Preterm Prelabour Rupture of Membranes at 34-37 Weeks’ Gestation: Intentional Delivery versus Expectant Management

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Abstract

Objectives: In this prospective study we wanted to prove that intentional delivery as compared to expectant management for PPROM at 34 – 37 weeks’ gestation will be associated with improved maternal and perinatal outcome.

Study Design: Consecutive 100 gravid women at >34 weeks 0 days and <36 weeks 6 days of gestation attending the labour emergency with PPROM fulfilling the selection criteria taken for study. They were randomized to receive misoprostol induction (n=50) or expectant (n=50) treatment only.

Result: In this study 12% women of expectant group developed chorioamnionitis and no chorioamnionitis occurred in any women Of induction group (12% vs. 0%, p=0.0353). Maternal hospital stay was significantly prolonged among patients in the expectant group (7.98±5.71 days vs. 3.28 ± 1.98 days, p=0.0001). Rate of Caesarean Section was more in induction group (16% vs. 10%, p= 0.5536). Birth
asphyxia (A.S < in 1 min) was more common in expectant group (14% vs. 10%, p=0.095), and neonatal sepsis also more common in expectant group (12% vs. 2%, p=0.1169).

**Conclusion:** In women whose pregnancy is complicated by PPROM at 34 weeks 0 days to 36 weeks 6 days, our study indicates that intentional delivery by induction of labour substantially improves pregnancy outcomes compared with expectant management.

**Key words:** Chorioamnionitis, Neonatal sepsis, Premature rupture of membranes

**INTRODUCTION**

Preterm prelabour rupture of foetal membrane (PPROM) is defined as rupture of foetal membrane at least one hour prior to the onset of labour at less than 37 weeks’ gestation (Penny C et al.)

The reported incidence of prelabour rupture of membrane averages from 6-10% and about 20% of these cases occur before 37 weeks of gestation. Although preterm prelabour rupture of membrane complicates about 1-2% of all pregnancies, it is associated with 40% preterm deliveries and result in significant perinatal morbidity and mortality.

Many studies have demonstrated significant benefits of expectant or conservative management in PPROM at less than 34 weeks of gestation but the management of PPROM between 34-37 weeks continues to be a controversial issue.

In planning the management of PPROM, several issues need to be considered. Prematurity is the principal risk to the fetus while infection morbidity is the primary maternal risk. Besides prematurity per se, the complication of PPROM includes umbilical cord compression due to oligohydraminos, cord prolapse, abruptio placenta and chorioamnionitis. Chorioamnionitis with PPROM is responsible for significant maternal and neonatal morbidity including early onset neonatal sepsis, bronchopulmonary dysplasia, intraventricular haemorrhage and periventricular white matter injury.

Obstetrical management remains a controversy when membrane rupture occurs between 34-37 weeks of gestation. Intentional delivery will remove the fetus from a hostile proinflammatory intrauterine environment. On the other hand, deliberately delivering a pregnancy preterm may adversely affect the neonatal outcome.

Many studies were undertaken for PPROM before 34 weeks’ gestation and those studies demonstrated significant benefit to expectant treatment at this early PPROM in reducing neonatal morbidities and death. Again several studies have demonstrated benefits of immediate induction of labour in PROM at term when the foetus is already mature.

Very few studies were done so far regarding management of PPROM at 34 – 37 weeks’
gestation. So it is not clear whether intentional delivery or expectant management will be beneficial to both mother and baby.

In this prospective study, we tried to find out the optimum management option of PPROM at 34-37 weeks’ gestation regarding neonatal or maternal morbidity.

**MATERIAL AND METHODS**

This prospective randomized study was conducted over 1 year period (2010 to 2011) & this trial was approved by the local ethical committee.

The gravid women attending the Labour Emergency with preterm PROM with singleton pregnancy between 34 wks 0 days to-36 wks 6 days gestation was included in the study. The diagnosis of preterm prelabour rupture of membrane was achieved by maternal history followed by a sterile speculum examination to visualize pooling of fluid in posterior vaginal fornix. Then a high vaginal swab was sent for culture and sensitivity. Digital examination was avoided in all women. Gestational age was confirmed by a reliable LMP or an early ultrasonography at first trimester or early second trimester. Exclusion factors included:

a) Non cephalic presentation  
b) Fetal distress  
c) Labour on admission  
d) Multiple gestation  
e) Post caesarean pregnancy  
f) Obstetric complication like antepartum haemorrhage, suspected chorioamnionitis, gross fetal anomalies  
g) Medical complications like hypertensive disorder, diabetes mellitus

All the women selected for study were received prophylactic antibiotic and observed in labour ward for 12 hours. If there was no initiation of labour and fetal heart rate was good, they were eligible for study and the written informed consent was taken from those who were willing to participate in the study. Eligible and consenting gravid women were randomly allotted to either expectant management or immediate induction of labour. Women assigned to expectant management were transferred to antenatal ward where vital signs and fetal heart rate was monitored every 8 hours. Women will be restricted to bed rest and remained in hospital till delivery. Antenatal test was done- women were observed for signs of clinical chorioamnionitis at least 12 hourly, which include maternal tachycardia, pyrexia, leucocytosis, uterine tenderness, offensive vaginal discharge and tachycardia. A weekly high vaginal swab and weekly maternal full blood count was considered.

Fetal monitoring with cardiotocography was done at 2 days’ interval and ultrasonography for gestational age, presentation and AFI was done weekly. Injection ceftriaxone (1 gram) IV was given 12 hourly. Criteria for delivery in this group were non reassuring fetal status (by CTG),
initiation of labour and sign of clinical chorioamnionitis.

The patient assigned to active management was received tablet misoprostol (50 microgram) orally 12 hourly for a maximum 4 doses. Digital examination was avoided till the patient goes into advanced labour (in the in the early stage of labour, cervical dilatation will be examined by speculum). Caesarean section was performed for standard obstetric indications. This patient also receive injection ceftriaxone (1 gram) IV twice daily till she remains afebrile for 48 hours postpartum.

Gibbs et al., (1982) describe that diagnosis of chorioamnionitis is clinical. It requires the presence of fever (>100.4 F or 37.8°C) and at least two of the following conditions:

- Maternal tachycardia (>100/min)
- Fetal tachycardia (>160/min)
- Uterine tenderness
- Foul smelling vaginal discharge
- Maternal leucocytosis

Neonatal sepsis was defined as presence in a newborn baby ("neonate") of a bacterial blood stream infection (BSI) (such as meningitis, pneumonia, pyelonephritis, or gastroenteritis) in the setting of fever.

The diagnosis of neonatal sepsis was made only in neonates with positive blood cultures. However, all babies with suspected sepsis received empiric broad-spectrum antibiotic therapy until cultures returned and were negative (usually 3 days). Antibiotic therapy was continued for 7 to 10 days in those neonates with culture-proved sepsis. RDS was defined as the early onset of tachypnea, retractions, and oxygen requirement for >24 hours or mechanical ventilation with radiographic confirmation.

Maternal variables like age, gestational age at the time of delivery, height, weight, birth weight of baby of both groups were represented by mean ± 2 S.D. The obstetric outcome of both groups of mothers was determined separately and their statistical significance was assessed by appropriate method with the help of Quickcalcs-GraphPad software. Statistical analysis of data of two groups were accomplished by the use of Chi square test and Fisher exact test for discrete data and Student t-test for continuous data. When p value <0.05, the result was considered statistically significant.

RESULT

Total 100 gravid women with PPROM at 34 to 37 weeks gestation fulfilling all selection criteria were included in the study. All of them had regular foetal heart rate and not in labour at the time of inclusion in the study. Those 100 eligible women were randomized to get immediate induction of labour (n=50) or expectant treatment (n=50 women).
TABLE I: Clinical characteristics

<table>
<thead>
<tr>
<th></th>
<th>Misoprostol (n=50)</th>
<th>Expectant (n=50)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age</td>
<td>21.80 ± 2.71</td>
<td>21.68 ± 2.18</td>
<td>P=0.1544</td>
</tr>
<tr>
<td>Gravidity</td>
<td>1.56± 0.67</td>
<td>1.62±0.70</td>
<td>P=0.6628</td>
</tr>
<tr>
<td>Nulliparous</td>
<td>29</td>
<td>26</td>
<td>P=0.6879</td>
</tr>
<tr>
<td>BMI</td>
<td>24.4900 ± 3.1264</td>
<td>24.5904 ± 2.8662</td>
<td>P=0.8674</td>
</tr>
<tr>
<td>EGA at PROM (Wks)</td>
<td>35.718±0.650</td>
<td>35.580 ± 0.642</td>
<td>P=0.2822</td>
</tr>
</tbody>
</table>

EGA, Estimated gestational age; PROM, premature rupture of membranes.

The clinical characteristics of each group are summarized in Table 1. Mean maternal age was similar in both group and there was no statistically significant difference (p=0.1544). Mean gravidity was 1.56 ± 0.67 in induction group and 1.62 ± 0.70 in expectant group and no significant difference (p=0.6628). 29 women in induction group and 26 women in expectant group were nulliparous. BMI of both groups was similar and no significant difference found. Gestational age at preterm premature rupture of membrane was similar in both group and there was no statistical significant difference (35.580±0.642 vs. 35.718 ± 0.650, p=0.2822).
TABLE II: Maternal outcome

<table>
<thead>
<tr>
<th>Maternal outcome</th>
<th>Misoprostol (n=50)</th>
<th>Expectant (n=50)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission to delivery interval (hr)</td>
<td>21.4520±4.2378</td>
<td>109.08±79.94 25</td>
<td>P=0.0001</td>
</tr>
<tr>
<td>Total hospital stay</td>
<td>3.28±1.98</td>
<td>7.98±5.71</td>
<td>P=0.0001</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>0</td>
<td>6 (12%)</td>
<td>P=0.0353</td>
</tr>
<tr>
<td>PPH</td>
<td>2%</td>
<td>8%</td>
<td>P=0.3622</td>
</tr>
<tr>
<td>Type of delivery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SVD</td>
<td>36 (72%)</td>
<td>39 (78%)</td>
<td>P=0.6442</td>
</tr>
<tr>
<td>Forceps</td>
<td>6 (12%)</td>
<td>6 (12%)</td>
<td>P=1.000</td>
</tr>
<tr>
<td>Caesarean section</td>
<td>8 (16%)</td>
<td>5 (10%)</td>
<td>P=0.5536</td>
</tr>
</tbody>
</table>

SVD, Spontaneous vaginal delivery

Maternal pregnancy outcome and maternal morbidity are summarized in table-II. As expected, the latency from admission to delivery was extremely significantly prolonged in expectant group (109.08±79.9425 hours vs. 21.4520 ± 4.2378 hours, p=0.0001). The overall incidence of clinical chorioamnionitis was much higher among women managed expectantly (12% vs. 0%). All patients had sign and symptoms of clinical chorioamnionitis before the onset of active labour for which labour was induced.

Similarly, maternal hospitalization was significantly prolonged for women in the expectant group, with these women having on the average 4 additional days in the hospital compared with patient who underwent induction of labour (7.98 ± 5.71 days vs. 3.28 ± 1.98 days, p=0.0001). Incidence of PPH was more in expectant group but difference was not significant.

The incidence of caesarean delivery was more in induction group compared with expectant group but the difference was not statistically significant. (16% vs. 10%, p=0.5536). Incidence of Caesarean section in either group was lower than the 20% incidence of C.S noted in our overall obstetric population during study period and probably this finding is the result of exclusion of patients with suspicious fetal heart rate tracings or meconium stained amniotic fluid. In both group similar numbers of patients required operative intervention during vaginal delivery (12% vs. 12%, p=0.1000).
TABLE III: Perinatal outcome

<table>
<thead>
<tr>
<th>Perinatal outcome</th>
<th>Misoprostol (n=50)</th>
<th>Expectant (n=50)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (in kg)</td>
<td>2.540 ± 0.2232</td>
<td>2.4676± 0.2153</td>
<td>P=0.1011</td>
</tr>
<tr>
<td>Apgar score 1m &lt;5</td>
<td>5 (10%)</td>
<td>7 (14%)</td>
<td>P=0.095</td>
</tr>
<tr>
<td>Apgar score 5m &lt;5</td>
<td>2 (4%)</td>
<td>3 (2%)</td>
<td>P=1.000</td>
</tr>
<tr>
<td>NICU admission</td>
<td>15 (30%)</td>
<td>19 (38%)</td>
<td>P=0.5269</td>
</tr>
<tr>
<td>RDS</td>
<td>2 (4%)</td>
<td>4 (8%)</td>
<td>P=0.6777</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>1(2%)</td>
<td>4 (8%)</td>
<td>P=0.3622</td>
</tr>
<tr>
<td>Sepsis</td>
<td>1 (2%)</td>
<td>6 (12%)</td>
<td>P=0.1169</td>
</tr>
<tr>
<td>Neonatal death</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
<td>P=0.3149</td>
</tr>
<tr>
<td>Total hospital stay (days)</td>
<td>2.28±1.98</td>
<td>3.18±2.85</td>
<td>P=0.0696</td>
</tr>
</tbody>
</table>

Perinatal outcome variables are summarized in Table-III. Birth weight was similar in both groups. Incidence of LBW baby slightly more in expectant group but difference was not statistically significant (2.4676±0.2153 kg vs. 2.540±0.2232 kg, p=0.1011). Apgar score at 1 and 5 minute were nearly identical. More babies in the expectant group were admitted to the neonatal intensive care unit, but the difference did not reach statistical significance (38% vs. 30%, p=0.5269).

Neonatal complications, such as hyaline membrane disease and the need for mechanical ventilation or supplemental oxygen >24 hours were nearly similar between two groups and difference was not statistically significant (RDS-8% vs. 4%, p=0.6777, mechanical ventilation- 8% vs. 2%, p=0.3622). Culture proved sepsis occurred in 6 (12%) neonate in expectant group, whereas only 1 (2%) infant in the induction group had sepsis but this difference was not statistically significant (12% vs. 2%, p=0.1169). The average neonatal hospital stay was similar between two groups (3.18±2.85 days vs. 2.28±1.98 days, p=0.0696). One neonatal death occurred in expectant group due to septicaemia with RDS. No neonatal death in induction group. There were no still births in either group.

DISCUSSION

Preterm prelabour rupture of the fetal membranes remains a major cause of preterm delivery,
neonatal morbidity and mortality. The underlying multifactorial aetiology, and the lack of differentiation of preterm labour with intact membranes and that following PPROM in research studies has made preventive strategies difficult to develop. Infection remains a major underlying cause, and greater understanding of the genetic basis of the immune-inflammatory response will identify women at increased risk more accurately. Treatment strategies including antibiotic therapy and use of corticosteroids in women who have already undergone PPROM have improved neonatal outcome significantly. However, the prediction and prevention of PPROM remains a significant challenge in obstetrics.

Preterm prelabour rupture of the membranes is an important clinical problem and a dilemma for the obstetricians. On the one hand, awaiting Spontaneous labor may lead to an increase in infectious disease for both mother and child, on the other hand induction of labor leads to preterm birth with an increase in neonatal morbidity due to prematurity. Prelabour rupture of the membranes occurs in 2% of all births and 40% of all preterm births. When prelabour rupture of the membranes occurs at term (PROM) there is good evidence that early delivery is associated with a lower incidence of maternal infection and increased maternal satisfaction compared with expectant management.

In our prospective study we compared the maternal and perinatal outcome associated with active (intentional delivery) versus expectant management of preterm prelabour rupture of membranes between 34 to 37 weeks’ gestation. 100 women were selected for the study were randomized to get intentional delivery (induction group) or expectant management (expectant group) having 50 women allotted in each group.

Several studies have been undertaken on patients with preterm premature rupture of the membranes at <37 weeks’ gestation. Naef et al.9 (1998) studied neonatal and maternal outcome in 120 gravid women with PROM at 34-37 weeks of gestation. In this study chorioamnionitis (16% versus 2%, p=0.007) and maternal hospital stay (5.2 + 6.8 days vs. 2.6 + 1.6 days, p=0.006) was significantly more in expectant group. Neonatal sepsis was also more common in the expectant group than among induction group, but the difference was not statistically significant. Spinnato et al.10 (1987) found significantly increased maternal infectious morbidity without identifiable neonatal benefit after expectant management of PROM below 37 weeks’ gestation. Nelson et al.11 found a similar incidence of caesarean delivery and neonatal infection with a 50% increase in maternal infectious morbidity with active management and induction of labor (18% vs. 12%, not significant). In contrast Mercer et al12 (1993) found a 52 % increase in maternal infectious morbidity (29.8% vs. 19.6%, not significant) with expectant management but a
similar incidence of abdominal delivery and neonatal infection in PROM < 37 weeks’ gestation. Alternatively another investigators found that maternal infection and caesarean section rates were more with induction of labor.\textsuperscript{13,14}

In our study we found that latency from admission to delivery was significantly prolonged in expectant group (109.08±79.9425 hours vs. 21.4520 ± 4.2378 hours, $p=0.0001$). Prolonged latency associated with a potential increase in infectious morbidity for both the mother and neonate. So the patient with preterm premature rupture of membranes at 34 weeks 0 days to 36 weeks 6 days of gestation may benefit from active intervention leading to delivery compared with expectant observation. We also found more women developed chorioamnionitis in expectant group and the difference was statistically significant (12\% vs. 0\%, $p=0.0353$). The total maternal hospital stay was significantly prolonged among patients in the expectant group and most of this increase is accounted for by the increased latency to delivery interval. But the rates of abdominal delivery were almost similar in both groups. We did not find an increase in abdominal delivery after active management with induction of labour.

Regarding perinatal outcome, we did not found any significant difference in mean birth weight, Apgar score, NICU admission, RDS, required mechanical ventilation, neonatal sepsis and perinatal mortality in both groups. But found chances of adverse perinatal outcome were more in induction group.

CONCLUSIONS

This small prospective study observed strong association of chorioamnionitis, prolong latency period with expectant management of PPROM at 34 to 37 weeks’ gestation. However it was carried out over a very short period of time with a small group of pregnant population, it demands a larger and long term comprehensive, prospective comparative study.

REFERENCE

5. Gibbs RS, Blanco JD, St. Clair PJ, et al. Quantitative bacteriology of amniotic fluid from patients with clinical intraamniotic


