

Neonatal Complications Related with Prolonged Rupture of Membranes

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Abstract

Citation: Boskabadi H, Maamouri G, Mafinejad S. Neonatal Complications Related with Prolonged Rupture of Membranes. *Maced J Med Sci.* 2011 Mar 15; 4(1):93-98. doi:10.3889/MJMS.1957-5773.2011.0159.

Key words: prolonged rupture of membranes (PROM); newborn; infection; complication.

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Received: 14-Jun-2010; Revised: 22-Jan-2011; Accepted: 26-Jan-2010; Online first: 01-Feb-2011

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Competing Interests: The author have declared that no competing interests exist.

Background. Prolonged rupture of membranes (PROM) is a common and significant cause of preterm labor and has a major impact on neonatal morbidity and mortality. The aim of this study was to determine maternal risk factors and the prevalence rate of neonatal complications following PROM. This study also detected the role of maternal antimicrobial treatment on neonatal complications.

Methods: This cross-sectional study was performed at Ghaem hospital, Mashhad, Iran; from March 2008 to April 2010 to evaluate newborns' outcome that were born from mothers with prolonged premature rupture of membranes (PROM > 18 hours). Maternal risk factors, antibiotic administration and its influences on neonatal complications were evaluated. Eligible infants were categorized into group I (symptomatic infants), II (mother with chorioamnionitis) and III (asymptomatic infants).

Results. 150 infants were included in the study. 12 (7.7%) infants had definitive infections (meningitis, sepsis, pneumonia), 101 (67%) infants were premature and 88 (58.6%) infants had mothers with a history of antibiotic intake. Maternal risk factors were reported in the following order: previous PROM (10%), addiction (8%), high urinary tract infection (5/3%), diabetes (4.7%), placenta abruption (4.7%), preeclampsia (3/3%) and cerclage (2%). Neonatal complications related with PROM were prematurity (67.3%), respiratory distress syndrome (22.6%), asphyxia (8.6%), meningitis (5.2%), sepsis (4%), pneumonia (1.3%) and death (4.6%). History of antibiotic administration to mothers with PROM was negative in four babies with sepsis and one with meningitis.

Conclusion. The most common complication of PROM was prematurity and its side effects, but infection is the most important modifiable complication. Although antimicrobial treatment of women with a history of PROM improves neonatal outcome through reducing neonatal sepsis and respiratory distress syndrome (RDS), but the incidence rate of meningitis and pneumonia may be increased.

Introduction

Premature rupture of fetal membranes by definition occurs before the onset of labor [1]. When this event lasts more than 18 hours before labor, it is defined as prolonged rupture of membranes (PROM), which is associated with increased rate of neonatal infectious to relatively ten folds [2]. Premature rupture of fetal membranes occurs in approximately 1-3% of all pregnancies

and 30-40% of preterm labors [3].

The etiology of PROM seems to be multifactorial. Several predisposing factors like black race, low socioeconomic level and smoking, history of PROM in previous pregnancy, vaginal bleeding, multifetal pregnancy and polyhydramnios may play role in PROM. Although prenatal care has been developed, but severe complications related to PROM is still occurring among mothers

and fetuses [5]. Serious maternal complications include chorioamnionitis and desiduitis [6]. Additionally, fetal and neonatal complications following PROM are significant and including prematurity, sepsis and respiratory distress syndrome (RDS) as major disorders [7, 8].

According to the importance of PROM and its effect on pregnancy outcome and the related maternal and neonatal complications, this descriptive study was performed to determine the incidence rate of PROM and evaluate the maternal risk factors and treatment, signs and symptoms in newborns and complications related to PROM. We also detected the influence of antibiotic administration to women with PROM on newborn's outcome.

Materials and Methods

This cross-sectional descriptive study was accomplished on 177 infants during March 2008 to April 2010 at Ghaem hospital, Mashhad, Iran. The ethic committee of Mashhad University of Medical Science approved this study and all parents signed informed consent. All infants who were born following PROM at least 18 hours were entered into the study. From 177 newborns, 27 cases were excluded due to parent's noncompliance, early discharge before completing evaluation and congenital anomalies.

Maternal history of pregnancy and delivery including age, smoking habit, addiction, high risk pregnancy, duration of pregnancy, gestational order, previous rupture of membrane, urinary tract infection within pregnancy, volume of amniotic fluid, duration of PROM, antibiotic intake, delivery problems, presentation of chorioamnionitis' symptoms and route of delivery were all recorded.

Neonatal characteristics like gestational age, birth weight, Apgar score, symptoms of sepsis and complications were collected. Therefore, complete physical examination was performed and abnormal findings were recorded.

Newborns were categorized into three groups due to maternal history and physical examination. Group 1 included infants who were symptomatic within 8 hours after birth (respiratory distress, poor feeding, severe prematurity, low Apgar, fever, apnea, cyanosis and pallor), group 2 included infants whose mothers had chorioamnionitis and group 3 was defined as asymptomatic infants. All babies within these groups were born

following PROM at least 18 hours. Infants of group 1 and 2 were admitted in NICU and full sepsis work up was performed [blood, cerebrospinal fluid (CSF) and urine cultures, CSF analysis (count of white blood cell (WBC), neutrophils' percentage and protein level), complete blood count (CBC), C-reactive protein (CRP) and chest-x-ray (CXR)]. These infants received empirical antibiotic treatment and then proper antibiotic was chosen due to the result of blood culture and antibiogram. Proven infection was defined as blood, CSF or urine culture became positive or CXR was compatible with pneumonia. Clinical sepsis included babies who were symptomatic and their laboratory values reported as WBC>20000 and/or CRP positive without any positive cultures. Infants with proven infection and clinical sepsis were treated for 10-21 and 5-7 days, respectively. Some cases, who had CSF pattern compatible with meningitis (WBC > 30 with neutrophils >25% and protein >150 mg/dl) but the CSF culture was negative, were treated at least for 10 days. In the current study, newborns also were placed into two groups due to antibiotic intake by mothers (at least 4 hours before labor); therefore newborns whose mother received or did not receive antibiotic, were compared together for signs and complications. We tried to find out the cause of death among babies, in this study. Statistical analysis was carried out using SPSS 11.5 statistical package, for comparing groups. The Student T-test and Chi-square test were performed on quantitative and qualitative variables. Mean values, standard deviation, frequency tables and charts were determined.

Results

From 2297 newborns who were born in our hospital in the course of study, 177(7.7%) were complicated with PROM (>18h). After excluding 27 babies, 150 cases were evaluated. The mean age of mothers was 26.5 ± 5.6 years. Relatively, 50 percent of women with PROM were primiparous. Route of delivery in 102 (68%) women was vaginal and 48 (32%) was cesarean section. 88 (58%) women had received antibiotic at least 4 hours before labor. Maternal predisposing factors were illustrated in Figure 1.

Twelve (12) women were diagnosed as oligohydramnios in which PROM lasted more than 72 hours in 10 cases. 101 (67.3%) babies were preterm and 49 (32.7%) were term.

From 150 infants who included in the study, 98 infants were admitted to NICU [79 were symptomatic

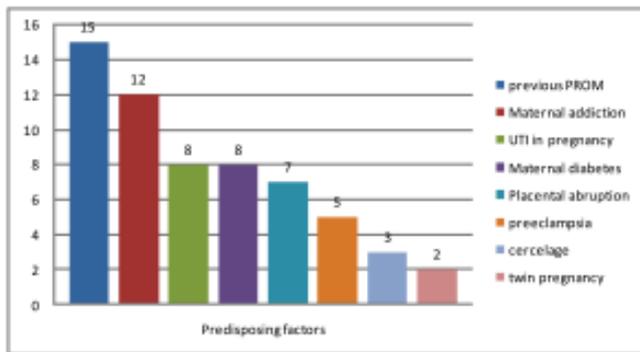


Figure 1: Predisposing factors in women with PROM.

within 8 hours after delivery (group 1) and 19 infants whose mothers had chorioamnionitis (group 2)]. 52 babies were asymptomatic (group3) and followed up in obstetric ward. The mean birth weight and five-minute's Apgar score of newborns following PROM was reported 2173 ± 700 gram and 7.8 ± 1.36 , respectively.

Positive CRP was detected in 18 infants, as well as 9 infants had proven infection and 9 infants had clinical sepsis. Positive CRP was determined in 21.6% of newborns, whose mothers received antibiotic, while it was reported 68.1% among babies whose mothers did not receive antibiotic ($p < 0.001$).

Leukocytosis ($WBC > 20000$) and leukopenia ($WBC < 5000$) were detected in 35 and 2 infants, respectively. Leukocytosis was reported in 4 cases with proven infection, 2 cases with meningitis and 13 cases with clinical sepsis. Although leukocyte count was lower among newborns whose mothers received antibiotic but the difference was not statistically significant ($p > 0.05$). Thrombocytopenia was detected within 19 babies, whereas 2 cases had meningitis and 17 cases were diagnosed as clinical sepsis.

Positive blood culture was reported in 6 cases in which *Kelebsiella*, *E.Coli* and *Staphylococcus epidermidis* were detected in 3, 2 and 1 cases, respectively. Meningitis was accompanied with 4 cases with positive blood culture (both *E.Coli* and *Kelebsiella*).

Table 1: Comparison of signs and problems among groups of newborns following PROM.

	Normal	Clinical sepsis	Proven sepsis	Probable infection	Positive CRP
Group 1	20	17	12	30	12
Group 2	1	13	0	5	6
Group 3	39	3	0	10	2

Culture negative meningitis was also detected in 4 babies ($WBC > 30$ with neutrophils > 6 and protein > 150 mg/dl in CSF fluid). Two babies were diagnosed as pneumonia due to chest- x-ray report. Significantly, all cases with sepsis or meningitis were placed before in symptomatic or maternal chorioamnionitis group (Table 1). Newborns complication was illustrated in Figure 2.

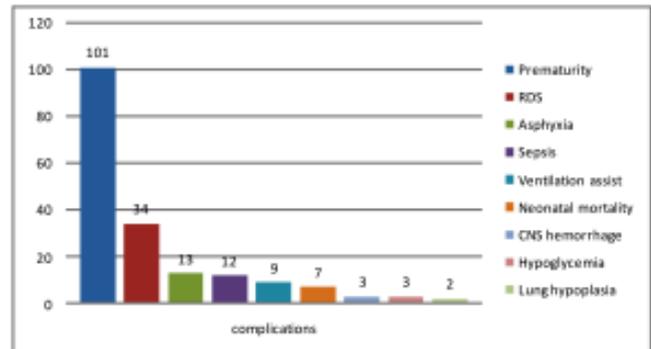


Figure 2: Neonatal complications following PROM.

In this study, newborns of mothers who received or did not receive antibiotic, were compared together (Table 2). Death was occurred in 7 infants following PROM.

Table 2: Comparison of neonatal problems among infants whose mother received or did not receive antibiotic.

	Mother received antibiotic	Mother did not receive antibiotic
Clinical sepsis	18	15
Proven sepsis	2	4
Sepsis evaluation	30	15
CNS hemorrhage	2	1
Asphyxia	6	7
Meningitis	3	1
pneumonia	2	0
RDS	11	23
Normal	22	27

Discussion

Prolonged rupture of membranes causes serious problems for mother, fetus and newborn. The current study determined that, despite the prematurity was the most common problem, infection was the most severe event following PROM ; therefore maternal antibiotic intake has reduced the neonatal complications related to infection.

In our study, the incidence of PROM was demon-

strated near 7.7 percent while other publishes have reported 1-8 percent [8, 9]. We found that two-thirds of the babies were born preterm and a similar study by AL QA showed that 62% of newborns were preterm following PROM. PROM in most pregnancies leads to preterm labor. As gestational age increases, the delivery following rupture of membrane takes place earlier. Usually PROM before 26 weeks of gestational age induces spontaneous delivery within a week in 57% of pregnancies and 22% within 4 weeks [10, 11].

In this study, 87.3% of women have labored spontaneously within 18-72 hours after PROM. 76% of preterm babies were born in the first week and 36% in the first day. Similarly, another study had reported that 42- 84% of deliveries were happened within a week after PROM [12].

Infection and inflammation of Choriodesidua was suggested as the mechanism of premature rupture of fetal membranes and collagen deficiency in fetal membranes is believed as a predisposing factor for premature rupture of membranes. Several predisposing factors were suggested for PROM. In this report, history of previous rupture of membranes, maternal addiction, UTI during pregnancy, maternal diabetes, preeclampsia, early placenta abruption, cerclage and twin pregnancy were accompanied with PROM. Other predisposing factors due to elevated pressure of amniotic fluid like polyhydramnios, multiple fetus, trauma, genetic disorders and enzymopathies and nutritional status were reported [12-14].

Strong correlation between PROM and intrauterine infection or inflammation was suggested. Possibly, genitourinary infection has an important role in the occurrence of PROM, especially in preterm deliveries [14]. Although, previous publishes have reported the risk factors of PROM, but their prevalence rates were undetermined [15-17]. We found that 40% of women with PROM had predisposing factors and previous rupture of membranes, addiction and UTI within pregnancy were diagnosed as the most common factors, respectively.

98(65.3%) babies were admitted to NICU following PROM, which included all symptomatic infants, preterm babies (<34week) and infants of women with chorioamnionitis. Chorioamnionitis among women with PROM was reported 12.7%, while other articles have reported this between 13-60% [17]. The rationale may be that chorioamnionitis was diagnosed by histopathological findings among preterm babies rather than clinical diagnosis which was performed in our study. High

incidence of neonatal admission following PROM indicated their problems within first days of life and recommended early and exact evaluation of mothers in order to reduce neonatal complications. Tanir et al. reported 75.8% of newborns, who were born before 34 weeks of gestation following PROM, were admitted in NICU and treated with antibiotics [18]. Their higher value of admission comparing with our study was described as their study was only performed on preterm babies; therefore more problems and higher rate of admission was predicted.

Respiratory Distress Syndrome (RDS) was reported 22.6 and 34 percent among all newborns and preterm infants, respectively. In previous studies the prevalence rate of RDS in preterm infants varies from 54to 90 percent [15, 17]. The explanation for lower incidence of RDS in this study was that we evaluated all the infants and one third of the babies were term.

Clinical and proven infection was increased significantly, among newborns following PROM. In the current study, 122 (81.2%) infants were evaluated for sepsis (at least, blood culture, CBC and CRP were performed) and 84 infants were completely evaluated (CSF, blood and urinary cultures were performed). Clinical sepsis, proven infection and proven sepsis among newborns were diagnosed in 22, 8 and 4 percent, respectively. This result indicated a strong relationship between PROM and neonatal infection. Medina et al. illustrated that, sepsis was occurred in 5.2% of newborns following PROM [17]. In previous studies, the prevalence rate of sepsis varies from 5.4 to 14 percent [15].

Pneumonia was determined in 1.3% of our babies while, Medina et al. had reported 0.9%, which is relatively similar to our result. *Klebsiella*, *E.Coli* and *Staphylococcus epidermidis* were defined as microbial agents among newborns with proven sepsis, while other publishes have reported group B *Streptococci* and sexual transmitted disease (STD) related microorganisms were common. This difference indicates that using Ampicillin as routine treatment for maternal PROM should be reevaluated and more effective antibiotics against gram negative microbial agents should be started.

CSF positive culture was determined in 2.6% of babies in the current study, whereas by including cases with culture negative meningitis, it rose to 5.2%. Almost, cases with meningitis had negative blood culture. The discordance in blood and cerebrospinal fluid cultures suggests that meningitis may be under diagnosed among infants due to routine antibiotic intake in women with

PROM and emphasizes the need for culture of CSF in symptomatic infants and those with maternal chorioamnionitis.

Asphyxia was occurred in 8.6% of babies following PROM and indicates, this increased rate was secondarily related to placenta abruption, abnormal position and premature labor. The rate of death among newborns was 4.6%, while previous studies reported 4-11%. Neonatal mortality rate was reported 19% by Tanir et al. The incidence of sepsis and death were inversely related with gestational age. Severe asphyxia, lung hypoplasia, sepsis, CNS hemorrhage and pneumothorax were determined as the main causes of death among our infants. High mortality rate was predicted, as asphyxia, sepsis and lung hypoplasia were increased significantly within preterm babies.

Several investigations illustrated different results for the effectiveness of chemoprophylaxis on the course of PROM. Infection is thought to be a predisposing factor for PROM, especially among preterm babies; therefore it is reasonable to use antibiotics.

In this study, proven sepsis and RDS were reduced significantly among group that received antibiotic ($p < 0.001$). Antibiotic administration also reduced the positive result of CRP ($p < 0.002$). Although the incidence rate of sepsis had declined among the group that received antibiotic, but the rate of meningitis and pneumonia had increased ($p < 0.001$). This result may be due to administration of inappropriate antibiotics to mothers, insufficient time for intrapartum prophylaxis or inappropriate penetration of drugs into infants' CSF and lungs. A number of trials have been reported in which, antibiotics administered to women with PROM decreased the incidence of neonatal sepsis [17], but Ohlsson' study did not find such results.

Conclusion

PROM is a common problem among women and a big challenge for neonatologists. Although prematurity and its associated problems is the most common complication of PROM but the incidence rate of sepsis, asphyxia and RDS were also increased. Great attention to maternal risk factors like previous PROM, addiction, diabetes and UTI within pregnancy as well as proper management may decrease the incidence rate and severity of maternal and neonatal complications associated with PROM. Although ampicillin administration to women with PROM improves neonatal outcome through

decreasing neonatal sepsis and RDS, but the number of meningitis and pneumonia may be increased. Entral gram negative microorganisms were commonly responsible for sepsis in our report; therefore the optimum antibiotic regimen for women with PROM should be reevaluated and a clinical trial for that is strictly advised.

Acknowledgment

The authors would like to thank the research vice chancellor of Mashhad University of Medical Science for supporting the budget of project. We are also thankful from personnel of midwifery and nursing, especially Miss Hajseyedi, Mollazade, Hassanzade, Tahery, Moghanni and Dinparvar.

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