Ectopic pregnancy

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Abstract

Ectopic pregnancy (EP) occurs in 1–2% of pregnancies, and is associated with significant morbidity and mortality. Women with abdominal pain or vaginal bleeding in early pregnancy, or risk factors for EP, are generally assessed by Early Pregnancy Assessment Units. Diagnosis is predominantly by trans-vaginal ultrasound supported by quantified serum human chorionic gonadotrophin (hCG). The resolution limit of trans-vaginal ultrasound means not all EPs can be identified, leaving women with a 'Pregnancy of Unknown Location'. Management for EP has moved away from surgery with growing experience in medical management, and evidence-based recognition of expectant management for selected women. Surgery will always have a role in the management of women with EP who are acutely unwell, when medical management is not likely to work, or has failed. On-going areas of research include improvements in women's risk stratification at their first attendance with symptoms, shortening time until diagnosis of EP, and combination medical treatments.

Keywords ectopic pregnancy; human chorionic gonadotrophin; methotrexate; salpingectomy; salpingotomy

Background

An ectopic pregnancy (EP) occurs when a fertilized oocyte implants outside the normal uterine cavity, and in the majority of women usually represents the loss of a desired pregnancy. The aetiology of an ectopic pregnancy is uncertain.

Each EP puts the woman at risk of morbidity and mortality, in the short term, from intraperitoneal bleeding or management-related complications, and longer term, from sub-fertility and pain. Despite advances in diagnosis and treatment no significant reductions in the number of deaths from EP are reported in the UK (Figure 1) in the most recent Centre for Maternal and Child Enquiries Report (CMACE). The psychological harm from such a pregnancy loss is apparent but more difficult to research and quantify.

Current areas of active research include studies to improve the time to making the diagnosis of an EP, risk stratification of symptomatic women at first presentation, and improving the time to resolution with medical management.

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Presentation and clinical symptoms

An EP on average occurs every 45 minutes in the UK. Within the approximate 12,000 cases each year there is an extremely wide range of clinical presentations of women, from asymptomatic to profound circulatory collapse. The presence of unilateral abdominal pain rather than vaginal bleeding tends to suggest EP rather than miscarriage but this is by no means conclusive. A high index of suspicion in all women of reproductive age until an EP is confirmed or excluded is needed. Non-gynaecological symptoms such as diarrhoea, vomiting or dizziness may predominate, and may not trigger consideration of pregnancy testing at first assessment, and furthermore direct the woman to other healthcare services such as medical or general surgical services.

There are many risk factors for ectopic pregnancy including past or present *Chlamydia trachomatis* infection, cigarette smoking, previous EP, pelvic surgery, termination of pregnancy, intrauterine contraceptive use and use of assisted reproductive technology amongst others. Women with EP often have none of these identifiable factors.

The UK now has a network of around 150 Early Pregnancy Assessment Units (EPAU) that provide a service to women at high risk of EP, such as those with symptoms of pain and vaginal bleeding in early pregnancy. EPAUs will have different and not always formalized risk assessment during first contact with the patient, typically by telephone or GP referral. Due to resource availability, the accessibility and timing of investigations that can be offered may not be ideal. Not all NHS trusts offer a gold-standard 'seven days per week' EPAU service, and women outwith the hours of the service are typically assessed by on-call gynaecology medical or nursing staff.

Diagnosis

After EPAU risk stratification based on clinical history and current symptoms, the main stay of EP diagnosis is trans-vaginal ultrasound scan (TV USS) supported by quantitative serum human chorionic gonadotrophin (hCG).

Amongst all women who experience first trimester pain or bleeding and present to an EPAU offering modern ultrasound, around 70% will have an intrauterine pregnancy identified of which approximate 40% will be confirmed as viable at the same examination. These proportions will vary considerably between centres depending on the underlying prevalence and nature of referral i.e. from GP referral to 'Walk-In' centres.

Ten percent, depending on the population served by the EPAU, will have a diagnosis of miscarriage, although fewer women than previously will be able to start active management due to refinements in the suggested criteria for the formal diagnosis of miscarriage (Table 1). The rationale behind this was to avoid inadvertent false positive diagnosis of a miscarriage instead of an early viable pregnancy.

A similar proportion will be classified as a 'Pregnancy of Unknown Location' (PUL), discussed below, and between 2 and 3% will have an EP. Of those with an EP the majority (98%) will have an implantation site within the Fallopian tube. The presence of an EP during a TV USS is highly likely if the following criteria are met.

- Absence of an intrauterine pregnancy (of confirmed, uncertain or absent viability) and
- Identification of an adnexal gestation scan (with or without yolk sac or fetal pole), or a heterogeneous adnexal mass.

Trends in deaths from ectopic pregnancy

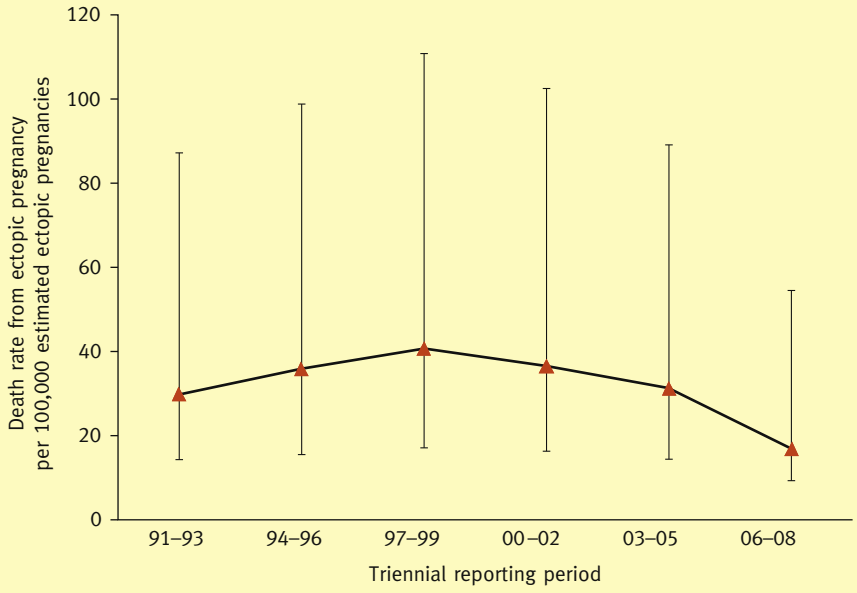

Figure 1

TV USS had a sensitivity 74% and specificity of 99%, with positive predictive value of 96.7% and a negative predictive value of 99.4% for identification of EP in a prospective observational study. The continued advances in TV USS quality mean that it is a constantly improving tool in EP diagnostics.

Correlation of less conclusive scan findings with quantitative measurement of serum hCG can be helpful. The concept of a 'discriminatory zone' was initially developed to determine at what level of serum hCG a normally sited and normally developing pregnancy should always be identified on a scan. Originally over 6000 IU/L for an abdominal scan, both improvements in resolution, and the use of TV USS have lowered this to between 1000 and 1500 IU/L. Serial hCG measurements around 48 hours apart are also helpful in this regard.

A viable intrauterine pregnancy would be expected to be associated with an 'optimal' rise in hCG from baseline of over 63% within 48 hours. EPs are often associated with a below optimal rise in hCG, or a largely static hCG. Miscarriage may become clinically apparent due to the amount of vaginal bleeding, and would correspond to a fall in hCG levels, with a 50% decrease over 48 hours meaning a viable pregnancy is very unlikely.

Caution is advised in interpretation however, in cases where imaging is technically sub-optimal such as with the presence of uterine fibroids, congenital uterine abnormalities and where a TV USS is not acceptable to the woman. A viable intrauterine twin pregnancy just below the threshold of resolution would demonstrate an apparently empty uterus with relatively high hCG levels, the combination of which may falsely suggest an EP.

Thus, although TV USS is a very safe investigation for women to undergo, the current route to making a firm diagnosis has drawbacks.

Recommendations on diagnosis of miscarriage

Scenario	A	B	C	D	E	F
Type of scan	Trans-vaginal	Trans-vaginal	Trans-abdominal	Trans-vaginal	Trans-vaginal	Trans-abdominal
Fetal heart activity	Absent	Absent	Absent	–	–	–
Fetal pole (Crown rump length)	≥7.0 mm	<7.0 mm	Any size	No Fetal Pole	No Fetal Pole	No Fetal Pole
Mean gestational sac diameter	–	–	–	≥25.0 mm	<25.0 mm	Any size
Action required to confirm diagnosis of miscarriage	Obtain 2nd opinion, or re-scan at least 7 days later	Re-scan 7 days later and reassess	Re-scan 14 days later and reassess	Obtain 2nd opinion, or re-scan at least 7 days later	Re-scan 7 days later and reassess	Re-scan 14 days later and reassess

Table 1