

2. Management of Ectopic Pregnancy

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Contents	Page
2.1 Scope of the guideline	29
2.1.1 Definition	29
2.1.2 Importance of ectopic pregnancy	29
2.2 Aetiology	30
2.3 Epidemiology	31
2.4 Diagnosis	32
2.4.1 History	32
2.4.2 Examination	33
2.4.3 Investigations	33
2.5 Management	34
2.5.1 Levels of management	34
2.5.2 Management strategies	35
2.□ Special circumstances	40
2.□.1 Ruptured ectopic pregnancy-management	40
2.□.2 Anti-D immunoglobulin	41
2.7 Summary	41
2.8 References	43

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Introduction

The aim of this guideline is to provide recommendations to aid General Practitioners and Gynaecologists in the management of **Ectopic Pregnancy**. This treatment could be initiated in a primary care setting or in centres with advanced facilities. The objective of management in ectopic pregnancy is to make an early diagnosis, treat, prevent complications, and consequently to improve quality of life

2.1 Scope of the guideline

2.1.1 Definition

An ectopic pregnancy is a pregnancy implanted in an abnormal location (outside of the uterus).

2.1.2 Importance of ectopic pregnancy.

Ectopic pregnancy account for maternal deaths. The incidence of ectopic pregnancy is 1.8/1000 (According to the UK data). Most of the ectopic pregnancies are sub clinical/biochemical; therefore true incidence may be higher. The most common site of ectopic implantation is the fallopian tube. Other sites such as the abdomen, ovary, cervix or cornu of the uterus are far less common but are associated with higher mortality. This higher mortality is due to greater detection difficulty and to massive bleeding that can result if rupture occurs at these sites. As a result of septic abortions and pelvic inflammatory disease (PID), the incidence of ectopic pregnancies show an increased trend over the past decades. (During the past 40 years its incidence has been steadily increasing concomitant with increased STD rates and associated salpingitis. Such abnormalities of the tubes prevent normal transport of the

fertilized egg to the uterus). On the other hand increase availability of Gynaecologists and ultrasonography (USS) facility, most of the ectopic pregnancies are diagnosed earlier and appropriate management carried out with reducing maternal mortality and morbidity. This guideline is intended to improve the morbidity and mortality associated with ectopic pregnancy.

2.2 Aetiology

- The commonest cause of ectopic pregnancy is salpingitis (causes 50% of first time ectopic pregnancies).
- 40% have no known cause. One hypothesis is that there is slowing of transport through the fallopian tube of the fertilized egg. This slow transport could possibly be due to hormonal imbalance (such as due to progesterone releasing IUD, progestin-only oral contraceptives). This could also happen in Artificial Reproductive Technique procedures (ART) or possibly an abnormality of the embryo. (e.g. chromosomal)
- Cigarette smoking significantly increases a woman's risk.
- Previous history of ectopic pregnancy increases the risk for another ectopic pregnancy. (Incidence is 7%)
- About 25% of women with an ectopic pregnancy have a history of previous surgery in the abdomen.

2.3 Epidemiology

How many women suffer from an ectopic pregnancy?

The occurrence of ectopic pregnancy is reported to be at a rate of about 1-2% of pregnancies and can occur in any sexually active fertile woman. The increase in incidence in the past few decades is thought to be due to two factors:

- I. Increased incidence of salpingitis (infection of the fallopian tube, usually due to a sexually transmitted disease (STD), such as Chlamydia or Gonorrhoea), and,
- II. Improved ability to detect ectopic pregnancies.

There is a marked increase in ectopic pregnancy rate with increasing age from 10 per 1000 pregnancies in women aged 15 to 24, to 21.5 per 1000 pregnancies in women aged 35 to 44.

Most ectopic pregnancies occur in women who have had more than one pregnancy. Only 10% to 15% of ectopic pregnancies occur in women who have never been pregnant before.

2.4 Diagnosis

2.4.1 History

What symptoms can a woman experience with ectopic pregnancy?

Women in whom it is suspected that they are in danger of ectopic pregnancy, with the use of testing and imaging it is now often possible to detect an ectopic pregnancy before symptoms develop. It is important to be aware of the symptoms of ectopic pregnancy because it can occur in any sexually active woman whether or not she is using contraceptives or has undergone tubal sterilization.

Symptoms occur as the embryo grows and as bleeding occurs due to leaking of blood through the fimbrial opening of the fallopian tube or from rupture of the tube. Mild bleeding can also occur without causing symptoms.

The most common symptoms that with which a woman presents to a doctor are abdominal pain (90-100% of women), delayed menses (75-90%) and unexpected bleeding through the vagina (50-80%).

Before rupture occurs, a vague soreness or spastic (colic) pain in the abdomen may be the only symptom present.

Abdominal pain can be generalized, or it can be localized on one side or both sides. About one quarter of women also have pain in the shoulder because of diaphragmatic irritation from blood in the abdomen.

During rupture, the pain usually becomes intense. Other symptoms also occur though less commonly. Dizziness and fainting occur in about one third of women with symptoms. Pregnancy symptoms also occur in about

20% of women with symptoms. 10% of the time, there can be an urge to have bowel movement.

2.4.2 Examination

2.4.2.1 Signs

The most common finding is tenderness in the abdomen and pelvis. Often, a mass is felt on the side of the uterus (adnexial mass). In about one third of women, an enlarged uterus is found which is smaller than would be found in a normal pregnancy, except when an interstitial pregnancy is present. Tachycardia and hypotension can be found if there has been profuse blood loss. **However, in most early ectopic pregnancies no abnormal findings can be found.**

2.4.3 Investigations

β-HCG Blood levels,
Transvaginal ultrasonography.

2.5 Management

2.5.1 Levels of management.

Level 1.

- General Practitioner (GP), Public Health Midwife (PHM), Medical Officer of Maternal Care (MOMC)

Identification of risk mothers of ectopic pregnancy:

Past history of;

- ectopic pregnancy,
- septic abortion,
- pelvic inflammatory disease (PID).

Recommendation:

Early referral to level 2

(Grade X)

Level 2.

- Base Hospital with Obstetrician and Gynaecologist.
Ultrasonography (USS) facility,
Laparotomy facility with or without Laparoscopy facility.

Level 3.

- General Hospital/Teaching Hospital with Obstetrician and Gynaecologist with all level 2 facilities.
Human Chorionic Gonadotrophin (hCG) level measurements available (24 hours)

2.5.2 Management strategies

2.5.2.1 Expectant management.

Ideal at *Level 3*.

(Grade Y)

Not all ectopic pregnancy ends up with maternal morbidity and mortality¹. There is 89.3 percent self-resolution of the ectopic pregnancies, but there is poor efficacy of this method.

Expectant management is an option for;

- When ectopic sac less than 2cm. with no identifiable fetal pole and less than 50ml. of haemoperitoneum on ultrasonography (USS).
- Clinically stable woman with minimal symptoms and a pregnancy of unknown location.
- Clinically stable asymptomatic woman with an ultrasound diagnosis of ectopic pregnancy and a decreasing serum human chorionic gonadotrophin levels (hCG), initially less than serum 1000 iu/l.

However, one need to realize that selection of patients for expectant management should be done selectively with full compliance of the patient following detailed counselling.

Women managed expectantly should be followed twice weekly with serial hCG measurements and weekly by transvaginal examinations to ensure a rapidly decreasing hCG level (ideally less than 50% of its initial level within seven days) and a reduction in the size of adnexial mass by seven days.

Thereafter weekly hCG and transvaginal ultrasound examinations are advised until serum hCG levels are less than 20 iu/l as **there are case reports of tubal rupture at low levels of β -hCG**. In addition, women selected for expectant management of pregnancy of unknown origin

should be counselled about the importance of compliance with follow-up and should be within easy access to the hospital.

2.5.2.2 Medical Management.

Ideal at *level 3*

(Grade Y)

Medical therapy should be offered to suitable women, and units should have treatment and follow-up protocols for the use of methotrexate in the treatment of ectopic pregnancy. In stable patients a variety of medical treatment options are as effective as surgery.¹⁷

If medical therapy is offered, women should be given clear information (preferably written) about the possible need for further treatment and adverse effects following treatment. Women should be able to return easily for assessment at any time during follow-up.

Medical therapy option may be considered for women with an hCG level below 3000 iu/l.^{20, 21}

The presence of cardiac activity in an ectopic pregnancy is associated with a reduced chance of success following medical therapy and should be considered a **contraindication to medical therapy.**^{11, 12}

The drug of choice is methotrexate. It can be given intravenous / intramuscular /oral or local injection at the site of the ectopic either laparoscopically, ultra sound guided hysteroscopically. Intramuscular methotrexate given as a single dose calculated from patient's body surface area (50 mg/m²). For most women this will be between 75 mg. and 90 mg. Serum hCG levels are checked on days four and seven and a further dose is given if hCG levels have failed to fall by more than 15% between day four and day seven.^{12, 18, 19}

However, the success rate is 75%. According to a small randomised controlled trial (RCT) there is no

difference in the outcome except in whom given by local injection. This also gives rise to relatively low drug related side effects. Therefore local injection of methotrexate is preferable to its use systemically.

There are no studies to comment on the subsequent fertility rate, as most of the trials are small. Method of administration needs to be addressed carefully after proper selection of patients.

For example there is high failure rate if the ectopic is more than 2cm. of fetal pole.

2.5.2.3 Surgical management

i. Laparotomy.

Ideal at level 2

(Grade Y)

Most of the ectopic pregnancies in Sri-lanka present after rupture and haemo-dynamically unstable. According to randomised controlled trials (RCT) there is controversies of stabilizing the patient and then proceeding with the laparotomy. However, results need to be considered cautiously. Laparotomy is preferred in haemo-dynamically unstable patients over laparoscopy. According to two randomised controlled trials (RCT), laparotomy patients give subsequent 55% intra-uterine pregnancy (IUP) rate, 1□□% of recurrent ectopic rate and 1.8% persistent trophoblastic activity.

ii. Laparoscopy.

Ideal at level 3. This depend on the consultant's preference, and is possible in *level 2* as well.

A laparoscopic approach in the surgical management of tubal pregnancy, in the haemo-dynamically stable patient, and is preferable to a laparotomy.

This method may be preferable for the ectopic when diagnosed early and unruptured.¹ According to three

randomised controlled trials (RCT) laparoscopic method give rise to less blood loss, less hospital stay, low cost and less post-operative analgesic requirements. This study shows higher intra-uterine pregnancy (IUP) (70%) rate, less recurrent ectopic (50%) and higher trophoblastic tissue activity (12.□□%).

Type of surgery

i. Salpingectomy.

According to meta analysis, this method gives rise less recurrent ectopic pregnancy rate (10%) and with no failure of removal of all ectopic tissue. However, there is no difference between laparotomy and laparoscopy except the advantages of laparoscopy.

In the presence of a healthy contralateral tube there is no clear evidence that salpingotomy should be used in preference to salpingectomy.^{0□-12}

ii. Salpingotomy.

According to good quality randomised controlled trials (RCT) there is higher rate of recurrent ectopic associated with this method (15%) and higher rate of trophoblastic activity (11%). However trophoblastic activity can be managed medically. There is no significant difference in intrauterine pregnancy (IUP) in both methods.

According to a randomised controlled trial (RCT), that there is no additional benefit of suturing the salpingostomy site, because the intrauterine pregnancy (IUP) rate is similar at 12 month after the surgery with or without suturing.

Randomised controlled trials (RCT) results suggest that there may be a higher subsequent intrauterine pregnancy rate associated with salpingotomy but the magnitude of this benefit may be small. Data from future randomised controlled trial (RCT) examining this question

is needed. The use of conservative surgical techniques exposes women to a small risk of tubal bleeding in the immediate postoperative period and the potential need for further treatment for persistent trophoblastic tissue. Both these risks and the possibility of further ectopic pregnancies in the conserved tube should be discussed if salpingotomy is being considered by the surgeon or requested by the patient¹³⁻¹⁴

Laparoscopic salpingotomy should be considered as the primary treatment when managing tubal pregnancy in the presence of contralateral tubal disease and the desire for future fertility.

In women with a damaged or absent contralateral tube, *in vitro* fertilization is likely to be required if salpingectomy is performed¹³⁻¹⁴. Because of the requirement for postoperative follow-up and the treatment of persistent trophoblasts, the short-term costs of salpingotomy are greater than salpingectomy.²¹ However, if the subsequent need for assisted conception is taken into account, an increase in intrauterine pregnancy rate of only 3% would make salpingotomy more cost effective than salpingectomy.¹⁹ In the presence of contralateral tubal disease the use of more conservative surgery is appropriate. These women must be made aware of the risk of a further ectopic pregnancy.¹³

Recommendations. **(Grade X)**

1. Laparoscopic method is superior to laparotomy method with regard to less cost, shorter hospital stay, less analgesic requirements, higher subsequent intrauterine pregnancy (IUP) and less recurrent ectopic rates. Therefore, laparoscopic method needs to be considered as a first option in unruptured ectopic.
2. Laparotomy is best in the case of life saving as well as with inadequate facilities.
3. Medical management should be conducted only by well-experienced consultants with emergency facilities at hand.
4. Expectant management should be carried out only with reliable and compliant patients.

2.6 Special circumstances

2.6.1 Ruptured Ectopic Pregnancy Management

Management of tubal pregnancy in the presence of haemodynamic instability should be by the most expedient method. In most cases this will be laparotomy.

There is no role for medical management in the treatment of tubal pregnancy or suspected tubal pregnancy when a patient shows signs of hypovolaemic shock. Transvaginal ultrasonography can rapidly confirm the presence of haemoperitoneum, if there is any diagnostic uncertainty. But expedient resuscitation and surgery should be undertaken. Experienced operators may be able to manage laparoscopically, women with even a large haemoperitoneum safely, but the surgical procedure which prevents further blood loss most quickly should be used. In most centers this will be laparotomy.

(Grade X)

2.6.2 Anti-D immunoglobulin

Non-sensitized women who are Rhesus negative with a confirmed or suspected ectopic pregnancy should receive anti-D immunoglobulin. **(Grade X)**

2.7 Summary

- Single dose methotrexate is best used for those who are asymptomatic, whose β -hCG is < 3000 mIU/ml, have tubal size < 3 cm, have no fetal cardiac activity on ultrasonography, and will come in to be followed closely. It cannot be used if there is a heterotopic pregnancy.
- Despite low and declining β -hCG levels, tubal rupture can still occur with methotrexate treatment. With severe pelvic pain, monitoring of vital signs and hematocrit can help differentiate between tubal abortion and tubal rupture.
- Most common side effects of methotrexate are;
 - a) stomatitis,
 - b) conjunctivitis,
 - c) mild abdominal pain of short duration. Rare side effects include dermatitis and pruritis.
- Surgery is done only if transvaginal ultrasonography shows an ectopic pregnancy.
- Laparoscopic surgery has been found to be superior to laparotomy and can treat most patients.
- Persistent ectopic pregnancy refers to the continued growth of trophoblastic tissue after surgery. Special attention should be given to the proximal portion during surgery and the ectopic pregnancy should be flushed out with suction irrigation.
- Expectant management is done when ectopic pregnancy is suspected, and transvaginal ultrasonography does not show an ectopic pregnancy. The patient is followed with weekly

- ultrasonography and weekly β -hCG measurements until the level is < 10 mIU/ml.
- All pregnant women who are Rh-negative should receive Rh immunoglobulin.

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