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## Original Article

### The effect of ultrasonography in predicting medical treatment success in ectopic pregnancy

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#### ABSTRACT

**Objective:** Ectopic pregnancy (EP) treatment success in a single dose methotrexate (MTX) regimen is decided by more than 15%  $\beta$  chorionic gonadotropin reduction in the 4th and 7th days after administration of 50mg/m<sup>2</sup> of medication. In our study, it was aimed whether the EP mass size less than 40mm detected by ultrasonography and the adnexal side on which it was located had an effect on the success of medical treatment. **Material and Methods:** 82 patients who treated with MTX included in the study were divided into two groups as those with a single dose of methotrexate success and those without (n:67 vs n:15). The groups were compared in terms of age, parity, size of adnexal mass detected on ultrasonography, and the side of ectopic pregnancy. **Results:** The parity rates and the age of patients were similar in both groups ( $p = 0.615$ ,  $p = 0.742$ ). Although the average adnexal mass size was found to be higher in the patient group those single dose MTX treatment was not successful, there was no statistically significant difference ( $p = 0.098$ ). Ectopic pregnancy was frequently observed on the right side in the group in which the medical treatment was successful (66 % vs 33%). **Conclusion:** The effect of ectopic pregnancy mass size on medical treatment prediction was investigated in cases with mass size less than 40mm. Ectopic pregnancy mass size, even if it is below 40 mm, may not indicate the medical treatment success.

**Keywords:** Ectopic pregnancy, Methotrexate, Treatment Failure, Ultrasonography

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## Introduction

Ectopic pregnancy (EP) is the placement of the blastocyst outside of the uterine endometrial cavity. Ectopic pregnancy is observed in approximately 2% of all pregnancies [1]. Ectopic pregnancy should be suspected especially in women with abnormal uterine bleeding, abdominal pain that starts locally on one side, and menstrual delay [2]. Delays in the diagnosis of ectopic pregnancy may result in mortality, and ruptured ectopic pregnancy-related hemorrhage is observed at 2.7 % among pregnancy-related deaths [3]. Ectopic pregnancy is located often in the fallopian tube and rarely ovarian, cesarean scar, abdominal and cervical [4].

EP is diagnosed by the patient's history, physical examination, beta chorionic gonadotropin (  $\beta$ hCG ) levels and ultrasonography (USG). However, definitive diagnosis is made by yolk sac(YS) and / or embryo observation in the gestational sac( GS) on the adnexal side in transvaginal ultrasonography or by laparoscopic observation [2,5]. An adnexal mass or intraabdominal free fluid may be detected in USG on these patients [6].

In patients who clinically contain two of the three symptoms such as menstrual delay, uterine bleeding, or abdominal pain, the diagnosis of EP can be confirmed by serial  $\beta$ - hCG and transvaginal USG examination in the absence of an emergency medical condition .

Rarely, non-viable intrauterine pregnancies without serial  $\beta$ -hCG increase and ectopic pregnancy distinction may require pathological diagnosis after dilatation curettage .

EP common risk factors are ectopic pregnancy history, tubal surgery history, smoking more than 20 cigarettes a day, previous pelvic inflammatory disease, three or more abortion, over 40 years old, infertility history, more than five sexual partners for life, intrauterine device is the use [7].

Methotrexate(MTX) can be used in the treatment of unruptured ectopic pregnancy or patients can be followed up without medication. Laparotomy or laparoscopy is planned in patients with unstable hemodynamic and MTX failure or MTX contraindications[8]. Treatment success in a single dose MTX regimen is decided by more than 15 %  $\beta$ - hCG reduction in the 4th and 7th days after administration of 50mg / m<sup>2</sup> of medication[4,9]. Two doses, multiple doses, leukoverine or mifepristone are also included with MTX regimens[10]. Surgical treatments vary depending on the localization of the ectopic pregnancy and the condition of rupture , but segmental salpingectomy , salpingostomy or mipting may be applied in the ectopic pregnancy observed[11].

There are many studies on the success of medical therapy in the treatment of ectopic pregnancy[2,4,12,13]. In our study , it was aimed whether the EP mass size less than 40 mm detected by ultrasonography and the adnexal side on which it was located had an effect on the success of medical treatment.

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## Materials and methods

Between 2016-2019 years, 215 patients who with abdominal pain, uterine bleeding, menstrual delay, adnexal mass or abdominal free fluid findings in USG admitted to our hospital which is a tertiary healthcare institution were retrospectively evaluated. Among these patients, 98 patients who were urgently operated at the time of admission due to ruptured EP and 35 patients who were followed up without treatment, such as expectant management, were not included in the analysis. 82 EP patients who did not have MTX contraindications and accepted treatment were included in the study.

In our clinic, when there is less than 15% decrease hCG values between on the 4th- 7th days in MTX treatment or patients had unstable hemodynamics as a result of tubal rupture or other reason, single dose MTX treatment failure is accepted. 15 patients included in the study had a single dose MTX treatment failure and the patients were operated. In the remaining 67 patients, a single dose of MTX therapy was sufficient.

The patients included in the study were divided into two groups as those with a single dose of methotrexate success and those without; the groups were compared in terms of age, parity, size of adnexal mass detected on ultrasonography, and the side of ectopic pregnancy.

### Statistical analysis

Results were considered significant if p value was <0.05. Independent t test was used for parametric variables such as age and parity between the two groups. Mann Whitney U test was used for the difference between non-parametric variables such as adnexal mass size. Chi-square test was used for assessing intergroup differences of categorical variables such as the side where ectopic pregnancy occurred and the results were given as n,% . All statistical analyses were performed using SPSS 22.0 programme for Windows (SPSS Inc., Chicago, IL).

## Results

Demographic data and USG findings of the patients included in the study are summarized in Table 1. The ages of the patients included in the study were similar ( $p = 0.742$ ). The parity rates were similar in both groups ( $p = 0.615$ ). Although the average adnexal mass size was found to be higher in the patient group those single dose MTX treatment was not successful, there was no statistically significant difference ( $p = 0.098$ ). Ectopic pregnancy was frequently observed on the right side in the group in which the medical treatment was successful. (66 % vs 33%), but there was no statistically significant difference between the two groups ( $p = 0.336$ ).

## Discussion

Ectopic pregnancy is an important complication of obstetric, which can lead to maternal mortality and morbidity. It is reported that if there is a delay in diagnosis, it may result in hemorrhage-related maternal death[3]. Following the diagnosis of ectopic pregnancy, MTX is applied as the first-line treatment in appropriate cases[8,14]. Operation options should be considered in cases which medical treatment is inappropriate or not responding to MTX[8,14].

The early prediction of medical treatment success in ectopic pregnancy has been frequently studied in the literature[2,4,12,13]. An ectopic pregnancy mass size of 40 mm, which is accepted by many others and recommended by ACOG, is a limit for selecting surgical methods in the treatment of ectopic pregnancy. In this study, the effect of

ectopic pregnancy mass size on medical treatment prediction was investigated in cases with mass size less than 40mm [8].

In our study, while EP mass diameter was larger in the patient group who failed treatment after a single dose of MTX, no statistically significant difference was found. Similarly, Akhatim et al. In a study they conducted in 2016 [15], they suggested that the ectopic pregnancy mass size, even if it is below 40 mm, may indicate the medical treatment success of EP.

Table 1: Ectopic pregnancy mass size and the effect of the side on treatment success

	Single dose mtx (n,67)	Operation (n,15)	p value
Age	30.08 ± 6.190	29.67 ± 5.821	0.742 <sup>a</sup>
Parity Nulliparous Multiparous	22 (29.1%) 45 (70.9%)	5 (33.3%) 10 (66.6%)	0.615 <sup>a</sup>
Average size of adnexal mass, mm	21 (10-43)	24 (10-42)	0.098 <sup>b</sup>
Ectopic pregnancy side Right Left	34 (50.7%) 33 (49.3%)	10 (66.6%) 5 (33.3%)	0.336 <sup>c</sup>

a, independent sample t test (mean ± std)

b, Mann-Whitney U test (median, min-max)

c, Chi-square test (%)

In our clinic, we recommend operation to patients as the primary treatment for cases over 4 cm. What makes our study strong is that the patients have an EP mass size below 4 cm in our patient selection. According to our study, we can not predict the failure to respond to MTX in tubal localized EP cases below this value and that tubal rupture will develop. Because of a non-ruptured ectopic pregnancy is usually below 4cm, we think that smaller reference values should be investigated to evaluate the success of MTX treatment.

In a 12-year wide-population retrospective analysis from China, EP was frequently observed on the right with 54.48%, similar to our study; Unlike our study, tubal rupture was more frequently observed in the left tube [16].

The weakness of our study is that the number of patients is limited. Patient selection criteria are the strengths of our study.

Early prediction of medical treatment success in ectopic pregnancy is important in terms of preventing morbidity and mortality due to ectopic pregnancy. There are publications suggesting that ultrasonography can be used to predict medical treatment success[17,18]. In our study, although the results were not statistically significant, they determined that the EP mass size and the side in which EP was determined differed in the surgical group. We think that prospective multicenter studies to be made in this subject will contribute to the literature.

## Disclosure

Authors have no potential conflicts of interest to disclose.

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