol Obstet* 2009;279:443–53. [CrossRef]
3. Karadeniz RS, Tasci Y, Altay M, Akkuş M, Akkurt O, Gelisen O. Tubal rupture in ectopic pregnancy: is it predictable? *Minerva Ginecol* 2015;67:13–9.
4. Bignardi T, Condous G. Does tubal ectopic pregnancy with hemoperitoneum always require surgery? *Ultrasound Obstet Gynecol* 2009;33:711–5. [CrossRef]
5. Alkatout I, Honemeyer U, Strauss A, Tinelli A, Malvasi A, Jonat W, et al. Clinical diagnosis and treatment of ectopic pregnancy. *Obstet Gynecol Surv* 2013;68:571–81. [CrossRef]
6. San Lazaro Campillo IS, Meaney S, O'Donoghue K, Corcoran P. Ectopic pregnancy hospitalisations: A national population-based study of rates, management and outcomes. *Eur J Obstet Gynecol Reprod Biol* 2018;231:174–9. [CrossRef]
7. Ecochard R, Gougeon A. Side of ovulation and cycle characteristics in normally fertile women. *Hum Reprod* 2000;15(4):752–5. [CrossRef]
8. Fukuda M, Fukuda K, Andersen CY, Byskov AG. Right-sided ovulation favours pregnancy more than left-sided ovulation. *Hum Reprod* 2000;15(9):1921–6. [CrossRef]
9. Järvelä I, Nuojua-Huttunen S, Martikainen H. Ovulation side and cycle fecundity: A retrospective analysis of frozen/thawed embryo transfer cycles. *Hum Reprod* 2000;15(6):1247–9. [CrossRef]
10. Diagnosis and management of ectopic pregnancy: Green-top guideline No. 21. *BJOG* 2016;123:15–55. [CrossRef]
11. Skubisz MM, Li J, Wallace EM, Tong S. Decline in β hCG levels between days 0 and 4 after a single dose of methotrexate for ectopic pregnancy predicts treatment success: A retrospective cohort study. *BJOG* 2011;118:1665–8. [CrossRef]
12. Gupta R, Porwal S, Swarnkar M, Sharma N, Maheshwari P. Incidence, trends and risk factors for ectopic pregnancies in a tertiary care hospital of Rajasthan. *J Pharm Biomed Sci* 2012;16:1–3.
13. Karaer A, Avsar FA, Batioglu S. Risk Factors for ectopic pregnancy: A case control study. *Aust N Z J Obstet Gynaecol* 2006;46:521–7. [CrossRef]
14. Islam A, Fawad A, Shah AA, Jadoon H, Sarwar I, Abbasi AU. Analysis of two years cases of ectopic pregnancy. *J Ayub Med Coll Abbottabad* 2017;29:65–7.
15. Xia W, Zhang J, Zhang D, Zhu Q, Zhang H, Huang Z, et al. Left-right asymmetry of tubal pregnancy: A 12-year retrospective hospital-based study. *J Minim Invasive Gynecol* 2019;26:671–8. [CrossRef]
16. Kurtoglu E, Kokcu A, Danaci M. Asynchronous bilateral ovarian torsion. A case report and mini review. *J Pediatr Adolesc Gynecol* 2014;27:122–4. [CrossRef]
17. Sznurkowski JJ, Emerich J. Endometriomas are more frequent on the left side. *Acta Obstet Gynecol Scand* 2008;87:104–6. [CrossRef]

ORİJİNAL ÇALIŞMA - ÖZ

Akut batın prezentasyonunda tubal ektopik gebelik: Bir olgu kontrol analizi

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AMAÇ: Klinik prezentasyonu akut batınla veya akut batın olmadan gerçekleşen tubal gebeliklerin (TG) demografik verileri, klinik bulguları, ektopik gebelik (EG) lokalizasyonunu (sol veya sağ taraflı) ve tedavilerini değerlendirmek.

GEREÇ VE YÖNTEM: Tubal gebelik tanılı gebeler akut batın olsun veya olmasın, EG lokalizasyonu (sağ/sol), yaş, parite, semptomlar (adet gecikmesi, vajinal kanama, kasık ağrısı), başlangıç β -hCG değeri, endometriyal kalınlık, rüptür varlığı ve tedavi tipi (metotreksat, cerrahi) açısından değerlendirilmiş ve karşılaştırılmıştır.

BULGULAR: Toplam 122 TG'li gebenin 32'si akut batın göstermekteydi, 45'inin sağ tüpünde ve 32'sinin sol tüpünde TG mevcuttu. Akut batın grubunda parite, başlangıç β -hCG düzeyi ve endometrial kalınlık akut batın olmayan gruba göre daha fazlaydı. Buna ek olarak, akut batın olmayan gruba göre kanama şikayetlerinin sıklığı, sağ taraflı TG olma, rüptür durumu ve ameliyat gerekliliği daha yüksekti. Sol taraflı TG olanlarda geçirilmiş EG ve metotreksat tedavi sıklığı, sağ taraflı TG olanlara göre daha yüksekti.

TARTIŞMA: Acil servise akut batın semptomları ile başvuran TG'li hastalardaki EG, çoğunlukla sağ tüpte yerleşmiş olup daha fazla sıklıkta açık cerrahi yoluyla salpenjektomiyi gerektirir.

Anahtar sözcükler: Akut batın; ektopik gebelik; metotreksat; salpenjektomi; tubal gebelik.

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