

## Ectopic Pregnancy: An Investigation into the Prevalence Bias Towards the Left Side

### ARTICLE INFO

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### ABSTRACT

Ectopic pregnancy (EP) is a term for the implantation of a fertilized egg in a location than the uterus. The fallopian tubes are the primary site of ectopic pregnancy implantation. In current paper, we examined the effects of anatomical, physiological, and hormonal factors to understand of the underlying reasons behind the left-sided predominance of EPs.

**Keywords:** Ectopic Pregnancy (EP); Left Side; Prevalence; Etiology.

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## Introduction

Ectopic pregnancy (EP) refers to the implantation of a fertilized egg outside the uterine cavity, most commonly occurring in the fallopian tubes. It is a serious medical condition that requires prompt diagnosis and appropriate management to prevent complications and preserve the health of the mother. EP poses a significant global health concern, affecting women of reproductive age worldwide (1-3). The epidemiology of EP demonstrates considerable regional and global variation. The incidence of EP varies across different populations, with rates influenced by factors such as age, reproductive history, and the presence of risk factors. According to global estimates, EP occurs in approximately 1-2% of all pregnancies. However, the prevalence may be higher in specific populations, such as women who have undergone assisted reproductive technologies or those with a history of pelvic inflammatory disease or previous EP. EP imposes a substantial burden on affected individuals and healthcare systems (4, 5). The clinical outcomes of EP can range from mild symptoms to life-threatening complications. Early diagnosis and appropriate management are crucial to prevent complications such as tubal rupture, internal bleeding, and even death. The main clinical presentation of EP includes abdominal pain, vaginal bleeding, and signs of early pregnancy, such as breast tenderness and missed periods. However, EP can manifest with a wide range of symptoms, making diagnosis challenging. The consequences of EP extend beyond the immediate health risks. EP can have significant emotional and psychological impacts on women and their partners, as it may disrupt fertility plans and cause distress (6-8). While ectopic pregnancies can be found in various locations, it has been observed that they are more commonly situated on the left side rather than the right side (9). This paper aims to explore and provide a comprehensive analysis to justify this prevalent bias. In current paper we examined anatomical, physiological, and hormonal factors to gain a deeper understanding of the underlying reasons behind the left-sided predominance of ectopic pregnancies.

### Anatomical Factors

Anatomical factors play a crucial role in understanding the left-sided prevalence bias in ectopic pregnancies. Here, we will delve into the anatomical characteristics of the female reproductive system that may contribute to this bias (10).

- **Fallopian Tube Length and Curvature:** The fallopian tubes are the primary site of EP implantation. Anatomical differences in the length and curvature of the fallopian tubes between the left and right sides can

influence the likelihood of ectopic pregnancies occurring on the left side. The left fallopian tube is generally longer than the right one. This elongation can provide a greater length for the fertilized egg to travel, increasing the chances of implantation outside the uterine cavity (11, 12).

- **Tubal Damage and Obstruction:** Pathological conditions, such as tubal damage or obstruction, can affect the chances of EP occurrence. The left fallopian tube's longer length may render it more susceptible to damage or obstruction, thereby increasing the likelihood of ectopic pregnancies on the left side. Conditions like pelvic inflammatory disease (PID), endometriosis, previous surgeries, or adhesions can lead to tubal scarring, narrowing, or complete blockage, creating an environment conducive to ectopic implantation (13, 14).

- **Blood Supply:** Vascular supply to the fallopian tubes also plays a role in EP prevalence bias. Variations in blood flow between the left and right sides may affect the local environment for implantation. Differences in blood flow dynamics, including the distribution of small blood vessels, capillaries, and nutrient supply, could potentially influence the favored site of implantation (15, 16).

- **Uterine Asymmetry:** The asymmetry of the uterus may also contribute to the left-sided prevalence bias. The uterus is not perfectly symmetrical, and variations in its shape or position can affect the movement and transport of the fertilized egg. A tilted uterus or an anatomical deviation towards the left side might create conditions favoring implantation in the left fallopian tube (17).

### Physiological Factors

Physiological factors related to the reproductive system can contribute to the left-sided prevalence bias observed in ectopic pregnancies (18).

- **Ciliary Beating Pattern:** The fallopian tubes are lined with tiny hair-like structures called cilia, which have a critical role in the movement of the fertilized egg toward the uterus. The coordinated beating of cilia helps propel the embryo through the fallopian tube. Variations in the ciliary beating pattern between the left and right sides of the fallopian tubes could influence the movement and transport of the fertilized egg. If there are differences in the speed, direction, or efficiency of ciliary movement, it could affect the likelihood of left-sided implantation (19, 20).

- **Tubal Motility:** Tubal motility refers to the ability of the fallopian tubes to undergo rhythmic contractions and movements. These movements help facilitate the transportation of the fertilized egg towards the uterus. Any disruptions in the normal motility patterns of the fallopian tubes, such as altered frequency or strength

of contractions, could affect the movement of the embryo. Variations in tubal motility between the left and right sides may influence the preferred site of implantation (21).

• **Muscle Tone and Peristalsis:** The smooth muscles within the fallopian tubes play a crucial role in their contractile activity. Variations in the muscle tone or peristaltic contractions of the fallopian tubes between the left and right sides may influence the implantation site preference. Differences in the strength or frequency of muscle contractions could impact the transport and movement of the fertilized egg, potentially favoring left-sided implantation (22, 23).

• **Local Microenvironment:** The physiological environment within the fallopian tubes can also impact the site of implantation. Factors such as pH, oxygen levels, nutrient availability, and immune response can create microenvironmental differences between the left and right fallopian tubes. These variations may influence the survival and development of the embryo, potentially leading to a left-sided prevalence bias (1, 24, 25).

#### Hormonal Factors

• **Progesterone:** Progesterone is a hormone essential for maintaining a healthy pregnancy by promoting uterine lining development and preventing contractions that could expel the embryo. Hormonal imbalances involving progesterone levels can affect tubal motility and contribute to the left-sided bias in EP prevalence (26, 27).

• **Hormone Receptor Expression:** The expression of progesterone receptors on the fallopian tube epithelium may differ between the left and right sides. Variations in receptor expression or function could influence the responsiveness of the fallopian tubes to progesterone. Differences in receptor density or affinity might favor left-sided implantation (28).  
Hormonal Environment: Hormonal environments within the fallopian tubes can vary between the left and right sides. Factors such as the local concentration of progesterone and other hormones may differ, potentially influencing the likelihood of implantation on the left side. Altered hormonal environments might disrupt the natural movement of the fertilized egg, favoring left-sided implantation (29).

• **Gonadotropins:** Gonadotropins, including follicle-stimulating hormone (FSH) and luteinizing hormone (LH), play crucial roles in regulating the menstrual cycle and ovulation. Variations in the levels or activity of these hormones could impact the implantation site preference in ectopic pregnancies. Imbalances in gonadotropin levels or aberrant hormonal patterns can disrupt the normal processes of ovulation, follicular development, and tube-uterine transport. These hormonal disruptions may affect the movement and positioning of the fertilized egg, potentially contributing to the left-sided prevalence bias (32, 33).

• **Other hormonal factors:** Other hormones, such as estrogen and inhibin, also play important roles in regulating the reproductive system. Imbalances in these hormones, or variations in their local concentrations or receptor expression, could potentially contribute to the left-sided prevalence bias. However, further research is needed to elucidate the specific mechanisms and interactions involved (32, 33).

#### Conclusion

Understanding the anatomical, physiological, and hormonal factors at play in ectopic pregnancies provides valuable insights into the underlying mechanisms and potential therapeutic approaches on the bias towards the left side EP.

#### Ethical Issue

There was no ethical issue in this review.

#### Conflict of Interests

There was no conflict of interest in this study.

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#### Reference:

1. Załęcka J, Pankiewicz K, Issat T, Laudański P. Molecular mechanisms underlying the association between endometriosis and ectopic pregnancy. *International Journal of Molecular Sciences*. 2022;23(7):3490.
2. Hendriks E, Rosenberg R, Prine L. Ectopic pregnancy: diagnosis and management. *American family physician*. 2020;101(10):599-606.
3. Al Naimi A, Moore P, Brüggmann D, Krysa L, Louwen F, Bahlmann F. Ectopic pregnancy: a single-center experience over ten years. *Reproductive Biology and Endocrinology*. 2021;19:1-6.
4. Moussa B, Serge TAE, David L, Adama D, Issa O. Ectopic Pregnancy: Epidemiological, Clinical, Therapeutical, Anatomopathological Aspects and Prognosis at the Department of Obstetrics and Gynecology of the Teaching Hospital Souro Sanou of Bobo-Dioulasso: About 79 Cases

- and Literature Review. *Open Journal of Obstetrics and Gynecology*. 2022;12(1):1-10.
- . Tulandi T. Ectopic pregnancy: epidemiology, risk factors, and anatomic sites. *UpToDate*, Waltham. 2019.
- ◧. Xue Y, Tong X, Zhang H, Zhang S. Pregnancy outcomes following in vitro fertilization treatment in women with previous recurrent ectopic pregnancy. *Plos one*. 2022;17(8):e0272949.
- ◨. Attali E, Yogev Y. The impact of advanced maternal age on pregnancy outcome. *Best Practice & Research Clinical Obstetrics & Gynaecology*. 2021;70:2-9.
- ∧. Chong KY, Solangon S, Barnhart K, Causa-Andrieu P, Capmas P, Condous G, et al. A core outcome set for future research in ectopic pregnancy: an international consensus development study. *Fertility and Sterility*. 2023;119(5):804-12.
- ∩. Xiao C, Shi Q, Cheng Q, Xu J. Non-surgical management of tubal ectopic pregnancy: a systematic review and meta-analysis. *Medicine*. 2021;100(50).
- ∪. Azhar E, Green L, Mohammadi S, Waheed A, Green S. Ruptured right broad ligament ectopic pregnancy in a patient with prior right salpingo-oophorectomy: a case report. *Cureus*. 2020;12(5).
- ∩∩. Cucinella G, Gullo G, Etrusco A, Dolce E, Culmone S, Buzzaccarini G. Early diagnosis and surgical management of heterotopic pregnancy allows us to save the intrauterine pregnancy. *Menopause Review/Przegląd Menopauzalny*. 2021;20(4):222-5.
- ∩∩. Zachariah SK, Fenn M, Jacob K, Arthungal SA, Zachariah SA. Management of acute abdomen in pregnancy: current perspectives. *International journal of women's health*. 2019:119-34.
- ∩∩. Zhang Y, Wang Q, Gao C-y, Tian H-j, He W-j, Zhang X, et al. Evaluation of the safety and effectiveness of tubal inflammatory drugs in patients with incomplete tubal obstruction after four-dimensional hysterosalpingo-contrast-sonography examination. *BMC Pregnancy and Childbirth*. 2022;22(1):1-7.
- ∩∩. Gebeh AK, Metwally M. Surgical management of tubal disease and infertility. *Obstetrics, Gynaecology & Reproductive Medicine*. 2019;29(5):123-8.
- ∩∩. Chen Y, Peng P, Li C, Teng L, Liu X, Liu J, et al. Abdominal pregnancy: a case report and review of 17 cases. *Archives of Gynecology and Obstetrics*. 2023;307(1):263-74.
- ∩∩. Xu H, Cheng D, Yang Q, Wang D. Multidisciplinary treatment of retroperitoneal ectopic pregnancy: a case report and literature review. *BMC Pregnancy and Childbirth*. 2022;22(1):472.
- ∩∩. Xue R-H, Li J, Huang Z, Li Z-Z, Chen L, Lin Q, et al. Is tubal endometriosis an asymmetric disease? A 17-year retrospective study. *Archives of Gynecology and Obstetrics*. 2020;301:721-7.
- ∩∩. AKSOY RT. CLINICAL MANIFESTATIONS OF ECTOPIC PREGNANCY. *Reviews in Medical and Health Science*. 2022:17.
- ∩∩. Sodeifian F, Samieefar N, Shahkarami S, Rayzan E, Seyedpour S, Rohlf M, et al. DNAH11 and a Novel Genetic Variant Associated with Situs Inversus: A Case Report and Review of the Literature. *Case Reports in Medicine*. 2023;2023.
- ∩∩. Leslie JS, Hjeij R, Vivante A, Bearce EA, Dyer L, Wang J, et al. Biallelic DAW1 variants cause a motile ciliopathy characterized by laterality defects and subtle ciliary beating abnormalities. *Genetics in Medicine*. 2022;24(11):2249-61.
- ∩∩. Sotelo C. Ovarian ectopic pregnancy: A clinical analysis. *The Journal for Nurse Practitioners*. 2019;15(3):224-7.
- ∩∩. Uma R, Banu OM. A Case Study of Histopathological Findings in Ectopic Tubal Pregnancies with Statistical Analysis in A Tertiary Care Center.
- ∩∩. Govender I, Rangiah S, Bongongo T, Mahuma P. A primary care approach to abdominal pain in adults. *South African Family Practice*. 2021;63(1).
- ∩∩. Zhang S, Yuan L, Wang Y, Sun Z. Effect of Fu Yan Qing prescription on pelvic effusion,

- mass absorption and microenvironment of pelvic blood stasis in patients with sequelae of pelvic inflammatory disease of accumulation of dampness heat and blood stasis type. *Pakistan Journal of Medical Sciences*. 2022;38(5):1376.
٢٥. Wrona A, Aleksandrovych V, Gil A, Kurnik-Łucka M, Walocha JA, Gil K. Retrospective analysis of a case report of a left ovarian ectopic pregnancy after the former tubal. *Folia Medica Cracoviensia*. 2022:121-35--35.
٢٦. Buck RH, Joubert SM, Norman RJ. Serum progesterone in the diagnosis of ectopic pregnancy: a valuable diagnostic test? *Fertility and sterility*. 1988;50(5):752-5.
٢٧. Warrick J, Gronowski A, Moffett C, Zhao Q, Bishop E, Woodworth A. Serum activin A does not predict ectopic pregnancy as a single measurement test, alone or as part of a multi-marker panel including progesterone and hCG. *Clinica chimica acta*. 2012;413(7-8):707-11.
٢٨. Dart R, Ramanujam P, Dart L. Progesterone as a predictor of ectopic pregnancy when the ultrasound is indeterminate. *The American journal of emergency medicine*. 2002;20(7):575-9.
٢٩. Murray H, Baakdah H, Bardell T, Tulandi T. Diagnosis and treatment of ectopic pregnancy. *Cmaj*. 2005;173(8):905-12.
٣٠. Kampioni M, Chmaj-Wierzchowska K, Wszolek K, Wilczak M. Interstitial Ectopic Pregnancy—Case Reports and Medical Management. *Medicina*. 2023;59(2):233.
٣١. Männistö J, Sammalkorpi H, Niinimäki M, Mentula M, Mentula P. Association of complicated appendicitis on the risk of later in vitro fertilization treatment requirement and ectopic pregnancy: a nationwide cohort study. *Acta Obstetrica et Gynecologica Scandinavica*. 2021;100(8):1490-6.
٣٢. Nabi U, Yousaf A, Ghaffar F, Sajid S, Ahmed MMH. Heterotopic pregnancy—a diagnostic challenge. Six case reports and literature review. *Cureus*. 2019;11(11).
٣٣. Egbe TO, Nana-Njamen T, Esome H, Enow-Orock GE. Vaginal birth after laparoscopic management of heterotopic pregnancy at the Douala general hospital, Cameroon: A case report. *Tropical Journal of Obstetrics and Gynaecology*. 2020;37(1):207-9.