**ECTOPIC PREGNANCY**

**DIAGNOSIS OF ECTOPIC PREGNANCY**

**DIAGNOSIS OF ECTOPIC PREGNANCY QRG**

*Initial assessment/history:*

Pregnant woman presents with **Symptoms/ Signs / Risk factors** for ectopic pregnancy (e.g. vaginal bleeding, abdominal pain, amenorrhoea).

**Trans vaginal ultrasound scan (TVS)**

Ectopic **diagnostic criteria** includes:

1. Positive pregnancy test
2. Empty intrauterine cavity
3. Complex adnexal mass +/- extrauterine gestation sac.

➢ **Other ectopic features include:** Bagel sign, pseudo sac, free pelvic fluid.

**Diagnostic algorithms (TVS + quantitative 8hCG)**

TVS + discriminatory zone hCG titre (>1500IU/L for TVS or >6500IU for transabdominal USS):

- **>1500 IU/L & no** intrauterine gestational sac = strongly suggests ectopic.
  - If no extrauterine sac evident, organise Consultant review or formal ultrasound in department. If no features suggestive of ectopic on formal USS, repeat TVS & hCG 48hours later in EPAS.
  - When repeated, if no intrauterine sac observed on TVS = abnormal pregnancy. If hCG rise or plateau = sign of ectopic. Falling hCG suggests failed pregnancy = **expectant management** may be offered if woman stable. Repeat hCG weekly until negative for pregnancy.
- **<1500 IU/L:** Repeat hCG in 72 hours: If **>1500** do TVS; If hCG **has not doubled** = abnormal pregnancy; If **falling hCG** = failed pregnancy & stable women can be offered **expectant management** with weekly hCG until hCG negative for pregnancy.

TVS + serial hCG +/- discriminatory zone hCG: If TVS & discriminatory zone hCG are inconclusive, hCG should be repeated. The slowest rise in hCG over 48hours in a **viable intrauterine** pregnancy is 53%.

**Subsequent management (if diagnosed with an ectopic pregnancy)**

**Medical, surgical or expectant** management dependent on individual clinical situation

**AIM**

- To provide information on **risk factors, symptoms, signs** and **diagnosis** of an ectopic pregnancy.

**KEY POINTS**

1. Ectopic pregnancy should be considered in all pregnant women who present to the Emergency Centre with abdominal pain or vaginal bleeding.
2. Untreated ectopic pregnancy in a fallopian tube can rupture and cause intra-abdominal bleeding.

**BACKGROUND**

Ectopic pregnancy occurs when the developing blastocyst becomes implanted at a site other than the endometrium of the uterine cavity and the most common extra-uterine location is the fallopian tube.
which accounts for 91-95% percent of all ectopic pregnancies. Other locations (and rates, out of all ectopic pregnancies) include the caesarean / hysterotomy scar (<6.1%), ovary (1-6%), rudimentary horn of a unicorneuterus (2%), cervix (<1%), and abdomen (0.9-1.4%). Contemporary management, associated with earlier diagnosis of ectopic pregnancy, involves (where possible) a conservative approach that attempts to save the fallopian tube, rather than salpingectomy.

Ectopic pregnancy is an important cause of maternal morbidity and mortality. Although deaths associated with ectopic pregnancy have declined with earlier and improved diagnosis, the majority (80%) of maternal first trimester deaths, and 10-15% of all pregnancy related deaths, are related to haemorrhage from ectopic pregnancy.

INCIDENCE
Of all reported pregnancies 1 to 2% are ectopic. The prevalence of ectopic pregnancy among women who go to an emergency department with first trimester bleeding, pain, or both, ranges from 6 - 16%. Over the past three decades, in many countries, the rate of ectopic pregnancy increased by a factor of three to six, and has remained stable.

RISK FACTORS
Some factors have been associated with an increased likelihood of ectopic pregnancy, however risk factors are only found in approximately 50 % of cases.

<table>
<thead>
<tr>
<th>Degree of additional risk</th>
<th>Risk factor</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Previous ectopic pregnancy</td>
<td>9.3 - 47</td>
</tr>
<tr>
<td></td>
<td>Previous tubal surgery</td>
<td>6.0 - 11.5</td>
</tr>
<tr>
<td></td>
<td>Failed tubal ligation</td>
<td>3.0 - 139</td>
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<tr>
<td></td>
<td>Documented tubal damage or pathology</td>
<td>3.5 - 25</td>
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<tr>
<td></td>
<td>Failed IUCD</td>
<td>1.1 - 45</td>
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<tr>
<td>Moderate</td>
<td>History of infertility</td>
<td>1.1 - 28</td>
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<tr>
<td></td>
<td>Previous pelvic/ genital infection</td>
<td>2.1 - 3.0</td>
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<tr>
<td></td>
<td>Cigarette smoking</td>
<td>2.3 - 3.9</td>
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<tr>
<td></td>
<td>Multiple sexual partners</td>
<td>1.4 - 4.8</td>
</tr>
<tr>
<td></td>
<td>Assisted reproductive technology</td>
<td>2.3 - 3.9</td>
</tr>
<tr>
<td>Low</td>
<td>Previous pelvic/ abdominal surgery</td>
<td>0.93 - 3.8</td>
</tr>
<tr>
<td></td>
<td>Early age at first sexual intercourse</td>
<td>1.1 – 2.5</td>
</tr>
<tr>
<td></td>
<td>Vaginal douching</td>
<td>1.1 – 3.1</td>
</tr>
</tbody>
</table>

Other factors include increased maternal age, pelvic inflammatory disease, and in-utero exposure to diethylstilbestrol.

SYMPTOMS
Clinical manifestations typically appear six to eight weeks after the last normal menstrual period, but can occur later, especially if the pregnancy is not in the fallopian tube. Normal pregnancy discomforts (e.g., breast tenderness, frequent urination, nausea) are often present in addition to the symptoms described below.

The typical triad of symptoms are:
- bleeding (75% of women)
- abdominal pain (80-90% of women)
- amenorrhoea

When the woman’s pain is disproportionately more severe than her bleeding, then ectopic pregnancy is likely, and if the bleeding is more severe than the pain, then intrauterine pregnancy is more likely.
BUT

- No symptoms before rupture\(^8\) - in 9%
- A third of women – No clinical signs
- Amenorrhoea is not universal
- Other presenting symptoms could be dizziness/fainting, shoulder tip pain, passage of tissue or gastrointestinal symptoms\(^1\) like diarrhoea or pain on defaecation\(^15\).

**SIGNS**

The clinical presentation and natural history of evolution of an ectopic pregnancy are unpredictable. It could range from complete absence of symptoms to shock/collapse. The physical examination is often unremarkable in a woman with a small, un-ruptured ectopic pregnancy.

Findings on physical examination may include\(^15\):

- Lower abdominal / pelvic / adnexal tenderness or mass\(^1\)
- Cervical motion tenderness\(^11\)
- Pallor / tachycardia / hypotension / shock / collapse / orthostatic hypotension.\(^1, 15\)

**DIAGNOSIS**

The recommended diagnostic tests include:

- Trans vaginal ultrasound scan alone (TVS)
- Diagnostic algorithms (TVS + quantitative \(\beta hCG\)).\(^11\)

The combination of tests with ultrasound scan +/- quantitative hCG estimation will permit a definitive diagnosis in almost all cases at a very early stage of pregnancy, thereby permitting treatment options less invasive than surgical excision.\(^16, 17\) Although progesterone concentrations can be used to predict a viable intrauterine or failed pregnancy, they do not assist clinicians to locate a pregnancy of unknown origin.\(^6, 11\) Currently, other diagnostic tests (e.g. Doppler or 3D ultrasound, curettage, laparoscopy, culdocentesis, magnetic resonance imaging) have not demonstrated improvement in current diagnosis sensitivity or specificity, and do not provide additional clinically useful information.\(^6\)

**ULTRASOUND SCAN ALONE**

Transvaginal ultrasound examination (TVS) is the most useful and primary investigation for determining the location of a pregnancy.\(^1\) If an ectopic pregnancy is present, the use of TVS should visualise 73-93% of cases.\(^6\) Visualisation of an adnexal mass separate from the ovary, on TVS, has been shown to have high sensitivity (84.4%) and specificity (98.9%) for diagnosing ectopic pregnancy.\(^1\)

The most appropriate diagnostic criteria include a combination of\(^6\):

- Positive pregnancy test
- Empty intrauterine cavity
- Complex adnexal mass +/- extrauterine gestation sac.\(^6\)

Other ultrasound features that may be suggestive of ectopic pregnancy are\(^5\):

- Bagel sign (a fluid filled adnexal mass surrounded by a hyperechogenic ring)
- Pseudo sac (collection of variable amount of fluid within the uterine cavity). They tend to be located in the middle of the uterine cavity and conform to the contour of the cavity unlike an intrauterine gestation sac embedded in the decidua.
- Pelvic free fluid.\(^6\)

**Note**: If the woman declines the TVS, offer a trans-abdominal ultrasound scan and explain how findings will be limited, with the low specificity of the test making an ectopic diagnosis difficult.\(^15\)

**DIAGNOSTIC ALGORITHMS (TVS + QUANTITATIVE \(\beta hCG\))**

Ultrasound is inconclusive in 8-31% of women, in whom one or more measurements of human chorionic gonadotrophin (hCG) concentration is necessary to guide the assessment.\(^1\)

- TVS + discriminatory zone hCG titre
TVS + serial hCG +/- discriminatory zone hCG.

**Discriminatory Zone HCG – 1500 IU/L**

It is defined as the serum hCG level above which a gestational sac should be visualized by ultrasound examination if an intrauterine pregnancy is present. At KEMH, this serum hCG level is 1500 with TVS (the level is higher [6500 IU/L] with transabdominal ultrasound). The absence of an intrauterine gestational sac at hCG concentrations above the discriminatory zone strongly suggests an ectopic pregnancy.

**HCG Above the Discriminatory Zone (>1500 IU/L)**

If no intra or extrauterine pregnancy is visualised on ultrasound scan in the Emergency Department/EPAS clinic, a Consultant review or a formal USS in the department should be organised. The diagnosis of ectopic pregnancy is less certain if no complex adnexal mass can be visualised, since there is variability in the level of expertise among ultrasonographers. Furthermore, a serum hCG greater than 1500 IU/L without visualisation of intrauterine or extrauterine pathology may represent a multiple gestation, since there is no proven discriminatory level for multiple gestations. For these reasons, in the absence of features suggestive of ectopic pregnancy on formal USS, the next step is to repeat the TVS examination and hCG concentration 48 hrs later in EPAS.

- If an intrauterine pregnancy is still not observed on TVS, then the pregnancy is abnormal.
- A rise or plateauing in the serum hCG concentration in the absence of ultrasound evidence of intrauterine pregnancy is diagnostic of ectopic pregnancy.
- A falling hCG concentration is most consistent with a failed pregnancy (intrauterine or extrauterine). Expectant management will be an option if the woman is stable, there is no fetal cardiac activity, and the levels are dropping steadily (ideally less than 50% of its initial level within seven days). These women should be observed closely for rupture or clinical deterioration. Weekly hCG concentrations should be monitored until the result is negative for pregnancy. Refer to Clinical Guideline Expectant Management.

**HCG Below the Discriminatory Zone**

A negative ultrasound examination at hCG levels below the discriminatory zone (1500IU/L) is consistent with an early viable intrauterine pregnancy, an ectopic pregnancy, or a nonviable intrauterine pregnancy. A serum hCG concentration less than 1500 IU/L should be followed by repetition of hCG in 72hrs to follow the rate of rise.

- If the hCG rises normally, then a TVS should be performed when hCG reaches / expected to reach the discriminatory zone.
- If the hCG concentration does not double over 72 hrs, then the pregnancy is abnormal. The clinician can be reasonably certain that a normal intrauterine pregnancy is not present.
- A falling hCG concentration is most consistent with a failed pregnancy (intrauterine or extrauterine). Expectant management will be an option if the woman is stable and the levels are dropping steadily (ideally less than 50% of its initial level within seven days). Weekly hCG concentrations should be monitored until the result is negative for pregnancy (Refer to Clinical Guideline Expectant Management).

**Serial HCG**

More than one measurement of hCG is needed if TVS + Discriminatory zone hCG are not conclusive. Studies in viable intrauterine pregnancies have reported the following changes in serum hCG:

- The mean doubling time for serum hCG ranges from 1.4 to 2.1 days in early pregnancy.
- In 85% of viable intrauterine pregnancies, the hCG concentration rises by at least 66% every 48 hours during the first 40 days of pregnancy; only 15% of viable pregnancies have a rate of rise less than this threshold.
- The slowest recorded rise over 48 hrs associated with a viable intrauterine pregnancy was 53%. 

DPMS Ref: 8462 All guidelines should be read in conjunction with the Disclaimer at the beginning of this manual
17. Kirk E, Papageorghiou AT, Condous G, Tan L, Bora S, Bourne T. The diagnostic effectiveness of an initial transvaginal


15. National Institute for Health and Clinical Excellence. NICE Clinical guideline 154: Ectopic pregnancy and miscarriage:


13. Ankum WM, Mol BW, Van der Veen F, Bossuyt PM, Ankum W, Van der Veen F, Hajenius PJ. Current evidence on surgery, systemic methotrexate and

12. Murray H, Baakdah H, Bardell T, Tulandi T. Diagnosis and treatment of ectopic pregnancy. Canadian Medical


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