

FOGSI GCPR

ON

ECTOPIC PREGNANCY

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Introduction:

Ectopic pregnancy is the leading cause of maternal death in early pregnancy. Ectopic pregnancy is defined as the implantation of a fertilized egg outside the uterine cavity. The most common ectopic site of implantation (97%) is the fallopian tube. The remaining 3% of ectopic pregnancies are implanted in the cervix, ovary, peritoneal cavity, or uterine scars. A growing ectopic pregnancy in any location can cause the tissue to become vascular, friable and eventually rupture resulting in internal bleeding. This situation can be life threatening and needs to be treated as medical emergency.

Risk factors:

- Pelvic inflammatory disease including pelvic tuberculosis
- Previous ectopic pregnancy
- Pregnancy which has occurred with an Intrauterine Device
- Tubal surgeries (ligations, reconstructions, re-implantations)
- Sexually transmitted diseases
- Smoking
- Infertility, ovulation induction and ART procedures

However, the majority of women with an ectopic pregnancy have no identifiable risk factor.

Incidence:

The incidence of ectopic pregnancy among all pregnancies is about 0.25-2.0% (1).

Indian studies have found a incidence of ectopic pregnancies ranging from 1-2%.(2). However, there is a marked disparity in case fatality rates. Some studies have shown no mortality, whereas, it is as high as 3.5% in others.(3). This is a reflection of the variable quality and infrastructure of care available in the country across various settings.

In India there is high prevalence of pelvic tuberculosis. Pelvic tuberculosis has been identified as an important etiological factor. In one study, genital tuberculosis was found in 13.2% of all cases of ectopic pregnancy.(4)

Clinical presentation

Ectopic pregnancy should be suspected in any woman with child bearing age presenting to the clinic or casualty with symptoms such as amenorrhea, abdominal pain and vaginal bleeding (5). The presentation may sometimes be dominated with the complaint of fainting, collapse, breathlessness, or dizziness. Uncommon symptoms include diarrhoea, pain in the shoulder, rectal pressure, urinary symptoms, and anaemia.

The range of presentations correspondingly produces a variety of features on examination. For a small, undisturbed ectopic pregnancy, the physical examination could be normal. In these situations, the diagnosis is based on investigations. On the other hand, with late presentations, there could be a disturbance of the vital signs and features of shock may be present including tachycardia, tachypnea, hypotension, and rarely bradycardia. Abdominal examination may reveal guarding, rigidity and tenderness. There may be cervical motion tenderness, adnexal tenderness or fullness in the adnexae and pouch of Douglas.

The presence of abdominal signs with altered vital parameters suggests a hemoperitoneum and mandates urgent resuscitation and management at a centre with appropriate facilities for surgery and blood transfusion.

Diagnostic tests

Diagnostic tests for ectopic pregnancy include a urine pregnancy tests, Serum beta hCG and ultrasound. Increased clinical suspicion combined with these tests plays a very important role in management and outcome.

The instant result of a urine pregnancy test is a useful pointer for the clinician to suspect an ectopic pregnancy. The easy availability, low cost and reliability of this test should be utilized. The test is a useful triage tool for clinicians to rule out a pregnancy when the clinical situation is not clear such as a patient who is not sure of dates, does not remember or is in a state of shock and the history cannot be elicited.

Laboratory tests

A single laboratory value of beta hCG should not be used to diagnose the location of a pregnancy. The typical level in a healthy pregnancy on the day of the missed period is 50 to 100 IU/L. In a healthy intrauterine pregnancy, levels of serum β -hCG will double every 1.4 to 2.1 days and peak between 50000 and 100000 IU/L at 8 to 10 weeks of pregnancy. Compared to the pattern observed in healthy intrauterine pregnancies, the rate of increase between two serum β -hCG levels done 48 hours apart is slower (<50% increase) in unhealthy pregnancies (those destined to miscarry or in ectopic locations)(6,7). There are, however exceptions to the rule. Viable pregnancies may have a slow rise in serum levels and ectopic pregnancies which are viable may mimic a healthy intrauterine pregnancy in terms of serum β -hCG levels(8). Also, interpreting levels and rates of rise are complicated in situations where the pregnancy is a result of assisted reproduction or a multiple pregnancy. Taking into view these considerations, paired serum β -hCG levels though useful, should be used in conjunction with transvaginal ultrasound to establish a diagnosis. This approach does not have a role in the diagnosis of caesarean scar and heterotopic pregnancy pregnancy.

The initial serum β -hCG level is a key prognostic indicator for the success of conservative management (expectant and medical) in cases of ultrasound visualized ectopic pregnancies in all locations.

A serum β -hCG level may not be available at short notice in all care settings. Depending on the clinical situation, pregnancy can be confirmed by a urine pregnancy test and one may proceed with emergency care as appropriate using clinical judgement. A single serum β -hCG should be carried out at diagnosis to help with management.

Progesterone levels are not useful for the diagnosis of an ectopic and maybe used in the prognostication of pregnancy of unknown location.

Imaging

Ultrasound remains the mainstay of the diagnosis(9). High index of suspicion and a detailed history are pre-requisite of scanning. In general, when carrying out a transabdominal or transvaginal ultrasound scan during early pregnancy, scan the uterus and adnexa to see if there is a heterotopic pregnancy. Transvaginal ultrasound gives earlier diagnosis as compared to a transabdominal scan on full bladder. In some circumstances, depending on patient acceptance and availability of machine probes, only a transabdominal scan may be possible. A transabdominal ultrasound scan is also useful for women with enlarged uterus such as fibroids or an ovarian cyst.

MRI is more useful for the diagnosis of ectopic pregnancies at unusual sites such as a uterine scar or an abdominal ectopic pregnancy. It may be used when there is diagnostic uncertainty in stable patients. For unstable patients with strong suspicion a low threshold to surgical approach is justified.

Diagnosis of an aborting ectopic: may be difficult in an isolated ultrasound examination. A repeat examination and/or laboratory tests such as urine pregnancy test, serum hCG levels are needed.

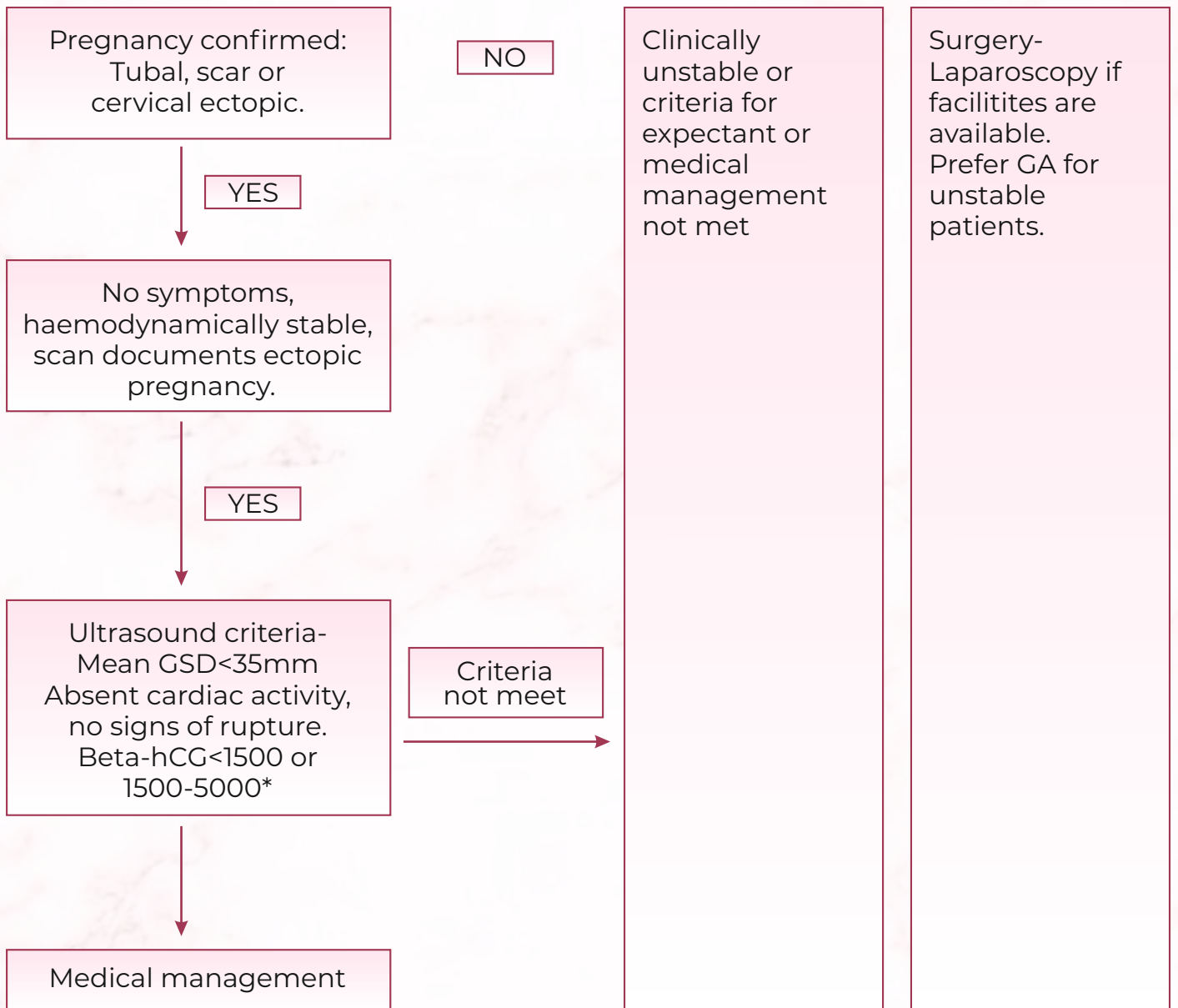
Diagnostic criteria and management options(10)

Suspected location	Ultrasound Diagnostic criteria (TVS/TAS)	Aid to diagnosis	Management options (see flowchart)
Tubal	Ultrasound- Non cystic adnexal mass, moving separate to the ovary, comprising a gestational sac containing a yolk sac/ fetal pole, with empty uterus or collected fluid. Ascites (hemoperitoneum) may or may not be present.	hCG levels, Progesterone Not recommended	Expectant Medical, Surgical
Cervical	An empty uterus, with a barrel-shaped cervix and a gestational sac present below the level of the internal cervical os. The absence of the 'sliding sign'. Blood flow around the gestational sac using colour Doppler.	Single Serum hCG levels Value greater than 10000iu are associated with decreased chance of successful medical management	Expectant Medical, Surgical
Caesarean Scar pregnancy	Empty uterine cavity with gestational sac or solid mass of trophoblast located anteriorly at the level of the internal os embedded at the site of the previous lower uterine segment caesarean section scar. Thin or absent layer of myometrium between the gestational sac and the bladder.	MRI can be used as second line if ultrasound diagnosis equivocal	Surgical preferred Medical management with ultrasound guided injection of methotrexate

	Evidence of prominent trophoblastic/ placental circulation on Doppler examination. Empty endocervical canal.		in the gestatio- nal sac. Intramuscular methotrexate may be used for very early presentations
Interstitial	Empty uterine cavity with products of conception / gestational sac located laterally in the interstitial (intramural) part of the tube and surrounded by less than 5 mm of myometrium in all imaging planes. Presence of the 'interstitial line sign'.	3D ultrasound or MRI to distinguish between angular and early intrauterine pregnancy.	Medical Surgical
Cornual rudimentary horn	Visualization of a single interstitial portion of fallopian tube in the main uterine body and gestational sac/products of conception seen mobile and separate from the uterus and completely surrounded by myometrium. Vascular pedicle adjoining the gestational sac to the unicornuate uterus.	3D ultrasound or MRI to distinguish between angular and early intrauterine pregnancy.	Medical Surgical
Ovarian	No specific agreed criteria Findings suggestive: Empty uterus Wide echogenic ring with an internal anechoic area on ovary Negative sliding organ sign- not possible to separate cystic structure from ovary on gentle probe palpation Corpus luteum identified separate from the ovary Presence of free fluid around the mass may represent ruptured ovarian ectopic	Single serum hCG	Surgical
Heterotropic	Ultrasound presence of an intrauterine pregnancy with a coexisting ectopic pregnancy	Persistent pain and rising hCG levels following miscarriage or termination of pregnancy	Surgical Medical/ Expectant if non-viable intrauterine pregnancy
Abdominal Ectopic	Absence of an intrauterine gestational sac Absence of both an evident dilated tube and a complex adnexal mass. A gestational cavity surrounded by loops of bowel and separated from them by peritoneum.	MRI, hCG levels,	Surgical Medical/ Expectant if non-viable intrauterine pregnancy

	A wide mobility similar to fluctuation of the sac, particularly evident with pressure of the transvaginal probe toward the posterior cul-de-sac.		
Pregnancy of unknown location	Scan cannot demonstrate a pregnancy however hCG levels confirm the same.	Serial hCG, scanning, high index of suspicion. SOS Surgery.	Expectant for confirmation of location. Persistent PUL can be offered medical or surgical treatment.

MEDICAL MANAGEMENT CRITERIA



MTX is the preferred treatment option when all of the following characteristics are present(10,11):

- Hemodynamic stability.
- Serum beta-human chorionic gonadotropin (hCG) concentration ≤ 5000 milli-international units/mL.
- Mean sac diameter < 3.5 cm with no fetal cardiac activity detected on transvaginal ultrasound (TVUS).
- Patients are willing and able to comply with post-treatment follow-up and have access to emergency medical services within a reasonable time frame in case of a deterioration in the clinical status.

MTX is contraindicated and surgery is required when the following are present :

- Hemodynamic instability.
- Intrauterine pregnancy, including a heterotopic pregnancy with coexisting viable intrauterine pregnancy.
- Signs or symptoms of impending or ongoing rupture of ectopic mass (eg, pelvic or abdominal pain or evidence of intraperitoneal bleeding suggestive of rupture).
- Clinically important abnormalities in baseline hematologic, renal, or hepatic laboratory values
- Medical conditions such as immunodeficiency, active pulmonary disease (eg, tuberculosis), and peptic ulcer disease
- Hypersensitivity to MTX.
- Breastfeeding.

MEDICAL MANAGEMENT

SINGLE DOSE REGIMEN

Single I/M dose on methotrexate 50 mg/m²

OR

Multiple dose regimen

Methotrexate 1mg/kg on day 1,3,5,7 with folinic acid rescue 0.1mg/kg im on day 2,4,6,8

Repeat beta hCG Day 4 and Day 7

Decrease in Beta hCG more than 15 % --

Successful medical Treatment ----

Measure Beta hCG weekly till non-pregnant value

Decrease in Beta hCG less than 15% --

Consider Repeat dose of methothrexate and repeat beta Hcg after 3 days

No Decrease in beta hCG after two doses – consider surgical management

Measure beta hCG on methotrexate dose days until it decreases by more than 15% from its previous value

Decrease in beta hCG greater than 15% — discontinue methotrexate --- Measure beta hCG weekly till non pregnant

No Decrease after 4 doses of methotrexate – consider surgical management

If BetahCG levels plateau or increase during weekly follow up consider administrating methotrexate for treatment of a persistent ectopic pregnancy

The focus group had concluded that single dose regimen only should be recommended.

Surgical management of tubal pregnancy(10,11):

Surgery is the first line of treatment when:

1. Criteria for expectant and medical management are not met with
 - Sac more than 35 mm
 - Cardiac activity present
 - Beta hCG more than 5000
 - Significant pain and hemoperitoneum
2. Failure of expectant or medical management
3. Clinical status of patient warrants urgent intervention
4. Compliance to medical management is doubtful

Approach: Laparoscopic or laparotomy

Approach depends on:

1. Clinical status of patient
2. Availability of laparoscopic facilities
3. Skill of the operating surgeon

Both the approaches are acceptable, especially in an emergency.

A laparoscopic surgical approach is preferable to an open approach.

A laparotomy is an acceptable alternative where there is no access or expertise in laparoscopy and especially in an acute clinical setting where operative intervention is a life-saving procedure.

It is desirable to take a consent for a laparotomy before laparoscopic surgery, especially for women with known pelvic inflammatory disease, pelvic masses, adhesions and previous surgeries.

Two options in surgical management for tubal pregnancy

Decision of salpingectomy or salpingotomy depends on the following factors

1. Patients clinical status
2. Desire for future fertility
3. Extent of tubal damage
4. Condition of contralateral tube

Salpingectomy

Complete or segmental removal of tube

Preferred when the tube is ruptured and damaged

Prerequisites:

Contralateral tube normal in fertility-desiring patients

Salpingotomy

Linear incision along the length of tube to enable removal of POCs

Preferred in unruptured ectopic

Prerequisites:

In women with a history of fertility-reducing factors (previous ectopic pregnancy, contralateral tubal damage, previous abdominal surgery, previous pelvic inflammatory disease), salpingotomy should be considered.

In either scenarios the tissue removed has to be sent for histopathology.

If a salpingotomy is performed, women should be informed about the risk of persistent trophoblast with the need for serum b-hCG level follow-up. They should also be counselled that there is a small risk that they may need further treatment in the form of systemic methotrexate or salpingectomy.

In India there is high prevalence of pelvic tuberculosis. This should be considered at the time of surgery for ectopic pregnancy. Appropriate sampling, testing and further treatment should be instituted for such situations.

Surgical management for ectopic pregnancy other than tubal(10,11):

Location of ectopic	Surgical management
Cervical	<p>First line of treatment: Medical/ conservative Indications for surgery: Failure of medical management or life threatening bleeding Surgical management to be carried out at tertiary care centre Options: 1.Suction and evacuation 2.Hysteroscopic resection under vision Additional measures to reduce bleeding: 1.Uterine artery embolization (UAE) 2.Laparoscopic or open uterine artery or internal iliac artery (ant div) ligation 3.Balloon tamponade 4.Hysterectomy</p>
Caesarean Scar pregnancy	<p>Surgical approach preferred over medical management Counselling regarding high risk of morbidity and mortality Options: 1.Suction evacuation or hysteroscopic guided resection 2.Laparotomy or laparoscopic approach – exposing the LUS by dissection the bladder and excision of the scar tissue with pregnancy --- reconstruction of LUS 3.Hysterectomy Additional measures to reduce bleeding: 1.Cervical cerclage 2.Uterine artery embolization (UAE) 3.Laparoscopic or open ligation of the uterine artery or anterior division of the internal iliac artery Balloon tamponade</p>
Interstitial	<p>First line of treatment: Medical/ conservative Indications for surgery: Failure of medical management or life threatening bleeding Options: 1.Laparoscopic or open cornual resection or salpingotomy- recommended approach 2.Hysterescopic resection under laparoscopic or usg guidance (Evidence is scant)</p>

Interstitial	Additional measures to reduce bleeding: 1. Use of diluted vasopressin for local infiltration 2. Uterine artery ligation at origin
Cornual/ rudimentary horn	Surgical approach is preferred Option: laparoscopic or open excision of rudimentary horn Attention to be paid to associated urinary tract anomalies
Ovarian	Surgical approach is preferred Option: laparoscopic or open removal of gestational products by enucleation or wedge resection Additional measures to reduce bleeding: Use of electrocautery or ovarian suturing Oophorectomy may be needed
Heterotopic pregnancy	Medical or conservative approach if intrauterine pregnancy non viable
Abdominal ectopic	Early first trimester abdominal pregnancy – laparoscopic approach Advanced abdominal pregnancy – laparotomy The placenta may be left insitu if the vascular attachment involves vascular structures or vital organs. Await spontaneous absorption or use adjuvant treatment with methotrexate or selective arterial embolization.

Role of anti D:

Offer anti D prophylaxis to all RhD negative women who have been treated medically or surgically for ectopic pregnancy(12).

Ectopic and future fertility:

In absence of history of subfertility or tubal pathology, women should be advised that there is no difference in the rate of fertility, risk of tubal pregnancy between the different management methods.

Women with previous history of subfertility should be advised that treatment of their tubal ectopic pregnancy with expectant or medical management is associated with better reproductive outcome as compared to surgical management

Summary

Ectopic pregnancies are a significant cause of maternal morbidity and mortality. Women at a high risk include those with previous pelvic surgery, ectopic, PID, smokers etc. The diagnosis may sometimes take a few days to establish and thus a high index of suspicion should be exercised. Individualised management should be offered considering mother's fertility history, type of ectopic, wishes, understanding, and access to the emergency services. Expectant and medical management may be offered judiciously to clinically stable patients with low threshold for emergency surgery. Due to chance of drug toxicity a single dose methotrexate is recommended over multi-dose regimen. Surgical management is preferred for patients who are unfit for the above or with ectopic at sites such as- caesarean scar, cornual/rudimentary horn, ovarian, interstitial. When offering surgery for tubal ectopics salpingectomy should be preferred over salpinogotomy which is associated with higher recurrence of ectopic in future.

Routine endometrial curettage to document Arias Stella reaction is NOT recommended. Anti-D should be offered to Rh negative mothers.

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