

## Case Series

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# Pregnancy outcomes of heterotopic pregnancy following IVF-ET: A case series

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## Abstract

Heterotopic pregnancy refers to the simultaneous presence of both an ectopic and an intrauterine pregnancy. This study presents a retrospective case series of Heterotopic Pregnancies (HP) subsequent to In Vitro Fertilization and Embryo Transfer (IVF-ET). Over the period spanning from July 1, 2020, to June 30, 2023, our fertility clinic encountered nine cases of HP among 4575 clinical pregnancies. All instances were identified through Transvaginal Sonography (TVS) during confirmation scans. The prevalence of HP is on the rise, likely attributed to the widespread utilization of assisted reproductive technologies. An early TVS conducted by a skilled fertility specialist or radiologist is considered crucial for prompt and effective diagnosis of HP.

**Objective:** To report a case series of Heterotopic Pregnancy (HP) following two blastocyst transfer following In Vitro Fertilization (IVF).

**Methods:** A Retrospective review study was performed to identify the HP cases after In Vitro Fertilization and Embryo Transfer (IVF-ET) in our reproductive center between July 2020 - June 2023.

**Results:** 9 out of 4575 pregnancies were diagnosed with HP. Incidence in our center is 1.96 per 1000 clinical pregnancies (0.19%) following IVF- ET. 8 patients underwent laparoscopic unilateral salpingectomy after diagnosis on the same day. Postoperatively all intrauterine pregnancies continued till term and resulted in live births.

**Conclusion:** The incidence of HP is increasing due to widespread use of assisted reproductive technology. An early diagnosis and early intervention is considered to be essential and beneficial for patient for optimal outcome of intrauterine pregnancy.

**Keywords:** Heterotopic pregnancy; In Vitro fertilization; Embryo transfer; Live birth.

## Introduction

The occurrence rate of heterotopic pregnancy in natural cycles ranges from approximately 1 in 30,000 pregnancies to 1 in 7963 pregnancies [1,2]. Factors such as increased instances of pelvic inflammatory diseases, widespread use of ovarian stimulation, and the prevalent use of Assisted Reproductive Techniques (ART) have contributed to the escalating prevalence of HP. Specifically, in women undergoing In Vitro Fertilization and

Embryo Transfer (IVF-ET), the incidence of HP can be notably high, reported as frequently as 1 in 100 pregnancies [1-4]. In our facility, the observed incidence stands at 1.96 per 1000 clinical pregnancies (0.19%) subsequent to IVF-ET procedures.

## Methodology

This case series originates from a reproductive medicine center spanning from July 2020 to June 2023. Data collection and analysis were conducted using Electronic Medical Records. Over

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**Table 1:** Results analysis.

S. No.	Type of infertility	Age	No of embryos transfer	Detection of GA at HP (weeks)	Management	Mode of art	Pregnancy outcome	Source of Oocyte	Site of Ectopic
1	Secondary	28	Two	6 weeks 6 days	Laparoscopic ectopic mass removal	ICSI-Fresh	Live Birth 38 weeks	Donor	Tubal stump
2	Secondary	31	Two	6 weeks 4 days	Laparoscopic LT salpingectomy	ICSI-FET	Live Birth 38 weeks	Self	Tubal
3	Primary	32	Two	6 weeks 2 days	Laparoscopic LT salpingectomy	ICSI-FET	Live Birth 40 weeks	Self	Tubal
4	Primary	33	Two	8 weeks	Laparoscopic RT salpingectomy	ICSI-FET	Live Birth 36 weeks 3 days	Self	Tubal
5	Secondary	30	Two	7 weeks 1 day	Laparoscopic RT salpingectomy + b/l clipping	ICSI-FET	Live Birth 36 weeks 2 days	Self	Tubal
6	Primary	33	Two	6 weeks 4 days	Laparoscopic RT salpingectomy	ICSI-FET	Live Birth 38 weeks	Self	Tubal
7	Secondary	33	Two	6 weeks 2 days	Laparoscopic LT salpingectomy	ICSI FET	Live Birth 37 weeks	Self	Tubal
8	Primary	36	Two	6 weeks 2 days	Laparoscopic left salpingectomy	ICSI Fresh	Ongoing pregnancy	Donor	Tubal
9	Primary	38	Two	6 weeks 4 days	Intracervical KCL injection under USG	ICSI FET	Live Birth 36 weeks	Self	Cervical

There was one case happened after B/L Salpingectomy, so it must be isthmic/other site

this three-year period, a total of 4575 pregnancies resulted from the IVF-ET procedure, which followed 5936 ET cycles performed at our reproductive center. The clinical pregnancy rate was documented at 77.07%. Among these pregnancies, nine cases were identified as Heterotopic Pregnancies (HP), with five patients experiencing primary infertility and four facing secondary infertility. Notably, two patients (22.2%) had a history of previous ectopic pregnancies. Additionally, in one patient, HP was detected following bilateral salpingectomy for an ectopic pregnancy.

### Case summary

Among the nine patients observed, eight experienced a tubal site for the heterotopic pregnancy, while one case occurred in the cervical region. The maternal age spanned from 28 to 38 years. Seven patients underwent ICSI-Frozen embryo transfer using their own oocytes, while two patients, facing poor ovarian reserve, opted for donor oocytes and received ICSI with fresh embryo transfer. Hemoperitoneum was detected in four cases during Transvaginal Sonography (TVS) examinations.

Among the seven patients with tubal ectopic gestation, laparoscopy and salpingectomy were chosen as the management strategy. Before surgery, all patients received intramuscular progesterone (100 mg), supplemented by vaginal progesterone gel (8% twice daily) and dihydroprogesterone (10 mg thrice daily) in the postoperative period, alongside antibiotic therapy. In one instance where a previous bilateral salpingectomy had been performed, the tubal stump retained the ectopic pregnancy, confirmed by histopathological examination.

For the patient with cervical heterotopic pregnancy, management involved KCL injection, followed by serial weekly ultrasounds monitoring the cervix. Subsequent scans indicated sac resorption, revealing a viable intrauterine pregnancy. At 13 weeks, cervical cerclage was performed. This intrauterine preg-

nancy progressed normally, culminating in preterm delivery at 36 weeks, resulting in a healthy baby despite preterm labor.

Among the eight patients with intrauterine pregnancies, all delivered healthy babies, yet three experienced preterm births (37.5%). Currently, one patient is in an ongoing pregnancy at 8 weeks. Feng Ge [17] reported a 93.8% live birth rate in sixty-five cases of heterotopic pregnancies, with surgical management conducted in 84.6% of cases.

### Discussion

The primary risk factors associated with Heterotopic Pregnancy (HP) include pelvic inflammatory disease, prior ectopic pregnancies, procedures involving assisted reproduction techniques, and ovarian hyperstimulation syndrome [11]. Notably, common clinical symptoms of HP encompass abdominal pain, the presence of an adnexal mass, peritoneal irritation, and an enlarged uterus, with vaginal bleeding being a rare occurrence compared to ectopic pregnancies.

The surge in HP cases directly correlates with the number of embryos transferred per ET cycle [5]. Several factors, including misplacement of the catheter tip, excess culture medium, or pressure during embryo injection, and endometrial bleeding from the ET procedure, might lead to embryo implantation in the fallopian tube [6].

High-resolution Transvaginal Ultrasound (TVUS) stands as a preferred and cost-effective method for diagnosing HP [7]. Research suggests that routine TVUS around Day 27 post ET can aid in the early diagnosis of HP, reducing missed diagnoses [12]. In our center, a lower incidence of HP was noted, possibly attributable to Blastocyst-stage Frozen Embryo Transfer (FET), which constituted around 65% of FET cases. Studies have demonstrated a decreased incidence of ectopic or HP occurrences after blastocyst-stage FET compared to cleavage-stage FET, with superior live birth rates [9,10].

Typically, HPs implant in the fallopian tube, with occurrences in the cervix, ovary, abdomen, and pelvis being extremely rare [16]. Approximately 60-70% of HPs result in live births, mirroring outcomes similar to singleton pregnancies [16]. However, delayed diagnosis could elevate the mortality rate for intrauterine gestation, potentially leading to maternal mortality [16]. Surgical interventions, primarily laparoscopy or laparotomy, are often used to manage HPs, with methotrexate avoided due to its teratogenic effects [11].

The surgical approach-often salpingectomy-remains the primary choice for HP treatment, tailored to each patient's clinical condition [13]. Minimizing uterine manipulation during surgery is crucial to safeguard the intrauterine pregnancy from potential complications [14]. Laparoscopic intervention is preferred for hemodynamically stable patients, ensuring minimal trauma, while laparotomy is reserved for cases of severe bleeding or hemorrhagic shock [15].

In our institute, laparoscopic surgery involved general intravenous anesthesia, maintaining CO<sub>2</sub> pneumoperitoneum pressure below 12 mmHg, and positioning the patient in a dorsal supine position. Studies have demonstrated the safety of this method for both mothers and newborns [17].



**Figure 1:** TVS image showing heterotopic live cervical pregnancy with concomitant intrauterine pregnancy.

Instances like the successful non-surgical intervention reported by Deka D involved transvaginal ultrasound-guided potassium chloride injection, resulting in a favorable outcome for a cervical heterotopic pregnancy [18]. Other cases have shown interventions like potassium chloride injections leading to delayed bleeding, necessitating additional measures like a cervical stay suture [19].

A limitation of our study was the small number of cases, and the retrospective nature made it challenging to precisely pinpoint the ectopic site in the fallopian tube, such as ampullary or interstitial locations.

### Conclusion

Heterotopic Pregnancies (HP) can occur in any woman of reproductive age, particularly in cases of induced ovulation or those undergoing IVF treatments. Increased vigilance is advised, especially during the initial ultrasound scan for patients undergoing IVF, particularly when multiple embryos are transferred. Thorough and attentive scanning of the uterus and surrounding areas is crucial for all women of reproductive age displaying clinical symptoms. Employing routine Transvaginal Ultrasound (TVUS) can aid in diagnosing HP, and early detection can significantly

impact the pregnancy's outcome, reducing complications for the patient. Laparoscopic intervention stands as the preferred treatment for hemodynamically stable patients, as it can effectively remove ectopic implantations with minimal trauma, averting intraperitoneal hemorrhage and potential complications associated with concurrent intrauterine pregnancies.

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