

## A Review on The Clinical Presentation and Management of Ectopic Pregnancy

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### Abstract:

Ectopic pregnancy (EP) is a serious condition in which implantation occurs outside the uterine cavity, accounting for about 1.2–1.4% of all pregnancies. It is a major cause of maternal morbidity and mortality during early pregnancy. Common maternal risk factors include pelvic inflammatory disease, Chlamydia trachomatis infection, smoking, previous tubal surgery, assisted reproductive techniques, and endometriosis, all of which may damage the fallopian tubes and impair embryo transport. Early diagnosis is essential to prevent complications such as tubal rupture and internal bleeding. Diagnostic methods include serum  $\beta$ -human chorionic gonadotropin ( $\beta$ -hCG), urinary hCG tests, progesterone estimation, transvaginal ultrasonography, computed tomography, and biomarkers such as vascular endothelial growth factor, creatine kinase, and ADAM-12. Among these, transvaginal ultrasound combined with serum  $\beta$ -hCG is widely used for accurate diagnosis. Treatment options depend on the patient's condition and include surgical management through laparotomy or laparoscopy, medical treatment with methotrexate, and expectant management in selected stable patients. The introduction of methotrexate has reduced the need for surgery in many cases. However, the decline in surgical treatment does not indicate a reduction in EP incidence, emphasizing the need for improved strategies for early detection and prevention.<sup>1</sup>

**Keywords:** PID (pelvic inflammatory disease),  $\beta$ -hCG, Methotrexate, laparotomy, EP (Ectopic pregnancy).

### I. INTRODUCTION:

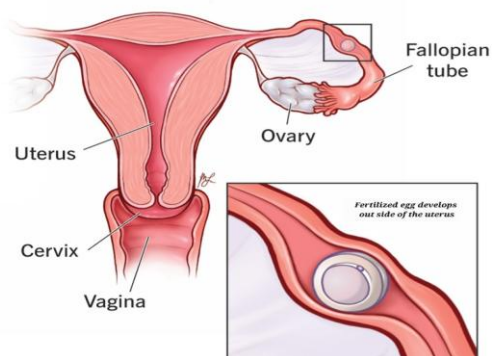
Ectopic Pregnancy, also known as extrauterine pregnancy, is derived from the Greek

word "ektos," meaning "out of place." It occurs when a fertilized egg implants outside the normal uterine cavity. More than 95% of ectopic pregnancies occur in the fallopian tubes, while less common implantation sites include the ovary and abdominal cavity. In most cases, the embryo does not survive or stops developing early. Ectopic pregnancy is a serious gynecological emergency and an important cause of maternal morbidity and mortality, especially during the first trimester of pregnancy. If not diagnosed early, it can lead to complications such as tubal rupture, severe intra-abdominal bleeding, infertility, and an increased risk of future ectopic pregnancies. Therefore, prompt diagnosis and immediate treatment are essential to prevent life-threatening outcomes.<sup>2</sup>

Over the past three decades, the incidence of ectopic pregnancy has increased worldwide. In developed countries, ectopic pregnancy accounts for approximately 4–10% of pregnancy-related deaths, and it is becoming an increasing health concern in developing nations as well. Although improvements in diagnostic techniques, such as transvaginal ultrasonography and serum  $\beta$ -hCG testing, have enabled earlier detection, ectopic pregnancy still remains a potentially life-threatening condition. Studies indicate that nearly 75% of maternal deaths during the first trimester are associated with ectopic pregnancy. In the United Kingdom, around 10,000 cases of ectopic pregnancy are diagnosed annually, with an incidence rate of approximately 11.1 per 1,000 pregnancies, which is comparable to rates reported in countries such as Norway and Australia. Research from France and several other countries has also shown a gradual increase in ectopic pregnancy rates over time. Similar rising trends have been observed in developing and Middle Eastern countries, including Saudi Arabia. These findings highlight the growing global burden of ectopic

pregnancy and emphasize the importance of early diagnosis, awareness, and effective management.<sup>3</sup>

#### Ectopic pregnancy



#### TYPES OF ECTOPIC PREGNANCY:

Ectopic pregnancy is a condition in which the fertilized ovum implants outside the normal uterine cavity. Depending on the site of implantation, ectopic pregnancy is classified into several types. Identification of the exact type is important because the clinical presentation, complications, and management may vary. The different types of ectopic pregnancy are described below.

##### 1. Tubal Pregnancy

Tubal pregnancy is the most common type of ectopic pregnancy, accounting for nearly 95% of all cases. In this condition, implantation occurs within the fallopian tube instead of the uterus. The fallopian tube is not designed to support the growth of a developing embryo; therefore, rupture and internal bleeding can occur if the condition is not diagnosed early. Tubal pregnancy is further classified into the following types based on the site of implantation within the tube.

- **Ampullary Pregnancy:** This is the most common form of tubal pregnancy. Implantation occurs in the ampulla, which is the widest portion of the fallopian tube. Because this area is relatively spacious, rupture may occur later compared to other tubal sites.
- **Isthmic Pregnancy:** Implantation occurs in the isthmus, the narrow part of the tube close to the uterus. Since this region is narrow and less elastic, rupture usually occurs earlier and may cause severe hemorrhage.
- **Fimbrial Pregnancy:** In this type, implantation occurs in the fimbrial end of the tube near the ovary. Sometimes the products of conception may be expelled into the abdominal cavity, leading to tubal abortion.

- **Interstitial (Cornual) Pregnancy:** The fertilized ovum implants in the interstitial part of the fallopian tube, which passes through the muscular wall of the uterus. This type may remain undetected for a longer period because the surrounding myometrium can stretch considerably. However, rupture can result in massive bleeding and may become life-threatening.<sup>4</sup>

##### 2. Ovarian Pregnancy

Ovarian pregnancy is a rare type of ectopic pregnancy in which the fertilized egg implants directly on or within the ovary. It may resemble a ruptured ovarian cyst clinically and is often difficult to diagnose before surgery. Risk factors include intrauterine contraceptive device usage and assisted reproductive techniques. Patients usually present with abdominal pain and vaginal bleeding. Early diagnosis and treatment are important to preserve ovarian function and prevent complications

##### 3. Abdominal Pregnancy:

Abdominal pregnancy occurs when implantation takes place within the abdominal cavity outside the uterus, fallopian tubes, and ovaries. The embryo may attach to structures such as the bowel, omentum, liver, or peritoneum. It is a rare but dangerous form of ectopic pregnancy because severe internal hemorrhage can occur due to placental attachment to abdominal organs. Patients may complain of abdominal pain, painful fetal movements, or gastrointestinal symptoms. Maternal morbidity and mortality rates are high in abdominal pregnancy.

##### 4. Cervical Pregnancy:

Cervical pregnancy is a rare ectopic pregnancy in which implantation occurs within the cervical canal below the internal os. It commonly presents with painless vaginal bleeding during early pregnancy. Risk factors include previous uterine surgeries, dilatation and curettage, and assisted reproductive procedures. Because the cervix contains abundant blood vessels and limited muscular tissue, heavy bleeding may occur during treatment. Early diagnosis through ultrasonography helps in conservative management and fertility preservation.

##### 5. Cesarean Scar Pregnancy:

Cesarean scar pregnancy is a rare but increasingly recognized type of ectopic pregnancy in which the embryo implants into the scar tissue of

a previous cesarean section. The incidence has increased with rising cesarean delivery rates worldwide. Patients may present with vaginal bleeding and abdominal pain during early pregnancy. If untreated, it may lead to uterine rupture, severe hemorrhage, and loss of fertility. Early ultrasonographic diagnosis is essential for proper management.

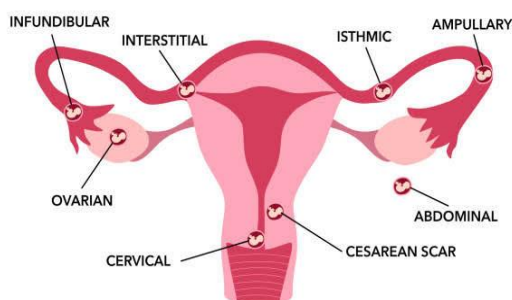
### 6. Heterotopic Pregnancy:

Heterotopic pregnancy refers to the simultaneous occurrence of both intrauterine and ectopic pregnancies. Although rare in natural conception, its incidence is higher in women undergoing assisted reproductive techniques such as in vitro fertilization (IVF). Diagnosis can be difficult because the presence of a normal intrauterine pregnancy may mask the ectopic pregnancy. Symptoms include abdominal pain and signs of internal bleeding. Early detection is important to save the intrauterine pregnancy and prevent maternal complications.

### 7. Cornual Pregnancy:

Cornual pregnancy occurs when implantation takes place in the horn of a bicornuate or malformed uterus. It is often confused with interstitial pregnancy but differs anatomically. Due to the ability of the uterine horn to stretch, rupture may occur later in pregnancy, leading to severe hemorrhage. This type is associated with high maternal risk if not diagnosed early.<sup>5</sup>

## TYPES OF ECTOPIC PREGNANCY



### ETIOLOGY:

The etiology of ectopic pregnancy refers to the causes and risk factors responsible for implantation of the fertilized ovum outside the normal uterine cavity. Normally, the fertilized egg travels through the fallopian tube and implants within the endometrium of the uterus. Any condition

that delays or interferes with the normal transport of the fertilized ovum can result in ectopic implantation. The exact **cause** of ectopic pregnancy is not always known, but several factors are strongly associated with its occurrence. Damage to the fallopian tube is considered the most important underlying factor. **Pelvic inflammatory disease (PID)**, especially infections caused by Chlamydia trachomatis and Neisseria gonorrhoeae, can damage the tubal epithelium and impair ciliary activity, increasing the risk of ectopic implantation. **Previous history of ectopic pregnancy** also significantly increases the risk of recurrence. Women who have undergone tubal surgeries, including tubal ligation, reconstructive surgery, or surgeries for infertility, are more likely to develop ectopic pregnancy due to scarring and adhesions within the tubes. Endometriosis and pelvic adhesions may also distort the normal anatomy of the reproductive organs and interfere with ovum transport.

Assisted reproductive techniques such as **In vitro fertilization (IVF)** and ovulation induction therapy are important risk factors. These procedures may alter normal embryo transport and increase the chance of implantation outside the uterus. The use of **intrauterine contraceptive devices (IUCDs)** does not increase the overall risk of pregnancy, but if pregnancy occurs with an IUCD in place, the likelihood of it being ectopic is higher.

**Smoking** is another significant risk factor because nicotine affects tubal motility and ciliary function, delaying the movement of the fertilized ovum. Hormonal imbalances, particularly altered progesterone levels, may also impair tubal contractions and contribute to abnormal implantation. **Congenital abnormalities** of the fallopian tubes or uterus can predispose women to ectopic pregnancy by interfering with the normal passage of the embryo. Increasing maternal age and multiple sexual partners are also associated with a higher risk due to the increased incidence of pelvic infections and tubal damage.<sup>6</sup>

### COMPLICATIONS:

Ectopic pregnancy is a serious medical condition that can lead to life-threatening complications if not diagnosed and treated early. Since the fertilized ovum implants outside the uterine cavity, the surrounding tissues are unable to support the growing pregnancy properly. As the pregnancy enlarges, it can damage nearby structures and cause severe maternal complications.

**1. Tubal Rupture:** Tubal rupture is the most common and dangerous complication of ectopic

pregnancy. As the embryo grows within the fallopian tube, the tube stretches and eventually ruptures because it cannot accommodate the expanding pregnancy. Rupture usually causes sudden severe abdominal pain and massive internal bleeding, requiring emergency surgical intervention.

**2. Intra-abdominal Hemorrhage:** Rupture of an ectopic pregnancy can lead to significant bleeding into the abdominal cavity. This internal hemorrhage may result in hypovolemic shock, loss of consciousness, and even death if immediate treatment is not provided.

**3. Hemorrhagic Shock:** Excessive blood loss from ruptured ectopic pregnancy may cause hemorrhagic shock. Patients may present with low blood pressure, rapid pulse, dizziness, pallor, sweating, and collapse. It is a life-threatening emergency that requires urgent resuscitation and surgery.

**4. Maternal Mortality:** Ectopic pregnancy remains one of the leading causes of maternal mortality during the first trimester of pregnancy. Delayed diagnosis and untreated rupture significantly increase the risk of maternal death.

**5. Infertility:** Damage to the fallopian tubes due to rupture, infection, or surgical removal may affect future fertility. Women with a history of ectopic pregnancy have an increased risk of infertility, especially if both tubes are damaged.<sup>7</sup>

**6. Recurrent Ectopic Pregnancy:** Women who have experienced one ectopic pregnancy are at greater risk of developing another ectopic pregnancy in future pregnancies due to persistent tubal damage or underlying risk factors.

**7. Pelvic Adhesions:** Internal bleeding and inflammation caused by ectopic pregnancy may result in the formation of pelvic adhesions. These adhesions can distort pelvic anatomy and contribute to chronic pelvic pain and infertility.

**8. Chronic Pelvic Pain:** Some women may develop long-term pelvic pain due to adhesions, scarring, or damage to reproductive organs following ectopic pregnancy or surgery.

**9. Psychological and Emotional Effects:** Ectopic pregnancy can have significant emotional and psychological impacts. Anxiety, depression, stress, grief, and fear regarding future pregnancies are common among affected women.<sup>8</sup>

#### DIAGNOSIS:

Earlier, ectopic pregnancy was diagnosed mainly through clinical symptoms such as **abdominal pain, vaginal bleeding, and amenorrhea**, but these methods were not reliable for early detection. Currently, diagnosis is mainly based on **serum  $\beta$ -hCG** estimation and

**transvaginal ultrasonography (TVS)**. Serial measurement of serum  $\beta$ -hCG levels helps assess pregnancy viability. In normal pregnancy,  $\beta$ -hCG levels usually double every 48 hours, whereas abnormal or slowly rising levels may suggest ectopic pregnancy. Serum progesterone measurement is also used as an additional marker because low progesterone levels are associated with nonviable and ectopic pregnancy. Transvaginal Ultrasonography is considered the gold standard for diagnosis. It helps identify the absence of an intrauterine gestational sac, adnexal masses, extrauterine pregnancy, and internal bleeding. Elevated  $\beta$ -hCG levels without evidence of intrauterine pregnancy on ultrasound strongly suggest ectopic pregnancy.

Other diagnostic methods include urinary hCG ratio tests, serum biomarkers such as Vascular Endothelial Growth Factor (VEGF), creatine kinase (CK), and ADAM-12, which may help in identifying ectopic pregnancy, although their clinical use is still limited. Magnetic Resonance Imaging and CT scans are rarely used but may assist in complicated or emergency cases. **Hysterosalpingography (HSG)** is useful for evaluating tubal abnormalities and infertility after treatment. Overall, early diagnosis using  $\beta$ -hCG estimation and transvaginal ultrasonography is essential to prevent complications such as tubal rupture, hemorrhage, infertility, and maternal mortality.<sup>9</sup>

#### MEDICAL MANAGEMENT:

Medical management is an important treatment option for ectopic pregnancy in carefully selected patients. It is mainly recommended for women who are hemodynamically stable, have an unruptured ectopic pregnancy, and do not show signs of severe internal bleeding. The purpose of medical treatment is to stop the growth of trophoblastic tissue, resolve the ectopic **pregnancy without surgery**, preserve the fallopian tube, and maintain future fertility. The drug most commonly used for medical management is **Methotrexate**. Methotrexate is a folic acid **antagonist that inhibits DNA synthesis** and prevents the **multiplication of rapidly dividing trophoblastic cells**. As a result, the ectopic pregnancy gradually resolves and is absorbed by the body. Medical management is considered appropriate in patients with a small ectopic mass, low serum  $\beta$ -hCG levels, absence of fetal cardiac activity, and no evidence of tubal rupture. Patients should also be willing to undergo regular follow-up and monitoring throughout the treatment period. However, methotrexate therapy is

contraindicated in women with ruptured ectopic pregnancy, severe liver or kidney disease, blood disorders, immunodeficiency, or hemodynamic instability.<sup>10</sup>

Several methotrexate treatment protocols are available. The single-dose regimen is the most commonly used method, in which **methotrexate is administered intramuscularly as a single injection**. Serum  $\beta$ -hCG levels are monitored on days 4 and 7 after treatment to evaluate response. If  $\beta$ -hCG levels decline appropriately, follow-up continues until the hormone becomes undetectable. In some patients with higher  $\beta$ -hCG levels or larger ectopic masses, multiple-dose or two-dose regimens may be used. Careful monitoring is essential during treatment. Serial  $\beta$ -hCG measurements help assess whether the ectopic pregnancy is resolving successfully.<sup>11</sup> Patients are also monitored for symptoms such as increasing abdominal pain, dizziness, or vaginal bleeding, which may indicate tubal rupture and require emergency surgery. During therapy, patients are advised to avoid alcohol, folic acid supplements, strenuous exercise, and sexual intercourse because these may interfere with treatment or increase the risk of complications. Although methotrexate is generally safe, some side effects may occur. Common adverse effects include nausea, vomiting, abdominal discomfort, stomatitis, fatigue, and transient elevation of liver enzymes. Rare complications include bone marrow suppression and severe toxicity.<sup>12</sup>

## II. SURGICAL METHOD:

Surgical treatment is an important method for managing ectopic pregnancy, especially in emergency situations such as **ruptured ectopic pregnancy, severe abdominal pain, heavy internal bleeding, or hemodynamic instability**. Historically, the first abdominal surgery for ectopic pregnancy in America was performed by **John Bard in 1759**. Later, in **1884, Robert Lawson Tait** introduced the successful surgical management of ruptured ectopic pregnancy by ligating bleeding vessels during laparotomy, which became a major advancement in treatment.<sup>13</sup> The main aim of surgery is to remove the ectopic pregnancy, control bleeding, prevent maternal complications, and preserve future fertility whenever possible. The type of surgery depends on the patient's condition, the size and location of the ectopic pregnancy, and the extent of tubal damage. **Two major surgical procedures** are commonly used for the treatment of ectopic pregnancy. The **first is salpingectomy**, in which the ectopic pregnancy is removed along with

the affected fallopian tube. This procedure is usually performed when the tube is severely damaged, ruptured, or actively bleeding. The **second procedure is salpingostomy**, where an incision is made over the fallopian tube, the ectopic pregnancy is carefully removed, and the tube is preserved. The incision may either be sutured or left to heal naturally.<sup>14</sup> Salpingostomy is mainly preferred in women who desire future fertility and have minimal tubal damage. Although surgical treatment is effective, complications such as infection, bleeding, pelvic adhesions, infertility, and anesthetic complications may occur.<sup>14</sup> Proper postoperative care, monitoring, and counseling regarding future pregnancies are important because women with previous ectopic pregnancy have an increased risk of recurrence.<sup>15</sup> Overall, early diagnosis and timely surgical intervention play a major role in reducing maternal morbidity and mortality associated with ectopic pregnancy.<sup>16</sup>

## III. CONCLUSION:

Ectopic Pregnancy remains a major cause of maternal morbidity and mortality during early pregnancy despite significant advances in diagnostic and therapeutic techniques. Early diagnosis through transvaginal ultrasonography and serum  $\beta$ -hCG estimation plays a crucial role in preventing serious complications such as tubal rupture, hemorrhage, infertility, and maternal death. Risk factors such as pelvic inflammatory disease, previous tubal surgery, smoking, and assisted reproductive techniques contribute significantly to the increasing incidence of ectopic pregnancy worldwide. Management depends on the clinical condition of the patient and includes medical treatment with Methotrexate, surgical intervention through laparoscopy or laparotomy, and careful follow-up. Early detection, proper management, and increased awareness are essential to reduce complications and improve reproductive outcomes in affected women.

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