



Non-tubal ectopic pregnancy treatment experiences of a tertiary care center

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Abstract

Aim To evaluate the incidence, the risk factors, and the treatment outcomes of Non-tubal ectopic pregnancies (NTEP) treated in a tertiary care center.

Material and methods A total of 110 NTEP cases treated between 2014 and 2019 were included in the retrospective study. The study cohort was divided into 6 groups according to the pregnancy localization: 87 cesarean scar pregnancies (CSPs), 7 ovarian pregnancies, 6 interstitial pregnancies, 4 rudimentary horn pregnancies, 4 abdominal pregnancies, and 2 cervical pregnancies. One woman rejected all treatment modalities. Demographic characteristics, treatment modalities, and outcomes of each group were evaluated.

Results In the study cohort, expectant management was performed in one (0.9%) woman. The methotrexate (MTX) treatment was administered in 29 (26.3%) women. Seventeen (15.4%) women underwent surgery, and 63 (57.2%) women underwent manual vacuum aspiration (MVA). A woman rejected all treatment modalities. Although 70.1% ($n=61$) of CSPs were cured with MVA, 24.1% ($n=21$) of them were treated with a single-dose MTX regimen in addition to MVA. The higher mean gestational sac size ($33,9 \pm 12,96$ mm vs. $17,34 \pm 9,87$ mm), the higher mean gestational week ($8,43 \pm 1,16$ w vs. $6,66 \pm 1,49$ w), the presence of fetal heartbeat (FHB) (90.5% vs. 26,2%) and the history of pelvic inflammatory disease (PID) (38.1% vs. 6,6%) were found in the CSPs with MVA treatment failure ($p < 0.05$).

Conclusion The management of NTEPs should be individualized according to the clinical and ultrasonographic findings. The size of the ectopic pregnancy mass, the gestational week, the presence of FHB, and the PID history were the predictive factors for the failure of MVA in CSP cases.

Keywords Non-Tubal · Ectopic Pregnancy · Cesarean Scar Pregnancy · Methotrexate · Manual vacuum aspiration · Surgery

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What does this study add to the clinical work?

Non-tubal ectopic pregnancy (NTEP) which causes severe morbidity and mortality, is a rare ectopic pregnancy. A total of 110 NTEP cases were divided into six groups; cesarean scar, ovarian, interstitial, rudimentary horn, abdominal, and cervical pregnancies. As a result, the management of NTEPs should be individualized according to the type of NTEPs, clinical features, and ultrasonographic findings. The size of the ectopic pregnancy mass, the gestational week, the presence of a fetal heart-beat, and the history of pelvic inflammatory disease were the predictive factors for the failure of manual vacuum aspiration in cesarean scar pregnancies and these cases need additional methotrexate treatment.

Introduction

Non-tubal ectopic pregnancy (NTEP) which causes serious morbidity and mortality, is a rare form of ectopic pregnancy (EP) that constitutes 2% of all pregnancies [1] and 10% of EPs [2]. The gestational sac is located neither in the uterine cavity nor in the tuba in NTEP cases. The types of NTEPs are cesarean scar pregnancy, cervical, interstitial, rudimentary horn, ovarian, and abdominal pregnancy. The incidence of NTEPs is increasing due to the enhancement in the number of pregnancies with assisted reproductive technology and cesarean delivery rates [3]. Particularly the incidence of cesarean scar pregnancy (CSP) has been rising over the years [4]. Other risk factors for NTEPs are previous ectopic pregnancy, pelvic infections, smoking, use of progesterone-only pills or intrauterine devices, previous tubal and uterine surgery including tubal sterilization, cesarean section, and uterine curettage [2, 5].

Increasing clinical experience due to the increasing risk factors, incidence, and radiological/ laboratory developments in this area have provided early diagnosis of NTEP. A review by Tsakiridis et al. presented a comparative review of the major national guidelines from the Royal College of Obstetricians and Gynaecologists (RCOG), the Royal College of Physicians of Ireland (RCPI), the Society of Obstetricians and Gynaecologists of Canada (SOGC), the American College of Obstetricians and Gynecologists (ACOG), the National Institute for Health (NIH), and Care Excellence on EP for the diagnosis and management of EP, whether tubal or non-tubal [6]. Treatment modalities in NTEP depend on many variables such as the type of NTEP, the patient's clinical characteristics, β -HCG values, patient preference, need

for urgent operative intervention, ultrasonographic findings, and clinician's approach [2, 5]. In addition, there are new guidelines from organizations such as ACOG [7] and the Society for Maternal–Fetal Medicine (SMFM) [8] regarding the effectiveness and safety of the treatment of EP cases, especially CSP. In this study, experiences of a tertiary care center are presented to contribute to the literature that still needs data on the management of NTEP and to draw the attention of the authors to this issue.

Methods

The NTEP cases that were treated in the obstetrics unit of a tertiary care center, between 2014 and 2019, were included in this retrospective study. Approval from the local ethics committee (dated 09.07.2020 and numbered 10) and signed informed consent from the patients were obtained for the study. All authors and the study protocol have complied with the Declaration of Helsinki regarding the ethical conduct of research involving human subjects.

The international criteria defined by Chetty and Elson [5] were strictly adhered to in the differentiation and diagnosis of subtypes of NTEP. Tubal ectopic pregnancies, pregnancies of unknown location, and intrauterine pregnancies were excluded from the study. Included cases diagnosed with NTEP were classified into 6 subtypes: CSP, ovarian, interstitial, rudimentary horn, abdominal, and cervical pregnancies.

Demographic and clinical characteristics of the women including the smoking status, the use of contraceptive methods, the previous pelvic surgery, the history of pelvic inflammatory disease (PID), the size of the gestational sac, the location of the pregnancy, the presence of fetal heart-beat (FHB), the β -HCG value at admission, the following β -HCG values during treatment, the time achieving the negative β -HCG value, and the duration of hospital stay were obtained from the medical records. The treatment modalities including expectant management, manual vacuum aspiration (MVA), systemic methotrexate (MTX) injection, and abdominal surgery were also recorded. Afterward, at least 2 years after the treatment, subsequent pregnancy results were obtained from the medical records, and the subsequent pregnancy outcomes of the participants were recorded.

In our clinic, the MVA technique was carried out in the treatment and management of CSP, as described by Altay et al. [9]. The MVA technique was also used in the treatment of some other types of NTEP, such as the communicating type rudimentary horn pregnancies. A Foley catheter was used in the treatment of bleeding to buffer the gross intrauterine bleeding that occurred and continued after MVA treatment. Considering the patient's compliance, preference, and the need for emergency surgery, MTX treatment was preferred in NTEPs including interstitial, abdominal, and

cervical pregnancies, and cases with MVA failures in CSPs. The single dose MTX regimen (50 mg/m², intramuscularly) was administered in these cases. The surgical therapy was carried out in hemodynamically unstable patients, ovarian pregnancies, and in cases with treatment failure or complications such as rupture during MTX treatment. Although we preferred laparoscopic techniques due to shorter hospital stays and less postoperative pain, we also used laparotomic surgery depending on the patient's clinical characteristics and preference, as well as the surgeon's preference.

The clinical characteristics, the treatment outcomes, and the subsequent pregnancy outcomes of the NTEP subtypes were analyzed. The CSP group, the largest subtype group, was also divided into 2 subgroups according to MVA treatment success. The cases that were cured with MVA treatment were included in the MVA group (Group 1). Treatment failure was considered as the presence of a plateau or increase in β -HCG value after the MVA procedure or the absence of a sufficient (at least 15%) decrease in β -HCG during weekly follow-ups. A single-dose MTX regimen is applied to the cases with no decrease in B-HCG values or a plateau after MVA, these cases that are considered as MVA failure group were included in the MTX after MVA group (Group 2). The clinical characteristics and the outcomes of the two groups were compared.

Analyses were carried out using the SPSS 21.0 program and were studied at a confidence level of 95%. In the presence of 2 independent groups, parametric variables were analyzed with a *t* test, and non-parametric variables were analyzed with the Mann–Whitney *U* test. The relationship between categorical variables was analyzed using the Chi-square test. Logistic regression analysis was carried out for the risk factors of MVA treatment failure in CSP cases.

Results

A total of 110 NTEP cases were divided into six groups as CSPs (*n* = 87), ovarian (*n* = 7), interstitial (*n* = 6), rudimentary horn (*n* = 4), abdominal (*n* = 4), and cervical (*n* = 2) pregnancies. The demographic and clinical characteristics of the groups are presented in Table 1 and treatment modalities, and subsequent pregnancy outcomes of the groups are presented in Table 2.

All four *abdominal pregnancies* in the study were FHB-negative. In one abdominal pregnancy case, the initial β -HCG value was 45,192 mIU/mL and the lesion size was 37 mm. The patient's rupture of ectopic pregnancy mass was at the hospital admission. Since the case was clinically unstable, surgery via laparotomy was performed. The MTX was administered to the other 3 patients in this group. Although the β -HCG value was 39,259 mIU/mL and the lesion size was 65 mm, the cure with 2 doses of MTX in

one patient, and patient was cured. Another patient with the β -HCG value of 7040 mIU/mL and a lesion size of 29 mm was cured with 3 doses of MTX. On the other hand, another case with a β -HCG value of 6010 mIU/mL and a lesion size of 33 mm ruptured 3 days after the first dose of MTX and was treated with emergency abdominal surgery.

Six cases in the study cohort had *interstitial pregnancies* and a single-dose MTX regimen was applied in all of them. The rupture was observed 43 days after the second dose of MTX in only one case of interstitial pregnancies which is the FHB was negative and the gestational sac diameter was 26 mm. The emergency laparotomy was performed due to hemodynamically instability and the patient was cured with salpingectomy and cornual resection. Although the MTX treatment was preferred primarily in *cervical pregnancies*, in one case with a B-HCG value of 1496 mIU/mL, MVA treatment was carried out. Because the patient was cured with MVA treatment refused the MTX treatment. In the other case with a β -HCG value of 2828 mIU/mL, the cure was achieved by applying a single dose MTX regimen.

In *ovarian pregnancies*, all of whom underwent abdominal surgery, unilateral salpingo-oophorectomy (USO) by laparotomy was performed in two cases, taking into account the severity of intra-abdominal bleeding, lesion size, β -HCG value, and age of the patient. Ovarian wedge resection (OWR) was performed in the other five cases and a cure was achieved with laparoscopic OWR in all these cases.

Among the *rudimentary horn pregnancies (RHPs)*, non-communicable type RHP that had no connection with the uterine cavity was detected in two cases. These two cases that were hemodynamically unstable due to ruptured mass and intra-abdominal bleeding were cured by laparoscopic resection. In the other two RHP cases, communicating type RHP was detected and one of them was cured with MVA by reaching the rudimentary cavity under the guidance of ultrasonography. However, in the other one, after the diagnosis, the spontaneous complete abortion occurred, and the cure was achieved with expectant management.

One of the primary data of this study is the subsequent pregnancy outcomes of the participants at least 2 years after the treatment (Table 2). The highest viable pregnancy rate was observed in the cervical (100%) pregnancies, followed by the abdominal (50%), the RHP (50%), the interstitial (33.3%), the CSP (31%), and the ovarian (14.3%) pregnancies, respectively. The subsequent pregnancy of 3.4% of CSPs resulted in recurrent CSP.

The clinical characteristics of CSPs cured with MVA (group 1) and MTX after MVA (group 2) are presented in Table 3. Although there was no significant difference between the groups in B-HCG values at admission ($16,002,19 \pm 22,416,07$ mIU/mL vs. $12,888,84 \pm 25,313,37$ mIU/mL), gestational sac diameter ($33,9 \pm 12,96$ mm vs. $17,34 \pm 9,87$ mm) and gestational week

Table 1 Demographic and clinical characteristics of types of non-tubal ectopic pregnancies

		Type of non-tubal ectopic pregnancies					
		Interstitial	Abdominal	Cervical	Ovarian	Rudimentary horn	Cesarean scar
		N=6	N=4	N=2	N=7	N=4	N=87
Age min_max (mean ± SD)		28_43 (33.67 ± 5.96)	29_33 (30.25 ± 1.89)	23_33 (28 ± 7.07)	22_41 (31.71 ± 7.78)	29_38 (33.75 ± 4.43)	18_43 (32.54 ± 6.08)
Body mass index min_max (mean ± SD)		19_29 (25.5 ± 4.04)	19_25 (23.5 ± 3)	27_29 (28 ± 1.41)	22_33 (27.57 ± 3.95)	24_37 (30.75 ± 6.24)	17_39 (26.2 ± 4.45)
Number of gravidea	1	3 (%50)	1 (%25)	1 (%50)	1 (%14.3)	0 (%0)	0 (%0)
	2–5	3 (%50)	3 (%75)	1 (%50)	6 (%85.7)	3 (%75)	78 (%89.8)
	≥ 6	0 (%0)	0 (%0)	0 (%0)	0 (%0)	1 (%25)	9 (%10.2)
Number of parity	0	3 (%50)	1 (%25)	2 (%100)	1 (%14.3)	1 (%25)	0 (%0)
	1	2 (%33.3)	1 (%25)	0 (%0)	2 (%28.6)	0 (%0)	32 (%36.8)
	≥ 2	1 (%16.7)	2 (%50)	0 (%0)	4 (%57.2)	3 (%75)	55 (%63.2)
Number of previous abortions	0	4 (%66.7)	4 (%100)	2 (%100)	7 (%100)	1 (%25)	48 (%55.2)
	1	2 (%33.3)	0 (%0)	0 (%0)	0 (%0)	2 (%50)	20 (%23)
	2	0 (%0)	0 (%0)	0 (%0)	0 (%0)	1 (%25)	13 (%14.9)
	≥ 3	0 (%0)	0 (%0)	0 (%0)	0 (%0)	0 (%0)	6 (%6.8)
History of previous dilatation and curettage		0 (%0)	0 (%0)	1 (%50)	0 (%0)	0 (%0)	11 (%12.6)
History of previous ectopic pregnancies		1 (%16.7)	0 (%0)	0 (%0)	2 (%28.6)	1 (%25)	2 (%2.3)
Number of previous cesarean section	0	5 (%83.3)	4 (%100)	2 (%100)	1 (%14.3)	4 (%100)	0 (%0)
	1–2	1 (%16.7)	0 (%0)	0 (%0)	4 (%57.2)	0 (%0)	77 (%88.5)
	≥ 3	0 (%0)	0 (%0)	0 (%0)	2 (%28.6)	0 (%0)	10 (%11.5)
Education status	Illiterate	0 (%0)	0 (%0)	0 (%0)	1 (%14.3)	1 (%25)	5 (%5.7)
	Primary school	1 (%16.7)	3 (%75)	0 (%0)	1 (%14.3)	2 (%50)	24 (%27.6)
	Secondary school	1 (%16.7)	0 (%0)	0 (%0)	2 (%28.6)	0 (%0)	25 (%28.7)
	High school	2 (%33.3)	0 (%0)	0 (%0)	1 (%14.3)	0 (%0)	14 (%16.1)
	University	2 (%33.3)	1 (%25)	2 (%100)	2 (%28.6)	1 (%25)	19 (%21.8)
Smokers		0 (%0)	0 (%0)	0 (%0)	1 (%14.3)	0 (%0)	22 (%25.3)
History of pelvic inflammatory disease		0 (%0)	0 (%0)	0 (%0)	1 (%14.3)	1 (%25)	12 (%13.8)
history of previous abdominal surgery		1 (%16.7)	1 (%25)	0 (%0)	6 (%85.7)	2 (%50)	87 (%100)
Contra-ceptive method	Not used	5 (%83.3)	4 (%100)	1 (%50)	3 (%42.9)	3 (%75)	43 (%49.4)
	Intrauterine device	0 (%0)	0 (%0)	0 (%0)	3 (%42.9)	0 (%0)	11 (%12.6)
	Male condom	1 (%16.7)	0 (%0)	0 (%0)	1 (%14.3)	1 (%25)	15 (%17.2)
	Coitus interruptus	0 (%0)	0 (%0)	0 (%0)	0 (%0)	0 (%0)	15 (%17.2)
	Combined oral contraceptive	0 (%0)	0 (%0)	1 (%50)	0 (%0)	0 (%0)	3 (%3.4)
Symptoms in the apply	Non-available	0 (%0)	1 (%25)	0 (%0)	0 (%0)	2 (%50)	14 (%16.1)
	Groin pain	0 (%0)	2 (%50)	0 (%0)	1 (%14.3)	0 (%0)	23 (%26.4)
	Vaginal bleeding	5 (%83.3)	0 (%0)	2 (%100)	6 (%85.7)	2 (%50)	36 (%41.4)
	Groin pain + vaginal bleeding	0 (%0)	1 (%25)	0 (%0)	0 (%0)	0 (%0)	8 (%9.2)
	Menstrual delay	1 (%16.7)	0 (%0)	0 (%0)	0 (%0)	0 (%0)	6 (%6.9)
Fetal heart-beat	Negative	6 (%100)	4 (%100)	2 (%100)	5 (%71.4)	2 (%50)	49 (%56.3)
	Positive	0 (%0)	0 (%0)	0 (%0)	2 (%28.6)	2 (%50)	38 (%43.7)
Gestational sac size(mm) min_max (Mean ± SD)		4_39 (17.83 ± 13.12)	26_65 (40.25 ± 17.11)	10_19 (14.5 ± 6.36)	13_45 (23.71 ± 11.6)	17_100 (50.25 ± 38.14)	5_68 (21.85 ± 13.64)
Initial B-HCG (mIU/mL) mean ± SD		34,225.83 ± 47,832.26	24,375.25 ± 20,757.78	2162 ± 666	7505.57 ± 6900.21	31,989 ± 49,915.73	14,660.3 ± 25,518.4

Table 2 Treatment and pregnancy outcomes of types of non-tubal ectopic pregnancies

		Type of non-tubal ectopic pregnancies					
		Interstitial	Abdominal	Cervical	Ovarian	Rudimentary horn	Cesarean scar
		N=6	N=4	N=2	N=7	N=4	N=87
Cases of injection of methotrexate		6 (%100)	3 (%75)	1 (%50)	0 (%0)	0 (%0)	21 (%24.1)
Cure with 1 dose of methotrexate		2	0	1	0	0	14
Cure with 2 dose of methotrexate		0	1	0	0	0	3
Cure with 3 dose of methotrexate		3	1	0	0	0	4
Rupture after injection of methotrexate		1 (%16.7)	1 (%33.3)	0 (%0)	0 (%0)	0 (%0)	0 (%0)
Rupture at admission		0 (%0)	1 (%25)	0 (%0)	2 (%28.6)	2 (%50)	2 (%2.3)
Type of treatment	Expectant approach	0 (%0)	0 (%0)	0 (%0)	0 (%0)	1 (%25)	0 (%0)
	Methotrexate therapy	5 (%83.3)	2 (%50)	1 (%50)	0 (%0)	0 (%0)	21 (%24.1)
	Abdominal surgery	1 (%16.7)	2 (%50)	0 (%0)	7 (%100)	2 (%50)	4 (%4.6)
	Treatment rejection	0 (%0)	0 (%0)	0 (%0)	0 (%0)	0 (%0)	1 (%1.1)
	Manual vacuum aspiration	0 (%0)	0 (%0)	1 (%50)	0 (%0)	1 (%25)	61 (%70.1)
Hospital stay (day) min_max (mean $\pm$ SD)		8_23 (12.67 $\pm$ 6.19)	4_14 (8.25 $\pm$ 5.06)	2_3 (2.5 $\pm$ 0.71)	1_11 (4.57 $\pm$ 3.15)	1_3 (1.75 $\pm$ 0.96)	1_20 (4.55 $\pm$ 5.11)
Time to negative B-HCG (day) min_max (mean $\pm$ SD)		35_120 (64.33 $\pm$ 35.02)	14_51 (36.5 $\pm$ 16.05)	10_16 (13 $\pm$ 4.24)	8_59 (20 $\pm$ 18.24)	7_45 (24 $\pm$ 17.68)	5_67 (23.63 $\pm$ 15.02)
Pregnancy outcome after cure	No pregnancy	3 (%50)	2 (%50)	0 (%0)	5 (%71.4)	2 (%50)	50 (%57.5)
	Viable pregnancy	2 (%33.3)	2 (%50)	2 (%100)	1 (%14.3)	2 (%50)	27 (%31)
	Abortion	1 (%16.7)	0 (%0)	0 (%0)	1 (%14.3)	0 (%0)	7 (%8)
	Cesarean Scar Pregnancy	0 (%0)	0 (%0)	0 (%0)	0 (%0)	0 (%0)	3 (%3.4)

In the type of treatment used in cesarean scar pregnancies, methotrexate was used as secondary management in case of failure of manual vacuum aspiration treatment

(8,43 $\pm$ 1,16w vs. 6,66 $\pm$ 1,49w) were found to be significantly higher in group 2 ($p < 0.05$). In addition, the rate of FHB positivity (90.5% vs. 26,2%) was found significantly higher in group 2 than group 1 ($p < 0.05$). The duration of hospital stay (1,87 $\pm$ 1,27d vs. 12,24 $\pm$ 4,35d) and the time required for β -HCG to become negative (17,36 $\pm$ 9,93d vs. 42,43 $\pm$ 12,87d) were found to be significantly shorter in group 1 than group 2 ($p < 0.05$). It was determined that the presence of FHB creates a 26.71-fold increase in risk for MVA failure (95% CI 5.58–127.75). In addition, the rate of PID history was found significantly higher in group 2 with a rate of 38.1% ($p < 0.05$). The presence of PID created an 8,769-fold risk of failure of MVA (95% CI 2.289–33.589). Although there was no statistically significant difference between the groups in subsequent pregnancy outcomes, there was a higher live pregnancy rate (35.4%) in group 1, while a higher CSP recurrence rate was found in group 2 with a rate of 9.5%.

Discussion

The study presented the management of rare NTEP cases in a tertiary care center. It also showed that the gestational sac size, the gestational week, the presence of FHB at admission,

and the history of PID were the predictive factors for failure of MVA treatment in CSP cases.

CSPs are seen in 1:2226 of all pregnancies and it is an NTEP that we will encounter frequently in the future with increasing cesarean rates [10]. Therefore, its management is important. The etiology of cesarean scar pregnancy is unclear. Previous cesarean section, previous dilatation, and curettage are the defined risk factors for CSP [11]. In this study, all the patients in CSPs had a history of previous cesarean delivery, 46% had an abortion, 12% had a previous curettage, and 25% had a history of smoking. In the SMFM Consult Series [8], expectation management is not recommended in CSP (GRADE 1B); in surgical treatment, it is recommended that operative resection (via transvaginal or laparoscopic approaches, if possible) or ultrasound-guided vacuum aspiration be considered and sharp curettage alone must be avoided (GRADE 2C). In CSPs, as described by Altay et al. [9], the conception product could be removed from the uterine cavity with MVA under ultrasonographic guidance. However, there was not enough evidence about the success rate and factors affecting the treatment success of this technique [12]. In the presented study, it was found that 70.1% of CSPs were cured with the MVA technique. It was observed that the higher gestational sac size, the higher gestational week, the presence

Table 3 Clinical characteristics of cesarean scar pregnancies according to the treatment modalities

		Subgroup of cesarean scar pregnancies		<i>p</i>
		Cure with MVA group 1 <i>N</i> =61	Cure with MTX after MVA group 2 <i>N</i> =21	
		Min_max (mean ± SD)	Min_max (mean ± SD)	
Age		18_43 (32.52 ± 5.89)	20_42 (32.57 ± 6.77)	.976 ^a
Body mass index		18_38 (25.98 ± 4.27)	17_39 (26.38 ± 4.98)	.726 ^a
Interval year with previous cesarean section		1_17 (4.67 ± 3.46)	1_10 (4.71 ± 2.31)	.959 ^a
Week of pregnancy		4_10 (6.66 ± 1.49)	6_10 (8.43 ± 1.16)	.000^a
Gestational sac size (mm)		5_54 (17.34 ± 9.87)	12_62 (33.9 ± 12.96)	.000^b
Hospitalization B-HCG (mIU/mL)		92_170088 (12,888.84 ± 25,313.37)	522_74853 (16,002.19 ± 22,416.07)	.636 ^b
Pre-treatment hemoglobin (gr/dl)		8.9_15.8 (12.56 ± 1.42)	8.9_14.7 (12.08 ± 1.39)	.185 ^a
Pre-treatment white blood cell (× 10 ³ /μl)		5_12 (8.54 ± 1.82)	4.5_15 (9.24 ± 2.67)	.198 ^a
Pre-treatment platelets (× 10 ³ /μl)		90_638 (280.36 ± 85.65)	162_389 (275.4 ± 69.45)	.909 ^b
Post-treatment hemoglobin (gr/dl)		8.5_13.8 (11.82 ± 1.33)	8.7_14.7 (11.48 ± 1.75)	.423 ^a
Post-treatment white blood cell (× 10 ³ /μl)		4.3_15 (9.46 ± 2.72)	4.5_13.9 (8.47 ± 2.49)	.204 ^a
Post-treatment platelets (× 10 ³ /μl)		164_445 (271.49 ± 61.99)	162_445 (263.12 ± 67.78)	.653 ^a
Hospital stay (days)		1_7 (1.87 ± 1.27)	7_20 (12.24 ± 4.35)	.000^a
Time to negative B-HCG (day)		5_47 (17.36 ± 9.93)	21_67 (42.43 ± 12.87)	.000^b
		<i>n</i> (%)	<i>n</i> (%)	<i>p</i>
Number of gravida	1	0(%0)	0(%0)	.203
	2	9 (%14.8)	7 (%33.3)	
	3	18 (%29.5)	7 (%33.3)	
	4	19 (%31.1)	3 (%14.3)	
	≥5	15 (%24.6)	4 (%19)	
Number of parity	0	0 (%0)	0 (%0)	.158
	1	20 (%32.8)	11 (%52.4)	
	2	32 (%52.5)	6 (%28.6)	
	≥ 3	9 (%14.8)	4 (%19)	
Number of previous abortions	0	30 (%49.2)	15 (%71.4)	.206
	1	17 (%27.9)	3 (%14.3)	
	≥2	14 (%23)	3 (%14.3)	
Number of previous D&C	0	54 (%88.5)	18 (%85.7)	.131
	1	7 (%11.5)	1 (%4.8)	
	2	0 (%0)	1 (%4.8)	
	3	0 (%0)	1 (%4.8)	
Number of previous ectopic pregnancies	0	60 (%98.4)	21 (%100)	.555
	1	1 (%1.6)	0 (%0)	
Number of previous cesarean section	1	21 (%34.4)	11 (%52.4)	.208
	2	34 (%55.7)	7 (%33.3)	
	≥ 3	6 (%9.8)	3 (%14.3)	
Education status	Illiterate	3 (%4.9)	2 (%9.5)	.498
	Primary school	14 (%23)	8 (%38.1)	
	Secondary school	21 (%34.4)	4 (%19)	
	High school	10(%16.4)	3(%14.3)	
	University	13(%21.3)	4(%19)	
Smoker	No	46(%75.4)	16(%76.2)	.943
	Yes	15(%24.6)	5(%23.8)	
History of pelvic inflammatory disease	No	57 (%93.4)	13 (%61.9)	.000
	Yes	4 (%6.6)	8 (%38.1)	

Table 3 (continued)

		<i>n</i> (%)	<i>n</i> (%)	<i>p</i>
Contraceptive method	No	25 (%41)	16 (%76.2)	.128
	Intrauterine devices	10 (%16.4)	1 (%4.8)	
	Male condom	11 (%18)	2 (%9.5)	
	Coitus interruptus	13 (%21.3)	2 (%9.5)	
	Combine oral contraceptives	2 (%3.3)	0 (%0)	
	Bilateral tubal ligation	0 (%0)	0 (%0)	
Symptoms in the apply	Non-available	12 (%19.7)	0 (%0)	.000
	Groin pain	16 (%26.2)	6 (%28.6)	
	Vaginal bleeding	26 (%42.6)	8 (%38.1)	
	Groin pain+vaginal bleeding	1 (%1.6)	7 (%33.3)	
	Menstrual delay	6 (%9.8)	0 (%0)	
Fetal heartbeat	Negative	45 (%73.8)	2 (%9.5)	.000
	Positive	16 (%26.2)	19 (%90.5)	
Pregnancy outcomes after cure	No pregnancy	33 (%54.1)	12 (%57.1)	.561
	Viable pregnancy	21 (%34.4)	6 (%28.6)	
	Abortion	5 (%8.2)	1 (%4.8)	
	Unwanted pregnancy	1 (%1.6)	0 (%0)	
	Cesarean scar pregnancy	1 (%1.6)	2 (%9.5)	
Buffer with Foley Catheter due to intrauterin bleeding	No	47 (%77)	19 (%90.5)	.181
	Yes	14 (%23)	2 (%9.5)	

Bold *p* value is statistically significant ($p < 0.05$)

MVA manuel vacuum aspiration, MTX methotrexate

^a*t* test; ^bMann Whitney *U* test; others Chi-square test

of FHB at admission, and the presence of a history of PID were associated with MVA treatment failure.

Careful selection of medical therapy is recommended in interstitial ectopic pregnancies [5]. In the series of Siew-Fei Ngu et al. [13], 51% of NTEPs were treated with surgery, 38% with medical treatment, and 10% with expectant management. Ramkrishna et al. [14] reported a higher success rate when compared to surgical treatment in cases with systemic or intra-sac MTX injection. In our series, 83.3% of interstitial ectopic pregnancy cases were treated with MTX and medical treatment failure occurred in a woman.

In ovarian pregnancies, laparoscopic partial or total oophorectomy is recommended while methotrexate can be used as a non-invasive alternative therapy [15, 16]. Wedge resection could be performed on patients wishing to preserve their fertility. In the series of Seiner et al. [17], three ovarian pregnancies had a fertility request and had wedge resection, of which one resulted in a viable pregnancy, one in abortion, and one in infertility. In our series, surgical management was performed in all ovarian pregnancies. One viable pregnancy in the case treated with OWR and one spontaneous abortion in the case treated with USO was observed after surgery in ovarian pregnancies.

In unicornuate uterus cases, isolated unicornuate uteruses are the most common type [18]. When a rudimentary horn is present, the cavitory but noncommunicating type is present in 22% of cases, and the cavitory and communicating type in 10% of cases [19]. Surgical excision is recommended in non-communicating rudimentary horn pregnancies [20]. Sanchez-Ferrer reported a 50% rate of unstable ruptured rudimentary horn pregnancy diagnosis by laparoscopic observation [20]. In our series, two of the four RHPs were the communicating type (50%). One of the cases was treated with an expectant approach since spontaneous abortion was seen, while MVA was performed in the other case with ultrasonography.

Fowler et. al. [21] showed that more than half of the patients required multiple interventions in the treatment of cervical pregnancies and a hysterectomy due to cervical bleeding was required in 9% of cases. In this study, one of the two cervical pregnancies was treated with MVA, and the other case was treated with MTX. No complication has occurred in the management of these cases. No balloon tamponade or additional intervention was needed.

It is thought that this study contributed to the literature by sharing the experience and treatment algorithms of a tertiary care center, providing detailed information on the

management of the extremely rare NTEP types, and presenting the factors affecting the success of the MVA technique used in the management of CSPs whose incidence is increasing day by day. However, the retrospective nature of the study and the small sample size of the subtype groups showed that further randomized controlled studies with larger cohorts are needed to standardize the management of NTEPs.

Conclusion

The higher gestational week, the larger gestational sac, the presence of FHB, and the history of PID were found as the risk factors for the failure of MVA in the management of CSPs. The management of NTEPs should be individualized according to the clinical characteristics of patients.

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Data availability The data supporting this study is available through the corresponding author upon reasonable request.

Declarations

Conflict of interest The authors declare no conflicts of interest.

Ethical approval Ethics committee approval was taken for this retrospective study from the Local Ethics Committee.

Human rights All authors and the study protocol have complied with the World Medical Association Declaration of Helsinki regarding the ethical conduct of research involving human subjects.

Consent to participate Informed consent was obtained from patients who participated in this study.

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