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PRACTICE

GUIDELINES

Ectopic pregnancy and miscarriage: diagnosis and initial management: summary of updated NICE guidance

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What you need to know

- The guideline now includes new recommendations on the ultrasound features for diagnosis of a tubal ectopic pregnancy
- Women without pain who have small ectopic pregnancies, low serum human chorionic gonadotropin (hCG) levels, and are able to return for follow-up may be offered the option of expectant management of ectopic pregnancy
- Women choosing expectant management for a diagnosed tubal ectopic pregnancy require close follow-up with immediate referral to secondary care if their condition deteriorates
- When diagnosing complete miscarriage on an ultrasound scan, in the absence of a previous scan confirming an intrauterine pregnancy, always be aware of the possibility of a pregnancy of unknown location. Advise these women to return for follow-up (for example, measurement of hCG levels, ultrasound scans) until a definitive diagnosis is obtained

Miscarriage and ectopic pregnancy have an adverse effect on the quality of life of many women, with early pregnancy loss accounting for over 50 000 hospital admissions in the UK annually.[1] Ectopic pregnancy (where the pregnancy implants outside the endometrial cavity, most commonly within the fallopian tube) occurs in approximately 11 per 1000 pregnancies.[2] Unfortunately, women still die during early pregnancy, with four maternal deaths reported in the UK between 2013 and 2015.[3] However, the case fatality rate has decreased over recent years,[2] suggesting that earlier diagnosis and treatment has made an impact. Accurate diagnosis and effective management of early pregnancy loss is therefore vital to avoid women dying unnecessarily, and to reduce the incidence of associated physical and psychological morbidity.

This article summarises the updated recommendations from the National Institute for Health and Care Excellence (NICE) on the diagnosis and management of tubal ectopic pregnancy and miscarriage in early pregnancy (up to 13 completed weeks of pregnancy).[4]

In addition to these updated recommendations, the guideline also contains recommendations on providing support and information, early pregnancy assessment services, symptoms and signs of ectopic pregnancy, diagnosis of viable intrauterine pregnancy and ectopic pregnancy, management of miscarriage, and management of ectopic pregnancy. However, these sections were not part of the guideline update, and remain unchanged from the 2012 guidance.

Updated recommendations

NICE recommendations are based on systematic reviews of best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the Guideline Committee's experience and opinion of what constitutes good practice. Evidence levels for the recommendations are given in italic in square brackets.

Diagnosis of tubal ectopic pregnancy

As with the previous version of this guideline, all women presenting with pain or bleeding in early pregnancy are recommended to undergo ultrasound scanning.

- Offer women who attend an early pregnancy assessment service (or out-of-hours gynaecology service if the early pregnancy assessment service is not available) a transvaginal ultrasound scan to identify the location of the pregnancy and whether there is a fetal pole and heartbeat. [*Based on moderate to very low quality evidence, and the experience and opinion of the Guideline Committee (GC)*]

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New recommendations have now been added to specifically highlight the ultrasound features that are associated with a tubal ectopic pregnancy. These include some features that are diagnostic of an ectopic pregnancy, as well as features which indicate a high probability or a possibility of ectopic pregnancy. The recommendations highlight the need to consider ultrasound features which indicate a high probability or possibility of an ectopic pregnancy in the context of other features (such as symptoms and signs, and serum human chorionic gonadotropin (hCG) levels) before making a diagnosis.

- When carrying out a transvaginal ultrasound scan in early pregnancy, look for these signs indicating there is a tubal ectopic pregnancy:
  - An adnexal mass, moving separate to the ovary, comprising a gestational sac containing a yolk sac *or*
  - An adnexal mass, moving separately to the ovary, comprising a gestational sac and fetal pole (with or without fetal heartbeat).

  [*Based on low quality evidence and the experience and opinion of the GC*]
- When carrying out a transvaginal ultrasound scan in early pregnancy, look for these signs indicating a high probability of a tubal ectopic pregnancy:
  - An adnexal mass, moving separately to the ovary, with an empty gestational sac (sometimes described as a "tubal ring" or "bagel sign") *or*
  - A complex, inhomogeneous adnexal mass, moving separate to the ovary.

  If these features are present, take into account other intrauterine and adnexal features on the scan, the woman's clinical presentation, and serum hCG levels before making a diagnosis. [*Based on moderate to very low quality evidence and the experience and opinion of the GC*]
- When carrying out a transvaginal ultrasound scan in early pregnancy, look for these signs indicating a possible ectopic pregnancy:
  - An empty uterus *or*
  - A collection of fluid within the uterine cavity (sometimes described as a pseudo-sac).

  If these features are present, take into account other intrauterine and adnexal features on the scan, the woman's clinical presentation, and serum hCG levels before making a diagnosis. [*Based on moderate to low quality evidence and the experience and opinion of the GC*]
- When carrying out a transabdominal or transvaginal ultrasound scan in early pregnancy, look for a moderate to large amount of free fluid in the peritoneal cavity or pouch of Douglas, which might represent haemoperitoneum. If this is present, take into account other intrauterine and adnexal features of the scan, the woman's clinical presentation, and hCG levels before making a diagnosis. [*Based on high to low quality evidence and the experience and opinion of the GC*]

The recommendations also describe the importance of checking the uterus and the adnexae when scanning in early pregnancy, to check for a co-existing intrauterine and extrauterine pregnancy (heterotopic pregnancy).

- When carrying out a transabdominal or transvaginal ultrasound scan during early pregnancy, scan the uterus and adnexae to see if there is a heterotopic pregnancy. [*Based on the experience and opinion of the GC*]

Finally, the recommendations now highlight the need for suitably trained individuals to be involved in the interpretation of early pregnancy ultrasound scans to improve the accuracy of diagnosis.

- All ultrasound scans should be performed or directly supervised and reviewed by appropriately qualified healthcare professionals with training in, and experience of, diagnosing ectopic pregnancies. [*Based on the experience and opinion of the GC*]

Management of tubal ectopic pregnancy

As with the previous version of the guideline, the options of medical management (using methotrexate) and surgical management (salpingectomy or salpingotomy) are still recommended, and guidance is given for the circumstances in which these should be favoured.

Expectant management of ectopic pregnancy has not previously been recommended as part of the guideline. However, an evidence review identified that expectant management of ectopic pregnancy may be appropriate, safe, and effective in certain circumstances. New recommendations have therefore been added to give guidance on situations in which expectant management may be suitable, and should be offered or considered for women with a confirmed tubal ectopic pregnancy. These include women who are pain-free with a small, tubal ectopic pregnancy and low hCG levels.

- Offer expectant management as an option to women who:
  - Are clinically stable and pain-free *and*
  - Have a tubal ectopic pregnancy measuring <35 mm with no visible heartbeat on transvaginal ultrasound scan *and*
  - Have serum hCG levels of ≤1000 IU/L *and*
  - Are able to return for follow-up.
- Consider expectant management as an option for women who:
  - Are clinically stable and pain-free *and*
  - Have a tubal ectopic pregnancy measuring <35 mm with no visible heartbeat on transvaginal ultrasound scan *and*
  - Have serum hCG levels >1000 IU/L and <1500 IU/L *and*
  - Are able to return for follow up.

  [*Based on moderate to very low quality evidence, and the experience and opinion of the GC*]

If the criteria above are not met, then women should be offered medical or surgical management of their ectopic pregnancy, according to the existing recommendations.

The guideline also provides recommendations regarding how often hCG levels should be checked, for women receiving expectant management, and how to act on the results:

- For women with a tubal ectopic pregnancy being managed expectantly, repeat hCG levels on days 2, 4, and 7 after the original test, and:
  - If hCG levels drop by ≥15% from the previous value on days 2, 4, and 7, then repeat weekly until a negative result (<20 IU/L) is obtained *or*
  - If hCG levels do not fall by 15%, stay the same, or rise from the previous value, review the woman's clinical condition and seek senior advice to help decide further management.

  [*Based on the experience and opinion of the GC*]

Finally, the recommendations include information to be provided to women about expectant management:

- Advise women that, based on limited evidence, there seems to be no difference following expectant or medical management in:
  - The rate of ectopic pregnancies ending naturally
  - The risk of tubal rupture
  - The need for additional treatment, but that they might need to be admitted urgently if their condition deteriorates
  - Health status, depression or anxiety scores.

  Advise women that the time taken for ectopic pregnancies to resolve and future fertility outcomes are likely to be the same with either expectant or medical management. [*Based on moderate to very low quality evidence, and the experience and opinion of the GC*]

Implementation

Early pregnancy units will need to ensure that they are able to provide care for women receiving expectant management of a tubal ectopic pregnancy. Local protocols will therefore need to be developed for assessment, monitoring, and follow-up of women who choose expectant management.

Guideline into practice

- How many women presenting with bleeding and/or pain in early pregnancy are referred for an ultrasound scan?
- How many women are offered the option of expectant management for ectopic pregnancy (of those in whom this would be appropriate)?

Future research

Ectopic pregnancy can have a considerable emotional impact on women and their partners, and it is unclear which of the treatment options may be beneficial at minimising this impact. There is currently no evidence which considers the psychological impact of the different treatments for ectopic pregnancy—this should be prioritised for future research.

How women were involved in the creation of this article

Committee members involved in this guideline update included lay members who contributed to the formulation of the recommendations summarised here.

Further information on the guidance

The guideline update was developed using the methods described in *Developing NICE guidelines: the manual* (https://www.nice.org.uk/process/pmg20/chapter/introduction-and-overview). Systematic literature searches were undertaken to identify all published clinical evidence and health economic evidence relevant to the review questions. The guideline committee comprised healthcare professionals and lay members, who considered the evidence identified and drafted recommendations on the basis of the evidence, and the expertise and opinion of the committee. Draft recommendations were subject to stakeholder consultation and revision before publication of the final guideline.

The members of the guideline committee were (in alphabetical order) Philip Barclay, Sarah Beswick, Alena Chong, Maria Clark, Sarah Fishburn (chair), Christine Harding, Geeta Kumar, Pramod Mainie, Sandra Morrissey, Munira Oza, Maryam Parisaei, Neelam Potdar, Rachel Small, Lisa Smith, Mark Tighe, Ashifa Trivedi, and Pensee Wu.

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