RECENT ADVANCES IN HIGH RISK PREGNANCY

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CHAPTER

2 Preterm Premature Rupture of Membranes (PPROMs)

Ambarisha Bhandiwad

Premature rupture of the membranes is defined as rupture of the fetal membranes occurring prior to the onset of the labor. The incidence of PROMs has remained constant through the years and has been reported to be between 3 to 18.5%.

Intact fetal membranes with normal amniotic fluid are necessary for normal fetal growth and development.

Preterm premature rupture of membranes (PPROMs) refers to occurrence of this event prior to 37 weeks gestation and accounts for about one fourth of all cases of ruptured membranes.

PPROMs is responsible for close to 40% of the cases of preterm births.

Because PPROMs is the leading cause of preterm birth and perinatal morbidity, it has a tremendous socio-economic impact in society.

PATHOPHYSIOLOGY

PPROMs is a complex and multifactorial entity. The fetal membranes are composed of the amnion and the chorion bound together by different layers composed of extracellular matrix. This matrix is the key factor for the elasticity and tensile strength of the fetal membranes. The tensile strength guarantees the role of the membranes as a physical and functional boundary for the fetus during human pregnancy. If the extracellular matrix is intact, the fetal membranes's elasticity and tensile strength is at its maximum, hence any process that weakens the matrix causes a release of enzymes such as matrix metalloproteinases (MMPs) increasing the risk of PPROMs.

Risks for PPROMs are previous pregnancy with PPROMs, which carries a recurrence rate of 21%, antepartum hemorrhage, multiple gestation, Polyhydromnios, (excessive membrane distention), smoking and illicit drug abuse such as heroin and cocaine, cervical insufficiency and infection (Box 2.1).

These risk factors are similar to those for preterm birth since they share the same or similar pathways.

The greater risk factor in PPROMs is infection. It has been demonstrated that the bacterial protease decreased the strength and elasticity of the chorioamniotic membranes. Women who are infected with gonorrhea, trichomonas, or Chlamydia

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Box 2.1: Risk factors for PPROMs

Previous pregnancy with PPROMs
Antepartum hemorrhage
Multiple gestation
Polyhydromnios, smoking
Illicit drug abuse such as heroin and cocaine
Cervical insufficiency
Infection
Iatrogenic – amniocentesis, fetoscopies.

and those colonized with Group B beta hemolytic streptococcous sp. (GBS) or Gardenella vaginalis also have an increased risk of PPROMs.

Bacteria which colonizes the genital tract have the capability of producing phospholipases which stimulates the release of prostaglandins from the break down of arachidonic acid leading to preterm contractions.

Infection also causes a host immune response, releasing pro inflammatory cytokines and mediators which cause weakening of the fetal membranes by disrupting its extracellular matrix and releasing MMPs. MMPs decreases the membrane strength by increasing collagen degradation.

Genetic susceptibility may be a risk factor for PPROMs. MMP-9 gene promoter activity and its association with PPROMs were described in 2002. Carriers for the SERPINHI gene T-allele are also at high risk for premature delivery. This T-allele reduces the promoter activity in amnion fibroblasts that deposit fibrillar collagen which gives the tensile strength to the amnion.

Cervical dilatation exposes fetal membranes to the vaginal microbial flora, causing weakening of the fetal membranes. Therefore infection plays an important role for the occurrence of this entity.

Rupture of the fetal membranes can be caused secondary to an iatrogenic process. Fluid leakage can complicate a pregnancy after amniocentesis or fetoscopies. Fluid leakage has been reported in 1% of genetic amniocentesis and 3-5% of diagnostic fetoscopies.

EVALUATION OF PPROMs (Box 2.2)

A patient with symptoms suggestive of PPROMs should have a prompt evaluation.

Patient history has a sensitivity of 90% for the diagnosis of PPROMs.

A patient who complains of leakage of fluid should have a speculum examination to evaluate for gross pooling of amniotic fluid in the vagina. If no fluid is seen on the speculum examination, the patient should be instructed to perform a valsalva maneuver such as coughing to evaluate if any leakage is visualized from the cervical OS. A digital examination should be avoided since

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this increases the risk of infection and little information is obtained from this examination.

Several tests have been utilized to assist in the diagnosis of PPROMs. The nitrazine paper test and the fern tests may be performed.

The combination of the patient's history, speculum examination, the nitrazine test, and the fern test for the evaluation of a patient with symptoms suggestive of PPROMs yields a sensitivity of 93.1%.

Nitrazine test: The normal pH of the vagina during pregnancy is between 4.5 and 5.0. When rupture of the membranes occurs and the vaginal mucosa is bathed in amniotic fluid whose pH is close to 7.3, the pH increases above 6.0, causing the nitrazine paper to turn from yellow to blue in color. However, the nitrazine test may give false-positive results if contaminated with semen, blood, some lubricants or if a vaginal infection is present.

The Fern test: This test has been described since the 1960s. The test is performed by placing a swab in the posterior fornix of the vagina to obtain vaginal fluid and then performing a smear on a glass slide which should be allowed to dry for 10 min. The microscopic appearance of the smear as arborization or fern pattern is a positive test. The reported specificity of the fern test has been reported to be 84-100%.

Patients with leakage of fluid from the vagina may also have a sonographic evaluation of amniotic fluid volume performed. It is also important to confirm a fetal heart rate, assess the gestational age of the pregnancy, and the position of the fetus. A finding of oligohydramnios may be useful in confirming rupture of the fetal membranes along with the above tests. The cervix can also be assessed by measuring the dilatation of the cervical OS, the cervical length, and to determine if funneling is present.

Fetal fibronectin (FFN): Another test that may be useful to assess leakage of fluid. This test can be performed after 18 weeks gestation. A negative test indicates that the membranes are infact since its negative predictive value is 98-99%. Nevertheless, it has a poor positive predictive value due to its high false positive rate and may not be needed or cost-effective.

If the diagnosis of rupture of the fetal membranes cannot be made with the above tests, an ultrasound guided invasive test can be performed. A 22 gauge needle is inserted under ultrasound guidance into the amniotic cavity. Amniotic fluid can be obtained and evaluated for glucose, white blood cells, gram stain, and sent for culture of the amniotic fluid. Indigo carmine or Evans blue (1ml) can be instilled. A tampon is placed in the vagina prior to instillation of dye and kept in place for 30-40 min; when removed, a blue tinged tampon will be seen if the patient has ruptured membranes.

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Box 2.2: Evaluation of PPROMs

- Patient history
- Speculum examination
- Perform valsalva maneuver
- Nitrazine test
- Fern test
- Sonographic evaluation
- Fetal fibronectin
- Ultrasound guided invasive test indigo carmine or Evans blue

NEONATAL COMPLICATIONS OF PPROMs

- Increased neonatal mortality and morbidity
- Prematurity is the main problem
- Birth asphyxia due to cord complications
- Neonatal sepsis
- Intrauterine fetal demise

Consequences of oligohydramnios such as pulmonary hypoplasia, postural deformities like talipses and craniofascial defects.

The reported incidence of these deformities varies between 3.5 to 50% for cases with severe oligohydramnios. The risk increases when the duration of PPROMs is greater than 14 days.

MATERNAL COMPLICATIONS OF PPROMs

Infection is the most important maternal complication of PPROMs. The risk of infection is inversely proportional to the duration of the latency period, chorioamniotis is a complication for both fetus and mother.

Non reassuring fetal heart occurs more commonly in pregnancies complicated by PPROMs. Cord compression due to oligohydramnios and a fetal cardiac response to infection are examples of why the incidence of non reassuring fetal status increases with PPROMs. Also, the incidence of fetal malpresentation increases with PPROMs. Because of these factors, the cesarean delivery rates for pregnancies complicated by PPROMs increases.

Mid-trimester PPROMs

The definition of mid trimester PPROMs is rupture of the fetal membranes occurring between 16-26 weeks gestation. If can occur secondary to an iatrogenic factor such as amniocentesis. Mid trimester PPROMs affects 0.7% of all pregnancies, less than 50% of patients will remain pregnant after 1 week of the event and 75.88% will be delivered by 28 days.

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PPROMs Occurring after 26 weeks Gestation

PPROMs after 26 weeks gestation is the most common obstetrical complication that leads to preterm deliveries. The major risks for the fetus are those of prematurity; therefore, therapy for PPROMs is aimed at prolonging labor to decrease the risks of prematurity. However, the timing of delivery is still controversial. Patients with PPROMs should be delivered if expectant management will not result in a significant prolongation of the pregnancy or if the risks of expectant management outweigh the neonatal risks associated with a preterm delivery.

After 34 weeks of gestation, expectant management is of little benefit, so most studies recommend delivery. If PPROMs occurs prior to 32 weeks, one may collect amniotic fluid for fetal lung maturity testing and expectant management with intravenous antimicrobials.

The controversial area is in the management of PPROMs that occurs between 32-34 weeks gestation.

Maternal surveillance for infection should be employed on every patient.

Fetal surveillance with non stress testing and biophysical profile testing may be employed. The interpretation of fetal heart rate changes that occur after PPROMs on the non stress test are often difficult to interpret. Fetal heart changes may be due to an immature fetal neurological development because of prematurity, or secondary to cord compression if oligohydramnios is present, or secondary to intra amniotic infection. This is an explanation for the many false positive readings. A biophysical profile may also be performed on patients with PPROMs. The absence of fetal breathing and fetal tone are predictive of fetal infection. Positive fetal breathing has a 95% negative predictive value for intra amniotic infection.

WHEN TO DELIVER?

PPROMs Occurring after 34 weeks Gestation

Most authorities recommend delivering patients presenting with PPROMs $\geq$ 34 weeks gestation since there is usually little benefit obtained from expectant management. Patients who present with PPROMs $\geq$ 34 weeks gestation should have genital cultures done, prescribed appropriate antimicrobials that covers GBS, and be delivered.

PPROMs Prior to 32 weeks Gestation

The evidence suggests that PPROMs prior to 32 weeks gestation should be managed expectantly. In the absence of complications like infections, abruption, active preterm labor, or a non reassuring fetal heart, expectant management with anti microbials and antenatal corticosteroids may help decrease the severe

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complications of prematurity. There is some evidence that, for extreme low birth weight (ELBW) premature neonates (< 1000 gm) there may be poor neurological development. In pregnancies complicated by preterm delivery, the incidence for ELBW of cerebral palsy was 9-26%, blindness 1-15%, deafness 9%, and up to 42% had cognitive disabilities.

Because of complications of prematurity and the severe complications of the extreme low birth weight infants, expectant management with the use of antimicrobials and antenatal steroids until 32 weeks of gestation unless infection is present or the status of the fetus or the mother are not re-assuring, is reassuring, is recommended.

PPROMs Occurring between 32-34 weeks Gestation

The management for patients presenting with PPROMs occurring between 32-34 weeks of gestation is unclear. Some authors recommend collection of amniotic fluid for fetal lung maturity testing and expectant management until 34 weeks gestation unless the fetal lung maturity test is positive.

Others recommend the same management as that of PPROMs occurring after 34 weeks gestation.

Many obstetricians collect amniotic fluid to evaluate for fetal lung maturity, and if positive, they would proceed to deliver the fetus.

Experimental ultrasound guided procedures have been reported to be successful in the management of PPROMs. Serial amnio infusions in selected cases can decrease morbidities associated with severe oligohydramnios and preterm birth. Another experimental modality that has been used is the use of intra-amniotic surfactant prior to delivery to decrease the incidence of severe RDS.

POINTS TO REMEMBER

Patients of 34 or more weeks gestation with PPROMs should be delivered. Patients less than 32 weeks gestation with PPROMs should be managed conservatively with corticosteroid and antimicrobial prophylaxis unless there is an indication for delivery. The management of patients with PPROMs between 32 and 34 weeks gestation is unclear.

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