Review Article

Ectopic Pregnancy Diagnosis and Management Approach: Literature Review

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Abstract

Background: Ectopic pregnancy is a condition in which the fertilized ovum, or blastocyst, gets faultily implanted at a site other than the uterine endometrium. It is not an uncommon condition. It presents in early pregnancy and could be potentially lethal to the mother. Hence, thorough knowledge of its risk factors, how it happens, how to diagnose it and treat it in the acute setting are of great importance in health care providers. **Objective:** Our aim is to discuss ectopic pregnancy in terms of anatomical sites, risk factors, clinical presentation, and emergency treatment. **Methods:** We searched PubMed for ectopic pregnancy, and its anatomical sites, presentation, risk factors, and treatment as keywords. **Conclusion:** Ectopic pregnancy is a potentially lethal condition that might turn the expected joy of a family into misery. In the vast majority of cases, it is tubal. Yet, extra-tubal ectopic pregnancy is not uncommon. It should be always put at the top of the differential diagnosis, whenever a lady in her childbearing age shows with first-trimester vaginal bleeding and/or abdominal pain. Once the diagnosis of ectopic pregnancy is confirmed, the patient should be first screened for the suitability of medical therapy using methotrexate before choosing a surgical approach.

Keywords: Ectopic pregnancy, vaginal bleeding, Extra- uterine pregnancy

Introduction

Female reproductive system consists of two ovaries, fallopian tubes and uterus. Ovaries are responsible for monthly release of an egg for possible fertilization by a sperm. Fallopian tubes are tubular structures that act as a pathway to allow passage of the female egg from ovaries to uterus for implantation. When sperm is introduced, it will pass its way through cervix and reach tubes in order to fertilize the egg forming an embryo. The fertilized egg will pass through fallopian tubes and will be implanted in uterus endometrium. Ectopic pregnancy occurs when fertilized egg is implanted elsewhere outside the uterus, mostly in the fallopian tubes [1].

Ectopic pregnancy is considered a common cause of morbidity and mortality in females of reproductive age. The causes that of ectopic pregnancy remains unclear, but various risk factors have been identified [2].

Ectopic pregnancy is one of the differentials of painful vaginal bleeding in early pregnancy. It is potentially life threatening and even if a patient is survived, it can be a possible source of distress to her and her family. The diagnosis of ectopic pregnancy might be challenging. At the moment, diagnosis depends on ultrasound scanning and serial serum beta-human chorionic gonadotrophin (β-hCG) measurements. Ectopic pregnancy can be managed medically or surgically, depending on the severity of the condition [2, 3].

Methodology

PubMed database was used for articles' selection through using the following keywords: Ectopic Pregnancy, Ectopic

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Pregnancy Management and Diagnosis. The Inclusion criteria were the articles relevant to the project having focused on ectopic pregnancy diagnosis and management, abdominal or ovarian pregnancy, and complication of ectopic pregnancy. The exclusion criteria were all other articles that did not have a related aspect to ectopic pregnancy as their primary endpoint or repeated studies.

Discussion

Ectopic pregnancy is when the blastocyst gets implanted outside (i.e. ectopic) the endometrium of the uterine cavity. Any place a blastocyst can get into is a potential site for ectopic pregnancy. Nevertheless, over 95% of cases are tubal pregnancies. Tubal pregnancy is an ectopic pregnancy in the Fallopian tube [1]. Within the tube, the most common site is the ampulla (over 70% of cases), followed by the isthmus, fimbriae and then tubal interstitium. Other extra-tubal locations include ovarian and abdominal [2].

Epidemiology:

Despite the great improvements that have been achieved in approaching and managing this condition, tubal ectopic pregnancy is still the leading cause of maternal mortality in the first trimester of pregnancy. The incidence of this potentially lethal condition is difficult to calculate considering that less patients are being treated as inpatients [4]. Also, its incidence varies across time and place. For example, in the United States, one study of one large health network for a 3-year period estimated the rate of ectopic pregnancy to be 20.7 per 1000 pregnancies [5]. Another and more recent study, which is also conducted in the US, showed much lower rate (6.4 per 1000 pregnancies). It also showed that older ages have the highest rates [6]. Similarly, a local study, which was a retrospective study done in Abha City of Saudi Arabia (SA), found an incidence of 0.74% with an impressive mortality of 0% [7]. In another study at King Fahd University Hospital at Al-Khobar where they conducted a retrospective analysis of a 10-year period, the results showed a prevalence of 1.13%, and concluded that this figure is within the range reported in the literature [8].

Risk factors:

Most risk factors have one thing in common, which is causing disruption in the normal tubal anatomy and/or function. By far, the most important risk factor is previous history of an ectopic pregnancy. If a lady developed it once, she is at risk of developing it again 3-to-8 times higher than pregnant ladies who have never experienced it [9]. Other risk factors include pelvic inflammatory disease (PID), tubal surgery, increasing age and cigarette smoking in the periconceptional period. One interesting risk factor is the use of contraception; either hormonal or the use of intra-uterine device. Ladies on these contraceptive methods have a very low chance of conceiving and getting pregnant. However, if they do get pregnant, they are at higher risk of developing ectopic pregnancy as compared to ladies who get pregnant off contraception. In other words, the absolute number of ectopic pregnancies among women on hormonal contraception or IUD is lower than other women, but proportions of pregnancies that are ectopic if higher. All these risk and others were explored in great depth in a large case-control study done in France between the years 1993 and 2000 [10].

Clinical Presentation:

Women with ectopic pregnancy can be asymptomatic in the first few weeks of pregnancy. In fact, they might even experience less pregnancy-related symptoms, such as nausea and breast tenderness compared to women with normal pregnancy because of the below-normal levels of estradiol, progesterone and human chorionic gonadotropin (hCG) observed in ectopic pregnancy [11-13].

When they start developing symptoms, they typically refer in the 6^{th}-8^{th} weeks of pregnancy to the emergency department with vaginal bleeding and/or abdominal pain. In a retrospective study, out of 2026 pregnant women who had been referred to the emergency department with first-trimester vaginal bleeding and/or abdominal pain, 18% were diagnosed with ectopic pregnancy. Of these, vaginal bleeding was slightly more common than abdominal pain (76% vs. 66%, respectively) [14]. This is similar to what was found in the previously mentioned study that was done in Al-Khobar City. Nevertheless, abdominal pain in the latter study was found to be more common than vaginal bleeding as the presenting symptom [8]. If the symptoms are persistent and severe, or the patient shows signs of hemodynamic instability, such as fainting, and decreased level of consciousness or shock, ruptured ectopic pregnancy should be suspected. In a population-based study done in France, the incidence of rupture was found to be 18% [15].

Although the presentation of first-trimester vaginal bleeding and/or abdominal pain is not specific to ectopic pregnancy (see Table 1 for the differential diagnosis), any female patient in her child-bearing age presented with this clinical picture should be actively investigated for the possible diagnosis of ectopic pregnancy. The investigative plan should include testing for pregnancy (unless the patient is already known to be pregnant), assessing the patient's hemodynamic status, locating the site of implantation, and finally some lab tests that might help in guiding the treatment.

Table 1: differential diagnosis of first-trimester vaginal bleeding and abdominal pain

Physiologic (due to implantation)	Gestational trophoblastic disease
Ectopic pregnancy	Sub-chorionic hematoma
Spontaneous abortion	Local gynecological pathology

Diagnosis:

To confirm the diagnosis, the clinical picture should be consistent, hCG level should be above the discriminatory zone (the level at which an intra-uterine pregnancy should be visible on ultrasonography) and no intra-uterine pregnancy should be found. Nevertheless, in rare cases, a lady might

have a heterotopic pregnancy in which she has a normal intra-uterine pregnancy and another ectopic. The incidence of heterotopic pregnancy is estimated to be around 1 in 7000 pregnancies [16]. If the hCG is not above the discriminatory zone, the patient should be kept under close observation with serial testing to confirm the diagnosis prior to providing treatment. If serial hCG levels show inappropriate increase with failure to visualize intra-uterine pregnancy, ectopic pregnancy can be diagnosed.

Management:

Once ectopic pregnancy is diagnosed, treatment will follow one of three options. These are expectant management, medical management with methotrexate or surgical management. Expectant management is rarely adopted considering that small proportion of patients meet the required criteria. Therefore, treatment is usually surgical or with methotrexate. In general, nonsurgical approach is preferred unless not possible (see Table 2).

Table 2: The cases in which ectopic pregnancy cannot be treated medically

	Hemodynamic instability
	hCG level is > 5,000 mIU/mL
	Trans-vaginal ultrasonography shows fatal cardiac activity
	Patient unwilling to comply with the close follow up required with medical therapy
Methotrexate therapy is contraindicated:	1. Heterotopic pregnancy with viable intra-uterine pregnancy 2. Methotrexate hypersensitivity 3. Baseline abnormalities in renal, hepatic or hematologic lab tests 4. Immunodeficiency 5. Breastfeeding 6. Active pulmonary disease of peptic ulcer disease

Conclusion

Ectopic pregnancy is a potentially lethal condition that might turn the expected joy of a family into misery. In the vast majority of cases, it is tubal. Yet, extra-tubal ectopic pregnancy is not uncommon. It should be always at the top of the differential diagnosis whenever a lady in her childbearing age shows with first-trimester vaginal bleeding and/or abdominal pain. When the diagnosis is confirmed, the patient should be first screened for the suitability of medical therapy with methotrexate before choosing a surgical approach.

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