

Maternal and neonatal outcome in preterm premature rupture of membranes

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Abstract

Background: Preterm premature rupture of membranes is defined as rupture of membranes before the onset of labor with the gestational age < 37 weeks. Preterm premature rupture of membranes is associated with 10% of the perinatal mortality, particularly associated with respiratory distress syndrome and neonatal infection. **Objective:** The study aims to assess the outcome of maternal and fetal outcome in preterm premature rupture of membranes. **Materials and Methods:** This cross-sectional study was performed on 136 pregnant women complicated by preterm premature rupture of membranes during May 2020 to June 2022 at Hue University of Medicine and Pharmacy Hospital and Hue Central Hospital. The pregnant women were managed to accord the current clinical practice of hospital. The information about objects is recorded until the time of discharge. **Results:** The rate of vaginal delivery is 52.9% and intra-amniotic infection is 8.8%. The gestational age < 34 weeks and closed cervix are associated with a greater frequency of cesarean section. The rate of neonatal infection is 34%, respiratory failure is 30%. The gestational age < 34 weeks and prolonged duration of membrane rupture to delivery > 48 hours increase the risk of early neonatal infection and neonatal respiratory failure, while the delivery methods are not increased these risks. **Conclusion:** Our findings provide insights to physicians when counseling parents on preterm premature rupture of membranes at periviable gestational age.

Keywords: preterm premature rupture of membranes, cesarean section, neonatal infection, neonatal respiratory failure.

1. INTRODUCTION

Premature rupture of membranes (PROM) is a rupture of the membranes (amniotic sac) before labor begins. If PROM occurs before 37 weeks of pregnancy, it is called preterm premature rupture of membranes (PPROM) [1].

According to the data in 2018 at Hue University of Medicine and Pharmacy Hospital, the rate of PPRM is about 16.4% [2]. According to American College of Obstetricians and Gynecologists, preterm birth occurs to approximately 10% of all births and is a major contributor to perinatal morbidity and mortality. PPRM complicates approximately 2-3% of all pregnancies, whereas term PROM occurs to approximately 8% of pregnancies. The rate of PPRM < 27 weeks was 0.5%; 27 - 34 weeks was 1% and 34 - 37 weeks was 1% [1, 3].

The gestational age, maternal risk, well-fetal being are so important for management, prognostic and counselling patient [1]. PPRM is accounted for 10% perinatal mortality. The most significant risks of the fetus after PPRM are complications from prematurity including respiratory distress, intraventricular hemorrhage, neonatal infection,

pulmonary hypoplasia. Overall, PPRM has been reported to be associated with a fourfold increase in perinatal mortality. Management and taking care a preterm baby is costly. The incidence of retained placenta, postpartum infection, cesarean section caused by abnormal fetal presentation, umbilical cord prolapse, amniotic infection are higher with preterm women [4].

The optimal management of pregnancies complicated by PPRM remains a challenge. The most challenging scenarios the OB doctors need to solve that is choosing whether expectant management or induction of labor. Some researches showed that early intervention can increase failed induction to labor, but delayed induction can increase the risk for maternal and fetal infection [5]. Royal College of Obstetricians and Gynaecologists provides age-based management guidelines between 24 and 37 weeks of pregnancy with careful monitoring to achieve better outcomes for the mother and her baby [6].

Although gestational age-based guidelines are essential to health care providers in the maternal/neonatal treatment decision-making, counselling

parents on the maternal outcome, rate of neonatal survival and long-term disabilities is a challenging complex issue, and present women with dilemmas in view of individual circumstances and patient values.

The study aims to assess the outcome of maternal and fetal outcome in preterm premature rupture of membranes.

2. MATERIALS AND METHODS

A cross-sectional study on women complicated by the preterm premature rupture of membranes (< 37 weeks) during May 2020 to June 2022 at Hue University of Medicine and Pharmacy Hospital and Hue Central Hospital.

Study population

All pregnancies complicated by PPRM during the study period.

Inclusion criteria

All pregnancies complicated by PPRM and have no sign of labor.

The gestational age from 22 weeks to 37 weeks was determined based on the first trimester ultrasound.

Pregnancy women agree to take part in study.

Exclusion criteria

Intrauterine fetal demise, birth defect, have no information about gestational age. Pregnancy women have some mental, neurological disorders.

Diagnosis of PPRM

The diagnosis of PPRM was confirmed based on the women have abnormal vaginal discharge, visualization of amniotic fluid passing from the cervical canal and pooling in the vagina through speculum and positive Nitrazine test.

Diagnosis of suspected intraamniotic infection

The diagnosis of suspected intraamniotic infection is made when the maternal temperature is greater than or equal to 39°C or when the maternal temperature is 38.0°C - 38.9°C lasts more than 30 minutes and one additional clinical risk factor is present: elevated maternal white blood cell, purulent cervical discharge, fetal tachycardia.

The pregnancy women were managed and treated according institutional protocol. The outcome measurement includes the duration of rupture of membranes to delivery, the methods of induction labor, the methods of delivery and neonatal complication such as respiratory distress and neonatal infection.

Diagnosis neonatal sepsis: Neonatal sepsis is a clinical syndrome in an infant 28 days of life or younger, manifested by systemic signs of infection and isolation of a bacterial pathogen from the

bloodstream. Sepsis is classified according to the neonate's age at the onset of symptoms.

- Early-onset sepsis is defined as the onset of symptoms before 72 hours of age.

- Late-onset sepsis is generally defined as the onset of symptoms at ≥ 72 hours of age.

It is often difficult to differentiate neonatal sepsis from other conditions. The differential diagnosis of neonatal sepsis includes systemic viral, fungal, and parasitic infections and noninfectious causes of temperature instability and respiratory, cardiocirculatory, and neurologic symptoms. The clinical history, disease course, and laboratory findings may help to distinguish neonatal sepsis from other infectious and noninfectious disorders. Ultimately, appropriate microbiologic testing is required to confirm the diagnosis.

Diagnosis neonatal respiratory distress

$\text{PaO}_2 < 50 - 60 \text{ mmHg}$ or/and $\text{PaCO}_2 > 60 \text{ mmHg}$ and $\text{pH} < 7.25$.

Statistics analysis

The variables about delivery, maternal and fetal complications before and after delivery were calculated by SPSS 20.0. Univariate analysis and multivariate logistic regression analysis were used for controlling the confounding factors. The tests were performed with 95% confidence interval.

3. RESULTS

During the study period from May 2020 to June 2022, there were 136 PPRM women that met the inclusion criteria.

The average age of the women participating in the study was 29.6, the age between 18 - 35 accounted for the majority of 81.6%. 65.4% of patients of PPRM mainly live in rural areas. PPRM women are mainly housewives (30.9%) and workers (22.1%).

The majority of PPRM happened to the gestational age of more than 34 weeks. The rate of gestational age from 34^{0/7} weeks to 36^{6/7} weeks contributed the major part with 72.1%. The proportions of nulligravida (49.3%) and multigravida (50.7%) was not too different.

Maternal outcome

Spontaneous onset of labor accounted for 51.5% and induction of labor accounted for 18.4% (Table 1). The duration of rupture of membrane to delivery less than 48 hours accounted for the majority of 75%. There were 12 cases were diagnosed with suspected intra-amniotic infection during the treatment. The rate of vaginal delivery was 52.9% and cesarean section was 47.1%.

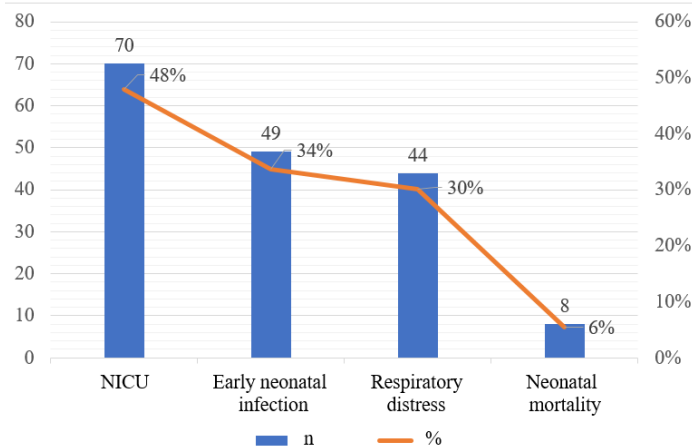
Table 1. Maternal outcomes

Characteristic	n	%
Gestational age		
< 28 weeks	7	5.1
28 - < 34 weeks	31	22.8
≥ 34 weeks	98	72.1
Duration between rupture of membrane to delivery		
< 48 hours	102	75.0
≥ 48 hours	34	25.0
Methods of induction labor		
Active cesarean section	41	16.2
Spontaneous onset of labor	70	51.5
Induction of labor	25	18.4
Amniotic infection		
Yes	12	8.8
No	124	91.2

The following parameters were identified as predictors of cesarean section in PPRM: twins had nearly 13 times higher risk of cesarean section than singletons with OR = 12.95 (95% CI: 2.19 - 76.70; p = 0.005); gestational age ≥ 34 weeks had nearly 6 times higher risk of cesarean section with OR = 5.85 (95%CI: 1.88-18.19; p = 0.002); the cervical is not dilated at the time of hospital admission which had three times higher risk of cesarean section with OR = 3.13 (95%CI: 1.04 - 9.43; p = 0.042). However, duration between rupture of membrane to delivery and gestational diabetes did not increase the risk of cesarean section (table 2).

Table 2. Multivariable logistic analysis of risk factors for cesarean section

Characteristic	Cesarean section		p	OR
	Yes (n = 64)	No (n = 72)		
Number of fetuses				
Singleton	57 (45.2)	69 (54.8)	-	1
Twin	7 (70.0)	3 (30.0)	0.005	12.95
Gestational age				
< 34 weeks	12 (31.6)	26 (68.4)		1
≥ 34 weeks	52 (53.1)	46 (46.9)	0.002	5.85
Dilation of cervix				
Not dilated	55 (50.9)	53 (49.1)	0.042	3.13
1 cm	9 (32.1)	19 (67.9)	-	1
Duration of PROM to delivery				
≥ 48h	15 (44.1)	19 (55.9)	0.224	1.85
< 48h	49 (48.0)	53 (52.0)	-	1
Gesational diabetes				
Yes	6 (85.7)	1 (14.3)	0.055	9.40
No	58 (45.0)	71 (55.0)	-	1

Neonatal outcome**Diagram 1.** Neonatal complications

There were 10 cases of twin in 136 PPRM women so the total neonatal were 146. The majority of neonatal had weight ≥ 1500 grams (91.8%). 70/146 newborns need to be admitted at neonatal intensive care unit (48%), 49/146 newborns had early onset neonatal infection (34%), 44/146 newborns had respiratory distress (30%) and 8/146 cases of neonatal mortality (6%) (Diagram 1).

Table 3. Risk factors of early neonatal infection

Characteristic	Early neonatal	infection	p	OR
	Yes	No		
Gestational age				
< 34 weeks	31 (68.9)	14 (31.1)	< 0.001	10.21
≥ 34 weeks	18 (17.8)	83 (82.2)		
Duration of PROM to delivery				
≥ 48 h	22 (59.5)	15 (40.5)	< 0.001	4.45
< 48h	27 (24.8)	82 (75.2)		
Amniotic infection				
Yes	9 (69.2)	4 (30.8)	0.01	5.23
No	40 (30.1)	93 (69.9)		
Methods of delivery				
Cesarean section	22 (31.0)	49 (69.0)	0.521	0.80
Vaginal delivery	27 (36.0)	48 (64.0)		

Table 4. Risk factors of Neonatal respiratory distress syndrome

Characteristic	Respiratory	distress	p	OR
	Yes	No		
Gestational age				
< 34 weeks	29 (64.4)	16 (35.6)	< 0.001	10.39
≥ 34 weeks	15 (14.9)	86 (85.1)		
Duration of PROM to delivery				
≥ 48 h	17 (45.9)	20 (54.1)	0.01	2.58
< 48h	27 (24.8)	82 (75.2)		

Amniotic infection				
Yes	7 (53.8)	6 (46.2)	0.06	3.03
No	37 (27.8)	96 (72.2)		
Methods of delivery				
Cesarean section	17 (23.9)	54 (76.1)	0.11	0.56
Vaginal delivery	27 (36.0)	48 (64.0)		
Early neonatal infection				
Yes	37 (75.5)	12 (24.5)	< 0.001	39.64
No	7 (7.2)	90 (92.8)		

The gestational age < 34 weeks increased 10 times higher of early neonatal infection with OR = 10.21 (95%CI: 4.54 - 22.98; $p < 0.001$). The duration of rupture of membrane to delivery > 48 hours increased 4 times higher of early neonatal infection with OR = 4.45 (95%CI: 2.03 - 9.79; $p < 0.001$). Intra-amniotic infection increased 5 times higher of early neonatal infection with OR = 5.23 (95%CI: 1.52 - 17.98; $p = 0.01$). The method of delivery (vaginal delivery/cesarean section) did not increase the risk of early neonatal infection.

The gestational age < 34 weeks increased 10 times higher of neonatal respiratory distress syndrome with OR = 10.39 (95%CI: 4.57 - 23.61; $p < 0.001$). The duration of rupture of membrane to delivery > 48 hours increased 2 times higher of neonatal respiratory distress syndrome with OR = 2.58 (95%CI: 1.18-5.63; $p < 0.015$). Newborns with early neonatal infection had 39 times higher of neonatal respiratory distress syndrome with OR = 39.64 (95%CI: 14.47 - 108.59; $p < 0.001$). Amniotic infection and the methods of delivery did not increase the risk of neonatal respiratory distress syndrome ($p > 0.05$).

4. DISCUSSION

Table 1 shows that the majority of PROM occurs to gestational age from 34 weeks or more with the rate of 72.1%. Gestational age plays an important role in the prognosis of PPRM. A study on 714 pregnant women with PPRM conducted by Ivana Chandra (2016) showed that the group of PPRM in preterm births, the percentage of newborns that needed special care was higher than the group of PPRM at the term ($p < 0.05$) [7]. In our study, the majority of cases of PPRM, labor occurs to the first 48 hours after rupture of membranes (75%). This result is similar to the study of Le Van Hoanh (2016) when the rate of preterm labor within 48 hours after rupture of membranes was 71.5% [8]. Hexia Xia (2015) has shown that early intervention can increase

the risk of failed induction into labor. Conversely, the delayed onset may lead to higher rates of maternal and fetal infections. The appropriate expectant time for rupture of membranes to spontaneous labor has varied according to several authors' reports, ranging from 12 to 96 hours [5].

According to table 1, the cases of spontaneous labor accounted for the highest rate of 70/136 cases (51.5%). According to many studies, approximately 50% of patients with PPRM go into spontaneous labor within 24 hours [9]. This result is consistent with our study.

In our study, there were 12/136 cases of suspected intra-amniotic infection diagnosed clinically during treatment, accounting for 8.8%. The clinical suspicion of intra-amniotic infection in our study was lower than in other studies. According to Xiang Han (2019), the rate of intra-amniotic infection is 15.7% [10]. The reason for the higher number of cases detected in Xiang Han's study may be because of the large sample size. According to research by Ji Hee Sung (2021), the accuracy of clinical criteria for diagnosing intra-amniotic infection is not high, about 50%. The diagnostic criteria for intra-amniotic fluid infection are ideally based on the outcome of early neonatal infection. Clinical practice in many places can define amniotic fluid infection more strictly or more loosely, thus this may lead to rates of amniotic infection that vary from studies and the association is not consistent with amniotic infection and neonatal outcomes [11].

In our study, the rate of vaginal birth was 52.9%, the rate of cesarean section was 47.1%. According to MICS, the report on the General Statistics Office of Vietnam in 2014, the cesarean section rate nationwide was 27.5% [12]. Increasing the rate of cesarean section is the current situation of many countries around the world. This is related to the disease model of the study, which was conducted in high-level healthcare facilities, where there are many high-risk pregnancies.

In addition, in PPROM women who have a high risk of preterm birth, the accompanying risk factors such as maternal obstetric status, some factors from the fetus, the appendages... increase the indications for cesarean section. Table 2 shows that independent factors can predict the risk of cesarean section in pregnant women: Twins (OR = 12.95; 95%CI: 2.19 - 76.70; $p = 0.005$); Gestational age ≥ 34 weeks (OR = 5.85; 95%CI: 1.88 - 18.19; $p = 0.002$); The fetal position is not favorable (OR = 8.35; 95%CI: 2.35 - 29.63; $p = 0.001$); Unopened cervix at admission (OR = 3.13; 95%CI: 1.04 - 9.43; $p = 0.042$). Meanwhile, the time of rupture of membranes to delivery and gestational diabetes did not increase the risk of cesarean section. According to a study by Le Thi Bich Huong (2018), the rate of vaginal birth to a full-term pregnancy with premature rupture of membranes was 79.1%. In multivariable regression analysis, latency period of more than 12 hours increased the risk of cesarean section by 56 times compared with the group of latency period less than 6 hours, the time for labor to delivery was between 6 and 12 hours and over 12 hours increased the rate of cesarean section by 9.56 times and 145.9 times, respectively, when compared with the group of less than 6 hours [13]. Meanwhile, according to research conducted by Al Riyami (2013), there is no significant association between risk factors such as gestational age, number of pregnancies, maternal age or maternal body mass index (BMI) and cesarean section rate [14].

Through our study and other studies, the majority of babies were born in a birth weight of more than 1500 grams, however this could be explained by the lower proportion of group with gestational age less than 34 weeks, this is the gestational age group of low fetal weight. On the other hand, with the development of the economy, the care and treatment services at medical facilities are better, which helps to nourish and take care of the fetus better, thus the weight of the fetus improved. In cases of PPROM, prolonging the potential time for fetal weight gains to continue. According to a study by Tigist Endale and his partners (2016), birth weight below 2500 grams was associated with a 7.8-fold increase in unfavorable neonatal outcomes (AOR = 7.8, 95%CI 1.2 - 51.2). Low birth weight is considered an important predictor of neonatal mortality, especially during the first month of life [15].

Table 3 shows that our study results show that the rate of early neonatal infection is quite high (34%). This can be explained: in our study, based on real conditions, early neonatal sepsis was diagnosed based on risk and symptoms, very

few cases received blood culture and follow-up treatment mainly based on clinical progression, thus increasing the number of cases diagnosed and treated. In multivariate regression analysis, some factors increase the risk of premature neonatal infection in children in our study: gestational age < 34 weeks (OR 10.21; 95% CI 4.54 - 22.98); $p < 0.001$), time to rupture of membranes to birth more than 48 hours (OR 4.45; 95% CI 2.03-9.79; $p < 0.001$) and amniotic infection (OR 5.23; 95% CI 1, 52 - 17.98; $p = 0.01$), whereas cesarean section or vaginal delivery did not increase the risk of neonatal infection. In the study of Nguyen Cuu Thien Thanh (2009), based on the multivariable regression equation to control for confounding factors, it was found that amniotic infection has a higher risk of causing neonatal bacteremia 9.53 (6.0 - 15.3). There is a relationship between neonatal infection and time to rupture of membranes, rupture of membranes more than 24 hours have a higher risk of neonatal bacteremia 7.75 (4.47 - 13.46) times higher than that of rupture of membranes < 24 hours. Using antibiotics after 12 hours the rupture of membranes is 4.2 times more likely to cause neonatal infection than antibiotics given before 12 hours [16]. Early neonatal infections in preterm neonates increases the risk of neonatal complications, prolong hospital stay, and increase mortality. Therefore, it is necessary to assess the risk factors and treat the child early.

Table 4 shows that there was 44/146 births to neonatal respiratory failure (30%). In multivariate regression analysis, some factors that increase the risk of neonatal respiratory failure of infants are gestational age < 34 weeks (OR 10.39; 95% CI 4.57 - 23.61; $p < 0.001$), the time of rupture of membranes to delivery ≥ 48 h (OR 2.58; 95% CI 1.18 - 5.63; $p = 0.015$) and early neonatal infection (OR 39.64; 95% CI 14.47 - 108.59; $p < 0.001$), while amniotic infection and termination method cesarean section or vaginal delivery did not increase the risk of neonatal respiratory failure. In the study of Nguyen Cuu Thien Thanh (2009), based on the multivariable regression equation, it was found that gestational age tends to protect the possibility of respiratory failure. Compared with gestational age of 28 weeks, in the group of gestational age more than 32 weeks, the possibility of respiratory failure is reduced by more than 73% [16]. According to Sarno and his partners (2019), amniotic infection did not affect respiratory failure (RR 0.93, 95% CI 1.08 - 1.67), however, after adjusting for gestational age, this risk decreased (RR 0.57, 95% CI 0.35 - 0.93) [17].

5. CONCLUSIONS

The rate of vaginal delivery of the preterm pregnancies with premature rupture of membranes was 52.9%, with the rate of amniotic infection was 8.8%, the rate of neonatal infection was 34% and the rate of neonatal respiratory failure is 30%. Factors affecting the likelihood of cesarean section are gestational age ≥ 34 weeks and unopened cervix at admission. Meanwhile, time of rupture of

membranes to delivery and gestational diabetes did not increase the risk of cesarean section.

Premature rupture of membranes at early term admitted to the hospital are cases confused clinical doctors, the goal of treatment is to do all that is possible to reduce the infant mortality rate. Clinically, the attending physician needs to understand the mechanism and therapy to avoid risk factors of respiratory failure and neonatal infection.

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