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COMPREHENSIVE REVIEW ON ECTOPIC PREGNANCY

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ABSTRACT

The implantation of a fertilized ovum outside the uterine cavity exists as a critical worldwide contributor to maternal death and serious medical conditions. A fertilized ovum developing outside the uterine cavity occurs most frequently in a fallopian tube. The review explores all aspects of ectopic pregnancy starting from its demographics to diverse risk elements along with the biological mechanisms and signs of patients and techniques for detection and approaches for management. The recent advancements in early detection together with imaging technology have improved patient survival rates but EP continues to be the major cause of pregnancy death during the first trimester. The treatment strategy for EP depends on clinical presentation and patient stability due to three available options of expectant management combined with medical and surgical treatments. The article features latest trends about pre-empting and treating early pregnancy losses together with requiring early detection along with customized treatment approaches.

KEYWORDS: Ectopic Pregnancy, Tubal Pregnancy, Diagnosis, Management, Complications.

INTRODUCTION

Pregnancy begins with a fertilized egg. Normally, the fertilized egg attaches to the lining of the uterus. An ectopic pregnancy occurs when a fertilized egg implants and grows outside the main cavity of the uterus. An ectopic pregnancy most often occurs in a fallopian tube, which carries eggs from the ovaries to the uterus. This type of ectopic pregnancy is called a tubal pregnancy. Sometimes, an ectopic pregnancy occurs in other areas of the body, such as the ovary, abdominal cavity or the lower part of the uterus (cervix), which connects to the vagina. An ectopic pregnancy can't proceed normally. The fertilized egg can't survive, and the growing tissue may cause life-threatening bleeding, if left untreated.[1]

Ectopic pregnancy

Ectopic pregnancy (EP) ruptures are the leading cause of maternal mortality within the first trimester of pregnancy with a rate of 9%–14% and an incidence of 5%–10% of all pregnancy-related deaths. A gestational sac (GS) that implants in a location that is not the uterus is defined as an EP. Women with an EP may have nonspecific symptoms such as lower abdominal pain and vaginal bleeding, often presenting clinically similar to appendicitis, urinary calculi, early pregnancy loss, or trauma. Women with this presentation in the first trimester have EP prevalence in emergency departments as high as 18%, which can be easily misdiagnosed as the previously described clinical mimics.

Table 1: Types of ectopic pregnancy (EP) and incidence.

EP type	Description	Incidence	Characteristics
Tubal	Gestational sac (GS) implants in the fallopian tube	95%	–
Interstitial	GS implants in interstitial portion of fallopian tube and transverses the myometrium in the uterine fundus	2%–4%	May present later in pregnancy[2]
Cesarean Scar (CSP)	GS implants into the anterior uterine wall of lower uterine segment where Cesarean scar resides	<1%	Treatment has a high success and high complication rate
Heterotopic	Concomitant intrauterine pregnancy (IUP) and EP	1%–3%	Difficult to manage if desired IUP
Cervical	GS implants in the mucosa of the endocervical canal	<1%	Dilation and curettage in a previous pregnancy in 70% of cases
Ovarian	GS implantation in the ovaries	<3%	81% associated with concomitant intrauterine devices
Abdominal	GS implants in the peritoneal cavity of the abdomen	~1%	There are some reported cases of term deliveries of healthy babies

METHODOLOGY

A systematic search was conducted using databases such as PubMed, Scopus, Web of Science, and Google Scholar. Keywords included ectopic pregnancy, tubal pregnancy, risk factors, diagnosis, management, and complications. Peer-reviewed journal articles, clinical trials, and meta-analyses published within the last two decades were prioritized.

DISCUSSION

How ectopic pregnancy occurs

Ectopic pregnancy is a condition in which a fertilized egg implants and begins to grow outside the main cavity of the uterus, most commonly in one of the fallopian tubes. Normally, a fertilized egg travels through the fallopian tube to the uterus, where it implants and grows. However, in an ectopic pregnancy, the egg becomes stuck in the tube or, less commonly, in other areas like the ovary, cervix, or abdominal cavity.

This type of pregnancy is not viable and can be life-threatening if not treated promptly. The growing embryo can cause the fallopian tube to rupture, leading to severe internal bleeding, which is a medical emergency. Symptoms of ectopic pregnancy can include abdominal pain, vaginal bleeding, dizziness, and shoulder pain, but these can also mimic symptoms of other conditions.

Epidemiology

It has been reported that 1.3–2.4% of all pregnancies are extrauterine. The true frequency cannot be estimated any more accurately than this, because statistics generally reflect only cases treated in the hospital and with surgery. In the mid-twentieth century, it was estimated that 0.4% of all pregnancies in the USA were extrauterine; recent data show a current figure higher than 1.4%. In Germany today, there are an estimated 20 extrauterine pregnancies for every 1000 live births.[7] The rising frequency of (diagnosed) extrauterine pregnancies is due to a number of factors, including:

- The increased utilization of assisted reproductive technology,
- The increasing number of operations performed on the fallopian tubes,
- Rising maternal age, and
- More sensitive diagnosis

Etiology

Ectopic pregnancy, in essence, is the implantation of an embryo outside of the uterine cavity most commonly in the fallopian tube. Smooth muscle contraction and ciliary beat within the fallopian tubes to assist the transport of an oocyte and embryo. Damage to the fallopian tubes, usually secondary to inflammation, induces tubal dysfunction which can result in retention of an oocyte or embryo. There are several local factors, such as toxic, infectious, immunologic, and hormonal, that can induce inflammation. There is upregulation of pro-inflammatory cytokines following tubal damage; this subsequently promotes embryo implantation, invasion, and angiogenesis within the fallopian tube. Chlamydia trachomatis infection results in the production of interleukin 1 by tubal epithelial cells; this happens to be a vital indicator for embryo implantation within the endometrium Interleukin 1 also has a role in downstream neutrophil recruitment which would further contribute to fallopian tubal damage. Cilia beat frequency is negatively affected by smoking and infection. Hormonal variations throughout the menstrual cycle additionally have demonstrated effects on cilia beat frequency.[8]

Ectopic implantation can occur in the cervix, uterine cornea, myometrium, ovaries, abdominal cavity, etc. Women with tubal ligation or other post-surgical alterations to their fallopian tubes are at risk for ectopic pregnancies as the native function of the fallopian tube would bealtered. The patient additionally can have an ectopic pregnancy with a concurrent intrauterine pregnancy, as known as a heterotopic pregnancy.[9]

Pathophysiology

The most common site of ectopic implantation is a fallopian tube, followed by the uterine cornua (referred to as a cornual or an interstitial pregnancy). Pregnancies implanted in the cervix, a caesarean scar, an ovary, or the abdomen are rare.

Heterotopic pregnancy (simultaneous ectopic and intrauterine pregnancies) occurs in only 1/10,000 to 30,000 pregnancies but may be more common among women who have had ovulation induction or used assisted reproductive technologies such as in vitro fertilization and gamete intrafallopian tube transfer (GIFT); in these women, the overall reported ectopic pregnancy rate is 1 to 2%.

The anatomic structure containing the fetus usually ruptures after about 6 to 16 weeks. Rupture results in bleeding that can be gradual or rapid enough to cause haemorrhagic shock. The later in the pregnancy the rupture occurs, the more rapidly blood is lost and the higher the risk of death[10]

Histopathology

The most common site for ectopic pregnancy adherence is in the ampullary region of the fallopian tube. Reportedly 95% of ectopic pregnancies develop in the ampulla, infundibular, and isthmic portions of the fallopian tubes.[11] With caesarean scar pregnancies, there is a migration of blastocyst into the myometrium due to residual scarring defect from prior c-section. The depth of implantation determines the type of caesarean scar pregnancy with type 1 having proximity to the uterine wall and type 2 implanting closer to the urinary bladder.[12]

Consequences

Ectopic pregnancy occurs when a fertilized egg implants outside the uterus, typically in one of the fallopian tubes. If it is not recognized and treated, there could be serious consequences, such as:

A dangerous medical condition is ectopic pregnancy rupture. If the ectopic pregnancy becomes large enough, the fallopian tube may rupture, causing internal bleeding. Given the potential for death, this requires immediate medical attention.

Severe Abdominal Pain and Internal Bleeding:

An ectopic pregnancy rupture can cause severe abdominal pain, fainting, confusion, and signs of shock from blood loss

- Infertility
- Severe pain
- Future ectopic pregnancy
- Death (if un treated)
- Shock (hypovolemic shock)
- Increased rate of mis carriage
- Emotional trauma[28]

Complications

Women who present early in pregnancy and have testing suggestive of an ectopic pregnancy would jeopardize the viability of an intrauterine pregnancy if given Methotrexate.[11] Women who receive the single-dose Methotrexate regimen are at high risk of treatment failure if the HCG level does not decrease by 15% from day 4 to day 7 thus prompting second-dose regimen.[13] Women presenting with vaginal bleeding and pelvic pain may be misdiagnosed as an abortion in progress if the ectopic pregnancy is at the cervicalos. The patient may have a cervical ectopic pregnancy and would thus run the risk of haemorrhage and potential hemodynamic instability if a dilation and curettage is performed.[4] Complications from management extend to treatment failure, in that women may present with/or develop hemodynamic instability which can result in death despite early operative interventions.

Reasons

- **Previous ectopic pregnancy:** There is an increased risk of a subsequent ectopic pregnancy after someone has experienced an ectopic pregnancy.
- **Fertility treatment:** There is a chance of ectopic pregnancy resulting from embryo transfer during IVF treatment as embryos can travel into the Fallopian tube, for example, during the implantation stage. The more embryos that are transferred, the higher the risk.

- **Pelvic Inflammatory Disease:** This is a past infection of the Fallopian tubes caused, for example, by a sexually transmitted infection like chlamydia trachomatis.
- **Endometriosis:** This is a condition where cells like the ones lining the womb grow elsewhere in the body but still react to the menstrual cycle each month and bleed despite there being no way for the blood to leave the body. It is not known why endometriosis increases the risk of ectopic pregnancy.
- **Abdominal surgery:** Any previous operation on the tummy, such as caesarean section or appendicectomy.
- **Intrauterine Device (IUD):** Intrauterine devices (coil) prevent pregnancy in the womb but is less effective in preventing pregnancy in a Fallopian tube.
- **Emergency contraception:** It is possible to become pregnant in the same cycle after trying to prevent pregnancy with emergency oral contraception. While not proven, there is the biological plausibility that emergency contraception could increase the risk of ectopic pregnancy. If the emergency contraception is effective and manages to prevent ovulation, it will decrease the risk, but if it fails to do so, there may be an increased risk of ectopic pregnancy.
- **Cigarette smoking:** Research by the University of Edinburgh shows that smokers have an increased level of the protein PROKR1 in their Fallopian tubes. The protein is instrumental in helping pregnancies implant in the womb, but when present in the Fallopian tubes can hinder the progress of a fertilised egg, increasing the chances of a pregnancy being ectopic.[14]

Prevention

There's no way to prevent an ectopic pregnancy, but here are some ways to decrease your risk:

- Limiting the number of sexual partners and using a condom during sex helps to prevent sexually transmitted infections and may reduce the risk of pelvic inflammatory disease.
- Don't smoke. If you do, quit before you try to get pregnant.

Symptoms

Nausea and breast soreness are common symptoms in both ectopic and uterine pregnancies.

The following symptoms are more common in an ectopic pregnancy and can indicate a medical emergency:

- Sharp waves of pain in the abdomen, pelvis, shoulder, or neck.
- Severe pain that occurs on one side of the abdomen.
- Light to heavy vaginal spotting or bleeding.
- Dizziness or fainting.
- Rectal pressure

Diagnosis and treatment of ectopic pregnancy

- If pregnancy cannot be found inside the uterus in a patient with b-hCG values higher than 2000 mIU/mL, physician must consider this situation very suspicious of EP until surely excluded.[16]
- Making EP diagnosis can be a real challenge, but transabdominal or, when possible, transvaginal ultrasound (TVUS) is a precious tool that in expert hands can be useful for diagnosis especially in initial work-up. Like reported until 6-week pregnancy, tool sensitivity is only 56%. When fetal heartbeat observed at an ectopic implantation by TVUS is evidence of an ectopic pregnancy. A common mistake in TVUS examination is recognizing as haemorrhagic corpus luteum or luteal cyst what in reality is a gestational chamber. For patients who

undergo in vitro fertilization (IVF) ultrasound detection can be even harder due to intense ovarian activity. Even if intrauterine pregnancy is found adnexa should be always checked, remembering that adnexal masses are not visible until mass size is around 2 cm, measures that are usually reached at 7 weeks of gestation, and that pulsation from embryonic pole is not always found. If high velocity, low resistance is found at Doppler examination, this could be a consequence of developing trophoblast, with increase of flow, in the typical “ring of fire” image. Identification of this is particular pattern in the adnexa increases sensitivity of EP diagnosis to 73%.[17,18]

- Some authors recommend using 3D ultrasound (US) with the scope of determine EP exact location. This ultrasound tool reproduces uterine coronal plane starting by orthogonal plans. Transparency mode functioning with this methodic provides complete vision of the whole salpinx even of the interstitial portion. This modality is very useful to precisely define EP site, such as angular and cornual pregnancy giving possibility to plan appropriate treatment in a short time.[19,20]
- Considering that these particular EP subtypes arise in high vascularized zones, a correct pre-surgical staging with ultrasound is fundamental.[21,22]
- 3D examination is also useful for differentiate between interstitial or angular pregnancy, due to a live baby can born.[23]
- Ultrasound can fail with abdominal pregnancies diagnosis. For these reasons, physician can use other imaging tools to locate pregnancy and, in a surgery-need scenario, make an accurate pre-surgical staging. Magnetic resonance imaging (MRI) and Computed Tomography (CT) have a key-role in confirming diagnosis, especially determining anatomic location and vascular supports excluding or confirming placental accretism. Frequently CT is used as imaging modality of choice in the evaluation of acute abdomen mainly in trauma setting. The pregnancy status should be checked before performing any radiologic imaging procedure. MRI does not provide ionizing radiation, can produce multiplanar imaging, gives great contrast between tissues and fluids. In the need of identification of haemorrhage and air bubbles T2-weighted images are the best choice. Contrast-enhanced imaging plays a main role in determining the presence of bleeding, as shown by extravasation, lesion vascularity and relation of the mass with pelvic vessels.[24,25]
- The ultrasonographic criteria for cornual pregnancy diagnosis are: an empty uterine cavity, a gestational sac located eccentrically and 1 cm from the most lateral wall of the uterine cavity, and a thin (<5 mm) myometrial layer surrounding the gestational sac.
- Traditionally, treatment of cornual pregnancy can been surgical and may include hysterectomy or cornual resection by laparotomy or laparoscopy.

Treatment options

A fertilized egg can't develop normally outside the uterus. To prevent life-threatening complications, the ectopic tissue needs to be removed. Depending on your symptoms and when the ectopic pregnancy is discovered, this may be done using medication, laparoscopic surgery or abdominal surgery.

Medication

An early ectopic pregnancy without unstable bleeding is most often treated with a medication called methotrexate, which stops cell growth and dissolves existing cells. The medication is given by injection. It's very important that the diagnosis of ectopic pregnancy is certain before receiving this treatment. After the injection, your doctor will order

another human chorionic gonadotropin (HCG) test to determine how well treatment is working, and if you need more medication.

Laparoscopic techniques

- Two laparoscopic procedures used to treat some ectopic pregnancies are salpingostomy and salpingectomy. In theoperation, a small incision is created in the belly, near or in the navel. Next, your physician views the tubal region using a laparoscope, a thin tube fitted with a camera lens and light.
- With a salpingostomy, the tube is allowed to heal naturally after the ectopic pregnancy is removed. A salpingectomy involves the removal of both the tube and the ectopic pregnancy.
- The extent of the damage and bleeding, as well as if the tube has burst, will determine which operation you need. Whether your other fallopian tube is healthy or exhibits symptoms of previous damage is another consideration.

Surgery during an emergency

If the bleeding is severe due to the ectopic pregnancy, you may require immediate surgery. Either a laparotomy or an abdominal incision can be employed for this. The fallopian tube might be saved in some situations. Typically, however, a ruptured tube must be removed.

The ectopic pregnancy is condition in which the fertilized egg implants and grows outside of the uterus and most commonly in a fallopian tube, which can be leads to the serious complications like internal bleeding, rupture of tissue and life threatening condition. the ectopic pregnancy is a major clinical problem ,world widely it occurring in 75,000 cases per year the rate of ectopic pregnancy is increased in nowadays and this condition is having the symptoms like severe pain on one side of the abdomen ,pelvis and shoulders light to heavy vaginal bleeding dizziness or fainting, rectal pressure the reason of this condition is previous ectopic pregnancy, fertility treatment, pelvic inflammatory disease, intrauterine devices, cigarette smoking during the pregnancy this are the main reason to cause the ectopic pregnancy.

Various types of ectopic pregnancy sites they are interstitial, ampullary, fimbria, ovarian, abdominal, cervical this conditions causes to the severe health problems in the Women's and the common presentation of EP is vaginal bleeding and lower abdominal pain in a women with amenorrhea was 47.5% The women who have this condition of EP typically complain of the brown vagina discharge soon after a missed period some times progressing to heavier bleeding similar to a miscarriage only bleeding was 18.3% ,and abdominal pain 9.7%. The diagnosis of this ectopic pregnancy based on the detection of beta human chorionic gonadotropin and ultra sound scan, beta-hCG can be detected in pregnancy as early as eight days after ovulation and laparoscopy methods can be detect the ectopic pregnancy condition in the women's the treatments options of the EP is expect management and methotrexate medicine and surgery is used to remove the pregnancy, usually along with the affected fallopian tube. The ectopic pregnancy is majorly occurred in the population some preventive measure should be taken that are limiting the number of sexual partner and using the condoms during the sex to prevent the STD and may be reduce the risk of pelvic inflammatory disease and don't smoke. If you do, quit before you try to get the pregnant.

CONCLUSION

Ectopic pregnancy, a serious condition requiring the prompt diagnosis and treatment can be leads to significant maternal morbidity and mortality if not managed effectively, early detection of an EP is fundamental for avoiding the

life threatening complications. The pelvic ultrasound still the best diagnostic tool for the peri uterine pregnancy and the proper medications are used to cure the condition and also emergency surgery method for EP.

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