Maternal and Fetal Outcomes of Spontaneous Preterm Premature Rupture of Membranes

Lee C. Yang, DO; Donald R. Taylor, DO; Howard H. Kaufman, DO; Roderick Hume, MD; Byron Calhoun, MD

The authors retrospectively evaluated maternal and fetal outcomes of 73 consecutive singleton pregnancies complicated by preterm premature rupture of amniotic membranes. When preterm labor occurred and fetuses were at a viable gestational age, pregnant patients were managed aggressively with tocolytic therapy, antenatal corticosteroid injections, and antenatal fetal testing. The mean gestational age at the onset of membrane rupture and delivery was 22.1 weeks and 23.8 weeks, respectively. The latency from membrane rupture to delivery ranged from 0 to 83 days with a mean of 8.6 days. Among the 73 pregnant patients, there were 22 (30.1%) stillbirths and 13 (17.8%) neonatal deaths, resulting in a perinatal death rate of 47.9%. The perinatal survival rate based on gestational age at the onset of fetal membrane rupture was 12.1% at less than 23 weeks of gestation, 60% at 23 weeks, and 100% at 24 to 26 weeks. Maternal morbidity was minimal with puerperal endomyometritis in 5 (6.8%) cases, one of which became septic; however, there was no long-term sequela. Eight (15.7%) liveborn infants had pulmonary hypoplasia, 5 (62.5%) of which resulted in neonatal death. In 33 (45.2%) patients, amniotic membranes ruptured before 23 weeks of gestation. At previable gestational age, the risk of neonatal pulmonary hypoplasia appears to be primarily dependent on gestational age at the onset of premature rupture of membrane rather than gestational age at delivery. Pregnancy outcomes remain dismal when the fetal membrane ruptures before 23 weeks of gestation.

Preterm premature rupture of membranes (PROM) at 16 through 26 weeks of gestation complicates approximately 1% of pregnancies in the United States and is associated with significant risk of neonatal morbidity and mortality.1,2 Perinatal mortality is high if PROM occurs when fetuses are of previable gestational age. Moretti and Sibai3 reported an overall survival rate of 50% to 70% after delivery at 24 to 26 weeks of gestation. Although neonatal morbidity remains significant, despite improvements in neonatal care for extremely premature newborns, neonatal survival has improved over recent years. Fortunato et al2 reported a prolonged latent phase, low infectious morbidity, and good neonatal outcomes when physicians manage these cases aggressively with active expectant management using tocolysis and prophylactic antibiotics.

In previous studies, investigators generally excluded newborns with chorioamnionitis or pregnant patients whose deliveries occurred shortly after PROM or on hospital admission. By excluding these patients from study protocols, outcomes—especially in the latency period—might appear better than expected. Therefore, this retrospective study aims to evaluate the outcome of every consecutive singleton pregnancy complicated by PROM that occurred when fetuses were at 16 to 26 weeks of gestation. Patients were treated at Rockford Memorial Hospital in Illinois, a regional perinatal center, from January 1995 to December 2001.

**Methods**
From January 1995 to December 2001, 73 pregnant patients who had preterm PROM at 16 to 26 weeks of gestation received medical care at Rockford Memorial Hospital. These patients were identified through the perinatal computer database and neonatal delivery logbooks. Institutional approval for a chart review was obtained from the Rockford Memorial Hospital Investigation Review Board.

Midtrimester PROM is defined as rupture of amniotic membranes occurring between 16 and 26 weeks of gestation.5 When fetuses were at viable gestational age (ie, 24 weeks of gestation), pregnant patients who had PROM were given tocolytic therapy if they went into spontaneous preterm labor, as well
as antenatal corticosteroids, fetal monitoring, and prophylactic antibiotics. For women whose fetuses were at previable gestational age during PROM, physicians opted instead to observe patients on an outpatient basis and then admitted them to the hospital at viability.

Initially, each patient was admitted to a labor and delivery suite for maternal and fetal assessment. After maternal condition was stabilized and there was no evidence of fetal distress when the fetus was viable, ultrasound evaluation was performed to assess fetal presentation, growth, anatomy, and the level of amniotic fluid. At the discretion of the attending physician, amniocentesis was performed to rule out infection.

Gestational age was estimated using the date of the patient’s last menstrual period and/or ultrasound dating. The attending physician ordered an ultrasound evaluation for every patient after hospital admission. Pelvic examination using a sterile speculum was performed. Digital examination was avoided unless the patient was committed to delivery. Diagnosis of preterm PROM was based on history and confirmed by the presence of pooled amniotic fluid on a sterile speculum, positive results from a ferning test, and transvaginal ultrasonographic evaluation that demonstrated oligohydramnios. Amniinfusion with warm physiologic saline solution and instillation of indigo carmine permitted a more comprehensive ultrasonographic evaluation to assist attending physicians in the diagnosis of oligohydramnios. Each patient was observed in the labor and delivery suite for at least 24 hours. At viability, external fetal monitoring assessed fetal well-being. Patients without evidence of infection were transferred to the high-risk maternal ward. Antenatal assessment included daily nonstress tests and an evaluation every 4 hours of patients’ vital signs and body temperatures.

Fetal growth was assessed every 3 to 4 weeks by ultrasound. At viability, patients with spontaneous preterm labor but no evidence of infection were treated with intravenous antibiotics: ampicillin sodium or, for patients with a hypersensitivity to penicillin, erythromycin. Treatment with MgSO4 was stopped and calcium channel blocker (20 mg of nifedipine orally every 6 hours) was started as a maintenance tocolysis once uterine quiescence was achieved for at least 48 hours. Patients received two intramuscular injections of antenatal corticosteroids (12 mg of betamethasone every 24 hours followed by a single weekly injection until delivery or up to 34 weeks of gestation).

Through 1999, all pregnant patients with PROM received weekly steroid injections until delivery or 34 weeks of gestation. However, since 2000, weekly or multiple courses of antenatal corticosteroid injections are no longer recommended.

Clinical chorioamnionitis was diagnosed by the attending physician if two or more of the following symptoms were present: maternal pyrexia (>38°C [>100.4°F]) in conjunction with uterine tenderness, purulent vaginal discharge, or fetal tachycardia. If amniocentesis was performed, the presence of organism or positive culture—with or without low glucose levels (<14 mg/dL)—would also be indicative of infection.

Indications for delivery included clinical chorioamnionitis, non-reassuring assessment for fetal well-being, fetal death, advanced labor, or failed tocolysis. If infection was identified, delivery was expedited and the use of broad-spectrum antibiotics was initiated.

Following delivery, all newborns were admitted to the neonatal intensive care unit and antibiotic therapy with ampicillin and gentamicin sulfate were initiated while the results of the septic work up were prepared. As a routine evaluation for potential intraventricular hemorrhage, roentgenography of the head was ordered by the attending physician for all newborns at 1 week of age—and as needed thereafter.

Diagnosis of respiratory distress syndrome was based on clinical and physical signs of respiratory distress and radiographic characteristics of the chest. Bronchopulmonary dysplasia was defined as the need for oxygen supplementation at 36 weeks of gestational age.

Results
Among the 73 patients included in this retrospective study, the mean maternal age was 26 years (range 16–38 years). Thirty (41.1%) patients were nulliparous. Thirteen (17.8%) patients had a history of tobacco use, seven (9.6%) had a history of preterm delivery, and 8 (11%) had a history of preterm PROM.

During the current pregnancy, 3 (4.1%) patients underwent cervical cerclage. Of the 3 patients who underwent this procedure, 2 cases were prophylactic and 1 was rescue.

Among these 73 patients, the gestational age distribution at the onset of PROM (Table 1) ranged between 16 and

<table>
<thead>
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<th>Gestational Age, wk</th>
<th>No. (%)</th>
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<tr>
<td>16</td>
<td>4 (5.5)</td>
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<td>25</td>
<td>13 (17.8)</td>
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<tr>
<td>26</td>
<td>7 (9.6)</td>
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* Percentages reported were rounded for each group by gestational age. Therefore, the sum of these percentages may not equal 100%.
26.9 weeks (mean 22.1 weeks; median 23 weeks). The mean gestational age at delivery was 23.8 weeks and the mean latency period from PROM to delivery was 8.6 days. Twenty-seven (37%) patients presented with clinical chorioamnionitis; however, placental examination demonstrated histologic chorioamnionitis in 49 (67.1%) cases.

Of the 22 (30.1%) stillbirths recorded in this group, the gestational age at the onset of PROM ranged from 16 to 23.1 weeks (mean 20.3 weeks, median 20.4 weeks). The mean gestational age at delivery was 20.7 weeks with a mean latency period from PROM to delivery of 3 days. Eleven (50%) of these patients presented with vaginal bleeding, whereas 10 (45%) patients initially had a clinical diagnosis of abruptio placentae. Fifteen (68.2%) patients went into labor spontaneously. Four (18.2%) patients presented with clinical chorioamnionitis. The rate of histologic chorioamnionitis was 63.6%, or 14 cases.

There were 13 (17.8%) neonatal deaths and the gestational age at the onset of PROM ranged from 16 to 23.4 weeks (mean 20.5 weeks, median 20.7 weeks). Two (15.4%) of the patients had abruptio placentae. All of these neonates died within 24 hours of birth because of extreme prematurity, respiratory insufficiency, and/or sepsis.

**Mode of Delivery**

Twenty-eight (38.4%) fetuses were in cephalic position and 45 (61.6%) fetuses were in breech presentation.

Twenty-three (31.5%) neonates were delivered by cesarean section. Indications for abdominal delivery were as follows: fetal distress and/or umbilical cord prolapsed (7 [30.4%]), fetal malpresentation (15 [65.2%]), or failed induction of a stillbirth (1 [4.3%]). There were 8 (11%) reported cases of prolapsed umbilical cord, but, as noted, not all of these fetuses were delivered abdominally.

**Maternal Morbidity**

Five (6.8%) of the 73 patients had puerperal endomyometritis. As noted, one of these became septic and was treated with broad-spectrum antibiotics, recovering without any sequela.

Nine (40.9%) of the 22 patients who delivered stillbirth had curettage to remove the retained placenta; one of these patients received a blood transfusion because of significant blood loss. There were no reported cases of maternal mortality or long-term morbidity.

**Perinatal Outcome**

The perinatal survival rate based on gestational age at the onset of PROM was 12.1% at fewer than 23 weeks of gestation, 60% at 23 weeks, and 100% in the 24 to 26 weeks' gestational age group (Table 2).

Among the 73 fetuses that were delivered, 22 (30.1%) were stillborn, and 13 (17.8%) died within 24 hours of delivery, resulting in an immediate perinatal death rate of 47.9%. Among the stillbirths, fetal membranes were ruptured at or before 23 weeks of gestation and all were delivered before 24 weeks of gestation.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Rupture of Membranes: Perinatal Outcome by Gestational Age (N=73)</th>
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<tr>
<td>Gestational Age, wk</td>
<td>No. (%)</td>
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<td>Total</td>
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* Percentages reported were rounded for each group by gestational age. Therefore, the sum of these percentages may not equal 100%.
Sixteen (42.1%) newborns had neonatal sepsis. Severe intra-ventricular hemorrhage (grade III or IV) occurred in 3 (7.9%) liveborn infants. Other significant premature complications are listed in (Table 4).

Discussion
Midtrimester PROM occurs in about 1% of pregnancies and continues to pose significant levels of morbidity among liveborn infants. The mean latency period from PROM to delivery was 8.6 days among all 73 patients analyzed, which is a shorter period of time than has been reported in previous studies (eg, 18.6 days).1,3,7,8

This shorter latency period can be explained in part by the large number of stillbirths recorded in our study (30.1%), whereas previous studies excluded from analysis those patients who delivered within 24 hours of PROM.

The incidence of clinical chorioamnionitis (37%) and histologic chorioamnionitis (67.1%) noted here is comparable with previous findings.1,4,9-11 Among patients with stillbirth, the incidence of clinical chorioamnionitis (18%) was low, but in line with figures reported by Beydoun and Yasin.4 Of the 27 (37%) patients who had clinical chorioamnionitis, 50% did so within the first 48 hours and 61.5% within 1 week following PROM.

The risk of infection is significant following preterm PROM. Five (6.8%) patients had endometritis, one incident of which resulted in maternal sepsis. There was no long-term maternal sequelae.

The level of maternal morbidity reported in our current study is low compared to previous studies.5,11,12 We theorize that this positive maternal outcome may be due in part to the consistent use of broad-spectrum antibiotics among the study group once infection was recognized by the attending physician, a decision that also allowed physicians to expedite delivery.5,12

Among the 73 patients, there were 22 stillbirths and 13 live births resulting in neonatal death. Therefore, the perinatal survival rate was 52.1%, a figure that is comparable to most previous studies.3,4 The perinatal survival rate based on gestational age at the onset of PROM was poor when the fetal membrane was ruptured before 23 weeks of gestation, however. The 100% survival rate at viable gestational age (ie, 24 weeks), however, is most likely a result of the use of antenatal antibiotics, corticosteroids, and improved neonatal care. No previous studies have reported such a high survival rate among this age group (ie, 24–26 weeks of gestation).3-5

In the current study, once fetuses had reached viable gestational age, pregnant patients were managed aggressively with tocolytic therapy in the presence of spontaneous uterine contraction, immediately receiving antenatal corticosteroids and prophylactic antibiotics. Amon et al13 demonstrated that prophylactic antibiotics prolonged the latency phase and reduced the incidence of neonatal infection.

In 1988, Moretti and Sibai3 evaluated maternal and neonatal outcomes for 118 midtrimester cases of PROM that were managed expectantly and occurred between 16 and 26 weeks of gestation. The mean gestational age at the onset of PROM was 23.1 weeks with a mean latency period of 13 days. Sixty-seven percent of patients delivered within 1 week following PROM. Perinatal mortality was recorded at 67.7%. The perinatal survival rate, based on gestational age at the
onset of PROM was 13% (8 of 60) at less than 23 weeks of gestation and 50% (32 of 64) at 24 to 26 weeks of gestation. There was one maternal death related to sepsis.

In 1984, Taylor and Garite\textsuperscript{5} reported on the outcome of 53 patients with preterm PROM between 16 and 25 weeks of gestation. These cases were also managed expectantly. Taylor and Garite reported a perinatal survival rate of 25% and a maternal morbidity rate of 58.5%.\textsuperscript{5} In addition, nearly as many deliveries resulted in live births with PROM before 23 weeks of gestation as after. However, our results suggest that perinatal survival is largely dependent on fetuses’ gestational age at PROM. When fetuses are of viable gestational age, the immediate perinatal survival rate we observed was 100%, but outcomes are discouraging when fetal membranes rupture before fetuses reach 23 weeks of gestation.

In the current study, the incidence of neonatal complications is high. All 36 surviving infants had respiratory distress syndrome. Further, 68.4% of surviving neonates had bronchopulmonary dysplasia. The number of neonatal complications documented in our study appear to be higher than those provided in previous studies.\textsuperscript{10,12,14,15} However, this unexpected result may be the effect of higher rates of neonatal survival when delivery occurred at an earlier gestational age, possibly indicating that the complications witnessed are related more closely to the effects of premature birth rather than PROM.

The incidence of neonatal sepsis was 18.4% (7 of 38), a figure that is in line with numbers reported elsewhere (ie, 2% to 19%).\textsuperscript{8,12} The incidence of necrotizing enterocolitis and contractures in our study were also comparatively low, at 5.3% and 2.6%, respectively.

The incidence of pulmonary hypoplasia—when occurrences among liveborn infants who survived were combined with those among neonates who later died—was 15.7% (8 of 51). In the current study, pulmonary hypoplasia occurred in patients with PROM that lasted longer than 2 weeks when the mean gestational age of the fetus at the onset of PROM was 18.9 weeks. Other studies\textsuperscript{5,16} suggest that the incidence of pulmonary hypoplasia increased significantly after 2 weeks of spontaneous rupture of membranes. It appears that the risk of pulmonary hypoplasia is dependent on gestational age at the time of PROM.

**Comment**

Despite progress in obstetric and neonatal care over the past 20 years, perinatal outcome in pregnancies with PROM before 23 weeks of gestation remains dismal. Thus, if expectant management is desired, physicians should counsel their patients thoroughly and well in advance with regard to the poor outcomes for neonates anticipated after this type of delivery. Alternatively, aggressive expectant management does not seem to increase maternal morbidity. However, the results of this report should be interpreted with caution because it is a small-scale retrospective study. Long-term neonatal morbidity will be the focus of future longitudinal studies.

**References**


