

# Risk factors and pregnancy outcomes of heterotopic pregnancy secondary to in vitro fertilization-embryo transfer: A case series study

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## Research article

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# Abstract

**Background:** The early diagnosis and treatment of heterotopic pregnancy (HP) remain one of the biggest challenges in the field of gynecology. A coexisting intrauterine gestation makes the ectopic pregnancy in HP more difficult to diagnose. This case series analysis is designed to explore factors affecting the incidence of HP secondary to in vitro fertilization-embryo transfer (IVF-ET) and that affecting pregnancy outcomes after surgical treatment of HP.

**Methods:** From the IVF registry system, the clinical data of 29 patients with HP and 92 with an intrauterine-only pregnancy (IUP) following embryo transfer from January 2009 to December 2017 were retrospectively analyzed.

Results HP had a higher proportion of previous ectopic pregnancies, multiple abortion history ( $\geq 2$  times) and tubal indication for IVF than IUP. In patients with HP, 31.03% had spontaneous abortion, 25.00% had preterm delivery and 58.62% resulted in a live birth. According to the results from logistic regression, history of multiple abortions (odds ratio (OR) 3.031, 95% confidence intervals (CI) 1.087-8.453;  $P=0.034$ ), tubal infertility (OR 3.844, 95% CI 1.268-11.656;  $P=0.017$ ), previous ectopic pregnancies (OR 2.303, 95% CI 0.625-8.490;  $P=0.021$ ) and multiple embryo transfer (OR 0.300, 95% CI 0.092-0.983;  $P=0.037$ ) resulted in an elevated proportion of HP in IVF cycles. Incidence of HP was comparable between patients transferred with blastocyst and cleavage embryos. Shorter operative duration, smaller size of the ectopic mass and location in the ampulla of the fallopian tube were associated with higher chance of survival in the coexistent intrauterine pregnancy after surgical treatment with HP.

**Conclusions:** The early diagnosis of HP remains a challenge. Previous history of ectopic pregnancy, multiple abortions, tubal infertility and multiple embryo transfer may be considered as meaningful risk factors of subsequent HP following IVF-ET. In patients with HP treated by surgery, shorter operative duration, smaller size of the ectopic mass and location in the ampulla of the fallopian tube means better reproductive prognosis.

## Background

HP, defined as simultaneous occurrence of ectopic and intrauterine pregnancy, is a rare disease in the general population. Previously, the incidence rate of HP was estimated from previous study between 1/7,963 and 1/30,000 in spontaneous pregnancies [1]. However, the incidence has risen, ranging from 1.5 in 1000 to 1 in 100 [2], with the widespread application of assisted reproduction technology (ART) and increased pelvic inflammatory disease. The early diagnosis and treatment of HP remain one of the biggest challenges in the field of gynecology. A coexisting intrauterine gestation makes the ectopic pregnancy in HP more difficult to diagnose. However, delay in diagnosis may increase the probability of tubal rupture, resulting in hemorrhagic shock and emergency blood transfusion [3]. Therefore, enhanced follow-up care should be performed in patients considered to be at high risk for HP. However, very little definite data exists regarding risk factors for HP after IVF-ET because of the rareness of the disease.

Several probable explanations for HP are suggested in recent years, such as transfer of multiple embryos, embryo transferring directly into the oviduct and transplantation in large volume of medium [4].

The ideal treatment of HP is to remove the ectopic pregnancy with least harm to the intrauterine gestational sac. It is well known that surgical treatment with HP is laparoscopy or laparotomy. In recent years, more and more patients with HP prefer to laparoscopy because of the minimally invasive approach [5]. Therefore, factors affecting prognosis after surgical therapy of HP are attention-attracting topic. However, the data on this issue are limited. The surgical characteristics associated with survival of the intrauterine pregnancy after surgical treatment with HP are not yet well known.

The purpose of the present retrospective study was to detect the risk factors of HP following IVF treatment. It also addressed factors influencing the pregnancy outcomes following the surgical treatment of HP.

## Materials And Methods

From February 2009 to January 2018, 4274 cycles following IVF-ET at the ART Center in Second Affiliated Hospital of Chengdu University of Traditional Chinese Medicine resulted in a pregnancy (clinical intrauterine, ectopic and heterotopic). 29 patients were diagnosed with HP and included in this study. Among the 29 patients with HP, 2 had a spontaneous miscarriage of the intrauterine pregnancy, and then were treated with Methotrexate for the ectopic pregnancy. In another 1 case, spontaneous resolution of the extrauterine gestation occurred, and the intrauterine pregnancy failed to survive after 2 weeks. One patient with cervical ectopic pregnancy was successfully treated with ultrasound-guided aspiration. The remaining 25 patients with HP received surgical treatment. During the same period, 92 patients were selected as controls by a random sampling of patient population with an intrauterine-only pregnancy after embryo transfer from the IVF registry system in our center.

IUP was defined as one or more gestational sacs located solely inside the uterus and visible by ultrasound. HP was defined as the simultaneous visualization of both intrauterine and extrauterine pregnancy. Diagnosis of HP was confirmed by postsurgical pathology in the present study. In our hospital, patients treated with IVF are required to return for a blood  $\beta$ -human chorionic gonadotrophin ( $\beta$ -hCG) test 14 and 18 days after embryo transfer. The patients who have elevated  $\beta$ -hCG levels will come back for transvaginal ultrasound examination 30 days after embryo transfer. After surgical treatment for HP, patients received intensive treatment with the goal of maintaining the intrauterine pregnancy. Besides, a weekly follow-up ultrasound scan was performed during the first trimester of pregnancy.

Maternal characteristics including body mass index (BMI), age, infertility diagnosis and previous pregnancy history were assessed. ART procedure characteristics: fresh or frozen-thawed cycles, number of embryos transferred, cleavage or blastocyst embryos, endometrial thickness and distance of air bubble to fundus were also assessed. In addition, the surgical characteristics were analyzed. The pregnancy outcomes of HP and IUP were compared in this study. Spontaneous abortion was defined as

embryonic/fetal loss before 20-week gestation. Preterm delivery was defined as delivery before 37 completed weeks.

To obtain data associated with the surgical characteristics and a superior view of the complex postoperative situation, a retrospective review of patients' hospital and outpatient medical records was performed. Reproductive outcomes were available via a phone-based follow-up.

This current study was approved by the hospital ethics committee. In our center, patients have permitted the use of their medical records for research by signing a written informed consent before IVF treatment.

All statistical analysis were performed using the SPSS 19.0 software. A multivariate logistic regression model was performed to obtain relative risk factors for HP. The T-test was used when variables obeyed a normal distribution. Chi-square tests were used to compare data shown as percentage. P values < .05 were considered significant.

## Results

### Maternal characteristics and pregnancy outcome

Among the 121 patients included in our study, no significant differences were detected between HP and IUP with respect to BMI, maternal age, infertility diagnosis, duration of infertility. However, HP had a higher proportion of previous ectopic pregnancies and multiple abortion history ( $\geq 2$  times) than IUP. Furthermore, HP had a higher proportion of patients treated with IVF due to tubal factor infertility. In patients with HP, 31.03% had spontaneous abortion, 25.00% had preterm delivery and 58.62% resulted in a live birth. No major infant malformations were diagnosed (Table 1).

Table 1  
Distribution of study population by maternal characteristics and pregnancy outcome

	Heterotopic pregnancies (N = 29)	Intrauterine pregnancies (N = 92)	P value
Age (y)	32.15 ± 3.21	32.06 ± 3.71	0.751
Body mass index(BMI), kg/m <sup>2</sup>	21.43 ± 2.15	22.32 ± 3.64	0.149
Infertility diagnosis			0.673
Primary infertility	12 (41.38)	43 (46.74)	
Secondary infertility	17 (58.62)	49 (53.26)	
Duration of infertility (y)	3.87 ± 2.74	4.15 ± 2.68	0.359
Previous abortions			0.017
≤ 1	11(37.93)	59 (64.13)	
≥ 2	18 (62.07)	33 (35.87)	
Previous ectopic pregnancies			0.037
0	21 (72.41)	82 (89.13)	
≥ 1	8 (27.59)	10 (10.87)	
Infertility diagnosis			0.034
Tubal factor	20 (68.97)	42 (45.65)	
Endometriosis	3 (10.34)	9 (9.78)	
Nontubal female factors	4 (13.79)	34 (36.96)	
Male factor	2 (6.90)	7 (7.61)	
Pregnancy outcome			
Spontaneous abortion	9 (31.03)	12 (13.04)	
Preterm delivery	5 (25.00)	6 (7.50)	
Live births	17 (58.62)	75 (81.52)	
Values are expressed as mean ± standard deviation or n (%).			

## IVF procedure characteristics

In the present study, the number of embryos transferred in patients with HP was significantly greater than those with intrauterine-only pregnancies ( 2.31 ± 0.47 vs.2.09 ± 0.39, p = 0.017 ). Results were similar after we analysis the incidence of OHSS (24.13% vs. 3.26%, p = 0.002). However, there was no difference in the

incidence of HP between thawed embryo and fresh embryo transfer cycles, and similar results were obtained when cleavage embryo and blastocyst transfer cycles were analyzed. In addition, no significant differences were detected in the number of retrieved oocytes, endometrial thickness, distance of air bubble to fundus between HP and IUP (Table 2).

Table 2  
Comparison of ART procedure characteristics between intrauterine-only and heterotopic pregnancies

	Heterotopic pregnancies (N = 29)	Intrauterine pregnancies (N = 92)	P value
Type of transfer cycles			0.668
Fresh embryo	16 (55.17)	49 (53.26)	
Frozen-thawed embryo	13 (44.83)	33 (46.74)	
Number of oocytes retrieved	13.76 ± 4.92	12.32 ± 4.28	0.133
Number of embryos transferred	2.31 ± 0.47	2.09 ± 0.39	0.017
Stage of embryo			0.479
Cleavage stage	23 (79.31)	66 (71.74)	
Blastocyst stage	6 (20.69)	26 (28.26)	
Endometrial thickness(mm)	10.20 ± 2.56	10.56 ± 1.93	0.425
Distance of air bubble to fundus (mm)	17.55 ± 1.80	17.32 ± 1.75	0.550
Ovarian hyperstimulation syndrome	7 (24.13)	3 (3.26)	0.002
β-hCG level (mIU/mL) after embryo transfer			
on day 14	399.10 ± 225.03	365.13 ± 157.37	0.454
on day 18	1837.28 ± 1091.85	1634.95 ± 729.76	0.356
Values are expressed as mean ± standard deviation or n (%).			

## Risk factors associated with HP

In order to assess the effects of different risk factors on incidence rate of HP after embryo transfer, multivariate logistic regression was used (Table 3). History of multiple abortions ( $\geq 2$  times) (OR 3.031, 95% CI 1.087–8.453; P = 0.034), tubal infertility (OR 3.844, 95% CI 1.268–11.656; P = 0.017), previous ectopic pregnancies (OR 2.303, 95% CI 0.625–8.490; P = 0.021) and multiple embryo transfer (OR 0.300,

95% CI 0.092–0.983; P = 0.037) were associated with an elevated incidence of HP following IVF treatment. The incidence rate of HP was comparable between patients with cleavage and blastocyst transfer. Interestingly, for all women involved in this research, endometrial thickness on the day embryo transfer showed no significant difference, lacking association with heterotopic pregnancies.

Table 3  
Risk factors associated with HP by logistic regression analysis.

Risk factors	OR (95% CI)*	P value
Previous ectopic pregnancies (yes/no)	2.303 (0.625–8.490)	0.021
Tubal factor (yes/no)	3.844 (1.268–11.656)	0.017
Previous abortion ( $\geq 2$ times)	3.031(1.087–8.453)	0.034
Number of transferred embryos	0.300 (0.092–0.983)	0.037
Endometrial thickness	1.077 (0.832–1.394)	0.575
Stage of embryo (cleavage/blastocyst)	2.140 (0.551–8.308)	0.272
* lower and upper bounds of a 95 percent confidence interval		

## Influence of surgical characteristics on survival of intrauterine pregnancy following surgical treatment of HP

25 patients with HP received surgical treatment on day of hospital admission. Among the patients, the ectopic pregnancy was located in the ampulla in 18 (72%), in the tubal interstitium in 3 (12%), and in the tubal isthmus in 4 (16%). The extrauterine gestation sac ruptured spontaneously in 3 patients. Among the 25 patients, 24 (96%) underwent treatment of HP by salpingectomy. Besides, the remaining one patient whose fallopian tubes had been removed was treated by placing a loop on stump of the tube. 20 (80%) underwent laparoscopic surgery, and 5 (20%) laparotomy. No serious complications associated with surgery or anesthesia were reported.

To explore influence of surgical characteristics on survival of intrauterine pregnancy following surgical treatment of HP, an additional sub-analysis was restricted to patients treated with surgery. Table 4 shows the surviving rate of the intrauterine pregnancy according to different surgical characters. As shown in Table 4, while duration of surgery increased, the surviving rate of the intrauterine pregnancy decreased significantly (100% vs. 75% vs. 33.33%,  $p = 0.034$ ). The similar result was given when the effect of adnexal masses size on the intrauterine pregnancy was assessed. Furthermore, when the fallopian tube ruptured, the surviving rate of intrauterine pregnancy decreased to 33.33% ( $P = 0.013$ ). When compared with other locations of ectopic pregnancy, the ampulla was strongly associated with a higher surviving rate of the intrauterine pregnancy (94.44%,  $P = 0.013$ ) (Table 4).

Table 4

Influence of surgical characteristics on survival of intrauterine pregnancy following surgical treatment of HP

	Number (N = 25)	Survival rate of intrauterine pregnancy (N = 20)	P value
Gestational age at the time of surgery(day,calculated from the date of embryo transfer )			0.245
≤ 30	5	4(80.00)	
31–56	16	14(87.50)	
> 56	4	2(50.00)	
Position of ectopic pregnancy			0.013
Ampullar	18	17 ( 94.44)	
Interstitial	3	1 (66.67)	
Isthmus	4	2 (50.00)	
Method of surgery			0.252
Laparoscopy	20	17 (85.00)	
Laparotomy	5	3 (60.00)	
Duration of surgery(min)			0.034
≤ 30	10	10 (100.00)	
30–60	12	9 (75.00)	
> 60	3	1 (33.33)	
sizes of the adnexal masses (cm)			0.013
≤ 5	18	17 (94.44)	
> 5	4	2 (50.00)	
tubal rupture	3	1 (33.33)	
Values are expressed as n (%).			

## Discussion

Heterotopic pregnancies are extremely rare forms of ectopic pregnancy in gynecology. However, in recent years the incidence rate has increased to 1% with widespread use of ART [6]. HP is a life-threatening condition which have a maternal mortality rate eight times greater than tubal ectopic pregnancies [7]. For this reason, early recognition and treatment is critical to improving the prognosis. Clinical features associated with HP vary widely among individuals. Some patients were asymptomatic and others may experience acute abdominal pain, pelvic hemorrhage and hypovolemic shock. The present study suggested no significant difference between the HP and IUP with aspect to blood level of  $\beta$ -hCG.  $\beta$ -hCG is usually low in ectopic pregnancies. However, it's probably unhelpful in diagnosis of heterotopic pregnancy, for they might indicate normal ranges in patients with HP. Transvaginal ultrasound provides a very important tool for the diagnosis of HP. However, the simultaneously presented concurrent intrauterine sac and bilaterally hyperstimulated ovaries greatly increased the difficulty in diagnosis. Given the above, diagnosis of HP is a major predicament for clinicians.

Many studies have shed light on the risk factors of HP over the past few years, with the hope of a clinical prediction model for it [4]. In our study, history of multiple abortions, tubal infertility, previous ectopic pregnancies and multiple embryo-transfer were associated with an increased incidence of HP following IVF treatment. Thus, HP should always be involved in differential diagnosis in symptomatic patients with risk factors suggested above. Furthermore, outpatient follow-up should be performed more frequently in patients with multiple embryo transfer, even though an intrauterine gestational sac is visible on ultrasound. A history of salpingitis and gross tubal damage in patients acts as a potential pathological mechanism of ectopic pregnancies following IVF and in natural conceptions [8]. The results are consistent with the present study which has shown that patients with history of tubal damage ( salpingitis and previous ectopic pregnancies ) are associated with increased rate of HP. A possible explanation is that altered tubal anatomy and function due to tubal damage may alter the mechanism of tubal transport and signaling molecules in tubal microenvironment which prevents embryonic implantation in the oviduct [9]. Compared with other indications for IVF treatment, tubal indications is a major risk for HP in the current study. The same results were also presented in Li's study [10]. The probable explanation of tubal pregnancies in those patients was that the embryos migrated into the oviduct after uterine placement, but the damaged tubal failed to transport the embryos back into the uterine.

The distance from the tip of transfer catheter to uterine fundus has also been evaluated as a potential risk factor for development of HP [11]. In our center, distance of air bubble to fundus was controlled in 15–20 millimetres range, and the data suggested no significant difference between HP and IUP ( $17.55 \pm 1.80$  mm vs.  $17.32 \pm 1.75$  mm,  $p = 0.55$ ). The result was consistent with study by Friedman et al. which reported that air bubble position too close to the fundus (10 mm) probably ended in a tubal pregnancy while a distance of 15–20 millimetres would achieved a higher rate of embryo implantation [12]. That is a possible explanation for the comparable data on distance of air bubble to fundus between the two groups in our center. The results of this study showed that multiple-embryo transfer was a risk factor associated with increased incidence of HP ( OR 0.300, 95% CI 0.092–0.983;  $P = 0.037$ ). This finding confirms and expands that of a previous study which believed that the diagnosis of HP must be

considered in patients with two or more embryos transferred in a cycle [13]. Therefore, selective single-embryo transfer probably is a preferred choice for a decreased risk of HP. Overall, in the present study, we found some factors from the cause of infertility, specific characteristics of IVF and embryo-transfer techniques which increased the risk of HP following embryo transfer. Patients treated with IVF-ET should have more frequent ultrasound examinations early in pregnancy, for delay in diagnosis of HP is more common than ectopic pregnancy. Therefore, it's important to increase clinicians' awareness of HP though an intrauterine pregnancy is present, especially in patients with risk factors given above.

Surgery is still the most frequently chosen method of treatment with HP. The surgical approaches are laparotomy and laparoscopy. The efficacy and safety of laparoscopic surgery during pregnancy is well certificated. It shows superiority over laparotomy approaches in postoperative recovery and subsequent reproductive outcomes [14]. In the present study, 20 (80%) patients were treated by laparoscopy. The surgical procedures were slightly modified, avoiding both excessive manipulation and cannulation due to co-existence of the gestational sac in uterine. Among the 25 patients, 24 (96%) underwent salpingectomy. A possible explanation is that, compared with salpingostomy, salpingectomy gives the competitive advantages of shortening the operation time, decreasing rates of persistent trophoblast, reducing intraoperative stimulation of uterine and avoiding the possibility of another ectopic pregnancy[15]. For the patients urgently needing a child, salpingectomy was acceptable if compensated by a higher survival rate of the intrauterine pregnancy following surgical treatment.

In the present study, the survival factors of intrauterine pregnancy following surgical treatment of HP were analyzed. We found that shorter operative duration, smaller size of the ectopic mass were associated with more chance to survive for the coexistent intrauterine pregnancy, and the prognosis would be better if ectopic pregnancies were in the ampulla of fallopian tube. As noted above, the factors are somewhat interrelated: a smaller size and ampulla located pregnancy involves a more simple surgical procedure and shorter duration of operation (salpingectomy), less manipulation of the uterus and surgical complications, which are key points for a better reproductive outcome. This finding is consistent with previous research [16], which suggests that salpingectomy may be a preferred choice in women with HP following IVF-embryo transfer.

In the current study, 3 patients had severe abdominal pain and massive pelvic hemorrhage due to tubal rupture. As a result, only one of them (33.3%) had the chance for an ongoing pregnancy after emergency surgery. Delayed diagnosis of HP in patients with a visible intrauterine pregnancy is life-threatening. It must be emphasized that for women treated with IVF-ET, even if an intrauterine gestational sac is confirmed, a high index of suspicion for HP is required, especially for these high-risk patients.

## Conclusions

In conclusion, HP is becoming more common with widespread use of ART, however, the most challenging aspect remains early diagnosis with certainty. Previous history of ectopic pregnancy, multiple abortions ( $\geq 2$  times), and cycles for tubal indication are probable risk factors for heterotopic pregnancies in

patients with IVF-ET treatment. Patients with these risk factors should be closely monitored by repeated ultrasonography after a positive pregnancy test. The surgical management of HP may result in a successful maternal outcome when early diagnosed. Finally, further expanded researches are needed to explore how to decrease incidence rate of ectopic pregnancy after IVF-ET.

## Declarations

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## Authors' contributions

Shaomi Zhu was the first author who acquired and analyzed the data and drafting the manuscript. Qinxiu Zhang revised the paper for some important content. All authors were responsible for data collection, data analysis, and data interpretation. All authors read and approved the final manuscript.

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## Availability of data and materials

The data are available from the corresponding author on reasonable request.

## Ethics approval and consent to participate

The present study was approved by the Institutional Review Board of Second Affiliated Hospital of Chengdu University of Traditional Chinese Medicine. The written informed consent of all subjects was obtained before participating the study.

## Declaration of interest

The authors report that they have no conflict of interest.

## References

1. Barrenetxea G, Barinaga-Rementeria L, Lopez de Larruzea A, Agirregoikoa JA, Mandiola M, Carbonero K. Heterotopic pregnancy: two cases and a comparative review. *Fertil Steril.* 2007; 87:417.e9-15.

2. Gergolet M, Klanjšček J, Steblovnik L, Teran N, Bizjak N, Di Bon N, et al. A case of avoidable heterotopic pregnancy after single embryo transfer. *Reprod Biomed Online*. 2015;30:622-4.
3. Soriano D, Shrim A, Seidman DS, Goldenberg M, Mashiach S, Oelsner G. Diagnosis and treatment of heterotopic pregnancy compared with ectopic pregnancy. *J Am Assoc Gynecol Laparosc*. 2002; 9: 352-8.
4. Verhulst G, Camus M, Bollen N, Van Steirteghem A, Devroey P. Analysis of the risk factors with regard to the occurrence of ectopic pregnancy after medically assisted procreation. *Hum Reprod*. 1993; 8:1284-7.
5. Mihmanli V, Kilickaya A, Cetinkaya N, Karahisar G, Uctas H. Spontaneous Heterotopic Pregnancy Presenting with Hemoperitoneum. *J Emerg Med*. 2016; 50 : 44 – 6.
6. Felekis T, Akrivis C, Tsirkas P, Korkontzelos I. Heterotopic triplet pregnancy after in vitro fertilization with favorable outcome of the intrauterine twin pregnancy subsequent to surgical treatment of the tubal pregnancy. *Case Rep Obstet Gynecol*. 2014; 2014: 356131.
7. Atrash HK, Friede A, Hogue CJ. Abdominal pregnancy in the United States: frequency and maternal mortality. *Obstet Gynecol*. 1987; 69: 333-7.
8. Refaat B, Dalton E, Ledger WL. Ectopic pregnancy secondary to in vitro fertilisation-embryo transfer: pathogenic mechanisms and management strategies. *Reprod Biol Endocrinol*. 2015; 12: 30.
9. Shaw JL, Dey SK, Critchley HO, Horne AW. Current knowledge of the aetiology of human tubal ectopic pregnancy. *Hum Reprod Update*. 2010;16:432 – 44.
10. Li C, Meng CX, Zhao WH, Lu HQ, Shi W, Zhang J. Risk factors for ectopic pregnancy in women with planned pregnancy: a case-control study. *Eur J Obstet Gynecol Reprod Biol*. 2014;181:176 – 82.
11. Yovich JL, Turner SR, Murphy AJ. Embryo transfer technique as a cause of ectopic pregnancies in in vitro fertilization. *Fertil Steril*. 1985; 44: 318 – 21.
12. Friedman BE, Lathi RB, Henne MB, Fisher SL, Milki AA. The effect of air bubble position after blastocyst transfer on pregnancy rates in IVF cycles. *Fertil Steril*. 2011;95:944-7.
13. Shavit T, Paz-Shalom E, Lachman E, Fainaru O, Ellenbogen A. Unusual case of recurrent heterotopic pregnancy after bilateral salpingectomy and literature review. *Reprod Biomed Online*. 2013;26:59– 61.
14. Paull C, Robson SJ. Hospital admission and surgical approach to tubal ectopic pregnancy in Australia 2000 to 2014: A population-based study. *Aust N Z J Obstet Gynaecol*. 2018;58:234-8.
15. Mol F, van Mello NM, Strandell A, Strandell K, Jurkovic D, Ross J, et al. Salpingotomy versus salpingectomy in women with tubal pregnancy (ESEP study): an open-label, multicentre, randomised controlled trial. *Lancet*. 2014; 383:1483-9.
16. Newbatt E, Beckles Z, Ullman R, Lumsden MA. Ectopic pregnancy and miscarriage: summary of NICE guidance. *BMJ*. 2012; 12: e8136.