# A comparative study of outcome of preterm neonate with and without history of preterm premature rupture of membrane

*S Khanal,[1] W Zhang,[1] N Rajbhandari Shrestha[2] and GR Dahal[3]*

[1]Department of Epidemiology, College of Public Health, Zhengzhou University, Henan, China,
[2]Department of Pediatrics, Third Affiliated Hospital of Zhengzhou University, Henan, China,
[3]Department of Pediatric Surgery, First Affiliated Hospital of Zhengzhou University, Henan, China

**Corresponding author:** Sirjana Khanal, Department of Epidemiology, College of Public Health, Zhengzhou University, Henan 450001, China, e-mail: khanalsirju@yahoo.com

## ABSTRACT

The aim of the study was to find put the neonatal outcome of infants born with history of preterm premature rupture of membrane (PPROM) and to compare with infants born without history of PPROM. It was a retrospective study that included 187 preterm newborn with history of PPROM admitted in neonatal intensive care unit of the third affiliated hospital of Zhengzhou University from January 2008 to December 2008. Another 150 preterm newborns from same department during same period were taken as control. Patient demographics, patient's problem, investigation, management and outcome were recorded from medical record department and compared. Chi square and t test were used for statistical analysis. There was no statistical difference of gestational age, mode of delivery, birth weight and gender between case and control group. Respiratory system related problems like birth asphyxia, respiratory distress syndrome, apnea and pneumonia were common in both group but not statistical significant ($p>0.05$). However, need of oxygen supply and mechanical ventilation was significantly more ($p<0.05$) in case group. Neonatal death was more in case group (5.3%) than in control group (0.7%) and was statistically significant ($p<0.001$). The morbidity of preterm neonate does not entirely depend on history of PPROM than prematurity itself. However severity of disease and death is more with history of PPROM.

**Keywords**: Preterm birth, premature rupture of membrane, neonatal outcome.

## INTRODUCTION

Preterm premature rupture of membrane (PPROM) is defined as rupture of fetal membrane before onset of labor at less than 37 completed weeks of gestation.[1] Incidence of PPROM ranges from 3.0-10.0% of all deliveries.[2-4] There are numerous risk factors for PPROM, such as physiologic changes, intrauterine infection at early gestational age, lower socioeconomic status of pregnant women, inadequate prenatal care and inadequate nutrition during pregnancy, sexually transmitted infections, vaginal bleeding, smoking during pregnancy etc.[2,5-7] Both mother and fetus are at greater risk of infection after PPROM. Approximately 60.0% of cases will go in to labor within first week of PPROM at 24 weeks and about 80% at 34 weeks.[8] One of the most common complication of PPROM is early delivery. Pre term delivery results in still birth or neonatal morbidity and mortality. Surviving neonates may develop respiratory distress syndrome (RDS), birth asphyxia, apnea, sepsis, necrotizing enterocolitis (NEC) and neurologic disorder.[2,9,10] Preterm delivery occurs in almost 11.0% of all births.[2] Prematurity itself is a cause of morbidity in neonates. In premature newborn, the organs are not developed to maturity level. We conducted a retrospective comparative study to find out the neonatal outcome in preterm babies born with or without history of PPROM.

## MATERIALS AND METHODS

It is a retrospective study from the Pediatric Department of 3rd affiliated hospital of Zhengzhou University, Zhengzhou, Henan, China. During a period of January 2008 to December 2008, 187 preterm neonates admitted in Neonatal Intensive Care Unit (NICU) with history of PPROM were eligible for this study. Another 150 preterm neonates born without history of PPROM (period of gestation and parity matched) was taken as control from the same NICU during the same period the comparison. Multiple pregnancy, full term birth and gross congenital anomalies were excluded from the study. Clinical information about the maternal history, history of PPROM, problem seen in newborn, investigations, management and outcome were recorded from the medical record department.

The gestational age was classified into two groups: very preterm (28 -32 weeks) and preterm (33- 36 weeks). Composite neonatal major and minor morbidity was defined as previously used criteria.[4] Composite neonatal major morbidity is presence of any of the following – RDS, sepsis, seizure, NEC, pneumonia, need of artificial

**Table-1:** Patient Characteristics

| Variables | Case(n= 187) | Control(n=150) | $X^2$/t-test | *p* | OR | 95.0% CI |
|---|---|---|---|---|---|---|
| Mean Gestational age (weeks) | 32.67±2.4 | 32.81±2.2 | 0.517 | 0.335 | - | - |
| Mode of Delivery | | | | | | |
| Normal (%) | 111 (59.4) | 80 (53.3) | 1.231 | 0.267 | 1.278 | 0.828-1.972 |
| Gender | | | | | | |
| Male (%) | 114 (61) | 84 (56) | 0.846 | 0.358 | 1.227 | 0.793-1.898 |
| Birth weight (grams) | 2160±620 | 2173±790 | 0.168 | 0.867 | - | - |
| AN Corticosteroid | | | | | | |
| Given (%) | 80 (42.7) | 64 (42.7) | 1.54 | 0.125 | 1.327 | 0.848-2.076 |

ventilation. Composite neonatal minor morbidity is presence of any of the following – Jaundice, transient hypo or hyperglycemia.

The outcome was defined as discharge with recovery, discharge on request of the parents as they did not want to continue treatment in the hospital and death in the hospital during treatment.

A statistical calculation was performed by SPSS 11.5 for windows. Chi square test was used for categorical data and t test for continuous data. Odds ratio and confidence interval was calculated where appropriate. P value less than 0.05 was taken as significant.

## RESULTS

The total numbers of neonates included in the study were 187 in case group and 150 in control group. Patient characteristics including gestational age, mode of delivery and birth weight were similar in case and control groups. Male neonates were more than the female but statistically not significant. The mothers who received antenatal corticosteroid were not significantly different between case and control. However there was a significant difference between preterm and very preterm group ($p$<0.05) (Table-1).

Out of the total ill babies, the most common illness was birth asphyxia in case (40.6%) and control (45.3%) group. Other respiratory problems like RDS, apnea and pneumonia were also high in both groups. All these respiratory problems were equally seen in both groups and statistically not significant ($p$>0.05). Similarly seizure and NEC were also found to be not statistically significant ($p$>0.05). The major composite morbidities include 142 (75.9%) patients in case group and 102 (68%) in control group. It failed to be significantly different.

Jaundice is a component of minor composite morbidity. In case group there were 76 neonates (40.6%) while in control group 106 (70.7%) with significant different ($p$<0.05). Details are shown in Table-2.

For all the ill babies in both the case and control groups, blood glucose, blood for culture/sensitivity and CRP investigations were performed. A positive blood culture was detected in 10 (5.3%) cases and 8 (6.7%) control positive. Blood culture and CRP was not found to be significant ($p$ > 0.05). However, there was significant difference in blood glucose level ($p$ < 0.05) as more abnormal level was found in control group (Table-3).

The treatment provided to ill babies was analyzed. Among the treatments, administration of oxygen, mechanical ventilation, antibiotics was more commonly used in case group ($p$<0.05). Phototherapy was used in more control group ($p$<0.05). Use of CPAP and pulmonary surfactant was not statistically significant ($p$>0.05). Treatment and managements are shown in Table-4.

Out of the total ill babies, 153 (81.8%) were recovered in case group and 147 (98.0%) in control group. The no.

**Table-2:** Problem seen in newborn babies

| Variable | Case(n= 187) | Control(n=150) | $X^2$/t-test | *p* | OR | 95.0% CI |
|---|---|---|---|---|---|---|
| Birth Asphyxia | 76 (40.6) | 68 (45.3) | 0.749 | 0.387 | 0.826 | 0.535-1.275 |
| RDS | 56 (29.9) | 52 (34.7) | 0.852 | 0.356 | 0.806 | 0.509-1.275 |
| Apnea | 55 (29.4) | 53 (35.6) | 1.442 | 0.230 | 0.755 | 0.477-1.195 |
| Pneumonia | 45 (24.1) | 37 (24.7) | 0.016 | 0.898 | 0.968 | 0.255-0.617 |
| Seizure | 22 (11.8) | 22 (14.7) | 0.617 | 0.432 | 0.776 | 0.411-1.463 |
| NEC | 12 (6.4) | 4 (2.7) | 2.589 | 0.108 | 2.503 | 0.790-7.926 |
| Jaundice | 76 (40.6) | 106 (70.7) | 30.20 | 0.0001 | 0.284 | 0.180-0.449 |

**Table-3:** Results of investigation

| Variable | Case(n= 187) | Control(n=150) | $X^2$/t-test | *p* | OR | 95.0% CI |
|---|---|---|---|---|---|---|
| Blood culture | | | | | | |
| Positive (+) | 10 (5.3) | 8 (5.3) | 0.248 | 0.618 | 0.784 | 0.300 -2.046 |
| C reactive Protein (+) | 15 (8) | 10 (6.7) | 0.222 | 0.637 | 1.221 | 0.532-2.802 |
| Blood Glucose | | | | | | |
| Normal | 147 (78.6) | 74 (49.3) | 25.52 | 0.0001 | 3.767 | 2.219-6.397 |
| Abnormal | 40 (21.4) | 76 (50.7) | | | | |

of ill patient discharged without recovery on request of parents were 24 in case group and 2 in control group. The no. of neonatal death recorded were 10 in case group and 1 in control group. The final outcome of baby was significantly better in control group ($p<0.001$). The mean hospital stay of the babies was $14\pm13.2$ days and $14.4\pm10.3$ days in case and control group respectively and is not significant ($p>0.05$)

## DISCUSSION

Preterm birth is a major health problem. Incidence of preterm birth ranges from 5.0-12.0% in most of the countries.[11-13] Prematurity is a major contributor for perinatal morbidity and mortality. Approximately 70% of neonatal mortality and 75.0% of morbidity results from preterm birth.[14,15] The incidence of preterm delivery which has increased in recent years is associated with various epidemiological and clinical risk factors.[16] Most preterm birth occurs after PPROM. PPROM results in loss of natural protection of fetus and intrauterine content. Both fetus and mother are at risk of infection. PPROM occurs in 2.0-4.0% of all pregnancies.[17-20] Approximately 10.0% of perinatal deaths are directly or indirectly attributable to PPROM.[21]

One of the important causes of death in preterm birth is pulmonary hypoplasia. This is related to gestational age of PPROM, early the gestational age higher the risk of pulmonary hypolasia. Incidence of pulmonary hypoplasia is 22.0% at 20-24 weeks and only 3% at 25-28 weeks of gestation.[22] Noor *et al* found that risk of PPROM was 43.5% in 30-35 weeks and 35.2% in 35-37 weeks of gestation.[17] Pulmonary hypoplasia results in RDS, apnea, pneumonia and asphyxia. Though there are various modern techniques and specific intervention that has added advantage in improving perinatal care, still outcome is very poor.[12] In many series,[23,24] the cut off line for poor outcome is 24 weeks and not recommended for prolongation of pregnancy.

Preterm labor before 34 weeks of gestation needs a course of antenatal corticosteroid. However, it is not recommended in PPROM with chorioamnionitis.[25] Crowley *et al* in a meta analysis, showed low incidence of RDS, periventricular hemorrhage and NEC after steroid administration.[26] Similarly many other studies revealed better neonatal outcome after administration of steroid.[27,28] In our study, administration of antenatal corticosteroid was not significantly different in case and control. But there was a difference when compared with term and very preterm newborn.

The incidence of cesarean section varied in different studies ranging from 14.0%[29] to 65.0%.[30] There was no difference in cases with or without PPROM. We reported a high caesarean section rate of 40.6% and 46.7% in case and control. The slightly higher male birth represents the current trends in many other literatures.[18,20,31]

In prematurity, lungs are immature and the problems related to lungs are high. Furman *et al* reported that RDS was affected by prematurity itself rather than the occurrence of PPROM.[32] Rate of different problems in recent publications are shown in table 6. The difference in rate is because of difference in selection of patient characteristics for study. In our study, birth asphyxia, RDS, apnea and pneumonia were high in both case and control group. Infection related problems like:

**Table-4:** Treatment measures

| Variable | Case(n= 187) | Control(n=150) | $X^2$/t-test | *p* | OR | 95.0% CI |
|---|---|---|---|---|---|---|
| Oxygen supply | 157 (84) | 74 (49.3) | 45.39 | 0.0001 | 5.304 | 3.199-8.794 |
| Mechanical ventilation | 33 (17.6) | 8 (5.3) | 11.934 | 0.001 | 3.828 | 1.711- 8.564 |
| CPAP | 31 (16.6) | 17 (11.3) | 1.874 | 0.171 | 1.555 | 0.824-2.934 |
| Pulmonary Surfactant | 40 (21.4) | 23 (15.3) | 2.009 | 0.156 | 1.503 | 0.854-2.644 |
| Phototherapy | 75 (40.1) | 92 (61.3) | 15.002 | 0.0001 | 0.422 | 0.272 -0.655 |
| Antibiotic | 180 (96.3) | 129 (86) | 11.494 | 0.001 | 4.186 | 1.728-10.140 |

**Table-5:** Neonatal outcome

| Variable | Case(n= 187) | Control(n=150) | $X^2$/t-test | *p* | OR | 95.0% CI |
|---|---|---|---|---|---|---|
| Recovered | 153 (81.8) | 147 (98) | | | | |
| Discharge on request | 24 (12.8) | 2 (1.3) | | | | |
| Died | 10 (5.3) | 1 (0.7) | 22.3 | 0.0001 | | |

pneumonia, NEC and sepsis were high in case group but still not sufficient to make a level of significance. Neonatal outcome largely depends on fetal gestational age than PPROM itself. [20,33,34] From this we can draw a conclusion that PPROM is not an independent risk factor for most of the neonatal problems than the prematurity itself. This finding is consistent with other studies.[30,35]

On the other hand, jaundice and transient hypo/ hyperglycemia was significantly more in control group. Probably, the neonates were admitted for these problems. Both jaundice and transient abnormal blood glucose are component of composite minor morbidity. Positive blood culture and CRP was found in less no. of patients and no difference in case and control group.

Several studies report a higher rate of morbidity in newborn after PPROM.[36,37] The composite major morbidity was 76.0% in patients with PPROM. The patients in control group were also premature and had composite major morbidity up to 67.9%. There is a difference but it was not statistical significant.

Respiratory support in the form of oxygen administration and mechanical ventilation was needed significantly more in case group. use of CPAP and pulmonary surfactant was also more in case group. However they fail to reach a level of significance. The final outcome as death was significantly more in case (5.3%) than in control (0.7%). Paumier *et al* found that the survival rate was approximately 50.0% at 26 weeks of gestation and 84.6% after 26 weeks. It reaches 97.5% at 30 weeks.[38] In a study by Newman *et al*, PPROM was associated with adverse perinatal outcome at 23-27 weeks of gestation.[39]

The individual morbidity of birth asphyxia, RDS, apnea, pneumonia, seizure, NEC and sepsis do not entirely depend on PPROM, rather than prematurity itself. Newborn with history of PPROM suffers more serious illness and need more respiratory support. The final outcome of PPROM is worse than without PPROM.

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**Table-6**: Rates of different illness due to PPROM revealed in few recent publications:

| Author(s) | Patient Characteristics | RDS | Pneumonia | Sepsis | NEC | Death |
|---|---|---|---|---|---|---|
| Paumier *et al*[38] | PPROM before 32 weeks (spontaneous labor) | 23.5% | - | 5.9% | 2.0% | 2.9% |
| Nili F *et al*[30] | PPROM < 37 weeks | 21.5% | 3.7% | - | - | - |
| Medina *et al*[2] | PPROM <37 weeks | 35.0% | - | - | - | 1.2% |
| Mehmet A *et al*[18] | PPROM with chorioamnionitis | 48.0% | - | - | 29.0% | 29.0% |
| Kifah Al *et al*[36] | PROM with antibiotic intake | 25.0% | - | - | 11.3% | - |
| Tanir HM *et al*[40] | PPROM & preterm delivery | 14.9% | - | 33.3% | - | 19.2% |
| Yang *et al*[20] | PPROM at 16 to 26 weeks | 100.0% | 15.8% | 42.0% | 13.2% | 17.8% |
| Our study* | PPROM <37 weeks admitted at NICU | 29.9% | 24.1% | - | 6.4% | 5.3% |

* However in our study birth asphyxia was reported high (40.6%) and Apnea 29.4% which are not shown in other studies mentioned above.

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