



Journal Homepage: - [www.journalijar.com](http://www.journalijar.com)

## INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/20647

DOI URL: <http://dx.doi.org/10.21474/IJAR01/20647>



### RESEARCH ARTICLE

#### HETEROTOPIC PREGNANCY WITH SUPERFETATION AFTER OVULATION INDUCTION WITH LETROZOLE FOLLOWED BY HEALTHY LIVE BIRTH: A CASE REPORT

Nancy S. Pillai, T. Jemela Bennet and Sukanya J.L

#### Manuscript Info

##### Manuscript History

Received: 21 January 2025

Final Accepted: 24 February 2025

Published: March 2025

##### Key words:-

Infertility Due to PCOS, Heterotopic Pregnancy, Letrozole-Assisted ovulation Induction

#### Abstract

Heterotopic pregnancy, a condition characterized by the simultaneous occurrence of intrauterine and extrauterine pregnancies, is a rare and challenging medical phenomenon. The advent of assisted reproductive technologies (ART) such as ovulation induction has further complicated the landscape of heterotopic pregnancies. This case study presents a unique occurrence of heterotopic pregnancy in a patient who underwent letrozole-assisted ovulation induction, shedding light on the complexity of this condition and its association with fertility treatments.

"© 2025 by the Author(s). Published by IJAR under CC BY 4.0. Unrestricted use allowed with credit to the author."

#### Introduction:-

Heterotopic pregnancy is a multifaceted reproductive condition defined by the coexistence of both intrauterine and extrauterine pregnancies<sup>1</sup>. While rare, its incidence has been increasing due to the rising popularity and advancements in assisted reproductive technologies (ART)<sup>2</sup>. Heterotopic pregnancies pose a diagnostic and therapeutic challenge, as their initial presentation can mimic common gynecological pathologies, leading to potential delays in accurate diagnosis and appropriate management<sup>3</sup>.

Letrozole and Clomiphene citrate are both medications commonly used for the treatment of infertility. Clomiphene citrate (CC) is a selective estrogen receptor modulator (SERM), widely used in the field of reproductive medicine. Letrozole, an aromatase inhibitor primarily used in ovulation induction, has gained significant traction in recent years as a fertility treatment option. By suppressing estrogen production, letrozole promotes follicular growth and subsequent ovulation<sup>4</sup>.

Several studies have compared the effectiveness of Letrozole and Clomiphene citrate in treating infertility<sup>5,6</sup>. Some research suggests that Letrozole may be more effective than Clomiphene citrate in achieving ovulation and

- <sup>1</sup>. Talbot K, Simpson R, Price N, Jackson SR. Heterotopic pregnancy. J Obstet Gynaecol 2011;31(1):7-12.
- <sup>2</sup>. Wang YN, Zheng LW, Fu LL, Xu Y, Zhang XY. Heterotopic pregnancy after assisted reproductive techniques with favorable outcome of the intrauterine pregnancy: A case report. World J Clin Cases 2023;11(3):669-676.
- <sup>3</sup>. Maleki A, Khalid N, Rajesh Patel C, El-Mahdi E. The rising incidence of heterotopic pregnancy: Current perspectives and associations with in-vitro fertilization. Eur J Obstet Gynecol Reprod Biol 2021;266:138-144.
- <sup>4</sup>. Kamath MS, George K. Letrozole or clomiphene citrate as first line for anovulatory infertility: a debate. Reprod Biol Endocrinol 2011;9:86.
- <sup>5</sup>. Legro RS, Brzyski RG, Diamond MP, et al. Letrozole versus clomiphene for infertility in the polycystic ovary syndrome. N Engl J Med 2014;371(2):119-29.

pregnancy rates, especially in women with PCOS. Additionally, Letrozole may have a lower risk of side effects such as thinning of the uterine lining<sup>7,8</sup>.

Understanding the complexities of heterotopic pregnancy and its association with letrozole-assisted ovulation induction is of utmost importance in the field of reproductive medicine. Such knowledge can aid healthcare professionals in timely diagnosis and appropriate management, ultimately improving patient outcomes and minimizing potential risks associated with this condition. Moreover, a comprehensive understanding of this rare occurrence will contribute to the development of evidence-based guidelines and counseling strategies for patients undergoing letrozole-based fertility treatments.

In conclusion, this case study highlights the significance of heterotopic pregnancy in the context of ovulation induction. By shedding light on the unique clinical aspects and challenges encountered in this particular case, we aim to provide valuable insights into the management of this condition and encourage further research in the field of reproductive medicine.

This study describes the ruptured tubal HTP in a patient who conceived with the aid of Letrozole, who presented at twelve weeks of gestation and was treated with an emergency laparotomy. The remaining course of the pregnancy was uneventful, with a normal full term normal vaginal delivery of a healthy infant at 38 weeks of gestation.

#### **Case Report:**

A 30-year-old second gravida at 11 weeks and 2 days of gestation, known case of PCOS (Polycystic ovary syndrome) presented to the Gynecology casualty of CSI Mission hospital, Kazhakootom with complaints of sudden onset of generalized weakness for half an hour. She was conceived after 2 cycles of Ovulation induction with Letrozole (2.5 mg once daily starting on day the second day of periods). She had a history of missed abortion at 3 months for which dilation and evacuation has done 2 years back.

On examination, patient was conscious, responding to verbal commands, pallor ++, hypotension (BP-70/50 mmHg) and Heart rate -107bpm, feeble and low volume pulse. Abdominal examination showed distended abdomen, tenderness over both right and left iliac fossa and supra pubic region. Local examination revealed no bleeding per vagina. Initially, foot end elevation given and one pint Normal saline was rushed intravenously after which her vitals was HR-100 bpm, SPO2- 98% at room air, BP -90/60 mmHg. Her hemoglobin - 7 g/dL, hematocrit - 21%

Ultrasonography revealed the presence of a viable intrauterine pregnancy with 12 weeks fetus and a massive hemoperitoneum. In view of massive hemoperitoneum patient was posted for emergency laparotomy under general anesthesia and proceed.

Initially Surgeon took over the case that revealed hemoperitoneum (1.5-2 L), blood clots present, uterus regularly enlarged at 12 weeks size, right tube slightly enlarged at the ampullary region with blood clot protruding out from the anti-mesenteric border and blood oozing from the site. Bilateral ovaries left fallopian tube and appendix was normal. So, Gynecologist was called in and Right salpingectomy was done.

Histopathology confirmed the diagnosis of ectopic pregnancy. Post operatively patient was transfused with 3 units of packed red cells and repeat Hb was 8.2 gm/dL. Patient was started on Inj. Tazomac (Piperacillin + Tazobactam). Drain was removed on post operative day 3 and the patient was discharged on post operative day 5 in good general condition.

A repeat ultrasound scan done after two weeks confirmed the viable intrauterine pregnancy. The pregnancy was continued without any significant complications. She has delivered a healthy female baby by full term normal vaginal delivery. Birth weight was 2.75 kg and her postnatal period was uneventful.

---

<sup>6</sup>. Kar S. Clomiphene citrate or letrozole as first-line ovulation induction drug in infertile PCOS women: A prospective randomized trial. *J Hum Reprod Sci* 2012;5(3):262-5.

<sup>7</sup>. Casper RF. Letrozole versus clomiphene citrate: which is better for ovulation induction? *Fertil Steril* 2009;92(3):858-859.

<sup>8</sup>. Yang AM, Cui N, Sun YF, Hao GM. Letrozole for Female Infertility. *Front Endocrinol (Lausanne)* 2021;12:676133.

**Discussion:-**

Heterotopic pregnancies, especially those accompanied by a ruptured tubal ectopic component, are an uncommon yet challenging clinical entity<sup>9</sup>. In this case report, we describe a 30-year-old woman with a history of anovulatory infertility who successfully conceived through Letrozole ovulation induction. The patient presented with symptoms of generalized weakness and supra pubic tenderness at twelve weeks of gestation, raising suspicion of an ectopic pregnancy. Our prompt diagnosis and timely intervention through emergency laparotomy proved crucial in preventing life-threatening complications. The intrauterine gestational sac corresponds to a gestational age of 11 weeks and 2 days, suggesting that intrauterine pregnancy very likely resulted from the ovulation induction that we performed. Therefore, we examined the possibility that the ruptured fimbrial ectopic pregnancy have been a superfetation pregnancy.

Superfetation is defined as the occurrence of ovulation, fertilization and implantation of a second or additional embryo(s) during a preexisting pregnancy. Commonly known to occur in various animals, superfetation has also been rarely reported in humans. Although heterotopic pregnancies suspected to be superfetation are extremely rare, there have been a few reported cases<sup>10,11</sup>. In this case report, assuming that the calculations for the establishment of the pregnancy occurred during the previous cycle, the rupture of the ectopic pregnancy may have occurred at a gestational age of 8-9 weeks considering the patient's cycles due to menstrual irregularities and unknown ovulation dates.

The risk of multiple pregnancies is elevated in patients undergoing ovulation induction, necessitating regular monitoring and early identification of such cases. In our patient, the initial presentation mimicked a possible ruptured tubal ectopic pregnancy, necessitating urgent evaluation to differentiate between heterotopic and isolated ectopic pregnancies.

Letrozole, an aromatase inhibitor commonly used for ovulation induction, increases the risk of multiple pregnancies, including heterotopic pregnancies. It is important for healthcare providers to be aware of this potential complication, especially when managing patients with PCOS and other ovulatory disorders. Counseling patients about the risk of multiple pregnancies, the possibility of heterotopic pregnancies, and the need for early prenatal care can improve outcomes in this patient population.

Early detection of heterotopic pregnancies is challenging, as they may present with variable symptoms and may be missed on routine ultrasound examinations. In our case, the presence of free fluid in the pelvis during ultrasound raised suspicion for an ectopic pregnancy, leading to further evaluation with laparotomy. Timely and accurate diagnosis is essential to initiate appropriate management and minimize adverse outcomes.

Management of heterotopic pregnancies involves the removal of the ectopic component while preserving the intrauterine pregnancy. The choice of surgical intervention, whether laparoscopy or laparotomy, depends on the clinical presentation, surgeon's expertise, and institutional resources. In our case, laparotomy proved to be an effective approach, resulting in the successful removal of the ruptured tubal ectopic pregnancy.

The remainder of the patient's pregnancy was uneventful, and she successfully delivered a healthy baby at full term through a normal vaginal delivery. The positive outcome in this case is encouraging, and it underscores the importance of prompt diagnosis and appropriate management of heterotopic pregnancies to achieve successful live births.

As demonstrated in this case, regular prenatal care and serial ultrasound assessments are essential to monitor the progress of the intrauterine pregnancy following the removal of the ectopic component. Close monitoring can help

- 
- <sup>9</sup>. Sivalingam VN, Duncan WC, Kirk E, Shephard LA, Horne AW. Diagnosis and management of ectopic pregnancy. *J Fam Plann Reprod Health Care* 2011;37(4):231-40.
- <sup>10</sup>. Kajdy A, Muzyka-Placzynska K, Filipecka-Tyczka D, Modzelewski J, Stanczyk M, Rabijewski M. A unique case of diagnosis of a heterotopic pregnancy at 26 weeks - case report and literature review. *BMC Pregnancy Childbirth* 2021;21(1):61.
- <sup>11</sup>. Ito A, Furukawa T, Nakaoka K, et al. Heterotopic pregnancy with suspicion of superfetation after the intrauterine insemination cycle with ovulation induction using clomiphene citrate: A case report. *Clin Pract* 2019;9(1):1129.

identify any potential complications, such as preterm labor or placental abnormalities, and ensure the overall well-being of both mother and baby.

**Conclusion:-**

This case illustrates a rare occurrence of heterotopic pregnancy with superfetation in a patient with a history of infertility due to PCOS who underwent ovulation induction with Letrozole. Early recognition of this complex condition and prompt intervention allowed for the successful management of the ectopic pregnancy while preserving the intrauterine pregnancy, ultimately resulting in the delivery of a healthy baby.

The management of such cases requires a multidisciplinary approach, involving gynecologists, fertility specialists, and skilled ultrasound technicians. Raising awareness about the possibility of heterotopic pregnancies with superfetation in high-risk patients undergoing ovulation induction can lead to earlier detection and improved outcomes. Further research is warranted to better understand the underlying mechanisms and risk factors associated with this unique clinical phenomenon.