Original Article

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Perinatal outcomes of pregnancies complicated by preterm premature rupture of the membranes before 34 weeks of gestation in a tertiary center in China: A retrospective review

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Summary **Preterm premature rupture of the membranes (PPROM) remains the leading cause of preterm deliveries and neonatal mortality and morbidity. The current cohort study sought to retrospectively examine perinatal outcomes in cases of PPROM < 34 weeks' gestation that were managed conservatively from 2010 to 2012 and to identify risk factors for short-term neonatal outcomes. Subjects were 510 pregnancies consisting of 114 twin and 396 singleton pregnancies. Clinical chorioamnionitis occurred in 17.8% of the pregnancies. Neonatal mortality was 7.4%, the rate of major neonatal conditions was 40%, and the rate of NICU admission was 72.9%. The latency period exceeded 48 h in 62.5% of the pregnancies and 7 days in 24.3% of the pregnancies. Twin pregnancies had a shorter latency period than singleton pregnancies (median of 2 days versus 4 days, $p < 0.001$). Pregnancies complicated with early vaginal bleeding had a higher neonatal mortality (13.95% *vs*. 6.36%, $p = 0.013$) and morbidity (51.16% *vs*. 38.32%, $p = 0.024$), fewer weeks of gestation at PPROM ($p = 0.029$). Multivariate logistic regression analysis revealed that weeks of gestation at PPROM (OR: 0.953, 95% CI: 0.939-0.966, $p < 0.001$) and a latency period (OR: 0.948, 95%CI: 0.926-0.970, $p < 0.001$) were associated with neonatal mortality or morbidity. A twin pregnancy (OR: 0.319, 95% CI: 0.17-0.6, $p < 0.001$) and weeks of gestation at PPROM (OR: 0.737, 95% CI: 0.66-0.822, $p < 0.001$) were associated with the latency period. Gestational age at PPROM, a twin pregnancy, and the latency period are associated with neonatal mortality and morbidity.**

Keywords: Preterm premature rupture of the membranes, neonatal morbidity, neonatal mortality, latency period

1. Introduction

Preterm birth occurs in approximately 12% of pregnancies (*1*). Preterm premature rupture of the membranes (PPROM), a subtype of preterm labor, is defined as spontaneous membrane rupture without onset of labor before 37 weeks of gestation. PPROM occurs in approximately 3% of pregnancies and results in one-third of preterm births. It remains the leading cause of preterm deliveries and neonatal mortality and morbidity (*2,3*).

Conditions due to prematurity include respiratory distress syndrome (RDS), intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL), necrotising enterocolitis (NEC), a prolonged stay in the neonatal intensive care unit (NICU), neonatal sepsis, required use of positive pressure ventilation (PPV), cardiac abnormalities, hyperbilirubinemia and hemolytic anemia, as well as cerebral palsy, and other long-term outcomes (*4*). Therefore, appropriate management of PPROM is crucial to improving neonatal and maternal outcomes. Obstetrical strategies to treat PPROM remain controversial and there is no consensus regarding active or conservative management of PPROM within 30 and 34 weeks' gestation. Conservative management to prolong a pregnancy is a classical approach to treating PPROM before 34 weeks' gestation in association with antibiotic therapy and corticosteroids. Delivery is recommended when PPROM occurs at or beyond 34 weeks' gestation (*5-7*).

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This Hospital, a tertiary care hospital in southwest China, conservatively manages PPROM < 34 weeks' gestation. This Hospital manages the majority of complicated pregnancies in this area. The aim of the present study was to evaluate neonatal and maternal outcomes in women with conservatively managed PPROM < 34 weeks' gestation and to identify risk factors for short-term neonatal outcomes.

2. Methods

This was a retrospective cohort study. Approval was obtained from the Institutional Review Board. Medical charts of women with spontaneous PPROM < 34 weeks' gestation who were admitted to Obstetrics at West China Second University Hospital from 2010 to 2012 were reviewed.

2.1. *Subjects*

Cases of triplets or higher order pregnancies, congenital malformations incompatible with life, a twin pregnancy with a delayed-interval delivery, fetal death before PPROM, and maternal and/or fetal indications for immediate delivery after admission were excluded.

2.2. *PPROM diagnosis*

Diagnosis of PPROM was based on the patient's history of watery discharge and leakage of amniotic fluid from the cervical os during a sterile speculum examination. Gestational age was determined based on the patient's last period or by ultrasound performed during the first trimester or early second trimester.

2.3. *Management of PPROM*

Couples were counseled by obstetricians about the adverse outcomes of an intentional delivery and conservative management and they selected conservative management when the patient was not in labor at admission. Dexamethasone was given for maturation of the fetal lungs, and the complete course was 4 doses of 5 mg *i.m*. within a 48-h interval. A broad-spectrum antibiotic (ampicillin, ceftezole, or clarithromycin) was administered from admission until delivery or for up to 7 days to prevent infection. Magnesium sulfate, a calcium channel blocker (nifedipine), or a betamimetic agent (ritodrine) was used as a tocolytic agent depending on the patient's status.

The status of the mother and fetus was closely monitored until delivery. Patients were checked by obstetricians daily. Maternal vital signs were monitored every 6 hours, and serum C-reactive protein (CRP) levels and the white blood cell count were checked weekly. Ultrasound scans were performed once a week to evaluate the status of the fetus. CTGs were performed daily to assess the status of the fetus. The treatment was promptly adjusted when necessary depending on the status of the mother and fetus. None of the pregnant women in this study underwent amniocentesis to assess infection or fetal lung maturity.

Clinical chorioamnionitis was performed if the patient presented with three or more of the following criteria: maternal body temperature ≥ 38°C, maternal tachycardia (≥ 110 beats/min), persistent fetal tachycardia (> 160 beats/min) or bradycardia (< 120 beats/min), presence of uterine tenderness, elevated CRP, malodorous vaginal discharge, and leukocytosis (≥ 15,000 cells/mm^3) in maternal blood.

When clinical chorioamnionitis was diagnosed during prolongation of a pregnancy, or there were maternal and/or fetal indications for delivery, or gestation reached 34 weeks, the pregnancy was managed with active induction of labor or a Cesarean delivery depending on the patient's obstetric history and the fetus' status.

2.4. *Data collection*

Maternal parameters including maternal age, parity, spontaneous or *in vitro* fertilization, singleton or twin pregnancy, and gestational age at PPROM were reviewed. Furthermore, parameters including weeks of gestation at delivery, mode of delivery, clinical chorioamnionitis, and obstetric complications were investigated. Recent studies of early vaginal bleeding in singleton and twin pregnancies have cited an increased risk of PPROM, preterm birth, preeclampsia, and placental abruption (*8,9*). Therefore, early vaginal bleeding during the pregnancy was reviewed during this study. Such bleeding was defined as the presence of blood in the vagina in the first or second trimester. Fetal parameters including fetal distress, birth weight, neonatal death, admission to the NICU, and major neonatal conditions (including patent ductus arteriosus (PDA), RDS, IVH, PVL, NEC, and sepsis) were also studied.

2.5. *Statistical analyses*

Maternal, fetal, and neonatal parameters were analyzed using a Chi-squared test, Fisher's exact test, a two-tailed student's *t*-test, and Mann-Whitney U test. Multivariate logistic regression was used to correlate the latency period, neonatal mortality, and neonatal morbidity with the parameters collected from medical charts. A p value < 0.05 was considered statistically significantly. Analysis was performed with the statistical software SPSS version 17.0.

3. Results

3.1. *Maternal characteristics*

Subjects were 510 patients who were diagnosed with

Table 1. Maternal characteristics of cases of PPROM < 34 weeks of gestation

Characteristics	PPROM, *n* = 510
Maternal age (mean ± S.D.)	28.4 ± 5.6
Maternal age > 35years, *n* (%)	72 (14.1%)
Weeks of gestation at admission (mean ± S.D.)	31.6 ± 1.9
Nulliparous, *n* (%)	361 (70.8%)
Conception	
Natural, *n* (%)	473 (92.8%)
IVF, *n* (%)	37 (7.3%)
Pregnancy	
Singleton, *n* (%)	396 (77.7%)
Twin, *n* (%)	114 (22.4%)
Previous cesarean section, *n* (%)	58 (11.4%)
History of preterm delivery, *n* (%)	6 (1.2%)
Early vaginal bleeding, *n* (%)	69 (13.5%)

PPROM < 34 weeks' gestation from 2010 to 2012. Of the 510 pregnancies, 396 were singleton pregnancies and 114 were twin pregnancies. The mean maternal age was 28.4 years (range: 17-45 years). The mean weeks of gestation at PPROM was 31.6 weeks (range: 20^{+2} -33^{+6} weeks). Of the 510 patients, 11.4% (58/510) had a previous Cesarean section, 1.2% (6/510) had one or more preterm births, and 13.5% (69/510) had a history of vaginal bleeding in early stages of the current pregnancy. The maternal characteristics of all patients in the study are shown in Table 1. There were no maternal deaths or severe morbidity noted in the current study.

3.2. *Clinical outcomes*

The mean weeks of gestation at delivery were 32.5 weeks (range 27^{+2} -34^{+3} weeks). Obstetrical complications such as hypertensive disorders of pregnancy, diabetes, intrahepatic cholestasis of pregnancy, umbilical prolapse, and placenta abruption were recorded based on medical charts and are shown in Table 2. The Cesarean section was performed in 37.1% of pregnancies with a medical complication such as breech presentation, fetal distress, or failure of labor to progress. During prolongation of a pregnancy, 284 patients (55.7%) went into labor spontaneously and delivered before 34 weeks. Indications for active induction of labor or a Cesarean delivery were as follows: 91 patients (17.8%) presented with clinical chorioamnionitis, 29 (5.7%) had maternal or fetal complications during prolongation of the pregnancy, and 106 (20.8%) had a pregnancy that lasted 34 weeks.

Fetal and neonatal data were reviewed. The mean neonatal birth weight was 1815.1 ± 462.6 g and 162 neonates (26.1%) were delivered with a birth weight < 1,500g (VLBW). Death of one twin occurred in three twin pregnancies that were conservatively managed. The neonatal mortality rate was 7.4% (46 cases) and the rate of major neonatal conditions was 40% (249 cases). Furthermore, the rate of NICU admission was 72.9%. Major neonatal conditions noted in the current study were IVH in 197 pregnancies (31.7%), RDS in 72 (11.6%), PDA in 10 (1.6%), PVL in 7 (1.1%), sepsis in 7 (1.1%), and NEC in 3 (0.5%). Data on these conditions are shown in Table 2.

Table 2. Clinical outcomes in cases of PPROM

Characteristics	PPROM, *n* = 510
Weeks of gestation at delivery (mean ± S.D.)	32.5 ± 1.7
Cesarean delivery, *n* (%)	189 (37.1%)
Obstetrical complications	
Diabetes[a], *n* (%)	109 (21.4%)
Intrahepatic cholestasis of pregnancy, *n* (%)	48 (9.4%)
Hypertensive disorders of pregnancy[b], *n* (%)	22 (4.3%)
Clinical chorioamnionitis, *n* (%)	91 (17.8%)
Fetal distress, *n* (%)	17 (3.3%)
Placenta abruption, *n* (%)	11 (2.2%)
Umbilical prolapse, *n* (%)	16 (3.1%)
Fetal death, *n* (%)	3 (0.6%)
Indications for termination	
Clinical chorioamnionitis, *n* (%)	91 (17.8%)
Maternal or fetal complications	29 (5.7%)
Pregnancy lasted 34 weeks	106 (20.8%)
Neonatal outcomes	
Birth weight (mean ± S.D.)	1815.1 ± 462.6
VLBW, *n* (%)	162 (26.1%)
NICU admission, *n* (%)	453 (72.9%)
Neonatal death, *n* (%)	46 (7.4%)
Major neonatal condition	
Intraventricular hemorrhage, *n* (%)	197 (31.7%)
Respiratory distress syndrome, *n* (%)	72 (11.6%)
Patent ductus arteriosus, *n* (%)	10 (1.6%)
Periventricular leukomalacia, *n* (%)	7 (1.1%)
Sepsis, *n* (%)	7 (1.1%)
Necrotizing enterocolitis, *n* (%)	3 (0.5%)

[a] Diabetes: includes type 1 diabetes, type 2 diabetes, gestational diabetes; [b] Hypertensive disorders of pregnancy: includes chronic hypertension, gestational hypertension, and preeclampsia.

3.3. *Neonatal mortality, major neonatal conditions, and NICU admission by gestational age at PPROM*

The gestational age at PPROM was divided into four periods to indicate perinatal outcomes by different weeks of gestation: < 28 weeks, 28-29^{+6} weeks, 30-31^{+6} weeks, and 32-33^{+6} weeks. The groups were analyzed in terms of the neonatal mortality, the rate of NICU admission, major neonatal conditions, and the latency period.

As gestational age at PPROM increased, the risk of an adverse neonatal outcome declined. The neonatal mortality rate was 7.4% (46 cases) in cases of PPROM, 50% in pregnancies < 28 weeks, 16.1% in pregnancies of 28-29^{+6} weeks, 5.7% in pregnancies of 30-31^{+6} weeks, and 2.2% in pregnancies of 32-33^{+6} weeks. The differences among the groups were statistically significantly (Table 3). As gestational age at PPROM increased, the rate of neonatal mortality significantly decreased.

The rate of major neonatal conditions was 40% (249 cases) in cases of PPROM, 57.1% in pregnancies < 28 weeks, 63.44% in pregnancies of 28-29^{+6} weeks,

Table 3. Neonatal mortality, major neonatal conditions, and NICU admission by gestational age at PPROM

Gestational age at PPROM	major neonatal condition, *n* (%)	neonatal mortality, *n* (%)	NICU admission, *n* (%)
< 28 w (*n* = 28)	16 (57.1)	14 (50)[a]	26 (92.9)[b]
28-29^{+6} w (*n* = 93)	59 (63.4)	15 (16.1)[a]	84 (90.3)[b]
30-31^{+6} w (*n* = 177)	71 (40.1)[c]	10 (5.7)[a]	149 (84.2)[b]
32-33^{+6} w (*n* = 323)	103 (31.9)[c]	7 (2.2)[a]	194 (60.1)
Total (*n* = 621)	249 (40)	46 (7.4)	453 (72.9)

Comparisons made by chi-square or Fisher's exact test, $p < 0.05$ is significant. [a] compared to each other, [b] compared to 32^{+0}-33^{+6} w, [c] compared to 28-29^{+6} w. Major neonatal condition: 28-29^{+6} w *vs*. 30-31^{+6} w, $p < 0.001$; 28-29^{+6} w *vs*. 32-33^{+6} w, $p < 0.001$; < 28 w *vs*. 32-33^{+6} w, $p = 0.007$. Neonatal mortality: < 28 w *vs*. 28-29^{+6} w, $p < 0.001$; < 28 w *vs*. 30-31^{+6} w, $p < 0.001$; < 28 w *vs*. 32-33^{+6} w, $p < 0.001$; 28-29^{+6} w *vs*. 30-31^{+6} w, $p = 0.005$; 28-29^{+6} w *vs*. 32-33^{+6} w, $p < 0.001$; 30-31^{+6} w *vs*. 32-33^{+6} w, $p = 0.04$. NICU admission: 32-33^{+6} w *vs*. < 28 w, $p = 0.001$; 32-33^{+6} w *vs*. 28-29^{+6} w, $p < 0.001$; 32-33^{+6} w *vs*. 30-31^{+6} w, $p < 0.001$.

Table 4. Perinatal outcomes in cases of PPROM with early vaginal bleeding

Characteristics	Present (*n* = 69)	Absent (*n* = 441)	*p*
Weeks of gestation at PPROM (mean ± S.D.)	31.1 ± 2.2	31.7 ± 1.8	0.029
Weeks of gestation at delivery (mean ± S.D.)	32.1 ± 2.0	32.6 ± 1.7	0.059
Neonatal birth weight (mean ± S.D.)	1766.2 ± 440.9	1822.9 ± 465.9	0.292
VLBW, %	27.9	25.4	0.625
Neonatal mortality, %	13.95	6.36	0.013
Neonatal morbidity, %	51.16	38.32	0.024

Comparisons done using a Student's *t*-test, chi-square test, or Fisher's exact test, $p < 0.05$ is significant.

40.11% in pregnancies of 30-31^{+6} weeks, and 31.9% in pregnancies of 32-33^{+6} weeks. The rate of major neonatal conditions decreased as the gestational age at PPROM increased (Table 3).

The rate of NICU admission was 60.1% in pregnancies of 32-33^{+6} weeks. This rate was significantly lower than that in pregnancies < 28 weeks, pregnancies of 28-29^{+6} weeks, and pregnancies of 30-31^{+6} weeks (Table 3).

3.4. *Perinatal outcomes in cases of early vaginal bleeding*

Perinatal outcomes were investigated in cases of early vaginal bleeding and cases where it was absent (Table 4). Cases of early vaginal bleeding involved a significantly higher rate of neonatal mortality (13.95% *vs*. 6.36%, $p = 0.013$) and morbidity (51.16% *vs*. 38.32%, $p = 0.024$). Cases of early vaginal bleeding were associated with significantly fewer weeks of gestation at PPROM (31.1 ± 2.2 weeks *vs*.31.7 ± 1.8 weeks, $p = 0.029$).

3.5. *Clinical chorioamnionitis*

The latency period and clinical chorioamnionitis were significant related. The latency period in cases of clinical chorioamnionitis was longer than that in cases where clinical chorioamnionitis was absent (median 5 days *vs*. 3 days, $p = 0.001$). Cases of clinical chorioamnionitis were associated with fewer weeks of gestation at PPROM than were cases where clinical chorioamnionitis was absent (31.2 ± 2.1 *vs*. 31.7 ± 1.9, $p = 0.014$). There was no significant correlation between clinical chorioamnionitis and neonatal mortality and morbidity.

3.6. *Latency period*

The latency period was defined as the time from membrane rupture to delivery. In this study, the median latency period was 4 days (range 0-56 days). The latency period was divided into three periods: ≤ 48 h, 3-7 days, and > 7 days. The latency period exceeded 48 h in 62.5% of pregnancies and 7 days in 24.3%. Moreover, twin pregnancies were associated with a shorter latency period than singleton pregnancies (median latency period of 2 days versus 4 days, $p < 0.001$, Mann-Whitney U test).

There was a strong inverse correlation between gestational age at PPROM and the latency period. PPROM at < 28 weeks was associated with a significantly higher rates of latency > 7 days than other groups (66.7% *vs*. 30.8%, 66.7% *vs*. 28.2%, 66.7% *vs*. 17.1%). PPROM at 32-33^{+6} weeks was associated with a significantly higher rates of latency ≤ 48 h than other groups (43.9% *vs*. 14.3%, 43.9% *vs*. 29.5%, 43.9% *vs*. 33.1%).

3.7. *Analysis of composite factors for the latency period*

Multivariate logistic regression was used to examine the correlation between the latency period and potential risk factors such as maternal age, method of conception, parity, singleton or twin pregnancy, history of early vaginal bleeding, weeks of gestation at PPROM, and clinical chorioamnionitis. Results indicated that a twin pregnancy (OR: 0.319, 95% CI: 0.17-0.6, $p < 0.001$) and weeks of gestation at PPROM were associated with

the latency interval (OR: 0.737, 95% CI: 0.66-0.822, $p < 0.001$).

3.8. *Analysis of composite factors for neonatal mortality or morbidity*

Multivariate logistic regression was used to examine the correlation between neonatal mortality or morbidity and potential risk factors such as maternal age, method of conception, parity, singleton or twin pregnancy, history of early vaginal bleeding, weeks of gestation at PPROM, clinical chorioamnionitis, and the latency period. Results indicated that weeks of gestation at PPROM (OR: 0.953, 95% CI: 0.939-0.966, $p < 0.001$) and the latency period (OR: 0.948, 95% CI: 0.926-0.970, $p < 0.001$) were associated with neonatal mortality or morbidity.

4. Discussion

One-third of preterm births are the result of PPROM. PPROM remains the leading cause of preterm deliveries and adverse neonatal outcomes. The etiology of PPROM remains elusive.

Obstetrical strategies to treat PPROM remain controversial. Intentional delivery should not be an option for women with PPROM between 28 and 34 weeks of gestation in the absence of other indications for early delivery since it increases the incidence of neonatal deaths and the rate of Cesarean sections (*10*). Expectant management is a classical approach to managing PPROM before 34 weeks' gestation, including admission to the hospital, administration of corticosteroids, and amniocentesis to exclude intra-amniotic infection and/or broad-spectrum antibiotics prophylaxis (*11*). Corticosteroids for fetal maturation have been proven to improve neonatal outcomes in preterm births and reduce perinatal mortality, RDS, and IVH (*12*). According to the guidelines of the SOGC, following PPROM at ≤ 32 weeks' gestation, antibiotics should be administered to women not in labor to prolong pregnancy and decrease maternal and neonatal morbidity; for PPROM at > 32 weeks' gestation, antibiotics should be administered to prolong a pregnancy if fetal lung maturity is not evident and/or delivery is not planned (*13*). Although there is no consensus regarding tocolysis, it may be used in women presenting with uterine contractions or can be used prophylactically to capitalize on the benefit of corticosteroids. Delivery is recommended when PROM occurs at or beyond 34 weeks' gestation (*14*). In the current study, management depended on Chinese guidelines for preterm labor and PPROM, which also recommend the conservative management of PPROM before 34 weeks' gestation in combination with antibiotic therapy and corticosteroids. Indications for active induction of labor or a Cesarean delivery during prolongation of a pregnancy were as follows: 17.8% of patients presented with clinical chorioamnionitis, 5.7% had maternal or fetal complications during prolongation of a pregnancy, and 20.8% had a pregnancy lasting 34 weeks.

During prolongation of a pregnancy, maternal and fetal infections can occur. This is especially true for chorioamnionitis, which is identified by means of clinical signs, histologic evidence, and the culture of microorganisms; chorioamnionitis is the most obvious infection associated with early labor and delivery (*15*). The current patients were treated with antibiotics. There were no maternal deaths or severe neonatal conditions noted in this study. In this study, clinical chorioamnionitis was noted in 17.8% of patients. This figure disagrees with those reported elsewhere due to differences in inclusion criteria. Ehsanipoor *et al*. studied cases of PPROM between 24 and $31^{6/7}$ weeks' gestation and noted clinical chorioamnionitis in 9.8% of twins and 23.2% of singletons; chorioamnionitis in the placenta was noted in 35.9% of twins and 67.7% in singletons (*16*). Goya *et al*. reported that clinical chorioamnionitis occurred in 23.1% of cases of expectantly managed PPROM < 34 weeks, and they diagnosed subclinical chorioamnionitis with amniocentesis in 4.6% of cases (*17*). In a retrospective study of women with singleton and twin pregnancies and PPROM between 24^{+0} and 36^{+6} weeks of gestation, 7.5% were found to have clinical chorioamnionitis (*18*). A disadvantage of the current study is that it did not include histopathological chorioamnionitis due to incomplete data on placental pathology, so the perinatal outcomes in cases of PPROM with histopathological chorioamnionitis could not be determined and the diagnosis of clinical chorioamnionitis could not be confirmed with histopathological results.

PPROM is responsible for 30% of the neonatal morbidity and mortality in premature births. In the current study, the fetal death rate was 0.6% and the neonatal mortality rate was 7.41%. These figures agree with those found in the literature (*17*). As expected, the risk of adverse neonatal outcomes declined with a higher gestational age at PPROM; this finding agrees with the results of a study by Pasquier *et al*. (*19*). In the current study, the neonatal mortality rate was 50% at < 28 weeks of gestation, 16.13% at 28-29^{+6} weeks, 5.65% at 30-31^{+6} weeks, and 2.17% at ≥ 32 weeks. Another study reported that the neonatal mortality rate was 53.6% at ≤ 28 weeks of gestation, 8.4% at 28-32 weeks, and 3.4% at ≥ 33 weeks (*4*). The rate of major neonatal conditions in the current study was 40%. These conditions consisted of IVH in 31.7% of cases, RDS in 11.6%, PDA in 1.6%, PVL in 1.1%, sepsis in 1.1%, and NEC in 0.5%. These figures agree with those reported by Gezer *et al*., who noted RDS in 30.7% of cases, IVH in 11.4%, sepsis in 13.6%, NEC in 0.4%, PDA in 4.4%, and leukomalacia in 0.4% (*4*).

In the present study, the rate of NICU admission was 72.9%, which is the same as in other studies. Walker *et al*. reported that PPROM for > 28 days was associated with an increased risk of death and morbidity (*20*). The current results indicated that weeks of gestation at PPROM (OR: 0.953, 95% CI: 0.939-0.966, $p < 0.001$) and the latency period (OR: 0.948, 95% CI: 0.926-0.970, $p < 0.001$) were significantly associated with neonatal mortality or morbidity. Thus, the contention by Walker *et al*. is correct. In light of maternal and fetal findings, a conservative approach can prove beneficial in cases of PPROM at < 34 weeks.

Vaginal bleeding in either the first or second trimester increased the risk of preterm delivery, PPROM, histological chorioamnionitis, and abruption. Ascending infection has been implicated as a possible etiology for PPROM. Data on early vaginal bleeding in cases of PPROM were analyzed to determine if early vaginal bleeding in cases of PPROM is associated with neonatal mortality and morbidity. Perinatal outcomes were compared in cases of early vaginal bleeding and cases where it was absent. Cases of early vaginal bleeding involved significantly fewer weeks of gestation at PPROM (31.07 ± 2.23 weeks *vs*. 31.69 ± 1.84 weeks, $p = 0.029$). Cases of early vaginal bleeding also involved a higher neonatal mortality and morbidity. Thus, early vaginal bleeding is a risk factor for fewer weeks of gestation at PPROM and adverse neonatal outcomes.

Some factors are known to affect the latency period, including gestational age, oligohydramnios, number of fetuses, and complications of pregnancy such as intra-amniotic infection, placental abruption, and active labor (*21*). In the current study, 37.5% of women with PPROM delivered within 48 h and 24.3% had a latency period of > 7 days. Gopalani *et al*. reported 38.8% of patients with PPROM at 24 to 31.9 weeks delivered within 48 h, but 32% had a latency period of > 7 days (*22*). The current study found that a younger gestational age at PPROM was associated with a longer latency period and that twin pregnancies were associated with a shorter latency period than singleton pregnancies (median latency period of 2 days versus 4 days, $p < 0.001$). Multivariate logistic regression analysis was performed after adjusting for confounding factors to determine risk factors for the latency period. Gestational age at PPROM ($p < 0.001$) and a twin pregnancy ($p < 0.001$) were found to be inversely correlated with the latency period. This finding agrees with the results of other studies (*18,23,24*).

The rate of Cesarean sections in this study was 37.06%. Other studies have reported a rate from 10% to 53% (*25,26*). The indications for a Cesarean section in the current cases were fetal distress, repeated Cesarean sections, abruptio placenta, failure of labor to progress, and breech presentation.

A limitation of this study was its retrospective nature. In addition, this study did not include histopathological chorioamnionitis due to incomplete data on placental pathology. Perinatal outcomes in cases of PPROM with histopathological chorioamnionitis were unable to be determined. Further prospective studies will focus on the associations revealed by this analysis.

In conclusion, the current results revealed that weeks of gestation at PPROM and the latency period were significantly associated with neonatal mortality or morbidity. A twin pregnancy and weeks of gestation at PPROM were significantly correlated with the latency period. Although early vaginal bleeding was not significantly associated with neonatal mortality or morbidity according to multivariate logistic regression, it may also be a risk factor for perinatal outcomes in cases of PPROM due to fewer weeks of gestation at PPROM and a higher neonatal mortality and morbidity.

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