

Original Paper

Short Term Outcomes of Neonates Born after Prolonged Premature Rupture of Membranes < 34 Weeks Gestation

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Abstract

Background: Preterm premature rupture of membranes (PPROM) is responsible for one-third of all preterm births worldwide. This aim of this study was to investigate the outcome of neonates born after prolonged PPRM with gestational age below 34 weeks.

Materials and methods: This retrospective study included 65 patients who were born to mothers with Prolonged PPRM <34 weeks gestation between January 2011 and December 2015 and admitted to the neonatal intensive care unit (NICU) at Jordan University Hospital.

Results: The mean gestational age of included patients was (31.9 ± 2.5 weeks), mean birth weight was (1840 ± 583 g) and 43 (66.2%) were males. The mortality rate in those infants was 12.3 %. Gestational age, birth weight, and Apgar score were significantly lower among mortality cases compared to surviving cases ($P < 0.05$).

Conclusion: Prolonged PPRM before the 34th gestational week is associated with high rate of morbidity and mortality, for which early identification of risk factors for developing PPRM can help in reducing the risk for preterm labors and subsequent burden on healthcare system.

Keywords

preterm premature rupture of membranes, neonatal outcomes, infection, respiratory morbidity

1. Introduction

Preterm premature rupture of membranes (PPROM) is defined as rupture of amniotic membranes prior to onset of labor and before the 37th week of pregnancy (Ye, Jiang, Lu, & Le, 2011). Despite recent advances in perinatal care, PPRM is considered a significant contributor to perinatal morbidity and

mortality (Linehan et al., 2016).

Despite having several risk factors for PPRM, infection and inflammation are considered key risk factors for both the primary event of rupture of membranes and successive fetal adverse events (Friedman & McElin, 1969; Simhan & Canavan, 2005), mainly; neonatal sepsis. Approximately 25-40% of amniotic fluid cultures were found positive upon presenting with PPRM (Simhan & Canavan, 2005), this risk is dramatically increased if the membranes were ruptured for more than 24 hours before delivery (Herbst & Kálán, 2007). Therefore, special precautions should be made to reduce the rate of neonatal sepsis (Simhan & Canavan, 2005).

The other major adverse effect for PPRM is respiratory morbidity, especially If PPRM occurs before the gestational age of 34 weeks, mainly respiratory distress syndrome (Usher, Allen, & McLean, 1971). In this case, efforts to prolong latency and reduce risk of premature delivery should be made, permitting the administration of corticosteroids (Vidaeff & Ramin, 2011; Yang, Choi, Roh, & Kim, 2004).

This study was conducted to investigate the outcome of neonates born after prolonged PPRM with gestational age below 34 weeks at Jordan university hospital.

2. Method

2.1 Patients & Materials

This is a retrospective study conducted at Jordan University Hospital's Neonatal Intensive Care Unit (NICU). The main objective is to evaluate the clinical outcomes of premature infants exposed to prolonged PPRM.

The University of Jordan Deanship of Scientific Research and Jordan University Hospital Institutional Review Board (IRB) approved this study. This study was conducted in compliance with the ethical standards of Jordan university hospital on human subjects as well as with the Helsinki Declaration.

All admitted neonates born to mothers with Prolonged PPRM <34 weeks gestation between January 2011 and December 2015 were included. Demographic and clinical data were extracted from the medical charts and the laboratory database.

Preterm premature rupture of membranes (PPROM) is defined as rupture of amniotic membranes prior to onset of labor and before the 37th week of pregnancy. Prolonged PPRM was defined as rupture of membranes of more than 24 hours prior to the delivery.

Respiratory distress is defined as the presence of one or more of the following signs: tachypnea with a respiratory rate >60 breaths/min, grunting, retractions, flaring ala nasi, cyanosis, and/or apnea. The diagnosis of respiratory distress syndrome (RDS) is based on both the presence of respiratory distress signs and radiographical finding of RDS.

Nasal CPAP is the treatment of choice for moderate to severe respiratory distress, in infants less than 26 weeks gestational age, the practice is to intubate and to administer surfactant prophylactically.

Our unit's protocol is to admit all newborns born to mothers with prolonged PPROM, Blood culture should be obtained at birth and empirical treatment with ampicillin and amikacin should be initiated.

Regarding blood investigations, CBC and CRP are usually done within the first 12 hours in all infants, and both will be repeated at 48 hours to determine the duration of treatment.

Early onset sepsis was defined as the presence of clinical signs and symptoms consistent with sepsis with or without positive blood culture in the first 72 hours of life. Culture-negative sepsis was defined as treatment with antibiotics for ≥ 7 days in neonates with negative blood cultures.

2.1.1 Statistical Analysis

Frequencies were compared using chi-square test. Comparisons between groups' means were performed using the t-test. Statistical significance was set at $p < .05$.

3. Result

A total of 65 neonates were included in our study, mean gestational age was (31.9 ± 2.5 weeks). Mean birth weight was (1840 ± 583 g). Male infants were 43 (66.2%). Caesarian section was the mode of delivery in 70.8%. Mean Apgar score was 7 in the first minute, and 9 in the fifth minute of age (Table 1).

Table 1. Demographic Characteristics of Neonates < 34 Weeks Gestational Age with Prolonged PPROM

Character	Distribution
Gestational age (weeks)	31.9 ± 2.5
23-27	4 (6.2%)
28-34	61 (93.8%)
Birth weight (mean \pm SD)g	1840.6 ± 583.6
Extremely low birth weight	3 (4.6%)
Small for age (number/%)	6 (9.2%)
Male gender (number/ %)	43 (66.2%)
Cesarean section delivery (number/%)	46 (70.8%)
Apgar scores (mean)	
First minute	7
Fifth minute	9
Low Apgar score	3 (4.6%)

Regarding infection risk factors, membranes were ruptured for more than 7 days in 33.8%, unknown GBS status was found in 100%, maternal chorioamnionitis in 7.7%. Overall rate of sepsis was 38.5%, blood culture positive sepsis rate was 3.1% (Table 2).

Table 2. Infection Risk Factors in Neonates < 34 Weeks Gestational Age with Prolonged PPROM

Characteristic	Number (frequency)
PPROM 1-2 days	32 (49.2)
PPROM 2-6 days	11 (16.9)
PPROM >7 days	22 (33.8)
Maternal UTI	2 (3.1)
Unknown GBS status	65 (100)
Maternal Chorioamnionitis	5 (7.7)
Peripartum maternal fever	10 (15.4)

Of the included infants, 86% had respiratory distress symptoms, 69.7% were treated with non-invasive ventilation. Approximate length of hospital stay was 16.9 days \pm 14.7, mortality rate was 12.3% (Table 3).

Table 3. Clinical Characteristics and Outcomes of Neonates < 34 Weeks Gestational Age with Prolonged PPROM

characteristic	Number (frequency)
Blood culture positive sepsis	2 (3.1)
Blood culture negative sepsis	23(35.0)
None invasive ventilation	46 (69.7)
Mechanical ventilation (any time)	23 (43.8)
Surfactant therapy	16 (24.0)
Length of hospital stay (average \pm SD)	16.9 \pm 14.7
Mortality	8 (12.3)
Respiratory related mortality	5 (62.5)*
Sepsis related mortality	3 (37.5)*

*of total mortality.

Mortality was higher in those with lower gestational age and lower birth weight. Low Apgar score was significantly associated with higher mortality rate (Table 4).

Table 4. Comparison of Neonatal Characteristics and Outcomes between Surviving Newborns and Mortality Cases

Characteristics	Death cases (8)	Surviving cases (57)	P value
Gestational age (weeks)	28.9 ± 3.1	32.6 ± 2.2	0.000*
23-27	3 (37.5%)	1 (1.8%)	0.005*
28-34	5 (62.5%)	56 (98.2%)	0.005*
Birth weight	1247.5 ± 678.2	1923.9 ± 523.9	0.002*
Extremely low birth weight	3 (37.5%)	0	0.001*
SGA	2 (25%)	4 (7%)	0.16
Male gender	6 (75%)	37 (64.9%)	0.71
Cesarean section	6 (75%)	40 (70.2%)	1.0
Mean Apgar score			
First minute	5	7	0.01*
Fifth minute	7	9	0.07
Low Apgar score	3 (37.5)	0 (0.0)	0.001*
Urinary tract infection	0 (0%)	4 (7%)	1.0
Maternal Fever	3 (37.5%)	7 (12.3%)	0.1
Chorioamnionitis	1 (12.5%)	4 (7%)	0.59
PPROM 1-2 days	5 (62.5%)	27 (47.4%)	0.48
PPROM 2-6 days	1 (12.5%)	10 (17.5%)	1.0
PPROM ≥7	2 (25%)	20 (35.1%)	0.71

*Significant P value < 0.05.

4. Discussion

PPROM is considered a major cause of preterm deliveries, with one third of preterm births being the result of PPRM (Pasquier et al., 2009). The frequency of neonatal complications in case of PPRM and their severity differ with the gestational age at which delivery occurs (Mercer, 2003).

The mortality rate in those infants was 12.3 %, of those 62.5 % were due to respiratory complication, and were as 37.5% were due to sepsis. The mortality rate was significantly higher in those with lower gestational age and with lower birth weight. 6% of the included infants were extremely premature below 28 weeks of gestation (Table 1). The mortality rate in this subgroup was 75% versus 8.2% in those with gestational age of 28 to 34 weeks, with a significant P value of < 0.005. A study done in Turkey reported similar observation with a neonatal mortality rate of 53.6% at ≤ 28 weeks of gestation, 8.4% at 29-32 weeks, and 3.4% at ≥ 33 weeks (Gezer et al., 2013). Moreover, Lieman, Brumfield, Carlo and Ramsey (2005) reported similar mortality trends in their cohort.

In our study, all patients with extremely low birth weight have died, all of which were born at

gestational age less than 28 week, emphasizing the fact that mortality rate in neonates with prolonged PPRM increases as birth weight decreases (Gezer et al., 2013; Lorenz, Wooliever, Jetton, & Paneth, 1998). Mortality rate was higher in those with lower Apgar scores at the 1st minute and 5th minute of age, which were similar to the findings of Lee, Subeh and Gould (2010), none of the infants who had low Apgar scores below 6 at the 5th minute survived (Weinberger et al., 2000). There was no relationship between latency period and mortality rate (Table 4).

Respiratory morbidities are the major complication of prematurity. It is most severe when the delivery occurs before 34 weeks (Caughey, Robinson, & Norwitz, 2008; Colin, McEvoy, & Castile, 2010). Lung development is linked to the presence of amniotic fluid, the earlier in gestation the rupture of membranes, the more is the risk of lung hypoplasia and respiratory complications (Vergani et al., 1994). In our study, only 14 % did not have any form of respiratory distress, and in those who were symptomatic, RDS was the most common cause. Non-invasive respiratory support was the most commonly used mode of ventilation (69.7 %), and only 24% of the included infants received surfactant therapy (Table 3).

All infants included in this study were born after prolonged PPRM, 49.2% within 48 hours and 33.8% had a latency period of more than 7 days. Since infection is the most common cause of premature membranes' rupture, neonatal sepsis is a major adverse event. This risk will be augmented in case of prolonged rupture of membranes (Herbst & Kállán, 2007).

In our cohort, the overall rate of sepsis was 40%. This includes those with culture positive sepsis (4.6%), and those with culture negative sepsis (35.4%) (Table 3). The later percentage might be over estimated due to the nonspecific symptoms of sepsis in this group, the overlap with the symptoms of other common morbidities like RDS, and the lack of reliable diagnostic tools (Schrag & Schuchat, 2005). These factors might influence the clinician decision regarding duration of antibiotic treatment in this high-risk group.

In conclusion, this study demonstrated that Prolonged PPRM is associated with high rate of morbidity and mortality. A prospective case control study is recommended to identify further factors that might influence the clinical outcomes in this population.

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