



# Preterm Premature Rupture of Membranes and Neonatal and Maternal Outcomes

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## Abstract

**Objective:** The management of Preterm Premature Rupture of Membranes (PPROM) remains controversial. PPRM may lead significant maternal and neonatal complications.

**Methods:** Retrospective data of PPRM cases managed in Suleymaniye Maternity Research and Training Hospital between 2008 and 2012 were collected and analyzed using SPSS.

**Results:** There were 192 women included in this analysis. Mean latency period was  $5.7 \pm 6.2$  days. Latency period differed significantly according to gestational age. Less advanced gestational age, higher values of initial leucocyte and CRP and lower level of initial AFI were associated with an increased risk of chorioamnionitis. Prolongation of latency period increased the risk febrile morbidity. The most common neonatal morbidities were respiratory distress syndrome (n=88, 45.8%), hyperbilirubinemia (n=67, 34.8%), sepsis (n=33, 17.1%), and congenital pneumonia (n=18, 9.3%). Neonatal mortality rate was 6.7%.

**Conclusion:** Prediction and diagnosis of maternal and neonatal complications are crucial in women with PPRM. Randomized controlled trials are needed to enlighten the controversial issues regarding PPRM management.

**Keywords:** PPRM; Preterm birth; Chorioamnionitis

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## Introduction

Preterm Premature Rupture of Membranes (PPROM) consists one third of preterm deliveries [1]. It is associated with increased incidence of neonatal and maternal complications, prior to 34<sup>th</sup> week of gestation, particularly [2].

Historically, PPRM cases have been managed expectantly with a median latency period of 1.5 days to 4.6 days [1,3]. Prolongation of latency period was shown to decrease neonatal morbidity and mortality as postnatal survival is related to gestational age at delivery and birth weight [4]. Use of antibiotics in the management of PPRM to prolong pregnancy, reduce neonatal and maternal infections has been recommended [5]. Surveillance should include regular recording of maternal vital signs and cardiotopography. Also, white cell count and C-Reactive Protein (CRP) level may be helpful in follow-up for a possible chorioamnionitis despite the fact that they are not specific [6]. Cervicovaginal swabs are routinely taken to direct antibiotic therapy.

In this study, we tried to investigate the neonatal and maternal outcomes in women with PPRM managed in our tertiary obstetric center.

## Material and Methods

This retrospective cohort study was conducted in the Department of Obstetrics and Gynecology at the Suleymaniye Maternity Research and Training Hospital, Istanbul, Turkey. PPRM was defined

**Table 1:** Maternal characteristic.

	Mean $\pm$ SD
Maternal age, years	27.7 $\pm$ 5.9
Gravidity	1.2 $\pm$ 1.6
Parity	1.0 $\pm$ 1.4
Gestational age at PPRM, weeks	30.9 $\pm$ 15.2

**Table 2:** Comparison between patients with and without chorioamnionitis.

Risk factors	Chorioamnionitis (-) n=164	Chorioamnionitis (+) n=28	P value
Mean gestational age at PPROM, weeks	g	27.6 ± 10.8	0.0001
Mean initial leucocyte, /mm <sup>3</sup>	9300 ± 2990	11820 ± 3360	0.001
Mean initial CRP	6 ± 5.9	11.6 ± 7.2	0.001
Mean initial AFI	80 ± 30	65 ± 20	0.05
Mean latency period, days	4.9 ± 3.9	8.2 ± 11.3	<0.0001

**Table 3:** Association between latency period and maternal morbidity.

	≤ 48 hours of latency, n=90	>48 hours of latency, n=102	P value
Febrile morbidity, n (%)	1 (1.1)	8 (7.8)	0.027
Postpartum bleeding, n (%)	3 (3.3)	4 (3.9)	0.825
Placental retention, n (%)	2 (2.2)	3 (2.9)	0.756

**Table 4:** Severe neonatal morbidity and mortality and gestational age.

	<30 weeks (n=89), n (%)	≥ 30 weeks (n=103), n (%)	P value
Severe neonatal morbidity*	70 (78.6)	30 (29.1)	<0.0001
Neonatal mortality	11 (12.3)	2 (1.9)	<0.0001

\*Severe neonatal morbidity: Respiratory distress syndrome, sepsis, intraventricular haemorrhage, congenital pneumonia, the need for intensive care unit

as rupture of membranes before 37<sup>th</sup> week of gestation. Patients who were hospitalized with a diagnosis of PPROM between January 2008 and December 2012 were retrospectively evaluated. Age, gravida-parity, history of prior pregnancies, amniotic volume, duration of latency period, use of antibiotic, tocolysis and corticosteroid, whole blood count parameters and CRP levels, gestational week at the time of birth, type of birth and maternal and neonatal morbidities were extracted from patients' files. Twin pregnancies and cases in whom ampicillin 4 x 1 gr intravenous (i.v.) or tocolysis was given were excluded. Diagnosis of PPROM was based on a history of leaking fluid and visualization of amniotic fluid in the vagina. If PPROM was not obvious after inspection, the diagnosis was confirmed by positive results from a nitrazine test and ultrasonographic evaluation that demonstrated oligohydramnios.

Last menstrual period and first trimester crown-rump length were used to determine gestational age. Cervical speculum and digital pelvic examinations, transabdominal ultrasound to measure amniotic fluid volume and fetal biometry was performed in all patients. Amniotic Fluid Index (AFI) was used to determine amniotic fluid volume. AFI less than 50 mm was accepted as oligohydramnios.

Cervicovaginal culture was obtained from all of the patients. Two grams of prophylactic Ampicillin was given intravenously every 6 hours. If the cervicovaginal culture was positive for any bacteria, a sensitive antibiotic was added to the treatment plan. All patients received single dose bethametasone injection.

Clinical chorioamnionitis was diagnosed based on maternal temperature ≥ 38°C and two or more of the following conditions: I. uterine tenderness; II. wbc count >15 000/mm<sup>3</sup>; III. foul-smelling vaginal discharge; IV. maternal tachycardia (<100 beats/min); and V. fetal tachycardia (>160 beats/min). RDS was diagnosed in symptomatic infants who required ventilator support for at least 24 hours. Neonatal sepsis was diagnosed if there was a positive blood culture result obtained during the first 72 hours after birth. Pneumonia was diagnosed when an infant had compatible symptoms with diagnostic X-ray findings.

Statistical analysis was done using statistical software (SPSS 10.0

for Windows) and Student's t-test, Mann-Whitney U test, McNemar's test and Friedman variance analysis were used, as appropriate. Significance level was defined as 0.05. Data were expressed as mean ± SD and percent (%), where appropriate.

## Results

A total of 192 patients were included into analysis. Maternal characteristics were presented in (Table 1). Maternal age ranged between 15 and 44.

Mean latency period was 5.7 ± 6.2 days, ranged between 0 and 40 days. Latency period differed significantly according to gestational age. Patients with a gestational age of less than 30 days and with a gestational age of 30 weeks or more had a latency period of 6.8 ± 7.1 days and 4.6 ± 5.5 days, respectively (p<0.001).

While 67 patients (34.8%) gave vaginal birth, 125 patients (65.2) underwent cesarean section (CS). The most common indications for CS were fetal distress (37%) and previous CS (35.4%).

Chorioamnionitis was diagnosed in 28 patients (14.5%). Possible risk factors for chorioamnionitis were demonstrated in (Table 2). Less advanced gestational age, higher values of initial leucocyte and CRP and lower level of initial AFI were associated with an increased risk of chorioamnionitis. In addition, the more the latency period, the higher the risk of chorioamnionitis.

Prolongation of latency period increased the risk febrile morbidity. However, latency period did not affect the incidence of the postpartum bleeding and the placental retention (Table 3). There was no maternal death in our series.

The most common neonatal morbidities were respiratory distress syndrome (n=88, 45.8%), hyperbilirubinemia (n=67, 34.8%), sepsis (n=33, 17.1%), and congenital pneumonia (n=18, 9.3%). Neonatal mortality rate was 6.7%. Comparison of neonatal morbidities and mortality in terms of gestational age showed a significantly increased incidence of severe neonatal morbidity and mortality under 30 weeks of gestation (Table 4).

## Discussion

Management of PPRM has still controversial issues, such as conservative vs active management, use of tocolytic drugs, antibiotic regimen and duration of antibiotic use, timing of antenatal corticosteroids, diagnostic challenges of maternal infection and timing of birth [7]. Herein, we presented the results of PPRM from a tertiary obstetric center. The included patients were managed conservatively using ampicillin and bethametasone and followed-up closely. Our study demonstrated that advanced gestational age at the time of membrane rupture is associated with shorter latency period. In addition, higher initial leucocyte and CRP levels and lower AFI were associated with chorioamnionitis. As expected, neonatal morbidity and mortality increased if the birth was given under 30 weeks of gestation.

A Cochrane review suggested the use of single dose antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth [8]. Consistently, a single dose of bethametasone was used for all patients in the present study. Respiratory distress syndrome occurred in 88 (45.8%) neonates.

Another Cochrane review from 2014 concluded that there is no enough evidence to support the use of tocolytics in PPRM [9]. Even though tocolytics may prolong latency period, this intervention increases the risk of chorioamnionitis and does not add any benefit to neonatal morbidity [9]. In the present study, none of the patients received tocolytics.

Chorioamnionitis was found in 14.5% of the patients, which is compatible with the reported incidence in English literature [9-11]. Prediction of patients with an increased risk of chorioamnionitis may allow obstetricians to choose active management instead of conservative management. In our study, possible risk factors for chorioamnionitis were investigated and earlier gestational ages, higher values of initial leucocyte and CRP and lower level of initial AFI were found to be associated with chorioamnionitis.

In conclusion, PPRM is one of the most important causes of preterm birth and management should include the use of the prophylactic antibiotics and the corticosteroids. Prediction and

diagnosis of maternal and neonatal complications are crucial. Randomized controlled trials are needed to enlighten the controversial issues regarding PPRM management.

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