Disorders of early pregnancy:

Early pregnancy disorders currently account for approximately three-quarters of emergency gynaecological admissions and are an important cause of maternal morbidity and mortality throughout the world. Pregnancy loss may have a profound effect on a woman and, appropriate counselling and support should be made available.

Introduction

The three main categories of early pregnancy disorders are:

1. spontaneous miscarriages
2. ectopic pregnancies
3. gestational trophoblastic disorders (GTDs).

Symptomatology:

The classical symptoms triad for early pregnancy disorders is:

1. amenorrhoea.
2. pelvic or low abdominal pain.
3. vaginal bleeding.

Pregnancy symptoms are often non-specific and many women of reproductive age have irregular menstrual cycles.

Pregnancy tests

Human chorionic gonadotrophin has a half-life of 6-24 hours and rises to a peak in pregnancy at 9-11 weeks' gestation. The first test to confirm the existence of pregnancy is for the detection of human chorionic gonadotrophin (hCG) in the patient's urine or plasma.

Human chorionic gonadotrophin is a placental derived glycoprotein, composed of two subunits, alpha and beta, which maintains the corpus luteum for the first 7 weeks of gestation. Extremely small quantities of hCG are produced by the pituitary gland and thus plasma hCG is almost exclusively produced by the placenta.
Definition:

An ectopic pregnancy occurs when the conceptus implants either outside the uterus (Fallopian tube, ovary or abdominal cavity) or in an abnormal position within the uterus (cornua, cervix). Combined tubal and uterine (heterotopic) pregnancies are uncommon.

Epidemiology and risk factors:

The incidence of ectopic pregnancy is about 1 %. Between 95 and 98 percent of ectopic pregnancies occur in the Fallopian tube.

Site of ectopic pregnancy:

Site of tubal ectopic pregnancy are:

1. More than 50 % of tubal pregnancies are situated in the **ampulla**.
2. Approximately 20 % occur in the **isthmus**.
3. Around 12 % are **fimbrial**.
4. Approximately 10 % are **interstiti**.

Pathogenesis

Sites of Implantation

Fallopian tube – most common site (ampulla) – 95%

Other 5% occur in:

- Ovary
- Uterine cornu
- Cervix
- Broad ligament
- Spleen
- Liver
- Retroperitoneum
- Diaphragm
- Cesarean scar
**Risk factors:**

The risk of ectopic pregnancy increases with:
1. maternal age,
2. number of sexual partners,
3. the use of an intrauterine device,
4. after proven pelvic inflammatory disease (gonorrhoea, *Chlamydia*) and
5. after pelvic surgery.

The risk of recurrence is around 10 per cent and is increased in those who have had a previous miscarriage or who have suffered tubal damage.

**Risk factor for ectopic pregnancy:**

1. Tubal sterilization
2. Previous ectopic pregnancy
3. Assisted reproduction & infertility
4. Intrauterine device
5. Documented tubal pathology
6. Infertility
7. Previous genital infection
8. Multiple partners
9. Previous pelvic/abdominal surgery
10. Smoking
11. Caesarean section
12. Tubal corrective surgery

**Mortality rate:**

Mortality from ectopic pregnancy remains high. Representing 13 per cent of all maternal deaths. The fatality rate of ectopic pregnancy is about four times that of childbirth.

**Ectopic pregnancy: Pathophysiology**

Any mechanical or functional factors that prevent or interfere with the passage of the fertilized egg to the uterine cavity may be aetiological factors for an ectopic pregnancy.

**Functional Factors:**

1. Progesteron only pill.
2. Intrauterine device.
3. Luteal phase defects
4. Cigarette smoking
5. Vaginal douching
It is believed that the main cause for a tubal implantation of the gestational sac is a low-grade infection, as approximately 50% of women operated on for an ectopic pregnancy have evidence of chronic pelvic inflammatory disease. A high proportion of women with a tubal pregnancy miscarry during the early stages of gestation. The products of conception may persist for a considerable period of time within the tube as one form of ‘chronic ectopic pregnancy’, or they may be gradually absorbed.

If implantation occurs into a site of the tube that offers a sufficient area for placentation, the process is very similar to that of an intrauterine pregnancy, for the conceptus penetrates the tubal mucosa and becomes embedded in the tissues of the tubal wall.

The extravillous trophoblast will penetrate the full thickness of the muscular layer of the tube to reach the subserosa and the tubo-ovarian circulation. Due to its limited distensibility, the tube will rupture and usually accompanied by fetal death, occasionally following rupture the fetus retains sufficient attachment to its blood supply to maintain viability and secondary abdominal pregnancy can proceed to term.

In an ectopic pregnancy, the uterine endometrium usually responds to the hormonal changes of pregnancy and undergoes focal decidua changes (Arias-Stella reaction). If the ectopic pregnancy miscarries, the uterine decidua may slough off as a cast, but more commonly as fragments mixed with small blood clots.

**Uterine Changes in Ectopic Pregnancy**

The uterus undergoes some of the changes associated with early normal pregnancy, including increase in size and softening of the cervix and isthmus. Lack of uterine changes does not exclude an ectopic pregnancy. The finding of uterine decidua without trophoblast suggests ectopic pregnancy but is not absolute.

*Arias-Stella reaction:*

Endometrial changes characterized by hypertrophic, hyperchromatic, lobular and irregularly shaped nuclei, and vacuolated, foamy cytoplasm with occasional mitoses Not specific for ectopic and may occur with normal implantation.

**Clinical features**

Compared to the other forms of early pregnancy disorders, there is no pathognomonic pain or findings on clinical examination that are diagnostic of a developing extrauterine pregnancy.

Vaginal bleeding (usually old blood in small amounts) and chronic pelvic pain (iliac fossa, sometimes bilateral) are the most commonly reported symptoms.

**Signs & Symptoms**

Often **subtle**, or even **absent**

1. **Pain:** Pelvic and abdominal pain – sharp, stabbing or tearing in character, rectal pain. Pleuritic chest pain – from diaphragmatic irritation caused by the hemorrhage
2. Abnormal Menstruation

Amenorrhea

Vaginal bleeding – may be scanty, dark brown, intermittent or continuous

3. Abdominal and pelvic Tenderness

Tenderness on abdominal and vaginal examination especially on motion of the cervix – ruptured or rupturing tubal pregnancies.

4. Uterine Changes

In 25% of women, the uterus enlarges due to hormonal stimulation of pregnancy.

5. Blood pressure and pulse

Before rupture vital signs are generally normal. Hypotension and tachycardia – if bleeding continues and hypovolemia becomes significant

6. Pelvic Mass

Almost always either posterior or lateral to the uterus, and typically soft and elastic

The mass may be firm with extensive infiltration of blood into the tubal wall.

General examination:

- This must include a record of pulse rate and blood pressure.
- Shoulder pain, which may occur secondary to blood irritating the diaphragm.
- Vascular instability characterized by low blood pressure, fainting, dizziness and rapid heart rate may be noted.

These symptoms are present in more than 50% of patients and are most typical of patients whose ectopic pregnancy has ruptured (intra-abdominal bleeding).

Gynecological examination:

- Speculum or bimanual examination must be performed in an environment where facilities for resuscitation are available,

as this examination may provoke the rupture of the tube.

Culdocentesis:

Culdocentesis: to exclude haemoperitoneum has also been a routine investigation in the emergency room to rule out ectopic pregnancy. Because this test is based on late development in the natural history of the ectopic pregnancy, it is obviously not going to be useful in detecting an early ectopic pregnancy.
The cervix is pulled toward the symphysis with a tenaculum, and a long 16- or 18-gauge needle is inserted through the posterior fornix into the cul-de-sac. Fluid containing fragments of old clots, or bloody fluid that does not clot, is compatible with the diagnosis of hemoperitoneum resulting from an ectopic pregnancy.

**Human chorionic gonadotrophin and transvaginal ultrasound:**

plasma hCG and transvaginal sonography have allowed for a less invasive evaluation of the patient with a suspected ectopic pregnancy. The hCG levels and ultrasound findings must be interpreted together.

One of the most important parameters is the discriminatory hCG level above which the gestational sac of an intrauterine pregnancy should be detectable by ultrasonography (usually 1000-1500 IU/L).

**Serum Progesterone Levels:**

- A value exceeding 25ng/mL excludes ectopic pregnancy.
- Values below 5ng/mL suggest either an intrauterine pregnancy with a dead fetus or an ectopic pregnancy

**Ultrasound:**

The presence or absence of an intrauterine gestational sac is the principal point of distinction between intrauterine and tubal pregnancy. The sonographic finding of an extraterine sac with an embryo or embryonic remnants is the most reliable diagnosis of ectopic pregnancy. An empty ectopic sac or a heterogeneous adnexal mass is a more common ultrasound feature.

The presence of fluid in the pouch of Douglas is a non-specific sign of ectopic pregnancy. In 10-20% of ectopic pregnancies, a pseudogestational sac is seen as a small, centrally located endometrial fluid collection surrounded by a single echogenic rim of endometrial tissue undergoing decidual reaction.

**Laparoscopy**

Laparoscopy should be considered in women with hCG above the discriminatory level and absence of an intrauterine gestational sac on ultrasound.

**Management:**

Ectopic pregnancy can be treated:

1. conservative (expectant).
2. medical.
3. surgical.
According to:

1. Clinical presentation.
2. Ultrasound finding.

**Anti-D Immunoglobulin:**

*D-negative* women with an ectopic pregnancy who are not sensitized to D-antigen should be given anti-D immunoglobulin.

**Expectant Management:**

**Criteria:**

1. Decreasing serial β-hCG levels.
2. Tubal pregnancies only.
3. No evidence of intra-abdominal bleeding or rupture as assessed by vaginal sonography.
4. Diameter of the ectopic mass not greater than 3.5 cm.

**Surgical Management:**

**CONSERVATIVE**

**Salpingostomy**

Used to remove a small pregnancy usually <2 cm in length. A 10-15 mm linear incision is made on the antimesenteric border immediately over the ectopic pregnancy, and is *left unsutured* to heal by secondary intention. Readily performed through a laparoscope *gold standard* surgical method used for unruptured ectopic pregnancy.

**Salpingotomy**

Procedure is the same as salpingostomy except that the incision is closed with a suture.

**Surgical Management: RADICAL**

**Salpingectomy**

Tubal resection may be used for both ruptured and unruptured ectopic pregnancies. Performed if the fallopian tube is extensively diseased or damaged.

**Management**

The classical approach to the treatment of ectopic pregnancy has always been surgical:

(salpingectomy or salpingotomy), either by laparotomy or laparoscopy.

The wider use of ultrasound, an early diagnosis is now possible in many cases before the onset of symptoms.
Medical Management: METHOTREXATE

An anti-neoplastic drug that acts as a folic acid antagonist, and is highly effective against rapidly proliferating trophoblasts.

Success is greatest if:

- The gestation is <6 weeks
- The tubal mass should be <3.5 cm in diameter
- The fetus is dead
- B-hCG is <15,000 mIU/mL

Contraindications:

1. Intra-abdominal hemorrhage
2. Breast feeding
3. Immunodeficiency
4. Alcoholism
5. Liver or renal disease
6. Blood dyscrasias
7. Active pulmonary disease
8. Peptic ulcer

Management

Non-surgical (medical) therapeutic approaches have been introduced, such as

1. puncture and aspiration of the ectopic sac,
2. local injections of prostaglandins.
3. potassium chloride.
4. hyperosmolar glucose.
5. methotrexate.

The advantages of treatment that does not involve surgery or the use of potentially toxic drugs are obvious. With earlier diagnosis it has also become apparent that spontaneous regression of tubal pregnancies is more common than previously thought. This has led to non-interventional expectant management, which is based on the assumption that a significant proportion of all tubal pregnancies will resolve without any treatment.

Unfortunately, not all patients will be suitable for this type of treatment or for a simple follow-up, and strict criteria must be observed in the selection of patients. Ultrasound examinations combined with serial hCG assessments are prerequisites for successful expectant management or in the follow-up of the patient treated medically.