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Ectopic Pregnancy: A Review

Emmanuel Ifeanyi Obeagu¹, Mohamud Hussein Faduma², Getrude Uzoma Obeagu³, Chekwube Catherine Agu⁴ and Sophia Kazibwe⁵

¹Department of Medical Laboratory Science, Kampala International University, Uganda.

²Department of Obstetrics and Gynaecology, Kampala International University, Uganda.

³Department of Nursing Science, Kampala International University, Uganda.

⁴University of Nigeria Teaching Hospital, Enugu, Nigeria.

⁵Department of Public Management, Management Science, Human Resource Management, Kampala International University, Uganda.

Abstract

Ectopic pregnancy is a life-threatening gynecological emergency and a major cause of maternal mortality and morbidity all over the world. It accounts for 75% of maternal deaths in early pregnancy thus in most developing countries including Uganda, ectopic pregnancy is among the common causes of first-trimester maternal death. All identified risk factors are maternal: pelvic inflammatory disease, Chlamydia trachomatis infection, smoking, tubal surgery, induced conception cycle, and endometriosis. Nonetheless, these risk factors vary from one study to another and from place to place.

Keywords: pregnancy, ectopic pregnancy, types of ectopic pregnancy, risk factors of ectopic pregnancy

Introduction

Ectopic pregnancy is an abnormal condition in which implantation of the blastocyst occurs outside the endometrium of the uterus [1-7]. Ectopic pregnancy may be asymptomatic [8], and its diagnosis depends on a clinical presentation together with serum beta-human chorionic Gonadotropin (-HCG) measurement and imaging using ultrasound [9].

The commonest clinical presentation are abdominal pain [10], vaginal bleeding and missed period [11]. Ectopic pregnancy can cause ruptures of fallopian tube, cervix and abdomen on which they are implanted [12]. At least 90% of all Ectopic pregnancies are located in the fallopian tube, and 80% of these are located in the ampullary segment of the tube [13].

Globally, ectopic pregnancy occurs in approximately 1–2% of pregnancies [12] and its global prevalence has been increasing exponentially [14]. A study done in China found that prevalence of ectopic pregnancies being 7.93% and most common presenting complaints were bleeding accompanied by abdominal pain [15] and in the kingdom of Saudi Arabia (KSA) it ranges between 0.58-1.5 % [16]. The prevalence of EP has been estimated to be 1-2 % of all natural pregnancies worldwide and in the kingdom of Saudi Arabia (KSA) it ranges between 0.58-15 % [17].

Ectopic pregnancies

The word “ectopic” defines a pregnancy that occurs anywhere apart from the uterus; the fallopian tube is the most commonly reported site of EP with over 95.5 % implanting in the fallopian tube [16]. Ectopic pregnancy (EP) or extra uterine pregnancy, accepted from the Greek word “ektapos” meaning out of place [18]. An ectopic pregnancy developing within the cervix is uncommon, accounting for less than 1% of all ectopic pregnancies. This type of pregnancy can be life-threatening because of the very high risk of hemorrhage [19]. EP is further common in women who have suffered with pelvic inflammatory disease (PID) and more than 50 % of women who have been infected are unaware of the exposure of PID. Moreover, it is due to difficulties in determining the effect of female genital chlamydial infection on reproductive outcome arise from flaws in specific study design and the lack of a reliable method for measuring a history of pelvic infection [18].

Various types of ectopic pregnancies

There are various types of ectopic pregnancies (EPs) but the fallopian tube is the dominant site in the majority of cases of tubal ectopic pregnancy. 75–80 % of EPs occur in the ampullary portion, 10–15 % of EPs occur in the isthmic portion and about 5 % of EP is in the fimbrial end of the fallopian tube [18]. The tubal EP can be detected by TVS, and implies an intact fallopian tube with a pregnancy that is likely to be growing and

visualized of an inhomogeneous mass that might well be a collapsed sac, which is less likely to contain active trophoblastic tissue [18].

Ovarian ectopic pregnancy (OEP) is one of the rarest variants, and incidence is estimated to be 0.15–3 % of all diagnosed OEP. Early diagnosis is necessary to avoid more serious complications and emergency invasive procedures; moreover, Panda et al. said that its preoperative diagnosis remains a challenge, and it cannot be early diagnosed. Medical therapy with MTX was not a possible option due to the occurrence of massive bleeding [18].

Cesarean scar ectopic pregnancy (CSEP) is another rarest form of EP with an incidence of 1:1,800 pregnancies due to increased number of cesarean deliveries over the last 30 years. It is widely spreading in society. Here, the gestational sac is implanted in the myometrium at the site of a previous cesarean section. Various complications, such as uterine rupture and massive hemorrhage, may be life threatening and impact negatively on future fertility in case of CSEP. The etiology of cesarean scar pregnancy is unclear although previous cesarean section, myomectomy, adenomyosis, IVF, previous dilatation and curettage, along with manual removal of placenta have been linked as risk factors for such type of EP [18].

Interstitial pregnancy (IP) constitutes 2.5 % of all EP. Correct diagnosis of IP can be quite difficult and it requires accurate ultrasound interpretation. The diagnosis relies heavily on ultrasound and potentially on laparoscopic evaluation. It is performed by visualization of the interstitial line adjoining the gestational sac and the lateral aspect of the uterine cavity followed by continuation of the myometrial mantle around the ectopic sac. The traditional treatment of interstitial pregnancy has been corneal resection or hysterectomy in cases of severely damaged uterus [18].

Risk factors of ectopic pregnancy

Many factors have been blamed for an increased prevalence of EP, the most common being advancing age, smoking, parity, previous EP, abortion, pelvic inflammatory disease (PID), sexually transmitted infections, and postabortion sepsis. In vitro fertilization is known to be a serious risk factor for EP [16].

Age is the risk of EP increases with advancing maternal age, with age over 35 years being a significant risk factor. Hypotheses for this association include the higher probability of exposure to most other risk factors with advancing age, increase in chromosomal abnormalities in trophoblastic tissue and age-related changes in tubal function delaying ovum transport, resulting in tubal implantation. The incidence of EP showed a steady increase with the increase in maternal age at conception from 1.4 % of all pregnancies at the age of 21 years to 6.9 % of pregnancies in women aged 44 years or more [20].

Cigarette smoking is the major cause of one-third of all cases of EP. Most studies investigating the effect of smoke on the fallopian tube have been performed in rodents and relate to cigarette smoke's effect on ciliary beat frequency and smooth muscle contraction. Furthermore, the reason why smoking cause tubal ectopic pregnancy is not understood. Tubal EP is thought to be a consequence of embryo retention within the fallopian tube due to impaired smooth muscle contractility and alterations in the tubal microenvironment. The cigarette smoking increases transcription of prokineticin receptor 1 (PROKR1), a G-protein-coupled receptor. The PRO-KRs are receptors for PROK1, a molecule known for its angiogenic properties, control of smooth muscle contractility, and regulation of genes important for intrauterine implantation [18].

EP is more common in women attending infertility clinics even in the absence of tubal disease. In addition, the **use of assisted reproductive technology (ART)** increases the

rate of EP. The rate of tubal EP following in vitro fertilization (IVF) still remains higher (approximately 2–5 %) than the rate of tubal EP with spontaneous pregnancy (1–2 %). The reason for the increased incidence of tubal EP by IVF is unclear. The technique of embryo transfer is a potential cause but there is little evidence to support this. The risk of tubal EP has also been reported to increase with the number of embryos that are transferred during IVF treatment [18].

Women with a **previous history of EP** also have an increased risk, which increases further in proportion to the number of previous EP. In Shaw et al.'s study, the OR for having an EP was 12.5 % after one previous EP and 76.6 % after two [17].

Prior tubal surgery (salpingostomy, neosalpingostomy, fimbrioplasty, tubal reanastomosis, and lysis of peritubal or periovarian adhesions) has an increased risk for developing EP. This in turn depends on the degree of damage and the extent of anatomic alteration [18].

Some **types of contraception**, such as progestogen only contraception and the intrauterine contraceptive device are associated with an increased incidence of EP when there is contraceptive failure, without necessarily increasing the absolute risk of EP. According to Patil et al., case control examination of the risk of the EP has been linked with the fourfold elevation after OI with clomiphene citrate or injectable gonadotrophins therapy [18].

Conclusion

Ectopic pregnancy (EP) presents a major health problem for women of child-bearing age. EP refers to the pregnancy occurring outside the uterine cavity that constitutes 1.2–1.4 % of all reported pregnancies. All identified risk factors are maternal: pelvic inflammatory disease, Chlamydia trachomatis infection, smoking, tubal surgery, induced conception cycle, and endometriosis. Nonetheless, these risk factors vary from one study to another and from place to place.

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