

Management of Preterm Premature rupture of the membranes (PPROM):

Introduction:

Preterm premature rupture of membranes (PPROM) is ROM prior to 37 weeks' gestation, but before the onset of labor. PPRM is far more difficult to manage than premature rupture of membranes (PROM) at term. Several issues need to be considered in formulating a plan of management. Prematurity is the principal risk to the fetus, while infection morbidity and its complications are the primary maternal risks.

The management of PPRM depends on the balance between the risks for fetal and neonatal complications with immediate delivery versus the risks and benefits of conservative treatment. The neonatal risks are primarily gestational age related. Therefore, the initial steps include confirmation of membrane rupture in addition to assessment of estimated gestational age, duration of membrane rupture, exclusion of maternal infection or abruption and assessment of fetal well being. Several areas of controversies exist regarding the best medical approach or management of PROM remote from term. Expectant management and immediate delivery are potential options in these patients, and each has its own advantages and disadvantages. With appropriate care, the maternal risks of expectant management are generally expected to be minimal and a clear neonatal advantage exists by reducing risks of prematurity. Some of the issues in management are discussed below with available guidelines from the august bodies.

Usual Outcome of Expectancy:

- In absence of adjunctive treatments, for any patient with preterm PROM, birth within 1 week is the most likely outcome,
- The earlier the PROM occurs, the greater is the latency period.
- Spontaneous sealing of the membranes does occur occasionally (< 10% of all cases), mostly after PPRM that has occurred subsequent to amniocentesis; however, this is the exception rather than the rule

Diagnosis:

- The diagnosis is made by a history suggestive of spontaneous rupture of membranes followed by a sterile speculum examination demonstrating pooling of fluid in the posterior vaginal fornix
- Digital vaginal examination is best avoided unless there is a strong suspicion that the woman may be in active labour or imminent delivery is anticipated

- If the diagnosis is not clear by history and examination, a Nitrazine paper test or fern test may be necessary. The combination of the aforementioned four procedures has a sensitivity of 93.1% in diagnosing PPROM.
- Ultrasound examination is useful in some cases to help confirm the diagnosis, in addition to providing information about the fetal condition and the status of the cervix.
- Fetal fibronectin test has a limitation of poor predictive value because of high false positive rate. Therefore despite high (98-99%) negative predictive value its use is not recommended.
- When the clinical history or physical examination is unclear, membrane rupture can be diagnosed unequivocally with USG guided transabdominal instillation of indigo carmine dye (1 mL in 9 mL of sterile normal saline), followed by observation for passage of blue fluid from the vagina.
- AmniSure, a rapid immunoassay, although accurate in the diagnosis, is still in the experimental stage. The sensitivity and specificity of AmniSure is 98.9% and 100% respectively.

General approaches of expectant management of preterm PROM:

- Modified bed rest to enhance re-accumulation of amniotic fluid and complete pelvic rest
- Periodic assessment for evidence of infection, abruption placentae, umbilical cord compression, fetal wellbeing, and labor
- The criteria for the diagnosis of clinical chorioamnionitis include maternal pyrexia, tachycardia, leucocytosis, uterine tenderness, offensive vaginal discharge and fetal tachycardia.
- It is not necessary to carry out weekly maternal full blood count or CRP.
- Leukocyte counts are nonspecific when there is no clinical evidence of infection, especially if antenatal corticosteroids have been administered.
- Periodic USG monitoring of amniotic fluid volume and fetal heart would be an acceptable strategy
- Weekly high vaginal swab need not be performed.
- CTG is useful and indeed fetal tachycardia is used in the definition of clinical chorioamnionitis.
- Biophysical profile score and Doppler velocimetry can be carried out, but these tests are of limited value in predicting fetal infection.
- An abnormal parameter or a combination of them may indicate intrauterine infection.
- There is insufficient evidence to recommend the use of amniocentesis in the diagnosis of intrauterine infection.
- There is no consensus on the frequency of optimal assessment,

Use of tocolytics in PPROM:

- Available data do not support the routine use of either prophylactic or therapeutic tocolysis after PPROM.
- In absence of any evidence, a specific recommendation for or against tocolysis in cases of PPROM cannot be made.

Corticosteroids in PPROM:

- A single course of antenatal steroid therapy before 32 weeks of gestation significantly reduces the risks of neonatal death, RDS, intraventricular hemorrhage, and necrotizing enterocolitis
- Available evidence demonstrates that antenatal steroid therapy does not increase the risks of neonatal or maternal infection irrespective of gestational age
- There is no data on the use of rescue administration of corticosteroids in women with PPROM.
- Based on available evidence, the efficacy of corticosteroid use at 32–33 completed weeks is unclear, but treatment may be beneficial particularly if pulmonary immaturity is documented. (ACOG)
- Corticosteroid use before fetal age of viability is not recommended, as sparse data exists on the efficacy. (ACOG)

Antibiotics use in PPROM:

- Women presenting with PPROM should be screened for UTI, STI, and GBS carrier, and treated with appropriate antibiotics if positive.
- Use of antibiotics in the setting of PPROM increases the latency and decreases the risks of chorioamnionitis and perinatal infection.
- There is no consensus in the choice of antibiotics and the duration of therapy
- Amoxicillin/clavulanic acid should not be used because of an increased risk of neonatal necrotizing enterocolitis. Amoxicillin without clavulanic acid is safe.
- Erythromycin or penicillin appears the antibiotic of choice. Erythromycin may be used in women who are allergic to penicillin
- Erythromycin should be given for 10 days following the diagnosis of PPROM. (RCOG)
- If group B streptococcus is isolated in cases of PPROM, antibiotics should be given. Penicillin should be administered, or Clindamycin in women who are allergic to penicillin. (RCOG).

- A 48-hour course of intravenous Ampicillin and erythromycin followed by 5 days of amoxicillin and erythromycin is recommended during expectant management of preterm PROM to prolong pregnancy and to reduce infectious and gestational age-dependent neonatal morbidity. (ACOG)
- All women with PROM and a viable fetus, including those known to be carriers of GBS and those who give birth before carrier status can be delineated, should receive intrapartum chemoprophylaxis to prevent vertical transmission regardless of earlier treatments. (ACOG)
- Revised guidelines from CDC recommend that women with PPROM who are not in labor should receive intravenous GBS coverage for at least the first 48 hours, until the GBS test results obtained on admission are available. However, GBS test results should not affect the duration of antibiotic therapy.
- If the patient completes the full course of antibiotic prophylaxis has no evidence of infection or labor, intrapartum GBS prophylaxis can be managed based on the results of the baseline GBS test at the time of PPROM, unless 5 weeks have passed. This is because a negative GBS test result is considered valid for 5 weeks
- SOGC Recommendation:
 - Antibiotic regimens may consist of an initial parenteral phase followed by an oral phase, or may consist of only an oral phase.
 - Ampicillin 2 g intravenously (IV) every 6 hours and erythromycin 250 mg IV every 6 hours for 48 hours followed by amoxicillin 250 mg orally every 8 hours and erythromycin 333 mg orally every 8 hours for 5 days
 - Erythromycin 250 mg orally every 6 hours for 10 days.

Time to deliver:

The conclusions were that there is insufficient evidence to guide clinical practice on the benefits and harms of immediate delivery compared with expectant management. (Cochrane 2010)

Prior to 32 weeks

- The evidence suggests expectant management with antibiotics and steroids in absence of any complication (infection, abruption, active labor or non-reassuring fetal heart).
- However, long term outcome of these preterm infants are a real concern.

PPROM ≥ 34 weeks

- Most recommend delivery since little benefit is likely to accrue following expectant management.
- GBS culture and use of appropriate antibiotics is recommended

PPROM between 32-34 weeks

- Some recommend collection of amniotic fluid for fetal lung maturity testing followed by expectant treatment until 34 weeks or until the lung maturity is positive
- Another group recommends aggressive approach to delivery since the risk of infection increases with expectancy.
- The management remains controversial until the long term outcome of the infants delivered electively during this gestational age is available from good quality evidences

Amniocentesis and USG guided procedures:

- There is insufficient evidence to guide clinical practice concerning the use of amnioinfusion during labor
- There is insufficient evidence to recommend transabdominal amnioinfusion in very preterm PPRM as a method to prevent pulmonary hypoplasia.
- The procedures may be helpful in selected situations both for diagnosis (rupture of membranes, evidence of infection) and treatment. However, these uses are still in experimental stage.

PPROM with cervical cerclage in place:

- Because the available studies are small and nonrandomized, the optimal timing of cerclage removal is unclear.
- The result of a multicentric RCT of removal vs retention of cerclage in PPRM is expected to be published in 2012 and would likely to provide some answer based on evidence.
- Until then following guidelines are suggested –
 - ≥ 32 weeks with PPRM – immediate removal of cerclage is recommended
 - Before the age of viability, cerclage removal is suggested as there would be very little, if any fetal/neonatal benefits with maternal risks only.
 - 24-31 weeks - The risks and benefits of short-term cerclage retention pending completion of antenatal corticosteroid therapy to enhance fetal maturation have not been evaluated.

Twin pregnancies with PPRM

- Data on twin and PPROM are sparse and not very robust. Therefore recommendations for management of such women are extrapolated from studies in singletons.
- Special considerations must be given in monochorionic twins and when PPROM occurs after invasive procedures before the age of fetal viability.
- Antenatal steroids and antibiotics seem reasonable during expectancy
- Management should better be individualized

HSV infection and PPROM

- The risk of prematurity should be weighed against the potential risk of vertical transmission.
- The risk of vertical transmission is higher in the setting of primary infection
- Recurrent active HSV infection –
 - Expectant management is recommended at 32-34 weeks with low risk of neonatal infection.
 - Prophylactic treatment with antiviral agents (eg, acyclovir) may be considered.
 - If at the time of delivery, active lesions or prodromal symptoms appear then CS is recommended.
 - Routine evaluation for viral shedding is not recommended
- Primary active HSV
 - The management is less clear, as insufficient data is available.
 - Although not very clear, 28-32 weeks is the likely gestational age at which the risk of neonatal infection outweighs the benefits of expectant management.
 - Maternal and neonatal treatment with acyclovir is recommended
 - If at the time of delivery, active lesions are present then CS is recommended.

PPROM in HIV positive women

- All women should receive zidovudine before delivery
- Those women managed expectantly should receive HAART
- Well controlled HIV infection – low risk of transmission. Expectant management until 32-34 weeks along with HAART is recommended.
- Untreated HIV infection – higher risk of transmission. Expectant management should be considered before 28-30 weeks or perhaps later depending upon the clinical circumstances

- CS does not diminish the risk of HIV transmission after rupture of the membranes

Role of fibrin glue in the sealing of membranes:

- There is insufficient evidence to recommend fibrin sealants as routine treatment for second-trimester oligohydramnios caused by PPROM to prevent pulmonary hypoplasia

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