

# Clinical Reviews in Emergency Medicine



## EMERGENCY MEDICINE MYTHS: ECTOPIC PREGNANCY EVALUATION, RISK FACTORS, AND PRESENTATION

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**Abstract—Background:** Ectopic pregnancy (EP) is an important cause of morbidity and mortality in females of reproductive age. Proper diagnosis and treatment are critical, as complications such as rupture, hemorrhagic shock, and even death can occur. **Objective:** EP is a condition emergency physicians are trained to detect, yet there are multiple myths concerning its evaluation and diagnosis. This article reviews several of these myths in order to improve emergency department (ED) evaluation and diagnosis. **Discussion:** EP is a difficult diagnosis and may be missed on initial ED visit. While the diagnosis is often delayed simply due to very early presentations, it can also be missed because patients may not have all the same risk factors or demonstrate the same symptoms. They may also not demonstrate the same serum B-human chorionic gonadotropin levels and trends or have the same ultrasound findings at equivalent gestational ages. Some patients with early EP may have positive ultrasound findings with serum  $\beta$ -hCG levels under a defined discriminatory zone (DZ). On the other hand, some patients with an early viable intrauterine pregnancy may have no visible findings on initial ultrasound, but have serum  $\beta$ -hCG (quantitative) levels well above the DZ. Although rare, EP has even been demonstrated in women with negative urine  $\beta$ -hCG tests or low serum  $\beta$ -hCG levels. **Conclusions:** While EP may be a challenging diagnosis, understanding the myths surrounding EP may help emergency physicians consider it, even when patient risk factors, symptoms, or ED laboratory or imaging studies do not initially or easily define the diagnosis. © 2017 Elsevier Inc. All rights reserved.

**Keywords—**ectopic; pregnancy; serum  $\beta$ -hCG; discriminatory zone; ultrasound

## INTRODUCTION

An ectopic pregnancy (EP) is a condition in which a fertilized ovum implants outside the endometrium (1). The largest percentage of EPs occur in the fallopian tubes, but they can also occur in the ovary, abdomen, and cervix (2). Although the incidence of EP approximates 2% of all pregnancies, it remains an important cause of morbidity and mortality (1,2). From 2003 to 2007, EP accounted for 0.26 maternal deaths per 100,000 live births in Caucasian women and 1.75 deaths per 100,000 live births in African-American women. Undiagnosed or untreated EP can also lead to complications, such as excessive hemorrhage, shock, or renal failure (1).

Although it is important to diagnose and treat EP early, the diagnosis can be challenging. Clinicians commonly misdiagnose EP on an initial medical encounter (3,4). Several recommendations attempt to simplify decision making and facilitate the diagnosis with obtaining accurate history, specific laboratory tests, and imaging studies (5,6). However, not every patient with EP will present similarly and, unfortunately, not every patient will demonstrate similar findings on these laboratory or imaging tests. The current article discusses EP and some of these discrepancies in the diagnosis of EP in the emergency department (ED). Of note, in this particular article, all serum  $\beta$ -human chorionic gonadotropin ( $\beta$ -hCG) levels refer to the quantitative test.

## DISCUSSION

### *Myth 1: If a Pregnant Patient Has a Serum hCG Above the Discriminatory Zone and No Visualized Intrauterine Pregnancy on Ultrasound, Then an Ectopic Pregnancy Must Be Present*

The discriminatory zone (DZ) describes the lowest serum  $\beta$ -hCG level where ultrasound (US) should detect visible signs of early pregnancy, such as yolk sac or fetal pole (7). With improving US technology, over time the DZ has fallen from a level of 6500 mIU/mL in the early 1980s to 1000–2000 mIU/mL in the present day (8–10). Women without evidence of a visible intrauterine pregnancy (IUP) on transvaginal US are considered to have pregnancy of unknown location (PUL), but it is often presumed that a patient with a PUL and a serum  $\beta$ -hCG level above the DZ has an EP, which may not be a correct assumption (11).

Recent research has questioned that a single hCG measurement can distinguish IUP from EP, even when the measurement is above the DZ (12,13). From the emergency practitioner's standpoint, the initial goal is to address a life-threatening condition. If any patient is unstable with concerning signs and symptoms, resuscitation and urgent obstetrics consultation is paramount. In stable patients, a more thorough evaluation can occur. The primary goal is to determine whether a viable IUP is present (12). If no IUP is seen on US, then PUL is present, and potential outcomes for this pregnancy may include early viable IUP, early non-viable IUP, or EP (12).

If a patient has an hCG level below the DZ, it is often thought an US is unnecessary because nothing can be visualized. However, as will be mentioned in Myth 2, this may not be the case. In situations where the hCG is above the DZ and no IUP is seen, then it is often presumed the pregnancy is not viable or an EP is present. However, the hCG DZ is a surrogate marker for gestational age. A normal gestational sac should be visualized around 5 weeks and 5 days from the last normal menstrual period, regardless if it is a singleton or multiple gestation (14). The  $\beta$ -hCG should be used in conjunction with suspected gestational age, and a single level should not be used alone in clinical decision making (15). Serum progesterone level is another laboratory test that has been used in conjunction with serum  $\beta$ -hCG level. It is thought that low serum progesterone levels (< 5 ng/mL) are associated with non-viable pregnancies (4,16–18). However, single progesterone levels are inadequate for determining EP vs. a non-viable IUP (18,19). Just as with US, the combination of the serum  $\beta$ -hCG level with a serum progesterone level may be useful in the diagnosis of EP in those patients who have PUL (20). This review will not discuss this further, but it is some-

thing for the emergency physician to note for reference purposes.

Indeed, there have been cases where patients with an initial PUL and serum  $\beta$ -hCG levels above the DZ have gone on to have viable pregnancies (13,21,22). In 2014, Ko et al. reviewed 113 patients with initial PUL and hCG levels > 1000 mIU/mL. They followed these patients for a specified time period to determine outcomes, including eventual viable IUPs (21). The authors evaluated only hemodynamically stable patients without significant vaginal bleeding who had serum  $\beta$ -hCG levels > 1000 mIU/mL taken within 12 h of US. Transvaginal US was repeated when the hCG level showed a rise > 53%. Laparoscopy occurred when there was suboptimal rise in hCG, a visualized EP on repeat US, or development of hemodynamic instability or hemoperitoneum. Overall, in those patients with eventual visualized IUPs (n = 42), 23 were viable. Of these 23 patients, the highest hCG level was 9083 mIU/mL, which occurred in a patient with a triplet pregnancy conceived through in vitro fertilization. Of the total 113 patients studied, 22 had EP diagnosed on laparoscopy, with initial serum  $\beta$ -hCG level range of 1155–21,770 mIU/mL. The other 49 patients without confirmed EP or IUP were grouped into "other," which included resolved PUL (n = 45), treated PUL (n = 2), and molar pregnancy (n = 2) (21). The authors suspect several factors contributed to the non-visualization of pregnancy on initial US, including maternal obesity, adenomyosis, and uterine fibroids. They conclude a single initial serum  $\beta$ -hCG level and inconclusive initial transvaginal US findings are not predictive of eventual IUP or EP (21).

Similarly, other studies have documented cases in which an embryo was not seen on initial US in patients with serum  $\beta$ -hCG levels above the DZ but was later seen on subsequent US scans (7,13,22). In 2013, Connolly et al. reviewed the records of 651 patients with known pregnancy outcomes who initially presented with symptoms of EP or miscarriage (7). They were evaluated with a serum  $\beta$ -hCG level and a transvaginal US within 6 h of each other. In this population, the highest observed hCG where no structure could be visualized was 2317 mIU/mL. Using a logistic regression model, the authors calculated the predicted probability of visualizing a gestational sac as a function of the serum hCG values. They found that in their population of patients with a DZ of 1500 mIU/mL, the predicted probability of visualizing a gestational sac in a viable pregnancy was 80.4% (7). The authors conclude that even with improving US technology, initial structural signs of pregnancy may not be seen on US in some patients who have initial serum  $\beta$ -hCG levels above the classically defined DZ of 1000–1500 mIU/mL (7).

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