**Preterm labor**

**Introduction:**

There are two major clinical subtypes of preterm birth. Indicated or iatrogenic (due to medical or obstetric complications) make up approximately one-third of all such birth. The remaining two-thirds are classified as spontaneous preterm births and have two subdivisions: spontaneous preterm labour and preterm pre-labour rapture of membrane (PPROM). This mean each is account for one third of the causes.

**Definition:** birth that occurs after viability but before 37 weeks.

In pregnancy term refers to the gestational period from 37+0 to 41+6 weeks. Preterm occur between 24+0 and 36+6 weeks.

**Prevalence:**

The prevalence in UK is about 6.6-7.4%. , however the incidence is differ according to the class of preterm birth. Significantly higher rate of preterm birth of up to 12% are reported from USA. Conversely many European countries quote rates below 5%. This may reflect differing etiological, socioeconomic and cultural factors.

**Classification:** for reasons related to etiology, outcome, and recurrence risk, preterm birth is subdivided into three gestational periods :

a- Mildly preterm: at 32+0 to 36+6 weeks (incidence 6.1%).

b- Very preterm: at 28+0 to 31.6 weeks (incidence0.9%).

c- Extremely preterm: at 24+0 to 27+6 weeks (incidence 0.4%).

**Etiology:** labor at term and prior to its share a common pathway involving uterine contractility, cervical effacement and dilatation and membrane rapture.
At term, the activation of this pathway is physiological. However, a variety of pathologies underlie labor remote from term. It has been suggested by some authors that preterm labor be considered a syndrome, in order to emphasize its multifactorial.

1- **Infection**: subclinical intrauterine infection of the choriodecidual space and amniotic fluid is the most widely studied etiological factor underlying spontaneous preterm births. The uterine cavity is normally sterile but the vagina contains commensal bacteria. Depending on the bacterial load and cervical resistance, the bacteria may ascend through the cervix and reach the fetal membranes. This may activate the deciduas, increase prostaglandin release and trigger contractions. Alternatively, it may weaken the membranes, leading to rapture. Early-onset neonatal sepsis, maternal postpartum endometritis and histological chorioamnionitis are all significantly more common after preterm birth, particularly those very early deliveries before 32 weeks.

2- **Vascular**: disturbance of the uteroplacental interface may lead to intrauterine bleeding. The blood can track down behind the membranes to the cervix and be revealed. Alternatively, it may track away from the cervix and be concealed. Either way, the blood irritates the uterus, leading to contractions, and damages the membranes, leading to early rapture.

3- **Uterine over distension**: overstretching of the myometrium (and possibly the membrane) leads to increased contractile activity and premature shortening and opening of the cervix. The possible causes are:
   a- **Multiple pregnancies**: this is the most common cause of uterine over distension. The median gestational age at delivery for twins is approximately 35 weeks and for triplets 33 weeks. Presently assisted reproductive techniques are responsible for majority of multiple pregnancies, although preterm delivery in this population can be decreased through multi-fetal reduction techniques.
   b- **Polyhydramnios**: fetal anomalies, such as atresias of the gastrointestinal tract are the most common cause of polyhydramnios leading to preterm delivery
4- **Cervical weakness or cervical insufficiency**: patients presenting with painless cervical dilatation without regular contraction were historically deemed to have cervical incompetence. Recently the features of cervical insufficiency is listed as follow:

a- History of two or more second trimester pregnancy losses
b- History of losing each pregnancy at an earlier gestational age.
c- History of painless cervical dilatation of up to 4-6cm.
d- Absence of clinical finding consistence with placental abruption.
e- History of cervical trauma caused by an operation or instrumentation on cervix e.g. cone biopsy, intrapartum cervical laceration or excessive forced cervical dilatation during curettage.

The normal cervical length is about 3.5cm. Studies suggested that the risk of preterm birth with increased progressively as the cervical length decreased. At a cervical length of 26mm the risk increases 6-fold.

5- **Abnormal uterine cavity**: a uterine cavity that is distorted by congenital malformation may be less able to accommodate the developing pregnancy. Associated abnormal placentation and cervical weakness may also contribute. Fibroids in a low position may also lead to complications. However, fibroids are common and most pregnancies are successful despite their presence.

6- **Surgical procedure and intercurrent illnesses**: serious maternal infective illnesses such as pyelonephritis, appendicitis and pneumonia are associated with preterm labor. In these cases, preterm labor is presumed to be due either to direct blood-born spread of infection to the uterine cavity or indirectly to chemical trigger such as endotoxins or cytokines. Many other illnesses, such as cholestasis of pregnancy, and non-obstetric surgical procedures are associated with preterm labor, although the mechanisms for this remain obscure.

Amniocentesis is a pregnancy-specific procedure associated with an increased risk of miscarriage and early birth. It’s usually performed after 15 weeks with a chance of 0.5 percent of subsequent pregnancy loss.
7- **Idiopathic**: in many case, especially in mildly preterm births between 34-36 weeks, no cause will be found. In these cases, the physiological pathways to parturition may simply have been turned on too early.

**Risk factors for preterm labor/PPROM:**

**A- Non-modifiable, major**
- One previous preterm birth: 20% risk.
- Two previous preterm birth: 40% risk.
- Twin pregnancy: 50% risk.
- Uterine abnormalities.
- Cervical anomalies like cervical damage e(cone biopsy, repeated dilatation) and cervical fibroid.
- Factors in current pregnancy like recurrent ante partum hemorrhage, intercurrent illness and any invasive procedure or surgery.

**B- Non-modifiable, minor**
- Teenagers having second or subsequent babies.
- Parity (0 or >5)
- Ethnicity (black women).
- Poor socioeconomic status.
- Education (not beyond secondary).

**C- Modifiable:**
- Smoking: two-fold increase of PPROM.
- Drugs of abuse: cocaine.
- Body mass index (BMI) <20: underweight women.
- Inter-pregnancy interval <1 year.

**Clinical feature:**

**History:** less than 50% of all women presenting with symptoms suggesting a risk of early delivery will delivery within 7 days. In isolation, contraction is poorly correlates with the risk of preterm birth. Markers of intensity such as analgesic requirements, or simple bedside clinical impression, may add refinement. Vague complaints such as increases discharge, pelvic pressure or low back ache are
sometime reported, with latter two often showing a cyclical pattern. Nonetheless, the diagnosis of preterm labor remains notoriously difficult unless contractions are accompanied by advanced dilatation >3cm, ruptured membranes or significant vaginal bleeding. Always check the dating of pregnancy by reviewing the menstrual history and if possible, any prior ultrasound examination.

**Examination:**

A brief general examination is important to assess overall health. This will include pulse, blood pressure, temperature, and state of hydration.

Abdominal examination may reveal the presence of uterine tenderness, suggesting abruption or chorioamnionitis. Digital examination should be limited, as they are known to stimulate prostaglandin production and may introduce organism into the cervical canal.

A careful speculum examination by an experienced clinician may yield valuable information; pooling of amniotic fluid, blood and/or abnormal discharge may be observed. A visual assessment of cervical dilatation is usually possible and has been shown to be as accurate as digital examination finding.

**Investigations:**

- **Bedside fibronectin testing:**
  Fetal fibronectin (fFN) is a glue-like protein binding the choriodecidual membranes. It is rarely present in vaginal secretion between 23 and 34 weeks. Any disruption at the choriodecidual interface results in fFN release and possible detection in the cervical secretions. This offers a rapid assessment of risk in asymptomatic women who do not have advanced dilatation. If done correctly, these tests have a greater predictive value than digital examination. In one study, 30% of women with a positive fibronectin test delivered within 7 days, compared with only 10 percent of women who were 2-3 cm dilated.

- **Cervical length:**
  Cervical length measurement by transvaginal ultrasound has also been shown to improve diagnostic accuracy. Significant cervical shortening is
often accompanied by dilatation and funneling of the membrane down the cervical canal. Ultrasound should also record presentation, amniotic fluid volume, and placental localization. Skilled ultrasonographer and suitable machines with transvaginal probes are required. Cervical incompetence if diagnosed clinically and proved by ultrasound is best treated by placing non absorbable suture material like mersallen tap around internal cervical os under anesthesia after first trimester by McDonald’s operation.

- Other investigations include CBP, ABO and Rh type, urine for culture and sensitivity and lower vaginal swab for culture and sensitivity

- Repeated vaginal examination: repeated vaginal examination in 1-4 hours should be considered essential in the absence of specialized tests. The interval between assessments should be guided by the severity of the symptoms.

**Differential diagnosis:**

1- Urinary tract infection.
2- Red degeneration of fibroid.
3- Placental abruption.
4- Constipation.
5- Gastroenteritis.

**Communication:** there are two important areas of communication in management of women with threatened preterm labor:

a- Communication with women and her family. And
b- Communication neonatologist.

**Drug therapy:**

**I-Steroids:**

Current evidence shows that a single course of maternal steroids given between 26 and 34 weeks gestation and received within 7 days of delivery results in markedly improved neonatal outcomes, with significant reduction in rates of
- Respiratory distress syndrome.
- Neonatal death.
- Intraventricular hemorrhage.

Maximum benefit from the injection is seen after 24 hours. Courses received less than 24 hours and more than 7 days before delivery did not produce a significant reduction in respiratory distress syndrome. Although there is reassuring evidence about the long term safety of steroid, repeated courses better to be avoided as it may causes:

- Increased risk of infection in PPROM.
- Restricted fetal body and brain growth.
- Adrenal suppression.

Corticosteroid can cause significant glycaemic disruption in diabetic women. They should be used in conjunction with increased glucose monitoring and adjusted insulin dose.

In general, no convincing difference is seen between betamethason and dexamethason, although a recent study shows improved neurological outcomes with betamethasone. The dose is 12 mg two times only with 12 hours apart.

**II-Tocolysis:**

The aim of tocolysis is to prolong gestation for at least until the administered corticosteroid will act which require 24 hours to 7 days for maximum effect to be achieved and also to allow time for inutero transfer to a unit with suitable premature unit. However, tocolytic may be harmful because:

1- It may prolong exposure of fetus to other wise harmful intrauterine environment like infection.
2- No improvement in neonatal outcome.

**Conditions that preclude the use of tocolytic:**

1- Progressive cervical dilatation.
2- Chorioamnionitis.
3- Fetal death or congenital anomalies.
4- Bleeding (abruption placenta).
5- Sever maternal medical or obstetrical conditions like sever maternal cardiac
disease or sever pre-eclampsia.

**Types of tocolytics:**

1- **Beta-agonist:** like ritordine and salbutamol, these drugs only prevent
delivery for 48 hours and not improve neonatal outcomes. These drugs
have significant side effects including hypotension, anxiety and palpitation.
Maternal death from acute cardiopulmonary compromise have been
described, with greatest risk if it given”
- In large fluid volume.
- In multiple pregnancies.
- In women with cardiac diseases.

In diabetic women additional care is needed as it causes significant extra
glycaemic disruption.

2- **Oxytocin antagonist:** like atosiban, this is principally an Argene
vasopressin receptor antagonist but also binds the oxytocin receptors. This
drug is widely used in UK because of significantly reduced side effects
compared to beta-agonist, but similarly dose not improves clinical
outcomes.

3- **Other agents:** other smooth muscle relaxants used to treat preterm labour
include magnesium sulphate, nifedipine, and GTN. There is little evidence
to suggest increased efficacy or improved outcomes.
Non-steroidal anti-inflammatory drugs (NSAIDs) such as indomethacin.
Although it might delay preterm delivery for up to 7 days, but its
undesirable drug because of its deleterious effects on renal ductus
arteriosus and renal artery causing oligohydramnios.

**III- Antibiotics:** it does seem to improve clinical outcome, but it may be beneficial
in PPROM.
**Fetal assessment:**

Monitoring of fetus is important although there are considerable difficulties surrounding the interpretation of the fetal heart rate in preterm infants, particularly at extremely early gestations.

**Mode of delivery:**

1- Every effort should be made to transfer a woman to a unit with facility of intensive preterm care unit.
2- Appropriate analgesia is required to prevent unnecessary maternal effort.
3- If gestational age is extremely low no need for C/S for fetal reason as neonatal outcomes at this early gestations are very poor.
4- As gestation advances, both neonatal outcome and ability to diagnose fetal compromise will improve, and intervention for fetal reason becomes universally appropriate.
5- Until now the evidence suggest that preterm breech better to be delivered by C/S.